

The Equine Acute Abdomen

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Contents

Part 1. Normal Anatomy and Physiology

Chapter
1 Gross and Microscopic Anatomy of the Equine Gastrointestinal Tract
Thomas M. Krunkosky, Carla Jarrett, and James N. Moore
Esophagus 5
Esophagus-Stomach Junction 7
Stomach 7
Stomach-Small Intestine Junction 11
Small Intestine 11
Large Intestine 14
Liver 17
Spleen 18
Pancreas 19

Chapter
2 Physiology of the Digestive Tract
Gastric Secretory Function – *Michael J. Murray* 22
Small Intestine Function – *David E. Freeman* 25
Digestive Physiology – Anatomy 25
Intraluminal Digestion 28
Absorption of Ions and Water 29
Absorption of Carbohydrate, Protein and Fat 32
Iron Absorption 33
Calcium and Magnesium Absorption 34
Intestinal Secretion 35
Motility 36
Control of Motility 37
Function of the Ileum 38
Large Bowel Function – *Marco A.F. Lopes* 41
Motility Patterns and Transit of Contents 41
Microbial Activity and Fermentation 42
Secretion and Absorption 45
Liver Function – *Tim S. Mair* 54
Bile Acid Metabolism and Excretion of Bile 54
Protein Metabolism 54
Carbohydrate Metabolism 55
Lipid Metabolism 55
Detoxification and Drug Metabolism 56
Storage 56

Chapter
3 Effects of Feeding on Equine Gastrointestinal Function or Physiology
Marco A.F. Lopes
Feeding Grain 58
Feeding Lush Grass 62
Replacing Grain With Fat 62
Feeding Mature Grass and Poor Quality Hay 62
Feeding Large Meals Intermittently and Fasting 62

Chapter
4 Intestinal Motility and Transit
Peter C. Rakestraw
Physiology of Normal Motility 68
Pathophysiology of Ileus 80
Treatment of Motility Disorders in the Horse 82

Part 2 Pathophysiology of Gastrointestinal Diseases

Chapter
5 Pathophysiology of Gastric Ulcer Disease
Michael J. Murray
Gastric Ulcer Disease 96

Chapter
6 Pathophysiology of Gastrointestinal Disease: Obstruction and Strangulation
Anthony T. Blikslager
Simple Obstruction 100
Strangulating Obstruction 101
Intestinal Reparative Mechanisms 107

Chapter
7 Prevention and Treatment of Postoperative Intraabdominal Adhesions in Horses
P.O. Eric Mueller
Current Concepts in Pathophysiology of Adhesion Formation 119
Diagnosis of Intraabdominal Adhesions 120
Current Concepts in Prevention of Adhesion Formation 121
Separation of Adhesiogenic Surfaces 122
Treatment of Intraabdominal Adhesions 125
Adhesion Prevention Strategies 125

Chapter
8 Pathophysiology of Peritonitis
John F. Peroni
Anatomy and Physiology of the Peritoneum 130
Etiology of Peritonitis 131
Clinical Presentation 131
Diagnostic Approach 132

Chapter
9 Pathophysiology of Enteritis and Colitis
Harold C. McKenzie
Inflammation 136
Pain 137
Ileus 137
Hypermotility 137
Hypersecretion 138
Osmotic Diarrhea 138
Decreased Absorption 138
Endothelial Dysfunction 138
Specific Diseases 138

Chapter
10 Malabsorption Syndromes
Tim S. Mair and Thomas J. Divers
Causes of Malabsorption Syndrome 148
Clinical Signs 155
Diagnosis 156
Treatment 158

Chapter
11 Liver Diseases and Liver Failure
Tim S. Mair and Thomas J. Divers
Causes of Liver Disease 162
Diagnosis of Liver Disease 165
Hyperlipemia 167
Theiler's Disease (Serum Hepatitis) 174
Other Causes of Acute Hepatic Disease and Failure in Adult Horses 178

Pyrrolizidine Alkaloid Intoxication 178
Cholangiohepatitis and Choledocholithiasis 182
Other Biliary Conditions 185
Chronic Active Hepatitis 185
Klein Grass (Panicium Coloratum) Toxicity 186
Alsike Clover Toxicity 186
Hepatic Neoplasia 187
Hepatic Amyloidosis 187
Iron Overload, Hemochromatosis 187
Right Hepatic Lobe Atrophy 188

Chapter
12 Systemic Inflammatory Response Syndrome: Endotoxemia Reconsidered
Clare E. Bryant and James N. Moore
Responses to Pathogen-Associated Molecular Patterns 192
Receptors for Gram-Negative Bacteria and Bacterial Ligands 193
Receptors for Gram-Positive Bacteria and Bacterial Ligands 195
Systemic Inflammatory Response Syndrome 196
Inflammatory Mediators and Their Source in the Horse 197

Part 3. Intestinal Parasitism
Chapter
13 Intestinal Parasitism
Christopher J. Proudman
Principles of Iintestinal Parasitism 204
Strongylus Vulgaris 204
Cyathostomins 207
Tapeworms 208
Parascaris Equorum 210
Other Intestinal Parasites 211
Prevention 211

Part 4. Epidemiology
Chapter
14 Epidemiology of Colic
Noah D. Cohen
General Epidemiologic Considerations 218
Incidence of Colic 222
Factors that Predispose to Colic 222
Factors Indicating the Need for Surgical Management of Colic 225
Frequency of and Factors Associated with Survival from Colic and Colic Surgery 226
Study of Colic Problems in Individuals and Herds 228

Part 5. Diagnosis
Chapter
15 Diagnosis of Gastrointestinal Disease
Emma L. Rowe and Nathaniel A.White
Signalment 236
History 237
Physical Examination 238
Hematology, Blood Gases, and Serum Biochemistry 270
Ultrasonography 271
Radiographs 276
Endoscopy 278
Laparoscopy 280
Fecal Examination 280
Transit Time 281
Exploratory Laparotomy 281
False Colic 281
Decision for Surgery 282

Part 6. Medical Management

Chapter
16 Medical Management of Gastrointestinal Diseases
Tim S. Mair
Analgesia 292
Choice of Analgesics in Colic 297
Treatment of Intestinal Spasm and Spasmodic Colic 298
Treatment of Obstruction 298
Treatment of Flatulence and Tympany 302
Treatment of Ileus 303

Chapter
17 Treatment of Shock
Kevin T. T. Corley
Support of the Cardiovascular System 310
Fluid Therapy 310
Acid Base Balance 312
Types of Fluid 316
Oral Fluids 324
Delivery Systems 326
Recognition of Hypovolemia and Dehydration 327
Treatment Strategies 329

Chapter
18 Treatment of Endotoxemia
Kevin T. T. Corley and Gayle D. Hallowell
Drugs that Bind or Block Endotoxin 338
Anti-Inflammatory Agents 340
Modulation of the Coagulation System 342
Drugs Affecting Intracellular Metabolism 344

Chapter
19 Treatment of Peritonitis
John F. Peroni
Medical Treatment 352
Interventional Treatment 352
Complications and Prognosis 354

Chapter
20 Diagnosis and Treatment of Enteritis and Colitis in the Horse
Harold C. McKenzie
Diagnosis 356
Specific Syndromes 356
Treatment 360
Supportive Therapies 360
Specific Therapies 366
Surgery 369
Specific Diseases 370

Chapter
21 Nonsurgical Management of Nephrosplenic Entrapment of the Large Colon
Joanne Hardy
Clinical Presentation 383
Diagnosis 383
Nonsurgical Correction 385
Complications and Prognosis 387
Prevention of Recurrence 387

Chapter
22 Colic in the Foal
Martin O. Furr
Abdominal Radiography 391
Gastroendoscopy 393
Ultrasonography 393
Abdominocentesis 394
Case Synthesis and Management 395
Surgical Treatment 396
Gastroduodenal Ulceration 397
Small-Intestinal Obstruction 397
Large-Colon Obstruction 397
Atresia 398

Part 7. Nutritional Management
Chapter
23 Nutritional Management of the Colic Patient
Ray J. Geor
Rationale for Early Initiation of Nutritional Support after Colic and Intestinal Surgery 404
Estimating Nutrient Requirements 405
Modes of Nutritional Therapy 406
Feeding Management of Specific Gastrointestinal Conditions 412

Part 8. Anesthesia for Abdominal Surgery
Chapter
24 Anesthesia for Horses with Colic
Cynthia M. Trim
Preanesthetic Assessment 420
Anesthetic Agents 421
Induction of Anesthesia 422
Maintenance of Anesthesia 422
Anesthetic Agents in Foals 424
Monitoring 424
Cardiovascular Support 428
Hypercapnia and Hypoxemia 434
Airway Management 435
Recovery from Anesthesia 436
Anesthesia for Surgery in the Standing Horse 437

Part 9. Surgery for Acute Abdominal Disease
Chapter
25 Preparation of the Patient
David E. Freeman
Patient Preparation 444
Antiseptics Agents 445
Draping the Surgery Site 446

Chapter
26 Surgical Exploration and Manipulation
David E. Freeman
Ventral Midline Incision 452
Inguinal Approach 454
Flank Laparotomy 455
Alternative Approaches 455
Abdominal Exploration 456
Examination and Handling of Small Intestine 468
Examination and Handling of Large Intestine 469
Special Circumstances 470
Intestinal Placement 472

Chapter
27 Surgical Techniques
David E. Freeman
Surgical Team 474
Surgical Environment and Equipment 475
Gowns, Drapes and Accessories 476
Decompression and Drainage 477
Laparotomy Sponges 482
Surgical Instruments and Suture 482
Stapling Instruments 485
Miscellaneous Instruments 489
Surgical Procedures in the Small Intestine 489

Chapter
28 Intestinal Viability
David E. Freeman
Small Intestine 502
Large Colon and Cecum 509
Small Colon 510

Chapter
29 Large-Colon Enterotomy, Resection and Anastomosis
Joanne Hardy
Large-Colon Enterotomy 514
Large Colon Resection 516

Chapter
30 Small Intestinal Resection and Anastomosis
David E. Freeman
Extent of Resection 522
Resection of Mesentery 522
Decompression 522
Resection and Anastomosis 523
Stoma Size 525
End-to-End Anastomosis 527
Stapled Jejunojejunostomy 528
Everted Triangulated Stapled Anastomosis 530
Stapled versus Handsewn Anastomoses for Jejunojejunostomy 530
Jejunoileostomy 531
Jejunocecal and Ileocecal Anastomoses 532
Pelvic Flexure Colotomy 536

Chapter
31 Abdominal Closure
David E. Freeman
Closure of the Peritoneum 540
Linea Alba Closure 540
Techniques and Principles 543
Subcutaneous Closure and Skin 544
Incisional Dressing 545
Recovery Stall 545
Abdominal Bandages 545
Postoperative Care 546
Healing of the Equine Linea Alba 546
Special Circumstances 547
Secondary Closure 548

Part 10. Intensive Care and Postoperative Care

Chapter
32 Monitoring Treatment for Abdominal Disease
Tim S. Mair and Thomas J. Divers
Frequency of Examinations 554
Physical Examinations 554
Monitoring Clinical Pathology Parameters 560

Chapter
33 Postoperative Complications
Christopher J. Proudman
Postoperative Colic 564
Postoperative Ileus (POI) 565
Jugular Thrombosis and Thrombophlebitis 566
Incisional Infection 568
Incisional Hernia Formation 569
Adhesions 570
Laminitis 572

Part 11. Specific Diseases

Chapter
34 Diseases of the Stomach
Michael J. Murray
Gastric Ulcer Syndromes 578
Gastric Impaction 582
Gastric Dilation 583
Neoplasia 583

Chapter
35 Liver Diseases In Foals
Tim S. Mair and Thomas J. Divers
Portosystemic Shunts 586
Tyzzer's Disease 586
Equine Herpes Virus 1 Hepatitis 588
Liver Failure in Foals after Neonatal Isoerythrolysis 588
Umbilical Vein Abscess Affecting the Liver 589
Portal Vein Thrombosis 589
Hyperammonemia of Morgan Foals 590
Bile Duct Obstruction 590
Toxic Hepatopathy 591

Chapter
36 Diseases Of The Small Intestine
David E. Freeman
Strangulating Obstruction 594
Nonstrangualting Obstruction 605
Inflammatory and Infiltrative Diseases 610

Chapter
37 Diseases of the Cecum; Cecocecal and cecocolic intussusception
James N. Moore and Joanne Hardy
Cecal Tympany 618
Cecal Impaction 619
Cecocecal and Cecocolic Intussusception 622

Chapter
38 Specific diseases of the large colon
Joanne Hardy
Large-Colon Tympany 628
Large Colon Impaction 628
Sand Impaction 631
Enterolithiasis 633
Large-Colon Displacement 634
Other Simple Obstructions of the Large Colon 639
Large-Colon Torsion/Volvulus 639
Right Dorsal Colitis 642
Mural Infarction (Thromboembolic Colic) 644
Other Strangulating Lesions of the Large Colon 644

Chapter
39 Disorders of the Small Colon
John F. Peroni
Surgical Considerations Affected by Anatomic Features of the Small Colon 650
Obstructive Lesions 651
Vascular and Strangulating Lesions 656

Chapter
40 Vascular and strangulating lesions
Peter C. Rakestraw
Anatomy 660
Etiology and Prevention 660
Location and Classification of Rectal Tears 660
Clinical Signs and Diagnosis 662
Emergency Management 663
Medical Management 664
Surgical Management 665
Temporary Indwelling Rectal Liner 665
Loop Colostomy 666
Primary Repair 671
Nonvisual Direct Suturing Per Rectum 671
Ventral Midline Exposure and Antimesenteric Enterotomy for Suture Repair 673
Prognosis and Recommendations 674

Chapter
41 Colic and Pregnancy
Elizabeth M. Santschi
Colic during Pregnancy 678
Colic in the Peripartum Period 683

Chapter
42 Colic From Alternative Systems – "False Colics"
Tim S. Mair
Pain Associated with the Female Reproductive Tract 689
Pain Associated with the Male Reproductive Tract 695
Pain Associated with the Urinary Tract 695
Liver Diseases 697
The Pancreas 697
The Spleen 698
Pain Associated with the Respiratory Tract 698
Pain Associated with Cardiovascular Disease 700
Pain Associated with the Musculoskeletal System 700

Chapter
43 Abdominal Injuries
John F. Peroni
Diagnostic Approach 704
Treatment 707

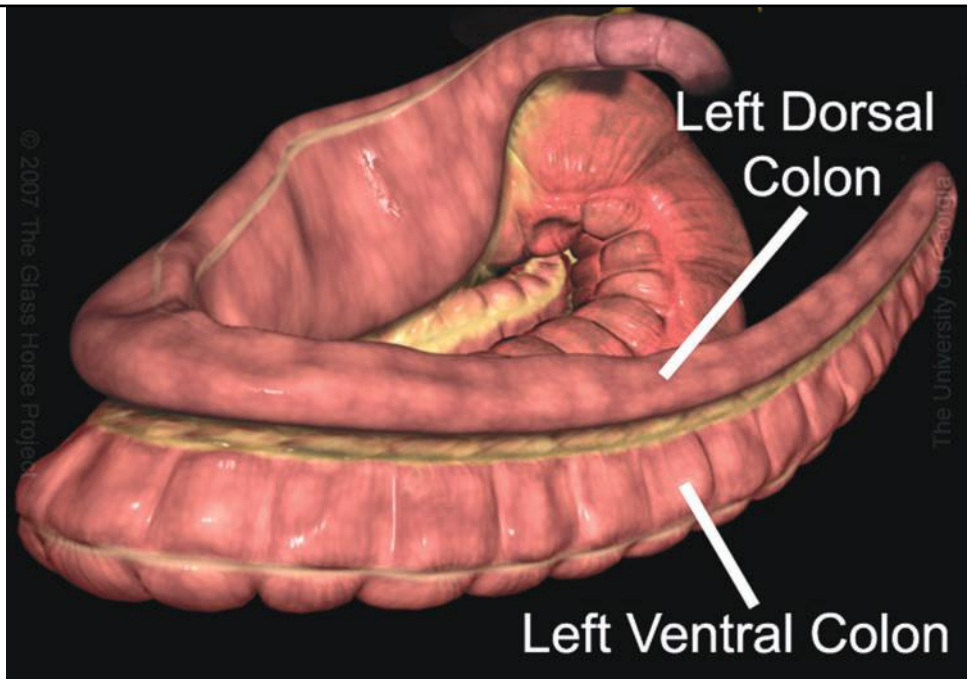
Chapter
44 Laminitis Associated with Acute Abdominal Disease
James K. Belknap and Andrew H. Parks
Pathogenesis 710
Clinical Presentation 716
Treatment 719

Index 731

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Normal Anatomy and Physiology

Part 1



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Gross and Microscopic Anatomy of the Equine Gastrointestinal Tract

Chapter 1

Thomas M. Krunkosky
Carla Jarrett
James N. Moore

Gaining a good working knowledge of the equine gastrointestinal tract and associated intra-abdominal organs can appear to be a daunting task, especially for people who are new to the area. However, veterinarians who examine and treat horses with conditions characterized by acute abdominal pain (colic) learn rather quickly that the key to the diagnosis often lies in recognizing changes in anatomic structures or relationships among different organs. With this in mind, this opening chapter focuses on the gross and microscopic structure of the horse's alimentary tract (Figure 1-1A, B, C & D), starting with the esophagus. Because some conditions characterized by colic involve other organs within the abdomen, we have reviewed the relevant structural aspects of the liver, spleen, and pancreas. In compiling this information, it is our goal to provide veterinary students and veterinarians with some of the foundational materials needed to fully understand clinical conditions that result in colic.

Figure 1-1A

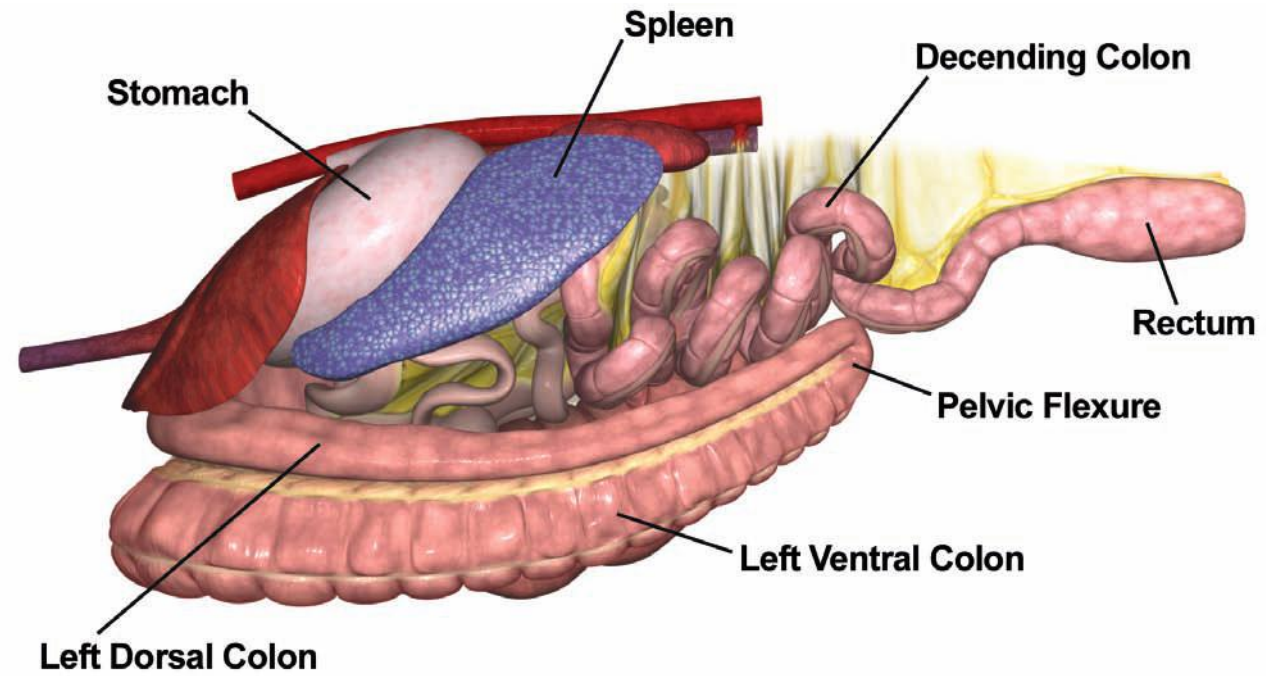


Figure 1-1B

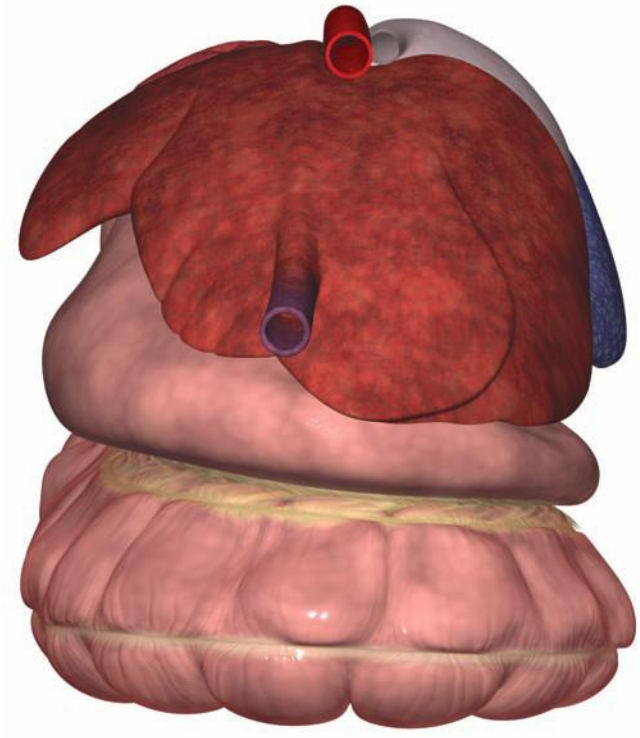


Figure 1-1C

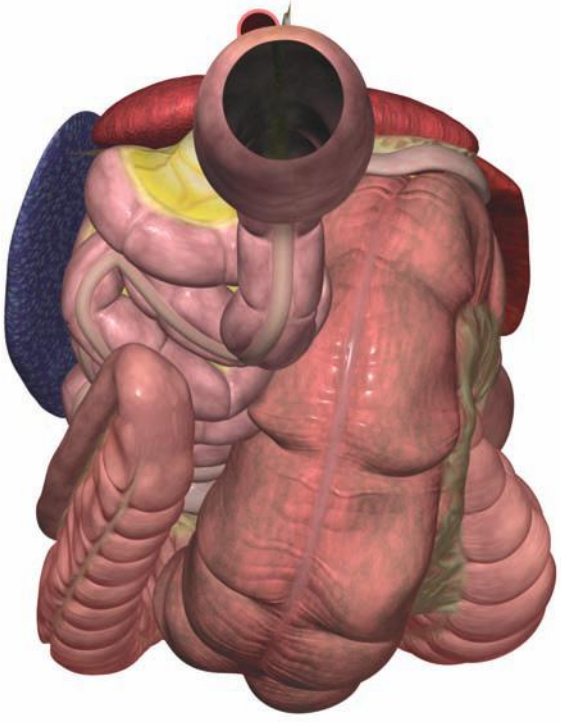
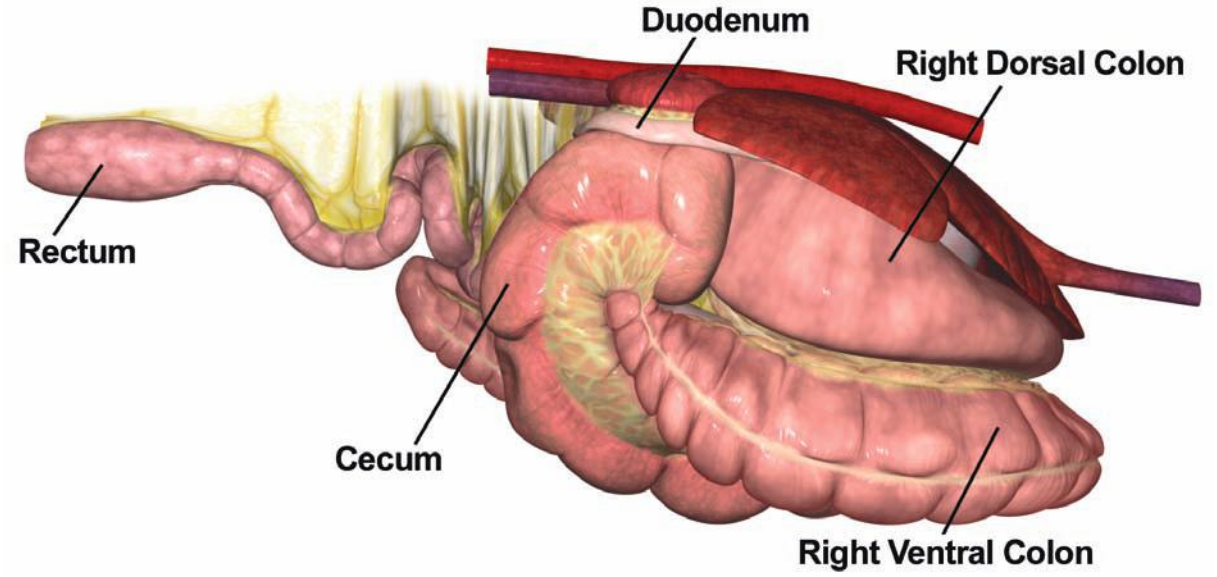


Figure 1-1D



A.) The abdominal organs from the left side of the horse. **B.)** A view from the cranial-most aspect of the abdomen. **C.)** The abdominal organs visible from the caudal-most aspect of the abdomen. **D.)** The abdominal organs from the horse's right side.

Esophagus

Gross Anatomic Features

Grossly, the esophagus consists of three portions: cervical, thoracic, and abdominal. In the cervical region of the neck, the esophagus is positioned on the dorsolateral aspect of the trachea adjacent to the carotid artery, the vagosympathetic trunk, and the left recurrent laryngeal nerve. The esophagus lies deep to the omohyoideus muscle and is enclosed within a sheath, the lateral wall of which comprises the medial wall of the carotid sheath. As the esophagus courses distally, it becomes positioned more laterally on the surface of the trachea. Near the thoracic inlet, the esophagus is positioned dorsal to the trachea. The thoracic portion of the esophagus passes through the mediastinum, over the heart, and through the esophageal hiatus in the diaphragm. The terminal portion of the esophagus in the abdominal cavity joins the stomach at the cardia.

Microscopic Features

The esophagus is a long muscular tube designed to facilitate the delivery of chewed ingesta to the stomach. Longitudinally oriented folds occur along the length of the mucosa of the esophagus to allow for expansion of the lumen during the passage of a food bolus. The mucosa of the esophagus is considerably mobile upon the underlying submucosa.

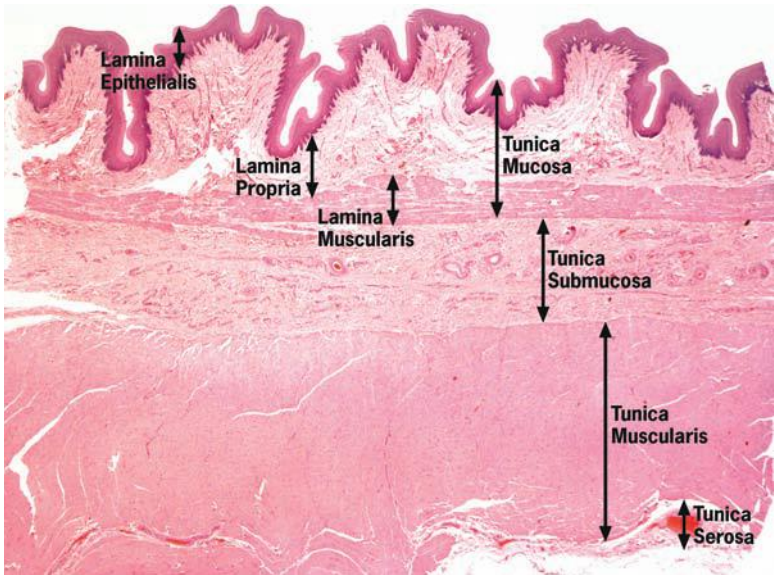
The tunica mucosa is made up of three layers, or laminae (Figure 1-2). The *lamina epithelialis* is nonkeratinized stratified squamous epithelium (Figure 1-3); mild to moderate keratinization of the epithelium may occur, depending on the nature of the ingesta. The *lamina propria* varies from loose to dense irregular connective tissue. The *lamina muscularis mucosa* is made up of isolated bundles of longitudinally oriented smooth muscle in the cranial esophagus. The muscle bundles increase in density and coalesce into a distinct layer toward the caudal esophagus. Because the lamina muscularis mucosa serves as a demarcation between the mucosa and the submucosa, it is difficult to distinguish these layers where the muscularis is sparse or absent.

The tunica submucosa is dense irregular connective tissue. The submucosa typically contains prominent vasculature and the submucosal nerve plexus. Simple branching tubuloalveolar mucous-secreting submucosal glands occur at the pharyngoesophageal junction (Figure 1-4).

The tunica muscularis is skeletal muscle in the cranial two thirds of the esophagus. The skeletal muscle transitions into smooth muscle in the caudal third of the esophagus. The tunica muscularis has two muscle layers; however, the layers are not always distinguishable because of spiraling and interlacing of the muscle bundles. The cervical region of the esophagus has a tunica adventitia of dense irregular connective tissue that blends with the surrounding tissues.

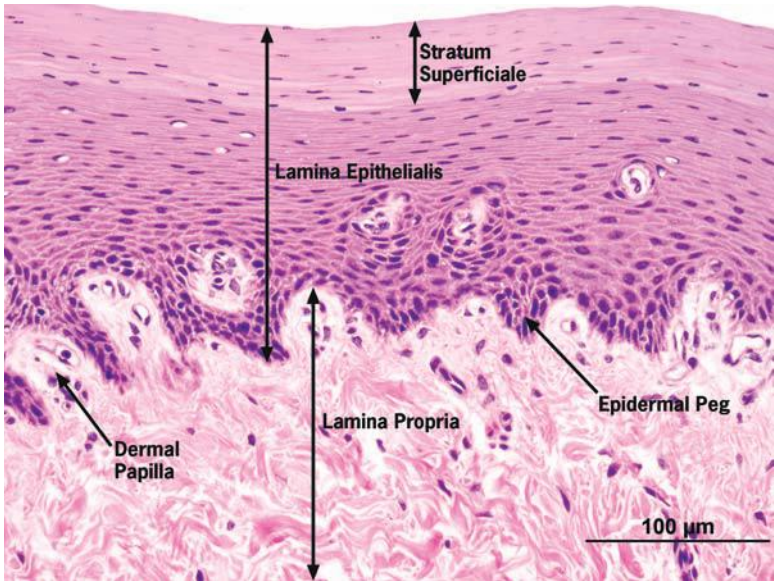
The thoracic and abdominal regions of the esophagus have a tunica serosa, which is made up of mediastinal pleura and visceral peritoneum, respectively.

Figure 1-2



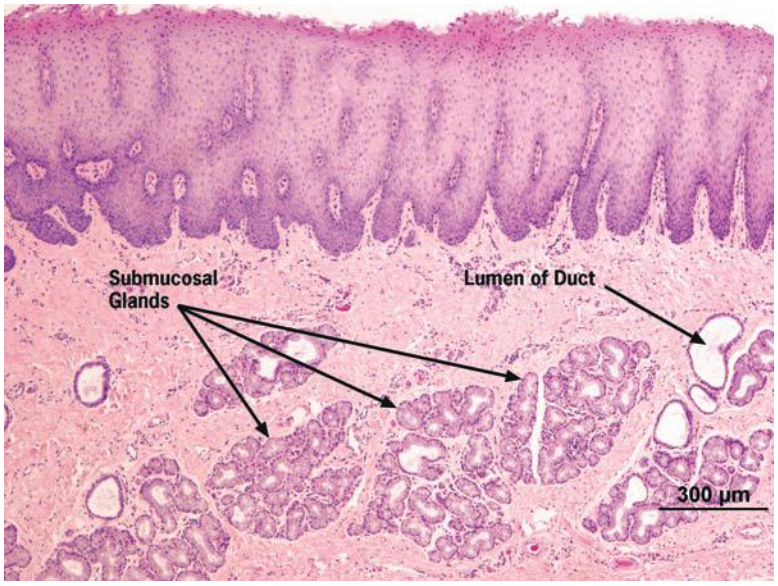
Full-thickness section of thoracic esophagus, showing: Tunica Mucosa; Tunica Submucosa; Tunica Muscularis; Tunica Serosa, and Lamina Epithelialis; Lamina Propria; and Lamina Muscularis Mucosa. H&E stain.

Figure 1-3



Lamina epithelialis of the esophagus. The epithelium is nonkeratinized with retention of nuclei throughout the most superficial layer (the stratum superficiale). The lamina propria is dense irregular connective tissue. The lamina propria and lamina epithelialis interdigitate via fingerlike projections of the epidermis (epidermal pegs) and dermis (dermal papillae). H&E stain.

Figure 1-4



Esophageal submucosal glands. The mucous secretory product of the submucosal glands are ducted into the esophageal lumen. The larger clear spaces are sections of ducts. H&E stain.

Esophagus–Stomach Junction

The true gastro-esophageal junction in the equine is microscopically similar to the caudal esophagus with the exception of a thickening in the inner circular layer of the tunica muscularis, which functions as a sphincter between the two organs. The combination of the muscular sphincter and the oblique angle by which the distal end of the esophagus joins the cardia of the stomach makes it virtually impossible for horses to vomit.

Stomach

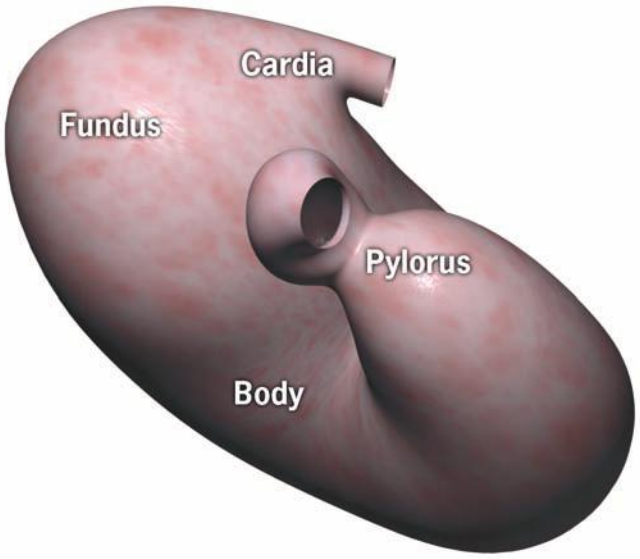
Gross Anatomic Features

Comparatively, the equine stomach is small, with a capacity of approximately 10 to 15 liters. The stomach is situated dorsocranially in the left side of the abdomen beneath the ribcage and caudal to the diaphragm. It is subdivided into four regions, the cardia, fundus, body, and pyloric region (Figure 1-5). The cardia, named because of its nearness to the heart, is the region in which the esophagus joins the stomach. Due to the shape of the horse's stomach, the cardia is near the pylorus, the two being separated by the short and concave lesser curvature of the stomach. The dilation of the stomach near the cardia is the fundus, which is large in the horse and includes a blind pouch, the saccus cecus. The body, which comprises the largest portion of the stomach, is defined by the long and convex greater curvature of the organ. The pyloric region is the narrowed ventral portion of the stomach that leads to the strong muscular sphincter, the pylorus. The pylorus is the only portion of the stomach situated to the right of the median plane.

The stomach has parietal and visceral surfaces. The parietal surface of the stomach is positioned adjacent to the diaphragm and the left lobe of the liver. The visceral surface faces caudoventrally, adjacent to the jejunum, pancreas, ascending colon and descending colon. The stomach is attached to surrounding organs by peritoneal folds which are loosely termed ligaments. The greater curvature of the stomach, which extends from the fundus to the pyloric region, is attached to the crura of the diaphragm by the gastrophrenic ligament. This ligament is continuous with the phrenicosplenic and gastrosplenic ligaments. The gastrosplenic ligament is continuous with the greater omentum.

The greater omentum is a thin, lacy tissue that attaches the stomach to portions of the gastrointestinal tract, and is itself attached along the greater curvature of the stomach. The greater omentum continues onto the cranial portion of the duodenum, the right dorsal colon, transverse colon, and the initial portion of the descending colon on the left of the median plane. Eventually the greater omentum proceeds cranially along the descending colon, onto the pancreas, and back to the greater curvature of the stomach where it joins the gastrophrenic ligament. Attachment of the greater omentum to these structures effectively encloses the visceral surface of the stomach, the initial portion of the duodenum, and portions of the right dorsal colon, transverse colon, descending colon, and the pancreas. The epiploic foramen is a narrow opening into the vestibule of the omental bursa, which is a cavity bounded by the greater and lesser omenta and their attachments. The boundaries of the epiploic foramen are the caudate process of the liver, the caudal vena cava, the portal vein, and the right lobe of the pancreas (see Chapter 26). The lesser omentum, which connects the lesser curvature of the stomach and a portion of the duodenum to the liver, is composed of the hepatogastric and hepatoduodenal ligaments.

Figure 1-5



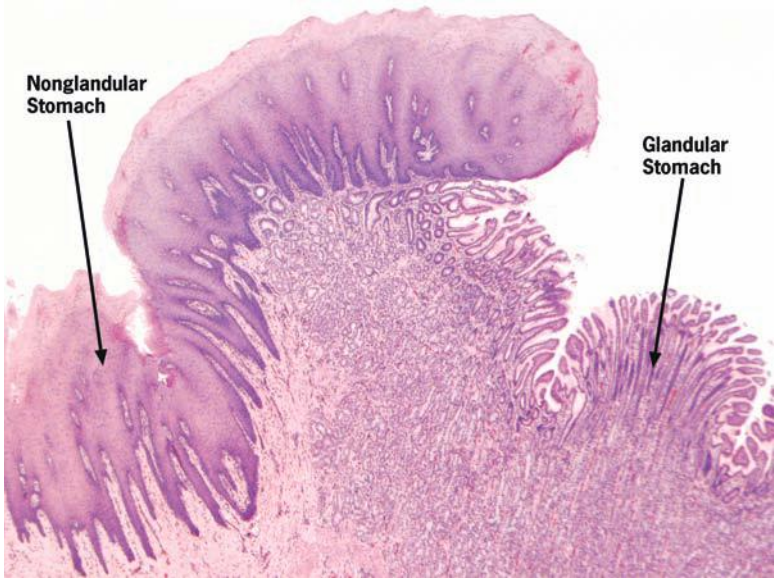
A view of the horse's stomach from the right side of the abdomen, permitting identification of the cardia, fundus, body, and pylorus.

Microscopic Features

The equine stomach has both nonglandular and glandular regions. Surface area is increased in the stomach by rugae grossly and by gastric glands microscopically. The nonglandular region of the stomach is microscopically similar to the caudal esophagus with a few exceptions. The lamina muscularis of the tunica mucosa in the stomach is organized into two distinct layers. The tunica muscularis is thicker in the stomach because of an additional layer of smooth muscle.

The junction of the nonglandular stomach with the glandular stomach forms a folded border, or margo plicatus (Figure 1-6). Microscopically, the margo plicatus is seen as an abrupt transition within the lamina epithelialis from a nonkeratinized stratified squamous epithelium to a simple columnar epithelium.

Figure 1-6



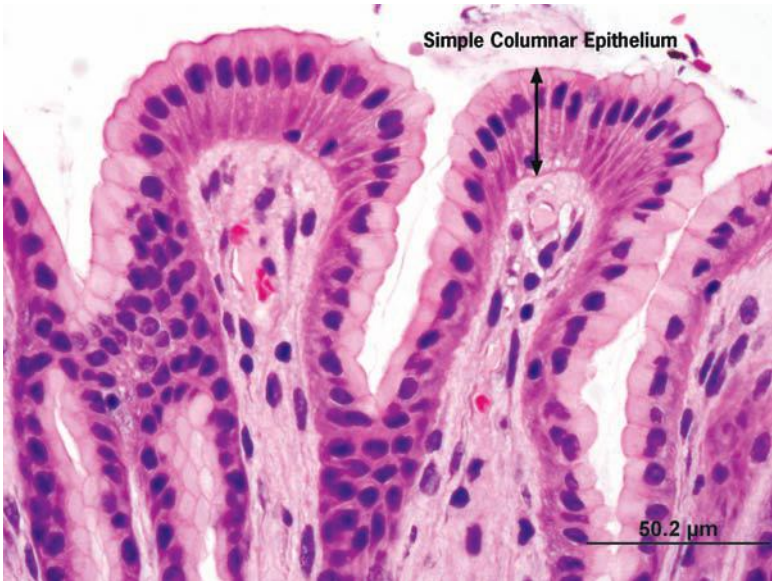
Junction of nonglandular and glandular regions of the equine stomach. The nonglandular region of the equine stomach slightly overlaps the glandular region of the stomach where the two adjoin, forming a folded border, or margo plicatus. H&E stain.

The glandular region of the stomach is further divided into a cardiac gland region, a proper gastric gland region, and a pyloric gland region. Microscopically, the distinction between these three regions may not be sharply demarcated, depending on where the tissue sample is taken and on the individual sampled. Mixing of the glandular regions may occur, some of which can be seen grossly. For example, small islands of proper gastric glands have been seen in the pyloric gland region of the fresh, unfixed organ. The demarcation between proper gastric glands and pyloric glands can be seen because they are colored differently in the fresh specimen and sometimes palpated grossly because the proper gastric glands are taller than the pyloric glands.

The lamina epithelialis of the tunica mucosa of the glandular stomach is a simple columnar epithelium (Figure 1-7). This epithelium lines the entire surface of the glandular region of the stomach, including the gastric pits (Figure 1-8), and provides a protective function by secreting mucus. The lamina epithelialis also includes the epithelium lining the individual gastric glands, which invaginate the lamina propria. The simple columnar epithelium lining the gastric glands varies in cell type, depending on the glandular region. Mitotic activity occurs in the neck region of all the gastric glands, and replenishes both the surface epithelium and the epithelium lining the gastric glands. The lamina propria is loose-to dense irregular connective tissue, and in all regions is highly cellular, with many lymphocytes, macrophages, plasma cells, and eosinophils. The lamina muscularis mucosa is an interwoven layer of smooth muscle bundles positioned perpendicularly to one another. Many smooth muscle fibers extend adluminally from the lamina muscularis into the lamina propria. The tunica submucosa is typical, containing dense irregular connective tissue, prominent vasculature, and the submucosal nerve plexus. The tunica muscularis is made up of smooth muscle bundles arranged in oblique, circular, and longitudinal layers. The tunica serosa is visceral peritoneum.

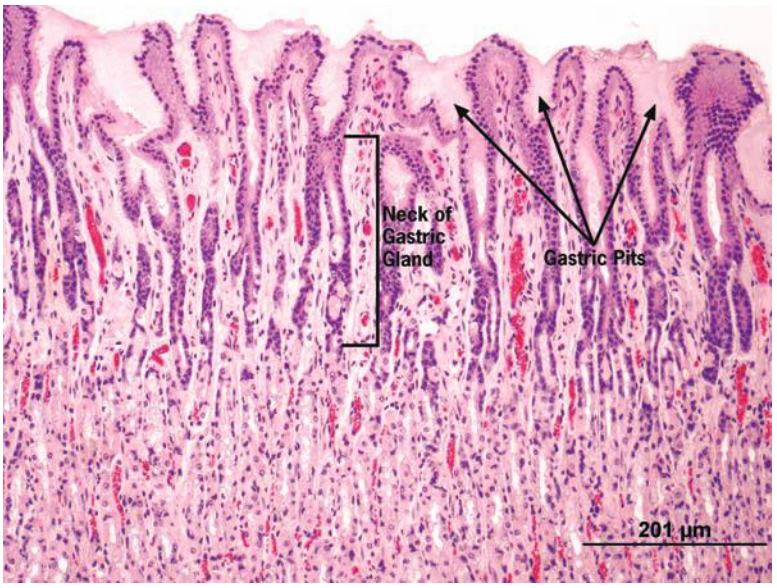
The cardiac gland region is a narrow region in equines that borders a portion of the margo plicatus. Cardiac glands are simple coiled tubular glands with some branching in the fundus of the glands. The length of the cardiac glands varies, particularly where the glands are juxtaposed against the margo plicatus. The glands are shortest immediately adjacent to the margo plicatus; otherwise, the glands are similar to the proper gastric glands in depth. The cardiac glands are primarily mucus-secreting (Figure 1-9). Chief cells and parietal cells are increasingly found within the cardiac glands as the glands slowly transition into proper gastric glands. Enteroendocrine cells are present in the cardiac glands, but require special stains for light microscopy.

Figure 1-7



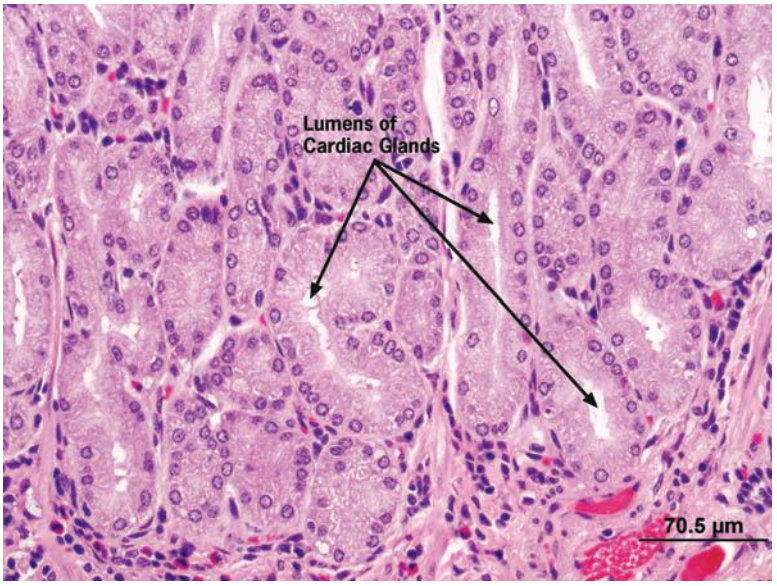
Simple columnar epithelium of the glandular portion of the equine stomach. This epithelium lines the surface of the glandular stomach and secretes a mucous product that is protective against the harsh acidic-fluid environment of the glandular stomach. H&E stain.

Figure 1-8



Gastric pits, necks, and upper portion of proper gastric glands. The gastric pits in this image are filled with protective mucus, which is secreted by the simple columnar epithelium lining the surface and pits. Deep to the gastric pits are narrowings in the glands referred to as the necks. The necks of the gastric glands are where the stem cells are located. The secretory product of the surface mucous cells differs from the secretory product of the neck mucous cells in both composition and staining characteristics. H&E stain.

Figure 1-9

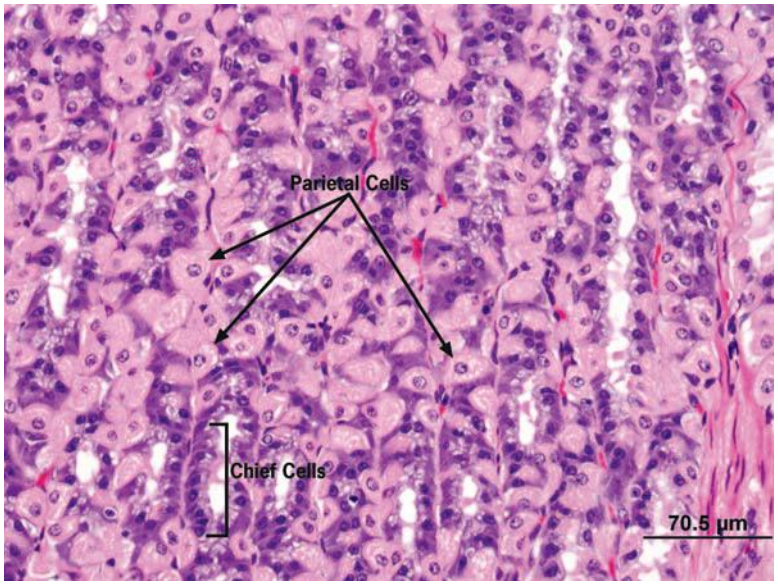


Deep portion of cardiac glands from the equine glandular stomach. This image illustrates the body and base (fundus) of the cardiac glands. Cardiac glands are coiled tubular glands; therefore, the glands appear to be in many different planes when sectioned, and it is difficult to trace the lumen of any one gland. The epithelium lining the glands secretes mucin, and the glandular secretory product is mucus. The vacuolation of the epithelial cytoplasm is due to mucin granules. Note the basally positioned nuclei of the glandular epithelium. H&E stain.

The proper gastric gland region occupies approximately two thirds of the body of the equine stomach. Proper gastric glands are long, simple tubular glands that are very straight but have some coiling and branching at their fundus. Proper gastric glands are divided into an isthmus (the funnel-shaped opening of the gastric pit into the neck), a short neck, a long body, and a fundus, or base. The gastric pits overlying the proper gastric glands tend to be shallower than the pits overlying the cardiac glands and pyloric glands, but this varies throughout the glandular stomach. The cells of the proper gastric glands include mucous neck cells, parietal cells, chief cells, and enteroendocrine cells (Figure 1-10). In general, predominantly parietal cells populate the neck and upper to mid-portions of the body of the glands, whereas predominantly chief cells populate the lower portions of the body and the fundus of the glands. Mucus-secreting cells are also present in the proper gastric glands in the regions where the proper gastric glands are transitioning with the cardiac glands or the pyloric glands.

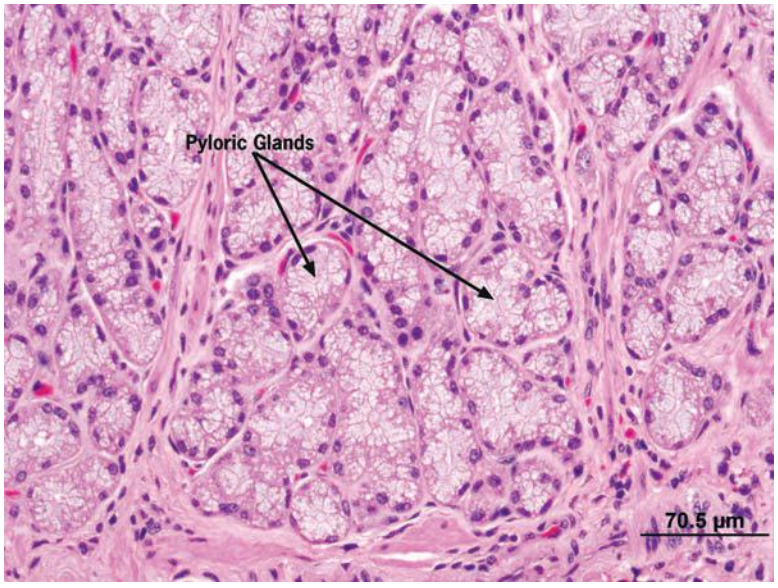
The pyloric gland region occupies the remaining one third of the glandular stomach near the pylorus. Some of the pyloric glands border the margo plicatus. Pyloric glands are simple coiled tubular glands with some branching in their fundus. The pyloric glands are primarily mucus-secreting (Figure 1-11), but may have scattered populations of parietal and chief cells, particularly near the junction of the pyloric glands with the proper gastric glands. Pyloric glands also have enteroendocrine cells.

Figure 1-10



Portion of proper gastric glands from the equine glandular stomach. This image illustrates the middle portion of the body of the proper gastric glands. Many eosinophilic parietal cells are visible; however, there are also many basophilic staining chief cells. The large parietal cells have a moth-eaten appearance due to the extensive canalicular system of the cells. The parietal cells produce and transport hydrogen and chloride ions into the cell canaliculi, where the ions combine to form hydrochloric acid. The chief cells produce proenzymes, particularly pepsinogen. H&E stain.

Figure 1-11



Deep portion of pyloric glands from the equine glandular stomach. This image illustrates the body and base (fundus) of the pyloric glands. Pyloric glands are similar to cardiac glands in that they both are coiled tubular glands that secrete mucous. H&E stain.

Stomach–Small Intestine Junction

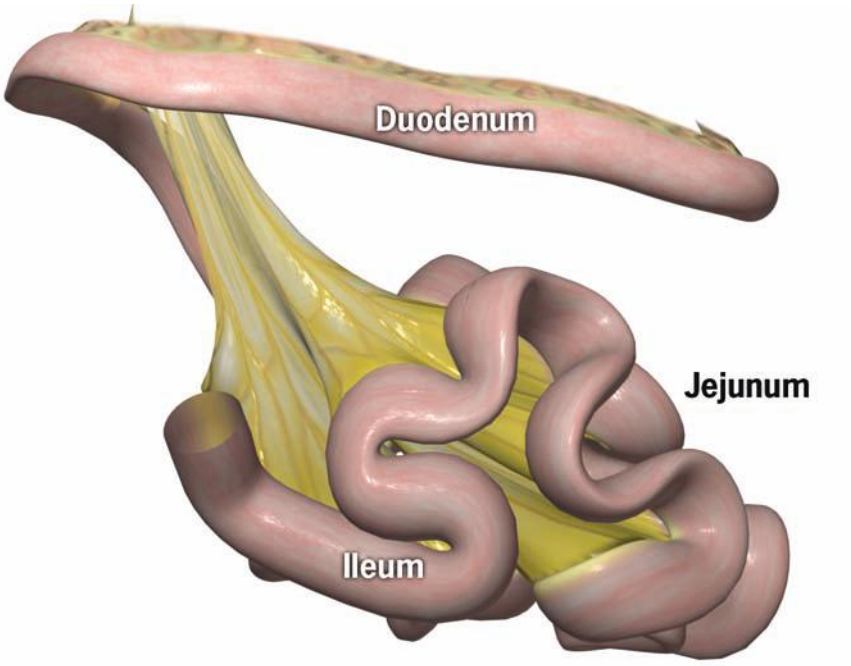
The gastrointestinal junction, or pyloric-duodenal junction, is the portal for release of chyme into the small intestine. At this junction there is a thickening in the inner circular layer of the tunica muscularis known as the pyloric sphincter muscle.

Small Intestine

Gross Anatomic Features

The equine small intestine is grossly divided into the duodenum, the jejunum, and the ileum (Figure 1-12), which are attached to the dorsal body wall by the mesoduodenum, mesojejunum, and mesoileum, respectively. The mesojejunum and mesoileum, which collectively are called the great mesentery, attach to the dorsal body wall via a narrow stalk through which blood vessels, lymphatic vessels, and nerves pass to the intestines. This narrow stalk, which commonly is called the root of the mesentery, can be palpated via rectal examination (see Chapter 15).

Figure 1-12



The duodenum, jejunum, and ileum, as viewed from the right side of the horse. Note the short mesoduodenum and long jejunal mesentery.

The duodenum is situated dorsally on the right side of the abdomen, adjacent to the base of the cecum and the right dorsal colon. The duodenum, which is approximately 1 meter long, arises from the pylorus and forms a loop caudal to the root of the mesentery. The mesoduodenum is a short mesentery attaching the duodenum to the dorsal body wall on the right side of the abdomen. The cranial portion of the duodenum is positioned against the visceral surface of the liver, where it has an initial sharp curve and two pouches or ampullae. The second curve in the duodenum is known as the cranial flexure, which encompasses the body of the pancreas. This portion of the duodenum is secured to the liver by the hepatoduodenal ligament, which contains the pancreatic and bile ducts. These ducts empty into the duodenum. The descending duodenum then passes dorsocaudally and is secured to the dorsal body wall by a short mesentery. At its caudal flexure, the duodenum passes medially around the base of the cecum, and crosses the median plane caudal to the root of the mesentery. The ascending duodenum then passes for a short distance in a cranial direction. At this point, the duodenum is adjacent to the descending mesocolon, and is connected to the transverse colon and initial portion of the descending colon by a portion of the mesoduodenum called the duodenocolic fold or ligament.

At the transition between the duodenum and the jejunum, the fanlike mesojejunum increases dramatically in length, averaging approximately 50 centimeters (cm). There are approximately 25 meters of jejunum in the adult horse, allowing coils of jejunum to mix together with coils of the descending colon. The length of the mesojejunum also allows movement of loops of the small intestine within the abdomen to become incarcerated through the epiploic foramen, inguinal canal, and rents in the mesentery, or twisted on the root of the mesentery (volvulus).

The terminal portion of the small intestine is the ileum, which is approximately 30 cm in length, and is characterized by a thick muscular wall, a long mesoileum, and an antimesenteric mesentery called the ileocecal fold. The ileocecal fold is a

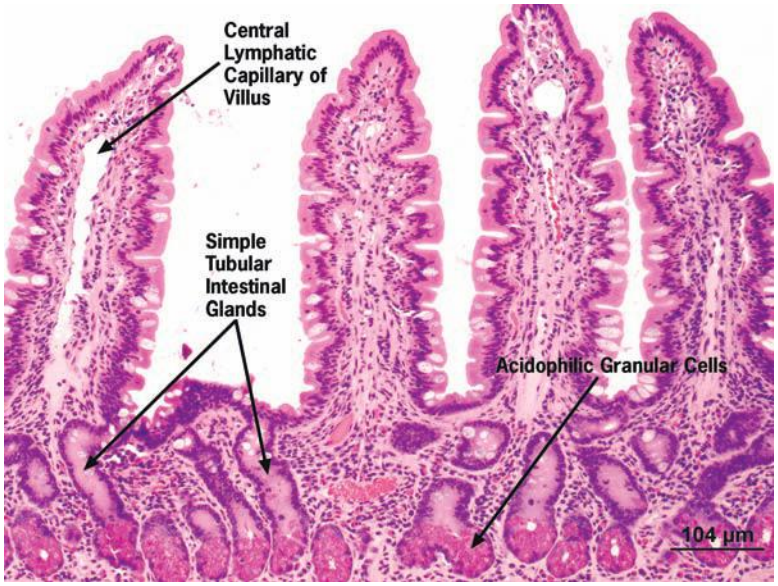
triangular-shaped fold of mesentery having a free edge and separate edges that attach to the ileum and to the dorsal band of the cecum. The ileum empties into the cecum on the dorsomedial aspect of the latter organ. The end of the ileum protrudes into the lumen of the cecum, and is surrounded by a raised annular fold of tissue, the ileal sphincter.

Microscopic Features

In the small intestine, surface area is grossly increased by the sheer length of the organ and by plicae circulares (circular folds). Surface area is increased microscopically by villi and by microvilli. The microvilli are referred to as the striated border. Microscopically, the three divisions of the small intestine are very similar. In the tunica mucosa, the lamina epithelialis lining the villi is made up of simple columnar cells that are interspersed with unicellular mucous glands, or goblet cells. The simple columnar cells are absorptive, and are referred to as enterocytes. The simple columnar epithelium also lines the intestinal glands (crypts of Lieberkuhn).

The small intestinal glands are simple tubular glands. The glands may coil and have some branching in the fundic region. The intestinal glands invaginate into the lamina propria. Cell division takes place in the fundic region of the intestinal glands; undifferentiated cells mature into goblet cells and enterocytes as they migrate toward the villi. In equines, another cell type, the acidophilic granular cell (Paneth cell) is also derived from the stem cells in the fundic region of the intestinal glands (Figure 1-13). Acidophilic granular cells occur in all divisions of the small intestine and are thought to play a role in mucosal immunity. In addition to these cell types, enteroendocrine cells are also present in the small intestinal glands.

Figure 1-13

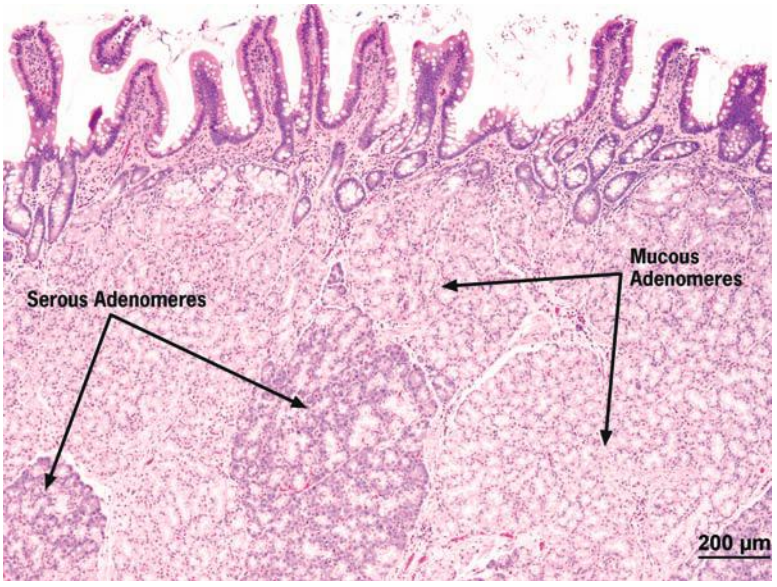


Villi and intestinal glands of equine jejunum. The small intestinal glands are simple tubular glands that empty into the intestinal lumen at the base of the villi. The bright eosinophilic-staining cells in the fundic region of these glands are the acidophilic granular (Paneth) cells. Lymphatic capillaries (central lacteals) are located within the lamina propria of the villi. H&E stain.

The lamina propria has variable cellularity, including but not limited to plasma cells, lymphocytes, macrophages and granulocytes, particularly eosinophils. The lamina propria within the villi has both blood capillaries and lymphatic capillaries (lacteals). The lamina muscularis mucosa is present and gives off smooth muscle fibers that extend adluminally into the villi. Contraction of these fibers allows for shortening of the villi and is thought to aid in emptying the capillaries, which become engorged during digestion.

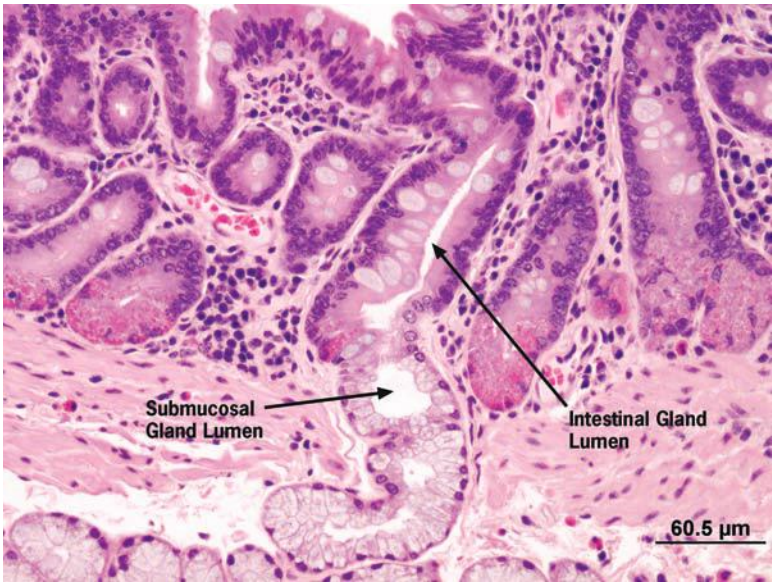
In general, the villi in the duodenum are blunt and wide, in the jejunum are long and slender and in the ileum are club-shaped. In the tunica submucosa, submucosal glands extend throughout the duodenum and into the jejunum (Figure 1-14). The submucosal glands are simple branching tubuloacinar glands that empty into the fundus of the intestinal glands (Figure 1-15). The glands predominantly contain mucous adenomeres with some serous adenomeres occurring occasionally. GALT (Gut Associated Lymphoid Tissue) occurs throughout the equine small intestine (Figure 1-16). GALT includes both nodular lymphoid tissue (primarily B cells) and diffuse lymphoid tissue (primarily T cells), which often occur together in aggregates (Peyer's patches). Lymphoid aggregates are grossly visible as thickened regions in the intestinal wall; the mucosa overlying these aggregates has a pitted surface. Microscopically, the aggregates are located in the tunica submucosa and extend adluminally into the tunica mucosa. The lamina muscularis is often disrupted by the lymphocytic infiltration. The lamina epithelialis overlying the pits is lacking in goblet cells and contains specialized epithelial cells known as microfold cells ("M" cells) that play a role in the immune process of monitoring intestinal antigens.

Figure 1-14



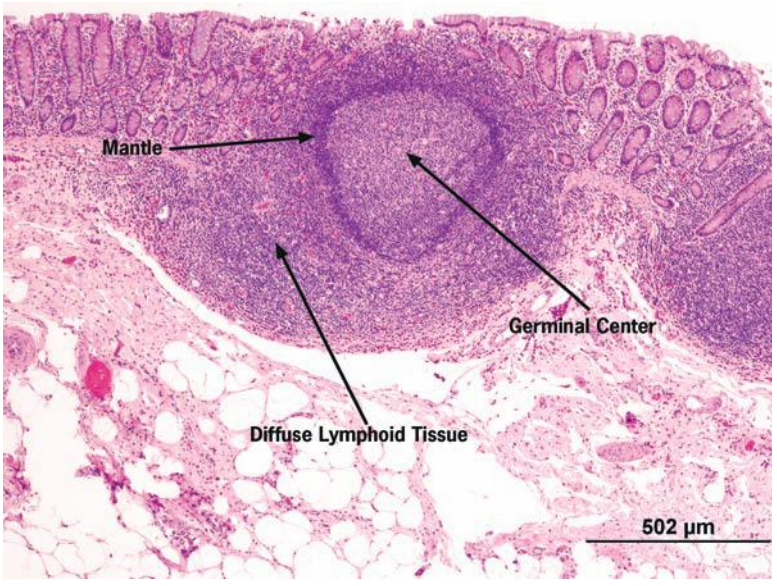
Submucosal glands of the equine jejunum. The submucosal glands are primarily composed of mucous adenomeres (light staining regions); however, serous adenomeres (darker staining regions) do occur. H&E stain.

Figure 1-15



Junction of submucosal and intestinal glands. The submucosal glands are not ducted directly to the intestinal lumen, but empty into the fundic region of the intestinal glands. H&E stain.

Figure 1-16



Gut associated lymphoid tissue (GALT). GALT may be found throughout the tubular digestive tract. GALT is composed of nodular (primarily B cells) and diffuse (primarily T cells) lymphoid tissue. The nodular lymphoid tissue in this image of ventral colon is undergoing proliferation in response to antigenic stimulation, forming a lighter-staining central germinal center surrounded by a darker-staining mantle of nonproliferative, nonreactive B cells. Surrounding the nodule is diffuse lymphoid tissue. H&E stain.

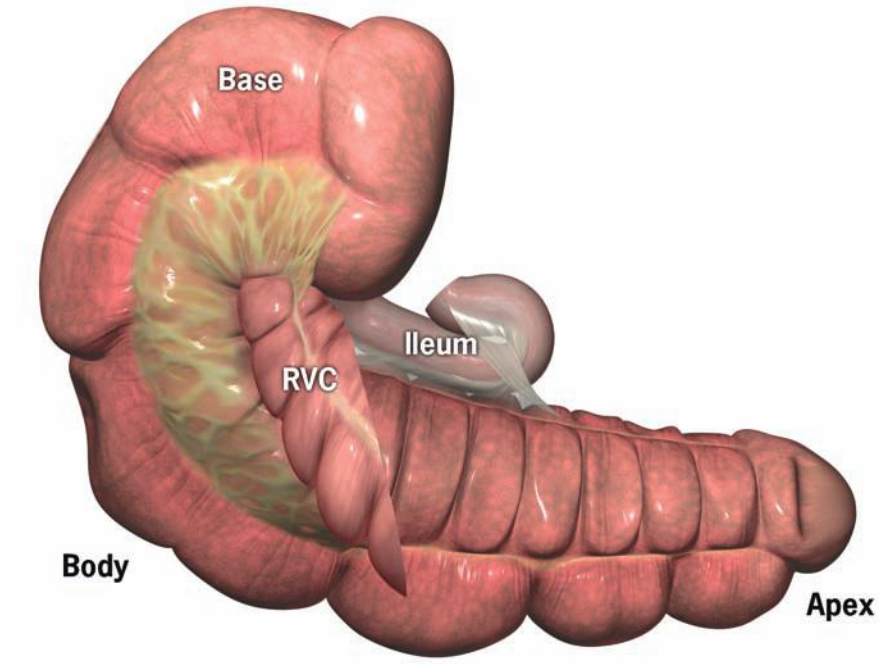
Large Intestine

Gross Anatomic Features

The equine large intestine is grossly divided into the cecum, the ascending (large), transverse, and descending (small) colons, and the rectum.

The cecum is a large comma-shaped fermentation vat that is situated primarily to the right of the midline. On the average, the cecum is approximately 1 meter in length and can accommodate 40 liters or more of ingesta. The cecum is composed of a base, body, and apex (Figure 1-17). The base is located dorsally in the right paralumbar fossa region, and the apex points to the xyphoid cartilage on the ventral midline. The cecum has a greater curvature on its dorsal aspect and a lesser curvature located ventrally. The dorsal aspect of the cecal base extends as far cranially as the costal portion of the diaphragm and the right lobe of the liver. The cecum is attached dorsally to the ventral surface of the right kidney, the root of the mesentery, and the pancreas.

Figure 1-17



The cecum, terminal ileum, and proximal portion of the right ventral colon (RVC) as viewed from the right side of the horse. The ileocecal fold is evident where it attaches the antimesenteric border of the ileum to the cecum. The base, body and apex of the cecum are also evident.

The cecum has haustra (sacculations) and four taenia (longitudinal bands). The cecal arteries, veins, and lymphatics pass through the mesentery overlying the medial and lateral cecal bands. The dorsal band of the cecum serves as the point of attachment for the ileocecal fold. The ventral cecal band is the most easily palpated band per rectum, running from the base toward the apex of the cecum (see Chapter 15). The ventral cecal band is almost entirely exposed, being concealed only where the cecum is attached to the dorsal body wall. A strong triangular fold of tissue, the cecocolic fold, attaches the lateral band of the cecum to the right ventral colon.

The ascending colon (large colon) is composed of two horseshoe-shaped lengths of intestine and can accommodate more than 100 liters of ingesta. The large colon originates on the right side of the abdomen at the cecocolic junction and terminates on the right side of the abdomen at the junction of the right dorsal colon with the transverse colon. In turn, ingesta moves through the right ventral colon, sternal flexure, left ventral colon, pelvic flexure, left dorsal colon, diaphragmatic flexure, and right dorsal colon (Figure 1-18A, B & C). The right and left ventral colons have an average diameter of approximately 25 cm. The most pronounced changes in the diameter occur at the pelvic flexure, where the diameter decreases to approximately 8 cm, and at the junction between the right dorsal and transverse colons, where the diameter changes from approximately 50 cm in the right dorsal colon to approximately 8 cm in the transverse colon. There are 4 longitudinal bands on the ventral colons, 1 on the left dorsal colon, 3 on the right dorsal colon, and 2 on the transverse and descending colons. The ventral colons each have 2 longitudinal bands on their dorsal surface; these bands are called the medial and lateral mesocolic bands, and are incorporated into the mesocolic attachments between the dorsal and ventral colons. The medial mesocolic band persists along the concave face of the bowel, whereas the lateral mesocolic band fades out. Ventrolateral and ventromedial bands are present on the ventral colons and are not covered by blood vessels or mesentery; these bands fade out near the pelvic flexure. The ventral colons also are characterized by sacculations; the dorsal colon lacks sacculations.

Figure 1-18A

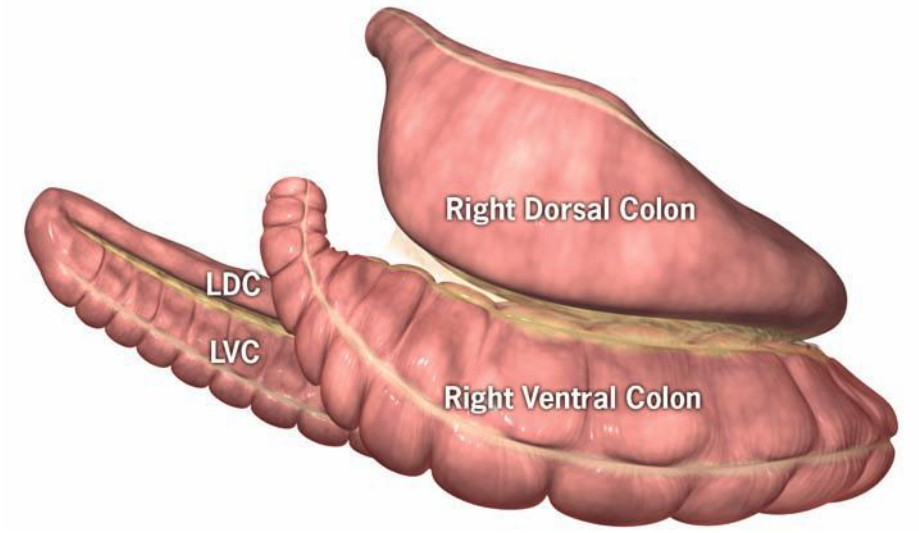


Figure 1-18B

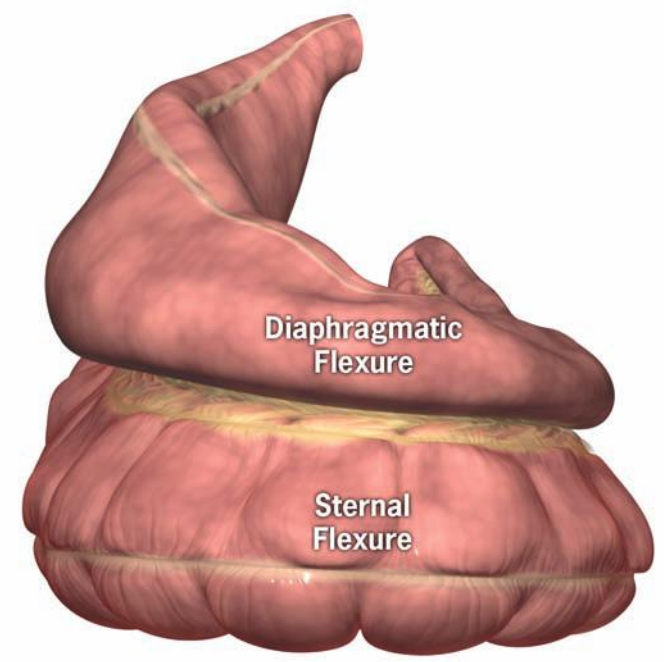
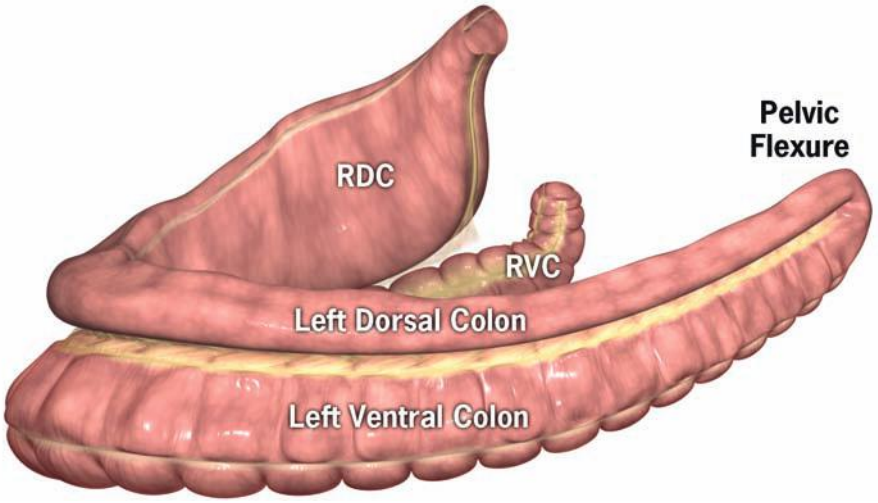


Figure 1-18C



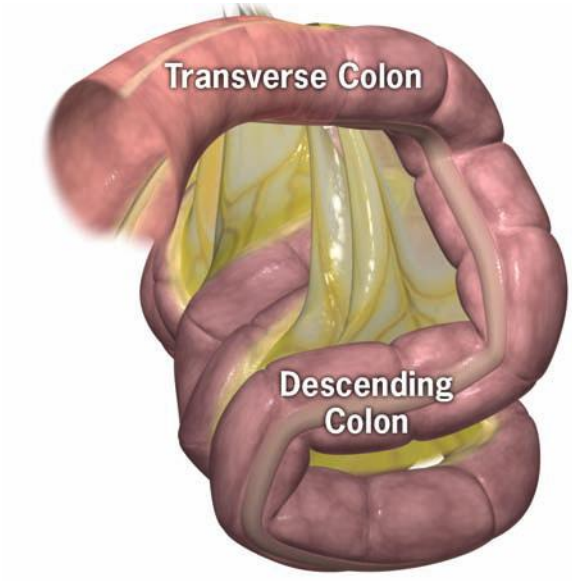
A.) The large colon, as viewed from the right side of the horse. The left ventral (LVC) and left dorsal (LDC) colons are evident toward the caudal aspect of the horse's abdomen. **B.)** The large colon from the cranial-most aspect of the abdomen, depicting the sternal flexure in the ventral colon and the diaphragmatic flexure in the dorsal colon. **C.)** The large colon, as viewed from the left side of the horse. The right ventral (RVC) and right dorsal (RDC) colons are identified.

The transverse colon is the short segment of intestine that connects the ascending (large) and descending (small) colons (Figure 1-19). It is situated dorsally, cranial to the cranial mesenteric artery and has a diameter of approximately 8 cm. It is tightly attached along its length to the dorsal aspect of the abdominal cavity by the transverse mesocolon.

The terminal 3 to 4 meters of large intestine are composed of the descending (small) colon and rectum (Figure 1-20). The descending colon has a diameter of approximately 8 cm, contains sacculations and a variable number of fecal balls, and has 2 longitudinal bands. One band is at the junction of the mesentery and the colon, and the other band is on the antimesenteric surface of the colon. The latter band is wide and easily palpable per rectum. Characteristically, the mesentery of the descending colon contains a large amount of fat, making palpation of the mesenteric vessels difficult.

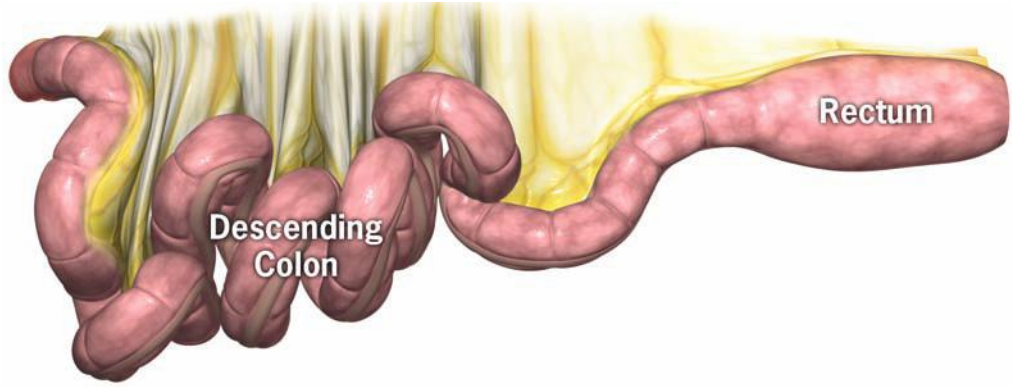
The rectum is approximately 25 cm in length, beginning at the pelvic inlet and terminating at the anus. Initially the rectum is covered by peritoneum and supported by the mesorectum. The distal portion of the rectum is retroperitoneal and is surrounded by connective tissue in the sacral region.

Figure 1-19



The transverse colon and initial portion of the descending colon as viewed from the cranial aspect of the abdomen.

Figure 1-20



The descending colon and rectum as viewed from the horse's left side.

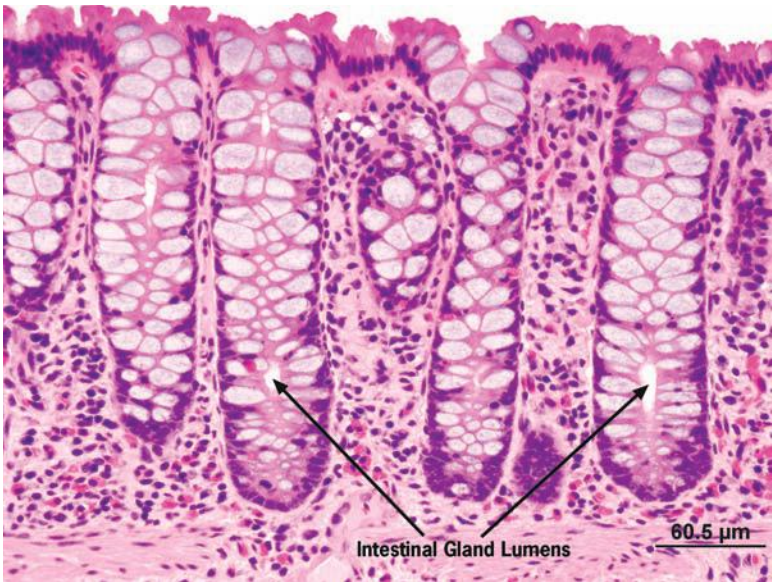
Microscopic Features

Microscopically, the divisions of the large intestine are very similar. Longitudinal folds increase the surface area of the large intestine. In the tunica mucosa, the luminal surface is smooth in comparison to the small intestine as there are no villi. The lamina epithelialis is made up of simple columnar epithelium; however, in the large intestine, the enterocytes may be difficult to distinguish because of the increased number of goblet cells, particularly in the intestinal glands. The intestinal glands are simple tubular glands that are straight with little coiling or branching (Figure 1-21). The intestinal glands invaginate the lamina propria, which has varying cellularity. The lamina muscularis mucosa is present. The tunica submucosa may contain lymphoid aggregates. The tunica muscularis has the most variation of all the tunics in the large intestine. The inner circular layer of smooth muscle is typical. The outer longitudinal layer of smooth muscle in the tunica muscularis is comparatively thin, except

where it forms thickened longitudinal bands called teniae. The teniae are reinforced with elastic fibers. The walls of the large intestine bulge out between the bands and form sacculations called haustra. The number of bands varies within the different regions of the large intestine.

Between the two layers of smooth muscle in the tunica muscularis is the myenteric plexus. This and the submucosal plexus are nerve plexuses of the autonomic nervous system (ANS), and they are present throughout the alimentary canal. The target tissues of the autonomic nervous system within the alimentary canal include both smooth muscle and glandular epithelium. Motility of the alimentary tract is achieved by dual means. Generally the ANS is responsible for gastric motility; however, local control also occurs in response to hormones, luminal stretching, and the composition of the ingesta (see Chapter 4).

Figure 1-21



Intestinal glands of equine descending colon. The large intestinal glands are simple straight tubular glands. The bright eosinophilic-staining cells in the lamina propria are eosinophils. H&E stain.

Liver

Gross Anatomic Features

The liver is positioned beneath the ribs, with approximately 60% of the liver being to the right of the median plane. The diaphragmatic surface of the liver is adjacent to the diaphragm, and the organ is positioned obliquely, running from dorsal on the right side to ventral on the left. The visceral surface of the liver contains impressions made by the stomach, colon, right kidney, duodenum, and cecum. The liver is attached to the diaphragm by the left and right triangular ligaments; the right triangular ligament is the shorter of the two. The falciform ligament attaches the liver ventrally to the sternal portion of the diaphragm, and the round ligament connects the ventral border of the liver to the umbilicus.

There is a fair amount of variability in the gross structure of the equine liver, with the left lobe being larger than the right lobe in some individuals and the right being the larger of the two lobes in others. The left lobe is divided into left lateral and left medial lobes, and the quadrate lobe is adjacent to a notch occupied by the round ligament. The right lobe is not divided, but the caudate process is positioned dorsal to the caudal vena cava and is one of the boundaries of the epiploic foramen (Figure 1-22). The epiploic foramen is a common site for strangulation obstruction of the distal jejunum and ileum. The dorsal aspect of the liver has an impression made by the right kidney, and a notch where the esophagus resides. The proximal portion of the duodenum is attached to the medial portion of the right lobe by the mesoduodenum, through which the bile duct passes from the portal fissure of the liver to the proximal duodenum. The mesoduodenum is continued by a band of fibrous tissue that attaches the right dorsal colon to the visceral surface of the liver.

Figure 1-22A

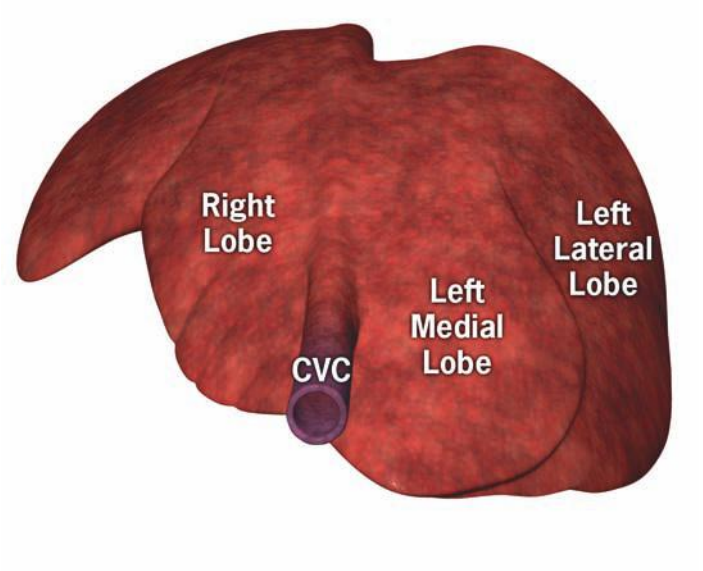
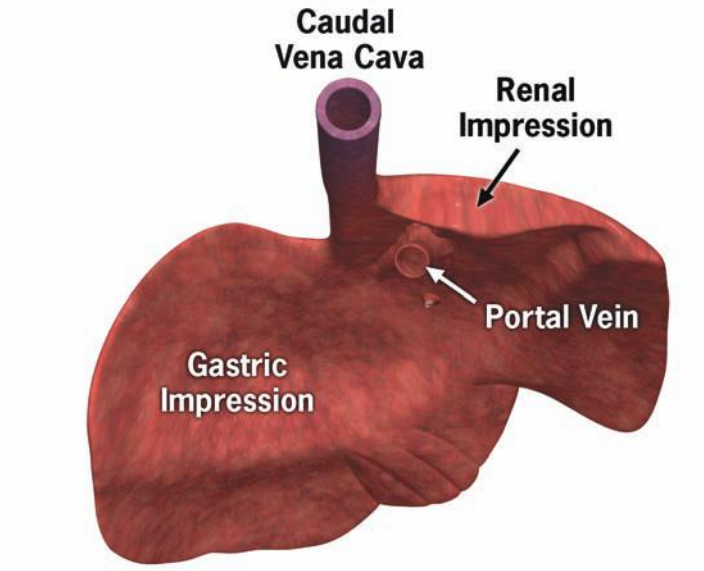


Figure 1-22B



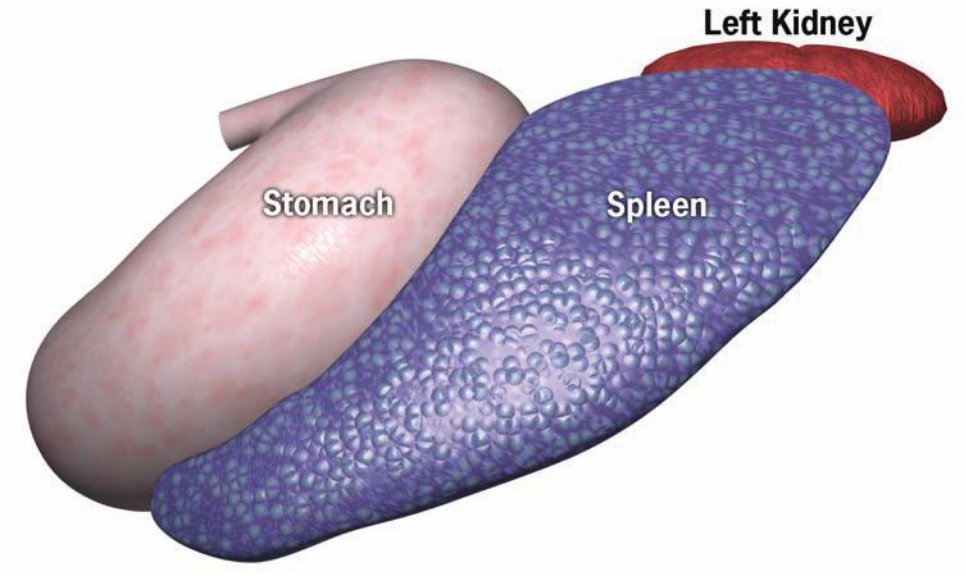
A.) The liver and caudal vena cava (CVC) as viewed from the cranial-most aspect of the abdomen. **B.)** The liver, caudal vena cava, and portal vein from a ventrocaudal point of view.

Spleen

Gross Anatomic Features

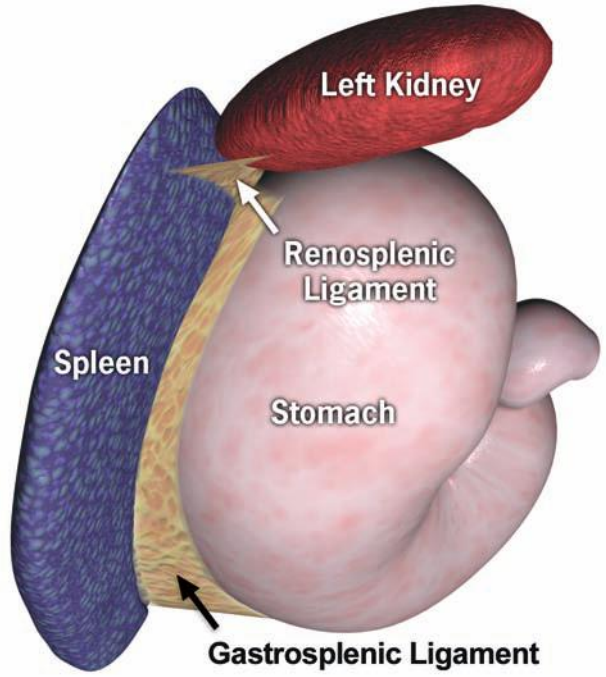
The spleen is part of the immune system rather than the digestive system. However, the fact that the ascending colon can become displaced dorsal to the renosplenic ligament necessitates inclusion of the spleen in the discussion of the abdomen. In the adult horse, the spleen is positioned against the left abdominal wall, with its wide dorsal portion near the left kidney and its more narrow ventral end directed cranioventrally (Figure 1-23). The cranial margin of the spleen is concave, while the caudal margin is convex. The caudal margin, which initially runs parallel to the costal arch, can be palpated per rectum in adult horses. The dorsal portion of the spleen is attached to the capsule of the left kidney by the renosplenic ligament (Figure 1-24). This ligament attaches to the medial aspect of the spleen in the region of the hilus. Consequently, the renosplenic ligament forms a "notch" in which the ascending colon can become displaced; the most dorsal aspect of the spleen prevents the colon from moving laterally, thus causing the colon to become entrapped.

Figure 1-23



The spleen, stomach and left kidney as viewed from the left side of the horse.

Figure 1-24



The spleen, stomach, and left kidney as viewed from the caudal aspect of the abdomen. The renosplenic ligament as well as the gastrosplenic ligament connecting the spleen to the stomach are evident.

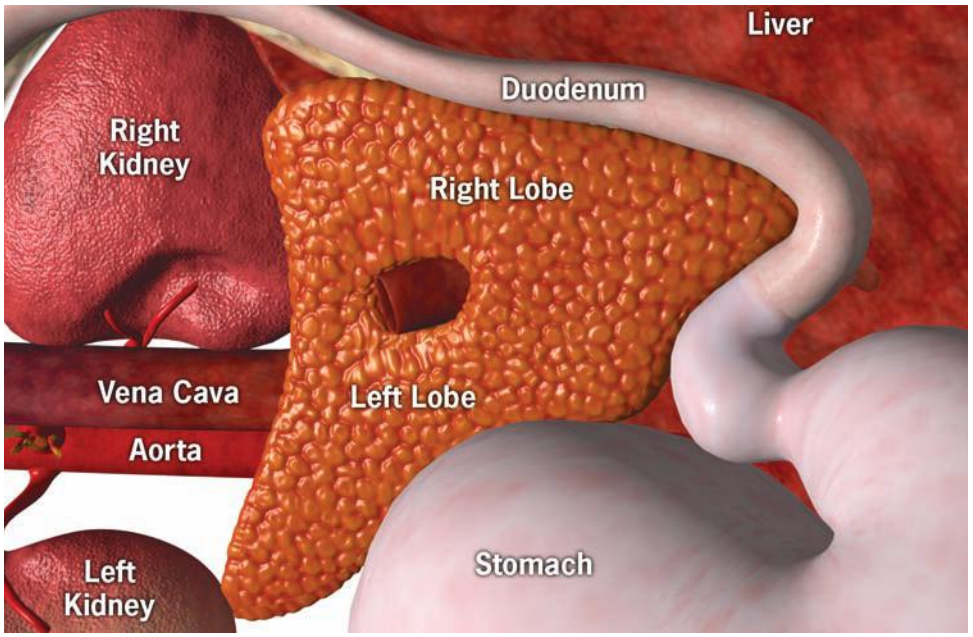
Pancreas

Gross Anatomic Features

Although acute pancreatitis appears to be a rare occurrence in the horse, evidence exists that pancreatic injury may occur in horses with acute intestinal obstruction. For this reason, a brief description of the pancreas is included as a final component of this chapter.

The pancreas is composed of left and right lobes and a body. In comparison with the right lobe, the left lobe is relatively long. The majority of the pancreas is situated adjacent to the stomach and liver, the cecal base, right dorsal colon, transverse colon, and cranial flexure of the duodenum (Figure 1-25). The right lobe extends to the right kidney, and the left lobe is attached to the stomach wall. The pancreatic duct runs adjacent to the bile duct and enters the duodenum at the hepatopancreatic ampulla. A smaller accessory pancreatic duct enters the duodenum at the minor duodenal papilla, a short distance from the major papilla.

Figure 1-25



The pancreas is confluent between the stomach, duodenum, and liver, extending to the right kidney with the left lobe extending along the right dorsal and transverse colons to the left kidney.

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Physiology of the Digestive Tract

Chapter 2

Gastric Secretory Function – Michael J. Murray
Small Intestine Function – David E. Freeman
Large Bowel Function – Marco A. F. Lopes
Liver Function – Tim Mair

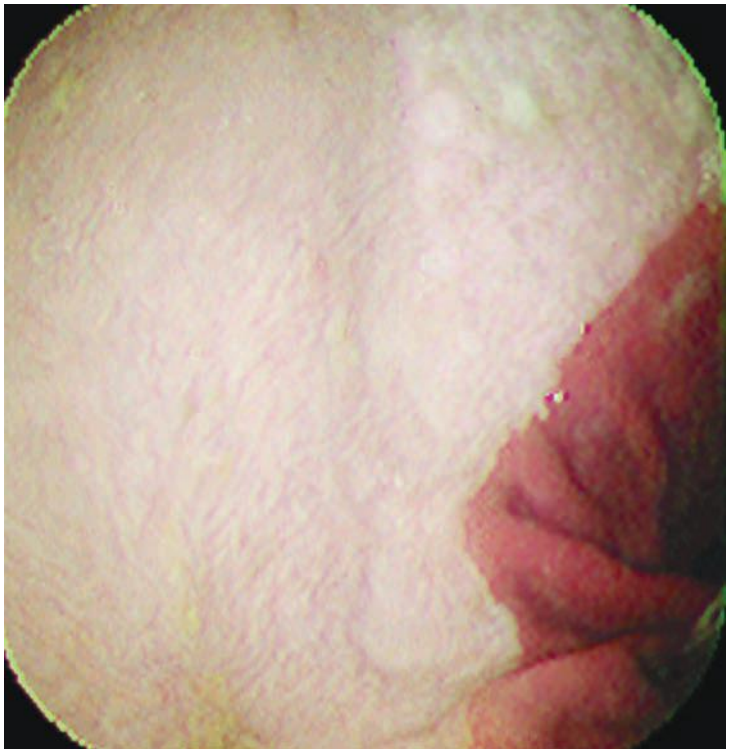
Gastric Secretory Function

Michael J. Murray

Stomach Anatomy–Physiology

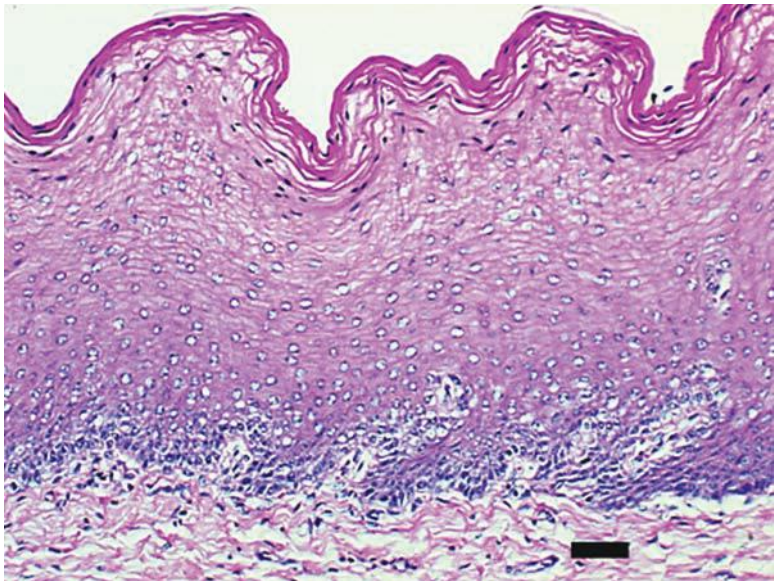
The dorsal fundus of the equine stomach is lined with non-glandular stratified squamous epithelial cells that are confluent with the lining of the esophagus (Figure 2-1). This lining is highly sensitive to acid, which can damage the cells within minutes of exposure.[1] This squamous epithelium has multiple cell layers covered by a superficial cornified layer (Figure 2-2), and mucosal protection in this area is primarily achieved by tight junctions between cells that form a barrier to acid. This is not a highly effective barrier, and exposure to even weak organic acids (e.g., acetic or propionic acid) can damage the barrier, particularly when the pH is low.[2] A hydrophobic phospholipid layer has been described on the surface of equine gastric squamous mucosa, which may offer some protection against damage by acid.[3] In addition to these mechanical protective factors, saliva provides a natural mechanism of neutralizing acid as well as coating the epithelium.[4]

Figure 2-1



Endoscopic view of normal equine stomach, including squamous (left) and glandular mucosal linings (right) of the stomach.

Figure 2-2



Microscopic appearance of equine gastric squamous mucosa (H&E).

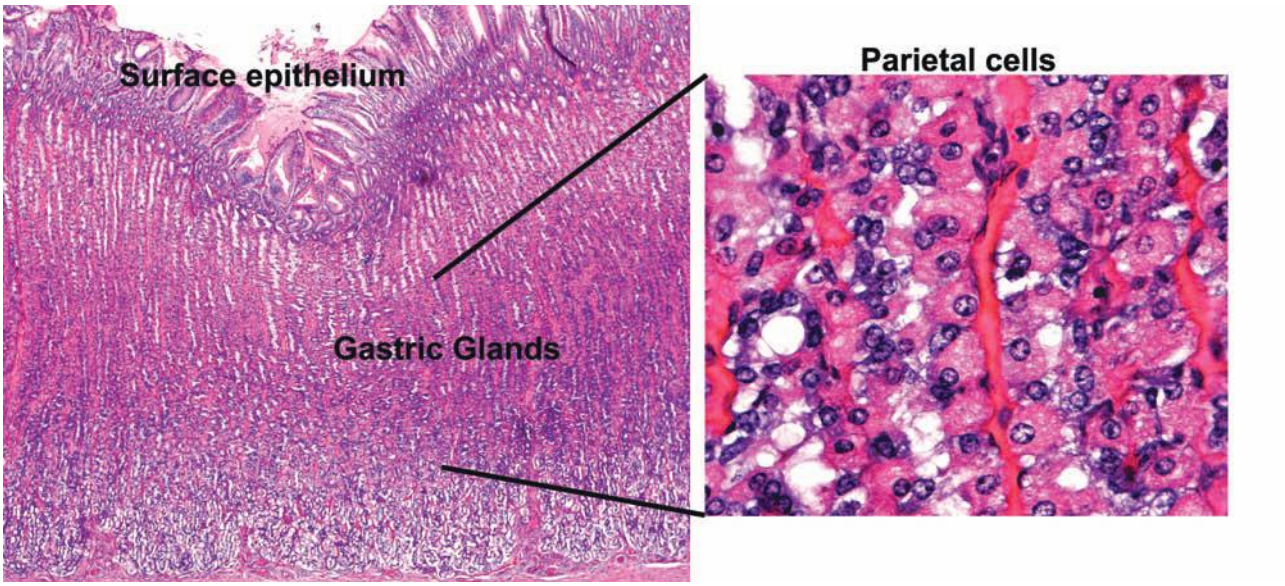
In neonatal foals, the developing gastric squamous epithelium is thin and possibly more susceptible to acid injury than is mature epithelium.[5] As part of normal gastric development in neonates, during the first month of life, the epithelium becomes thicker as it is exposed to hydrochloric acid. The developing epithelium may resist acid less effectively than more mature gastric squamous epithelium, thereby predisposing it to injury.

An irregular raised ridge, the margo plicatus, separates the squamous compartment from the glandular compartment of the stomach. Most equine gastric ulcers occur in the squamous mucosa in close proximity to this border, as a result of the proximity of this tissue to acidic gastric contents.

The ventral gastric mucosa is a highly differentiated glandular tissue with many cell types, including cells that secrete hydrochloric acid and digestive enzymes, and cells that stimulate and inhibit acid secretion (Figure 2-3). The glandular mucosa is not only highly differentiated, but the distribution of cells varies by region. The oxyntic (acid-secreting) portion of the glandular mucosa is in the region of the body of the stomach. This is where acid-secreting parietal cells, pepsinogen-secreting chief cells, histamine-secreting cells, and some somatostatin-secreting cells are located. These cells are aligned vertically from the lumen to the muscularis mucosa, such that the secreted hydrochloric acid is transported along channels toward the luminal surface. As the glandular mucosa transitions from the body towards the antrum, there are fewer oxyntic glands, and these glands are absent in the antrum. Within the mucosa of the antrum are abundant mucus and mucin-secreting cells, as well as endocrine cells (Figure 2-4). Gastrin-secreting G cells are located in this region of the stomach.

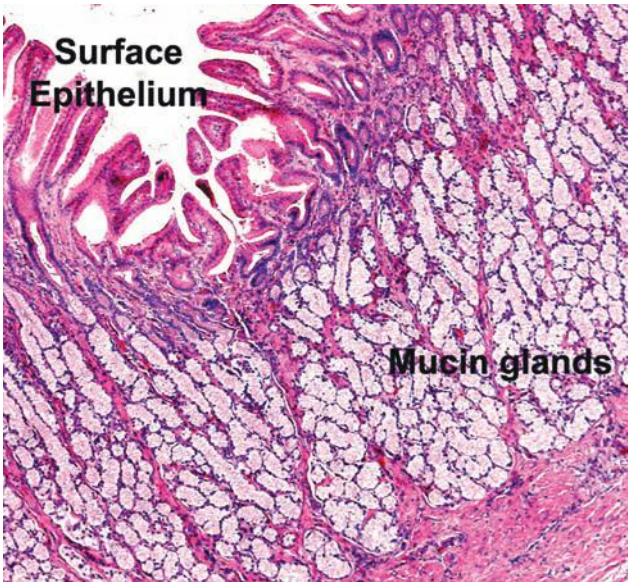
The glandular mucosa also contains highly developed self-protective mechanisms. Unique to the glandular mucosa is the ability to form a bicarbonate-rich protective mucus layer within which a pH gradient reduces the acidity at the mucosal surface to near neutral pH. Phospholipids in the mucus help repel gastric acid, and these phospholipids can be found in the secretory canals of the gastric gland.

Figure 2-3



Microscopic appearance of equine gastric glandular (oxyntic) mucosa. The area of the gastric glands is enlarged to show the parietal cells arranged in parallel rows (H&E).

Figure 2-4



Microscopic appearance of equine gastric glandular (antral) mucosa. There are abundant mucosal mucin-secreting glands (H&E).

Gastric Secretory Function

Hydrochloric acid is secreted by parietal cells via H^+, K^+–ATPase pumps, of which there are more than one million pumps per cell. The H^+,K^+–ATPase pumps utilize phosphorylation of ATP to exchange water solvated protons (protonated water, hydroxonium ion, H_3O^+) for potassium ions. In conjunction with parallel potassium and chloride ion conductances, this ATPase is responsible for the secretion of hydrochloric acid into the secretory canaliculus of the parietal cell, the enclosed space reaching a pH of near 1.0.[6] In the resting parietal cell, these pumps reside within the membranes of vesicles in the cell cytoplasm. When activated by histamine and gastrin, the parietal cells alter their shape and the vesicles merge with the outer cell membrane to form secretory canaliculi.

The equine stomach secretes hydrochloric acid continuously, even when the foal or horse is not eating.[7] Gastric acid secretion is pronounced as early as 2 days of age in neonatal foals.[8] Gastric acidity is lowest when the horse eats or the foal nurses, because eating stimulates the secretion of bicarbonate-rich saliva that can neutralize some gastric acid, and roughage or milk absorb gastric secretions so that they do not contact the mucosal surface. Once a horse stops eating or a foal ceases nursing, the gastric pH can rapidly decrease to less than 2.0, and the acidity will remain high until eating or nursing resumes.[8,9]

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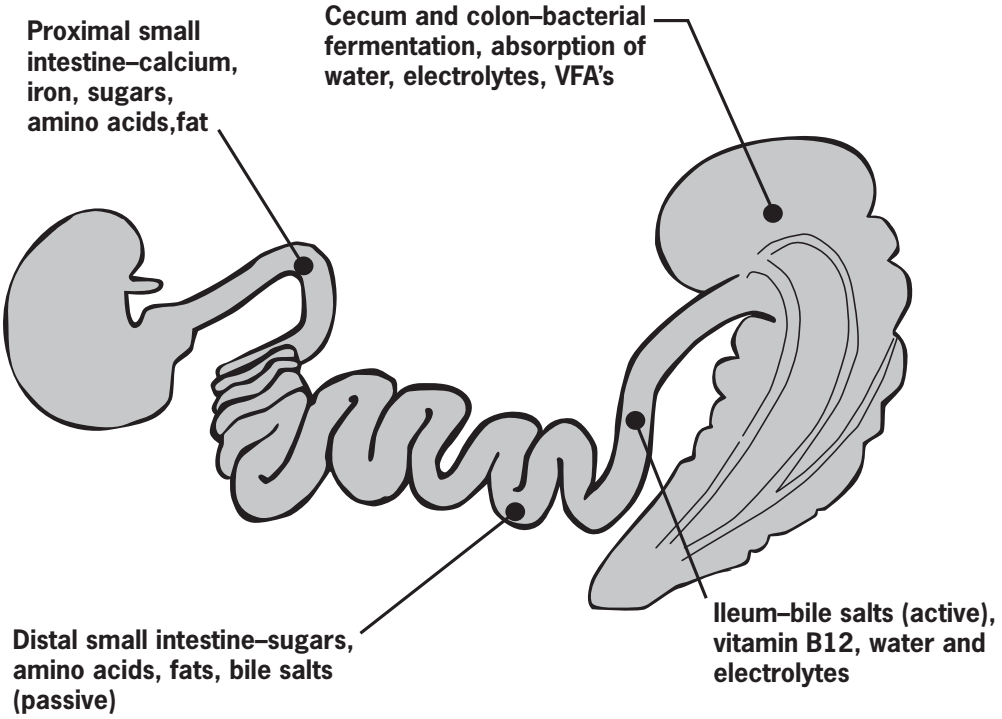
Small Intestine Function

David E. Freeman

Digestive Physiology–Anatomy

Digestion and absorption of nutrients take place predominantly in the proximal half of the small intestine (Figure 2-5) so that the ileum is exposed to a relatively low nutrient load.[1] The digestive/absorptive units of the small intestinal mucosa are finger-like projections of the epithelial surface, the villi (Figure 2-6), and each villus is surrounded by approximately 6 to 9 crypts of Lieberkühn.[2] Villi are considerably shorter in the horse than in most domestic animals,[3] and villus height and crypt depth decline from the proximal to distal segments of the intestine.[1] The importance of surface amplification by mucosal folds or plicae circulares does not apply to the horse.[3]

Figure 2-5



Distribution of major sites of absorption in the equine small intestine based on information from other species.

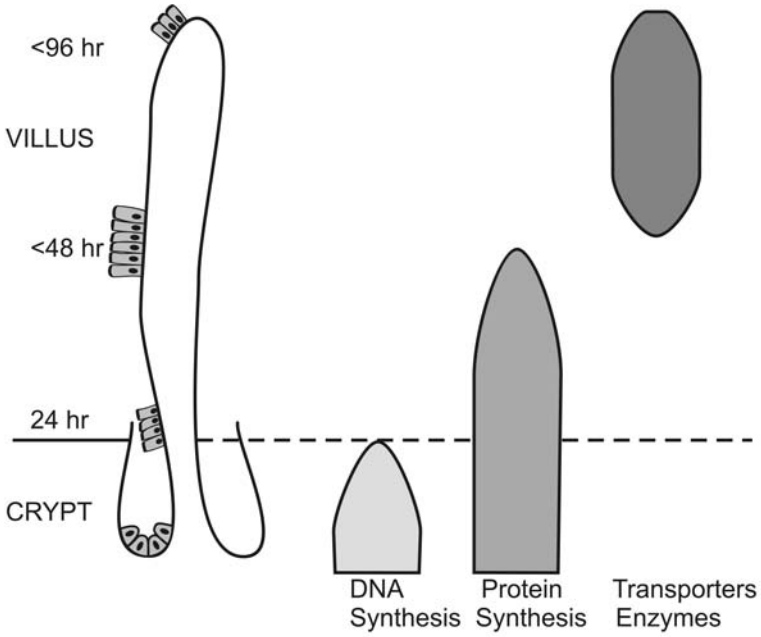
Figure 2-6



Typical appearance of jejunal villi in equine small intestine on scanning electron microscopy. Bar = 100 m.

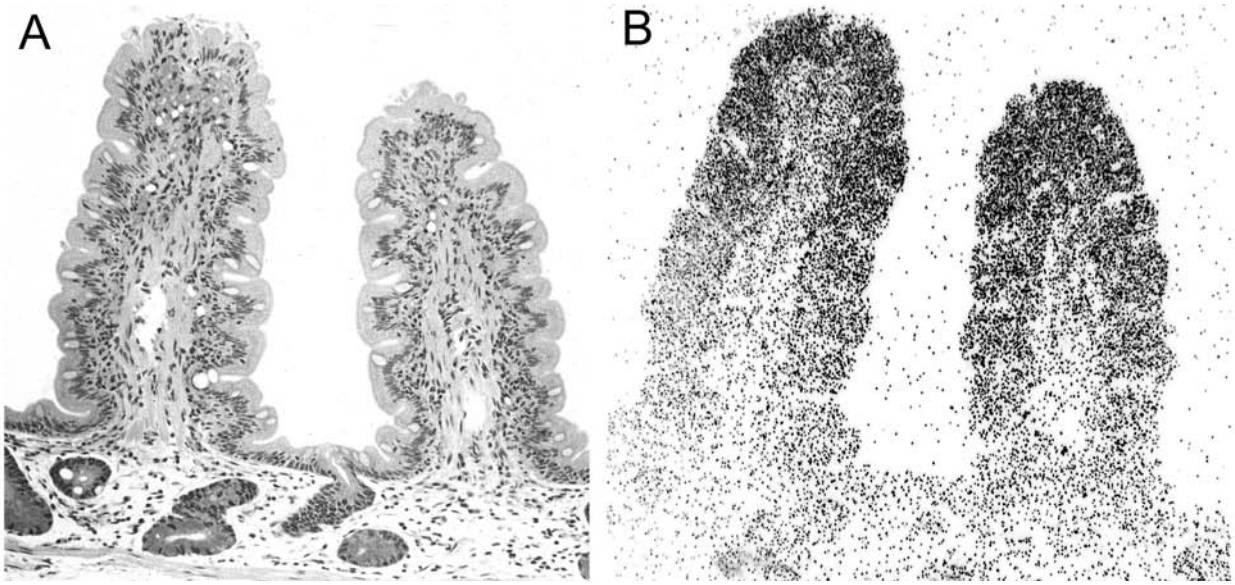
The major cell types of the small intestinal mucosa are columnar absorptive cells or enterocytes (~90%), mucous (goblet) cells, enteroendocrine cells, Paneth cells, and undifferentiated columnar cells.[2] These cells arise from progenitor or stem cells at the base of crypts.[1] After at least 2 divisions within the crypt, the columnar cells migrate onto the villus as mature absorptive cells and are finally extruded at the villus tip, usually with a turnover time of 2 to 3 days.[1,2] As cells migrate from the crypts, they acquire the properties of mature cells, and are capable of surface digestion of nutrients and active transport of digestion products (Figure 2-7). These functions are most pronounced in the upper third of the villi, which makes it unlikely that the villi are designed to increase the absorptive surface area (Figure 2-7). For example, there is a gradient of RNA abundance from the villus base to the tip with 6 times more of the D-glucose transporter (SGLT1, see later) being present in mature cells near the tip than in the immature cells at the base.[2] A similar gradient for amino acid absorption has been demonstrated by autoradiographic methods in equine jejunum (Figure 2-8). Although the crypts of both small and large intestines have zones of proliferation, migration, and differentiation, only the small intestine has villi with unique digestive and absorptive capabilities (Figure 2-9).

Figure 2-7



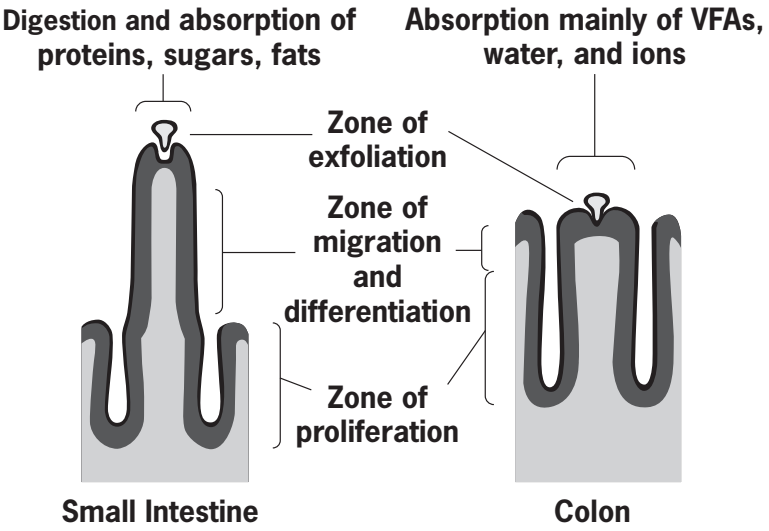
Distribution of different activities in the small intestinal crypt and villus, demonstrating steps in the maturation of epithelial cells leading to development of transporters and enzymes in the upper third of villi.

Figure 2-8A, B



Autoradiographic location of transport sites for L-alanine in villi from equine jejunum, with section stained with H & E **A.)** and unstained section **B.)** Note that silver grains that identify tritiated L-alanine are concentrated towards the villus tip.

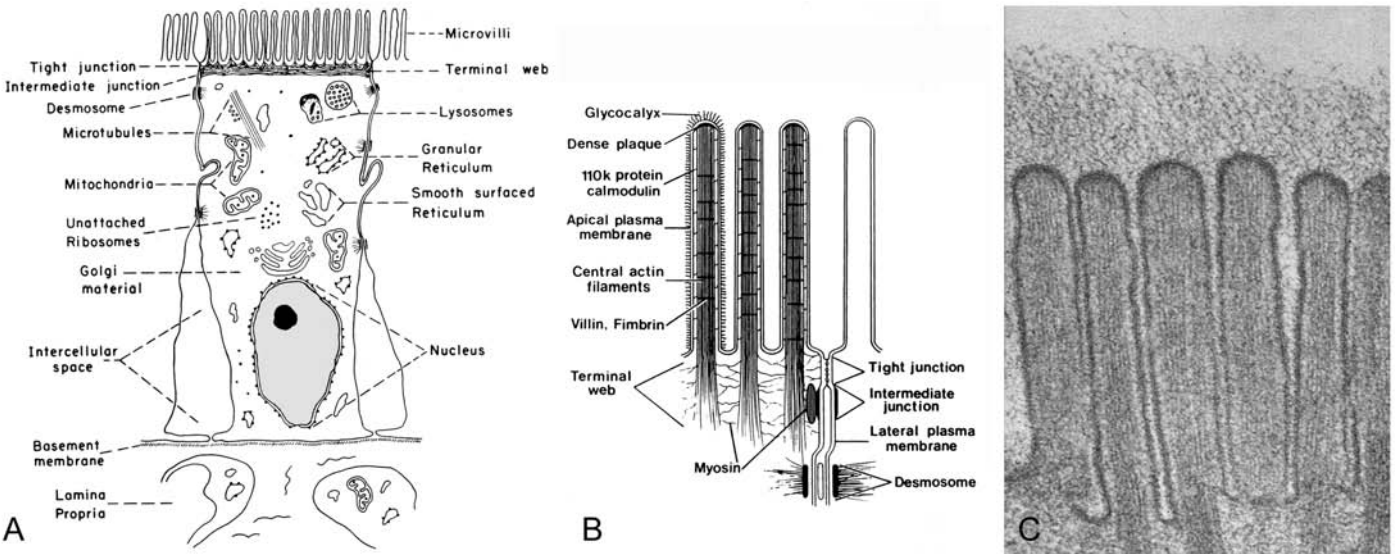
Figure 2-9



Structural differences in mucosa between small intestine and colon, particularly demonstrating villi in small intestine with digestive and absorptive capabilities that are lacking in the colon.

The apical surface of a mature enterocyte is also arranged to form microvilli, which is described as a brush border membrane (Figure 2-10). Enzymes that complete digestion of carbohydrates (disaccharidases) and proteins (peptidases) and render them absorbable are located within the microvilli. The microvillar membrane also contains various specific transport systems for absorbing digestive end-products into the enterocyte. An aqueous layer approximately 35μ thick, called the unstirred water layer, and the glycocalyx, or "fuzzy coat," coat the brush border of surface epithelial cells and present additional barriers to movement of solutes (Figure 2-10).[4] Enterocytes are connected to each other by tight junctions, which restrict the transmucosal flux of large molecules, although these tight junctions are permeable to water and many low-molecular weight substances (Figure 2-10).[5,6] The tight junction is more permeable to Na^+ and K^+ than to Cl^-, resulting in the creation of electrical potentials.[7] The space between cells is called the intercellular space and it combines with the tight junctional complexes to form the paracellular channel (Figure 2-10).[8] This space expands during water absorption.[6]

Figure 2-10A, B & C

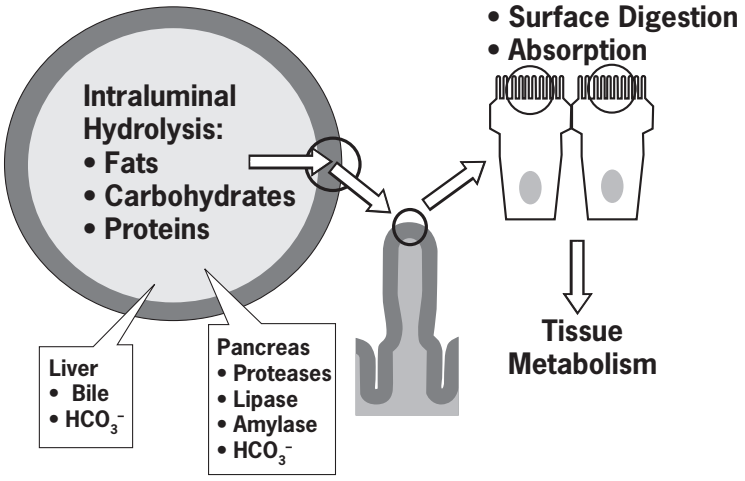


Typical absorptive epithelial cell or enterocyte in small intestine **A.)**, schematic of the structural features of the apical plasma membrane and junctional complexes of intestinal absorptive cells **B.)**, and transmission electron microscopic image of microvilli **C.)** with obvious actin filaments that form rootlets in the terminal web. Reproduced from Johnson LR (ed): Physiology of the Gastrointestinal Tract. New York: Raven Press, 1987 and 1994.

Intraluminal Digestion

In the small intestine, dietary carbohydrates, fats, and proteins are broken down by pancreatic enzymes, and the products of carbohydrate and protein digestion are hydrolyzed further by brush border enzymes (Figure 2-11).[2,9,10] Hydrogen ion in the duodenum causes the release of secretin from S cells, which stimulates the pancreas and liver to secrete HCO_3^- and water (Figure 2-11).[9,11,12] Bicarbonate neutralizes H+ ion in the proximal small intestine and thereby prevents acid-pepsin damage to the duodenal mucosa, provides a functional pH for pancreatic and brush border enzymes, and increases solubility of bile acids and fatty acids.[9,12] Proteins and fats in the duodenum stimulate the release of cholecystokinin (CCK) from I cells, which causes the pancreas to secrete enzymes for the digestion of carbohydrates, fats, and proteins, as well as cofactors (colipase) that aid in enzymatic digestion (Figure 2-11).[11,12] Trypsinogen, the precursor form (zymogen) of trypsin, must reach the small intestine to be activated by the brush border enzyme enterokinase.[12] Trypsin can also activate trypsinogen, but this occurs at a much slower rate than activation by enterokinase. All other zymogens can only be activated by trypsin. The principal pancreatic enzymes are amylase for starch digestion, trypsin, chymotrypsin, carboxypeptidase, and elastase for protein digestion, and lipase and colipase for fat digestion.[12]

Figure 2-11



Interaction between intraluminal digestion, surface digestion, and absorption in small intestine, showing the contribution of liver and pancreas to the process.

Basal pancreatic secretions in the horse are profuse and apparently continuous (10 to 12 L/100 kg body weight/day), but they can be increased rapidly as the horse eats.[13] The concentration of HCO_3^- is low and does not exceed that of Cl^- at any rate of secretion, so that Cl^- remains the predominant inorganic anion in the horse's pancreatic secretion at all rates of flow.[13] As a result, pancreatic secretion may provide a source of anion (Cl^-) for exchange with HCO_3^- in the terminal ileum to buffer contents prior to fermentation in the colon.[13,14] Although content and output of pancreatic enzymes is small in the horse compared with other animals,[13] digestion and absorption appear to be as efficient.[15]

Lipolysis in the small intestine requires emulsification of fat by bile salts, which allows the intestine to break the fat globules into minute particles by agitation, and thereby increase the surface area of lipids.[12] The precursor of bile salts is cholesterol, which is converted in the liver to cholic acid or chenodeoxycholic acid.[16] These acids then combine principally with glycine and taurine to form glyco and tauro conjugated bile salts. Conjugation lowers the pKa to below the physiologic range of intestinal pH, causing the conjugated bile acids to become ionized anions (referred to as bile salts) rather than undissociated bile acids. In the ionized form, they are more soluble.[16] Micelles form when the bile salts reach a particular concentration in the intestine, called the critical micellar concentration (CMC), and they aid in absorption (see later).

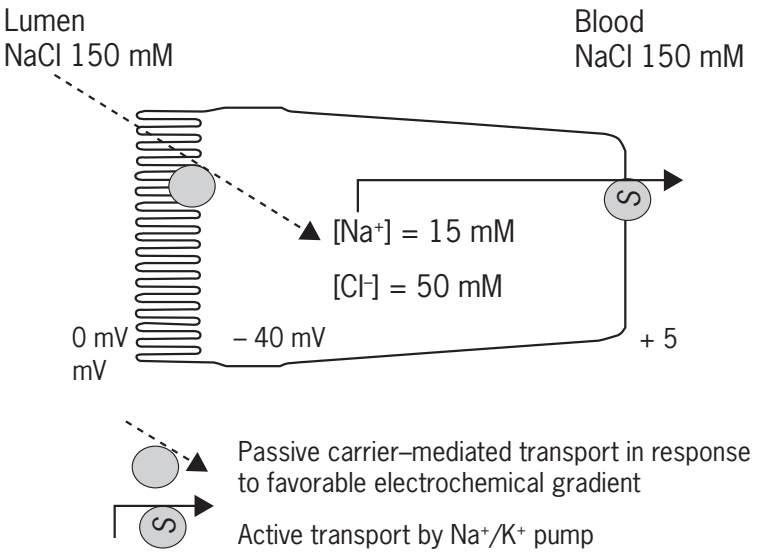
Approximately 94% of bile salts are reabsorbed by the small intestinal mucosa, pass to the liver, and then are resecreted in a process called enterohepatic circulation of bile.[12,16] Active transport by a Na^+– dependent process in the ileum (see Figure 2-5) and passive absorption by the jejunum combine to reclaim intraluminal bile. Secondary bile salts are produced from bacterial deconjugation and dehydroxylation of bile salts that are not absorbed in the small intestine and enter the colon. These secondary bile salts are relatively insoluble at the pH of colonic contents, and form precipitates that are excreted in feces. The small quantities lost in feces are replaced continually by liver cells.[12,16]

Absorption of Ions and Water

Reabsorption of ions and water by the intestine is critical to recover the large volume of digestive secretions from the salivary glands, pancreas, liver, stomach, and small intestine itself. Most of the small intestinal absorption of water takes place in the distal third of the small intestine, but the bulk of intestinal water is absorbed by the large intestine.[14] However, Na^+ absorption in the small intestine plays an important role in absorption of several nutrients and other ions.

The four mechanisms by which electrolytes can move across the mucosa are 1) passive diffusion (paracellular or transcellular, and driven by an electrochemical gradient); 2) neutral exchange (transcellular exchange of cations or anions); 3) carrier-mediated cotransport (transcellular, primarily with Na^+); and 4) active transport (energy-consuming, such as the Na^+/K^+–ATPase). The routes for transepithelial movement of ions and water are through the cells (transcellular) and through paracellular spaces (extracellular).[6,8] Transcellular movement of Na^+ involves entry from the lumen into the cell down an electrochemical gradient (Figure 2-12). In contrast, exit of Na^+ from the cell is against an electrochemical gradient and, therefore, is an active process that requires energy. The source of this energy is the Na^+/K^+–ATPase, or so called Na^+ pump, located along the basal and lateral membranes (Figure 2-12).[8,14] The active transport of Na^+ across the cell creates a transmucosal electrical potential difference, with the serosal side being positive (Figure 2-12). Ultimately, every Na^+ ion that crosses the cell by any route is accompanied by an anion, usually Cl^-, to maintain electroneutrality, and water to maintain osmolality.

Figure 2-12



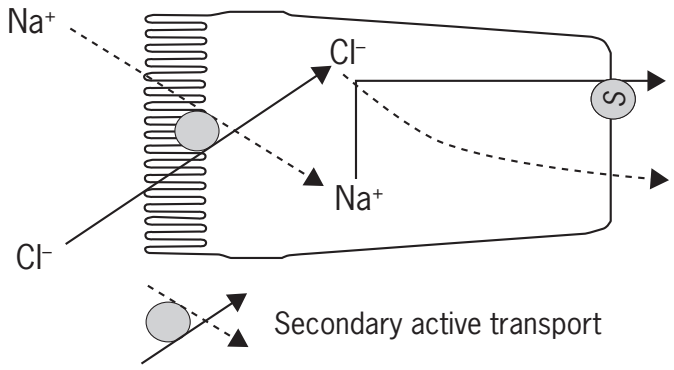
Mechanism of Na^+ absorption in the small intestine, with Na^+ entering the cell passively down its electrochemical gradient (low intracellular concentration and cell interior negative). The Na^+ is then pumped out of the cell against an electrochemical gradient by the energy-dependent Na^+/K^+ pump. The active transport of Na^+ across the cell creates a transmucosal electrical potential difference, with the serosal side being positive.

Net Cl^- absorption requires a source of energy with sufficient magnitude to offset the electrochemical gradient that opposes its entry into the cell (cell interior is negative and intracellular concentration of Cl^- is high).[7] The electrochemical gradient for Na^+ across this membrane has more than sufficient potential energy, as calculated from the Nernst equation, to move Cl^- into the cell, if it can be coupled to Na^+ movement (Figure 2-13A). This coupling is brought about by a carrier mechanism on the luminal membrane that is specific for Na^+ and Cl^- (Figure 2-13A). The ultimate driving force that energizes transport by this shared transporter is the Na^+ pump on the basolateral membrane, because this maintains the electrochemical gradient that favors Na^+ entry into the cell. The net movement of Cl^- by this mechanism is called secondary active transport (Figure 2-13A).[7]

The Na^+ gradient also energizes uptake of hexoses (glucose), amino acids, and most B vitamins against their chemical gradients into the cell (Figure 2-13B).[7] Although absorption of these compounds is usually considered to be active, in reality they are absorbed by secondary active transport (Figure 2-13B). This is also called the ion gradient hypothesis. The Na^+ gradient can also energize countertransport, by which an intracellular H^+ ion can be exchanged for extracellular Na^+ at the luminal membrane (Figure 2-13C).[7]

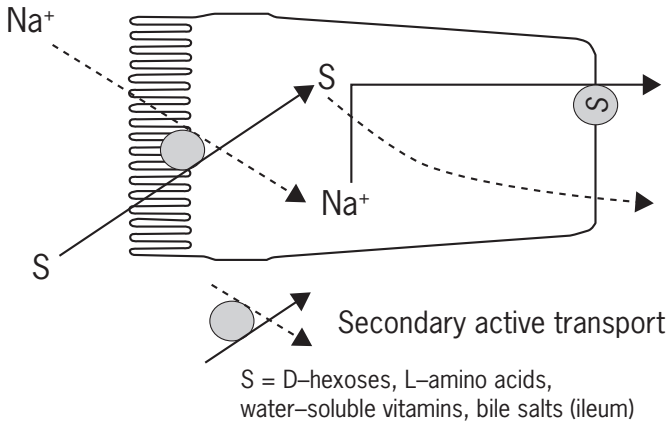
Transepithelial driving forces for movement of water and ions include chemical, osmotic, and electrical gradients between lumen and blood. Water transport is passive, closely coupled to solute movement, and is primarily paracellular.[8] As absorbed Na+ is pumped across the basolateral membrane, it creates an osmotic gradient that draws water into the intercellular space (Figure 2-14).[7,8] As water accumulates in this space, it increases the hydrostatic pressure, and this pressure forces the water across the basolateral membrane toward the capillary (Figure 2-14). Although the tight junction favors this process by restricting backflow of absorbed water and electrolytes into the lumen, paracellular permeability and reverse flow through this

Figure 2-13A



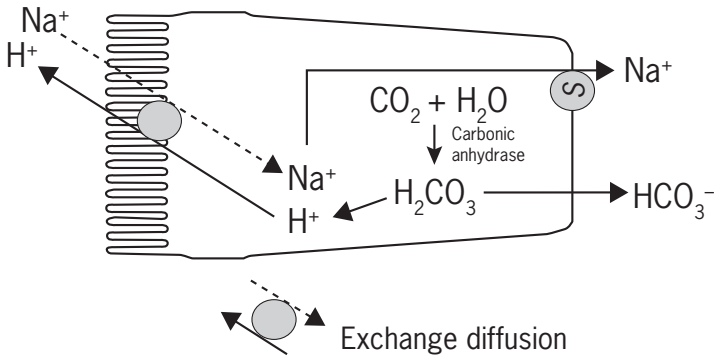
Method of Cl^- entry against an electrical gradient (cell interior negative) by neutral cotransport with Na^+. This is an example of secondary active transport, with the Na^+ transport providing the driving force. The passive exit of Cl^- is facilitated by the electrical gradient.

Figure 2-13B



Method of substrate (S) entry against a chemical gradient (caused by buildup of substrate within the cell) by cotransport with Na^+. This is another example of secondary active transport, with the Na^+ transport providing the driving force. The passive exit of substrate is facilitated by the chemical gradient created by substrate accumulation within the cell.

Figure 2-13C



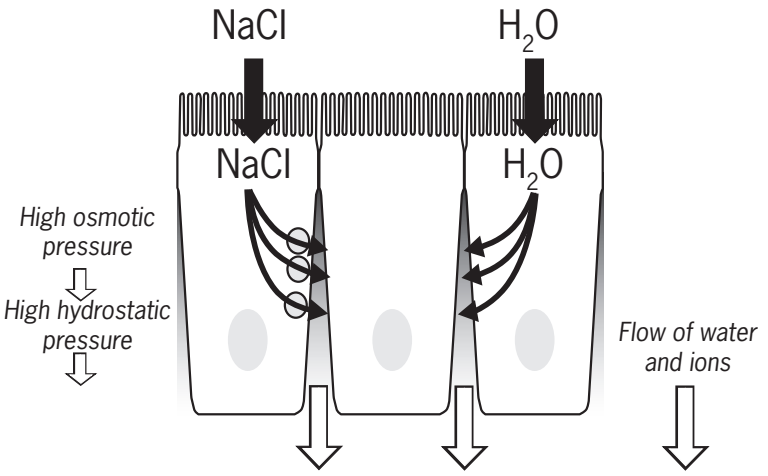
An example of exchange of a proton generated within the cell for Na^+ in the lumen by a countertransport mechanism. This mechanism would provide intraluminal H^+ for cotransport systems with peptides or for protonation of anions to improve absorption.

route are actually high in the jejunum (Figure 2-15). Paracellular permeability decreases from jejunum to colon, so that Starling forces have much more influence on ion and fluid transport in the proximal bowel, just as in the proximal tubule of the kidney.[6,14]

Net water movement from lumen to plasma through the paracellular route "drag" permeant ions and low molecular weight substances with it; this transport mechanism is called solvent drag or convection (Figure 2-16).[6,14] Solvent drag or convection is another means by which small water soluble substrates, such as sugars, amino acids, Ca^{++},and Mg^{++}, are drawn across the epithelium (Figure 2-16).

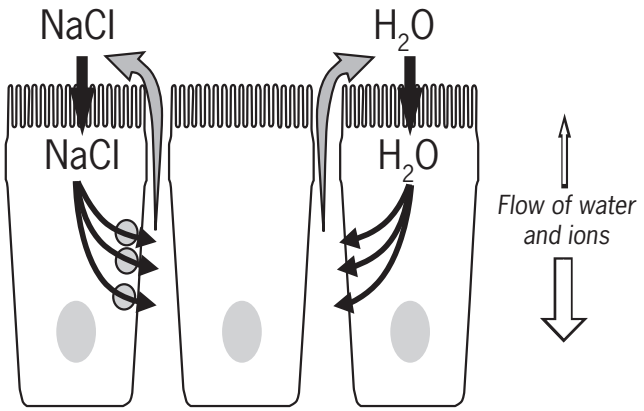
Fluid absorbed by the epithelium moves from the interstitium into the central lacteal of the villus.[10] The villus contracts through the action of its smooth muscle fibers and "pumps" the fluid from the central lacteal into the deeper lymphatics.[8] Although the popular hypothesis that the intestinal villus has a countercurrent multiplier that could enhance water and solute absorption, there is no evidence for such a system, at least in the dog, a species with the ideal vascular anatomy in its villus.[17]

Figure 2-14



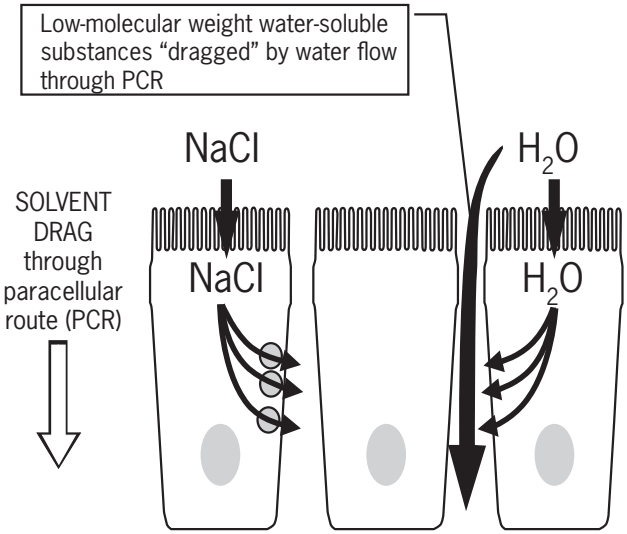
The standing gradient hypothesis invoked to explain water absorption. As absorbed Na^+ is pumped across the basolateral membrane, it creates an osmotic gradient that draws water into the intercellular space. As water accumulates in this space, it increases the hydrostatic pressure, and this pressure forces the water across the basolateral membrane towards the capillary. The tight junction favors this process by restricting backflow of absorbed water and electrolytes into the lumen.

Figure 2-15



In a "leaky" epithelium, the tight junctions are sufficiently loose or permeable to allow backflux of some absorbed water and ions into the lumen, so that water absorption is less efficient (in the jejunum) than in a tight epithelium (colon).

Figure 2-16



In an epithelium where the bulk of water flow is toward the basement membrane, low molecular weight substances will be entrained to follow the absorbed water and be absorbed. This is called "solvent drag" and is analogous to a stream carrying material with it in the direction of the current flow.

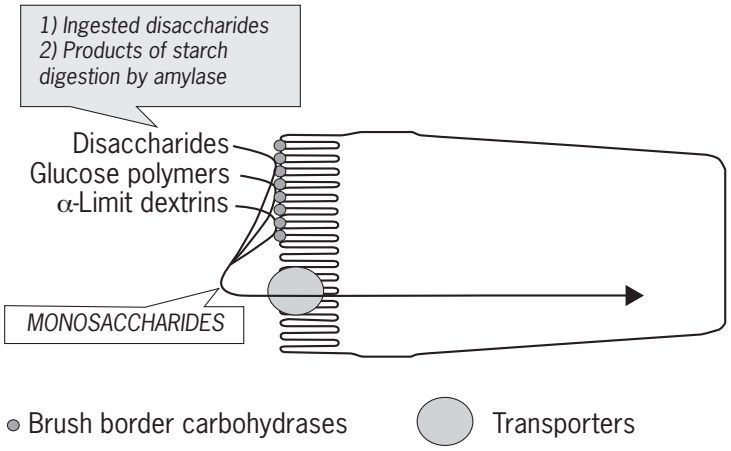
Absorption of Carbohydrate, Protein and Fat

Absorption of nutrients is the final step in the digestive process. Before these nutrients can be absorbed by the brush border membrane, however, they must be modified by intraluminal and brush border processes (see Figure 2-11).

Carbohydrate Absorption

Several brush border oligosaccharidases hydrolyze initial products of starch digestion derived from amylase, and the final monomeric D+–isomer forms are produced by brush border disaccharidases (Figure 2-17).[2] Sucrase activity is highest in the proximal small intestine of the horse on a grass-based diet, with activity levels comparable to those reported in other nonruminants.[18] Maltase activity is distributed evenly along the equine small intestine, and is higher than in other species.[18] Lactase activity is higher in equine jejunum than in other parts of equine small intestine, but decreases as the animal matures.[18]

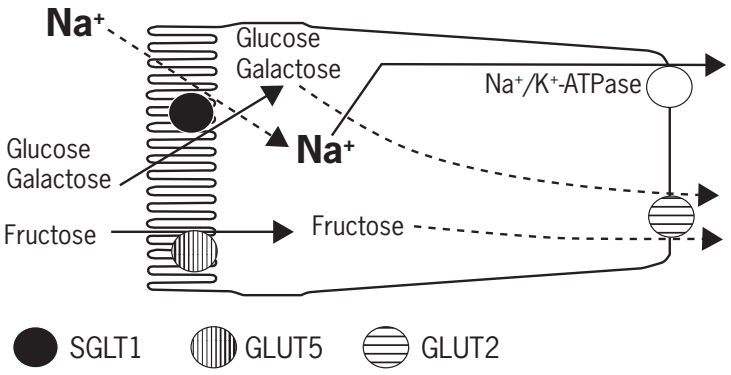
Figure 2-17



Surface hydrolysis of the carbohydrate polymers produced by intraluminal digestion and the subsequent absorption of the same as monosaccharides.
Reproduced from Johnson LR (ed): Physiology of the Gastrointestinal Tract. New York: Raven Press, 1987.

The monosaccharides produced by brush border hydrolysis, such as D-glucose and D-galactose, are transported across the enterocyte membrane by a high-affinity, low-capacity, Na^+-dependent cotransporter *type* 1 isoform, SGLT1 (Figure 2-18).[2,18] In horses maintained on conventional grass-based diets, the major site of D-glucose uptake by the SGLT1 transporter is the duodenum, followed by the jejunum, and then the ileum.[18] The D+ isomer form of fructose moves from lumen into the cell by facilitated diffusion through the GLUT5 transport system, which is not Na^+ dependent (Figure 2-18).[2] The monosachharides diffuse down their concentration gradient from the absorptive cell into the plasma through a GLUT2 passive transport mechanism and then enter the portal venous system (Figure 2-18).[2,12]

Figure 2-18

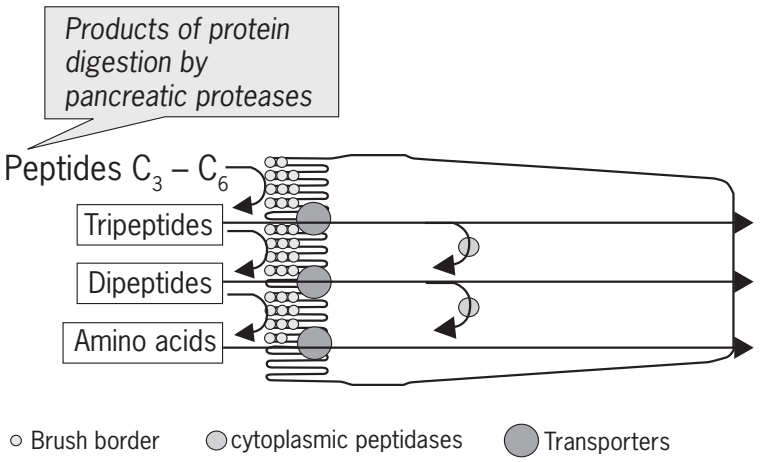


Monosaccharide transporters in intestinal epithelium, showing the Na^+-dependent process for glucose and galactose (SGLT1) and the Na^+-independent process for fructose (GLUT5) on the brush border and the basolateral transporter used by all three monosaccharides (GLUT2).

Protein Absorption

Brush border oligopeptidases break down the small neutral peptides yielded by pancreatic peptidases into constituent di- and tripeptides [~25%] or amino acids [~75%].[10,12] Within the enterocyte, the peptides are hydrolyzed by soluble cytoplasmic oligopeptidases into constituent amino acids, which move passively into portal blood down a concentration gradient (Figure 2-19). Consequently, many dipeptides and tripeptides are transported into the cell, but mostly free amino acids enter portal circulation (Figure 2-19).[10] The intestine has several distinct amino acid transport systems, with varying degrees of specificity for L^+ isomer forms of the amino acids and differences in Na^+ dependence.[10] The peptide transport systems are H^+-dependent.[10] Circulating and intraluminal amino acids can also be used by the intestinal epithelial cells as a source of metabolic fuel.[1]

Figure 2-19

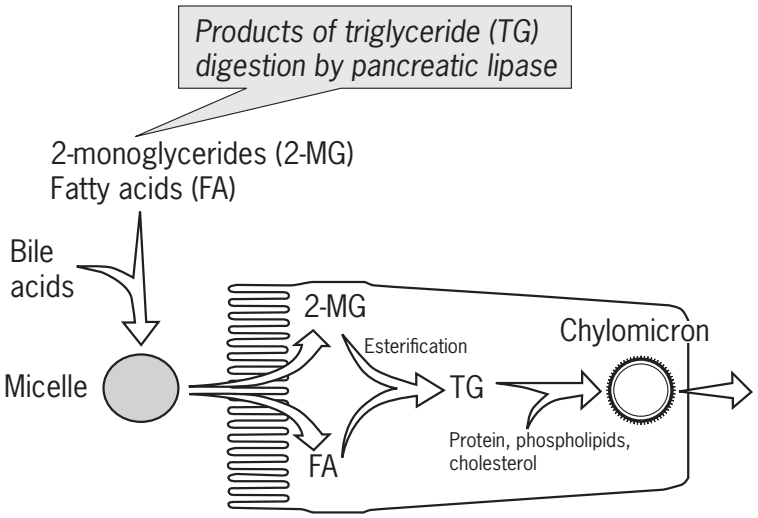


Surface hydrolysis of the protein polymers produced by intraluminal digestion and the subsequent absorption of the same as small peptides and amino acids.
Reproduced from Johnson LR (ed): Physiology of the Gastrointestinal Tract. New York: Raven Press, 1987.

Fat Absorption

Long- and medium-chain triglycerides are split into constituent fatty acids and monoglycerides by pancreatic lipase and colipase.[12] After lipolysis, the resulting long-chain fatty acids and 2-monoglycerides, as well as fat soluble vitamins and cholesterol, must combine with bile acids to form a water-soluble mixed micelle (Figure 2-20).[19] A mixed micelle has the fat-soluble part of its components directed inward and the water-soluble portion directed outward. In this arrangement, micelles facilitate movement of lipids through the unstirred water layer to the intestinal epithelial cells, where they release their constituents for absorption.[19] Because of their fat solubility, the released long-chain fatty acids and 2-monoglycerides can traverse the membrane down a concentration gradient. Fatty acids and 2-monoglycerides in the mucosal cell undergo re esterification and formation of chylomicrons, and chylomicrons are taken up by the lymphatic system (Figure 2-20).[19]

Figure 2-20



Role of micellar solubilization and chylomicron formation on absorption of 2-monoglycerides and fatty acids. Micelles allow these products to cross the unstirred aqueous layer to reach the apical membrane, and the chylomicrons are taken up by the lymphatics.

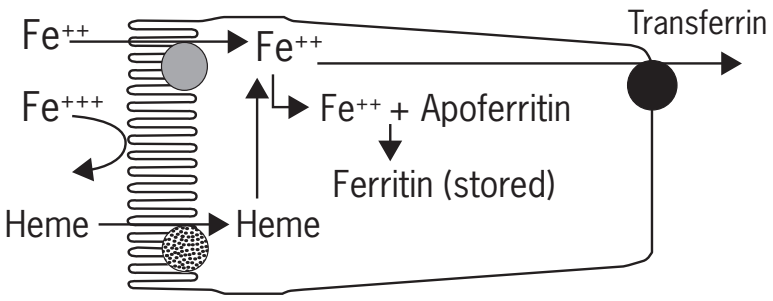
Iron Absorption

Iron has no avenue for excretion from the body so its transport must be closely regulated. The ferrous form of iron (Fe^{++}) is absorbed better than the ferric form (Fe^{+++}), although the precise mechanism is not known (Figure 2-21).[20] Some absorbed iron combines with an intracellular protein, called apoferritin, to form an iron complex called ferritin (Figure 2-21).[20] If no binding protein is available, absorbed ferrous iron is transported across the serosal border of the cell through transferrin receptors and is released to the circulation (Figure 2-21).[7,20]

If iron stores in the body are low, little iron enters the crypt cells from the blood (Figure 2-22). Consequently, little iron is available to stimulate synthesis of iron-binding proteins or ferritin in the crypt cell. As a result, cells migrating to the villus tip as mature cells are low in this protein (Figure 2-22);[20] however, the same cells are high in basolateral transferrin receptor (Figure 2-22).[20] Therefore, as ferrous iron enters the cell from the lumen, it is not bound and is free to enter the circulation and contribute to replenishing iron stores (Figure 2-22). Conversely, a large iron store in the body causes the ferrous iron to diffuse

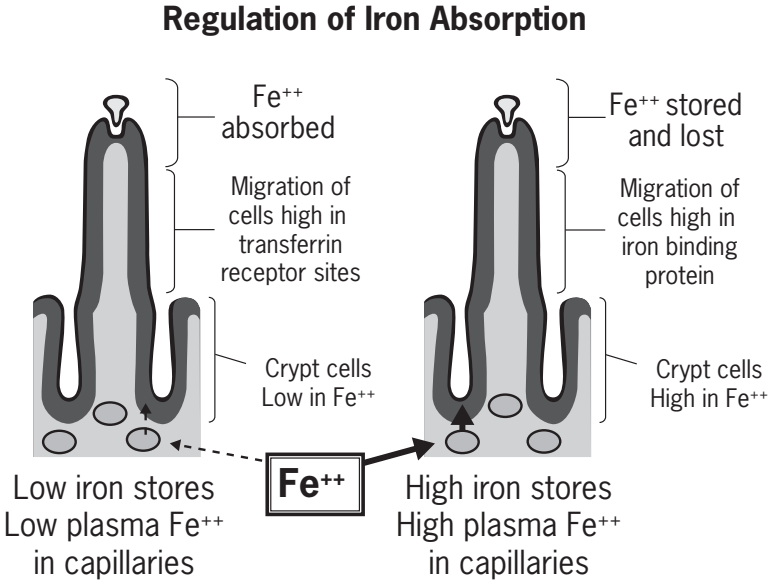
from its high concentrations in blood into the crypt cell, where it induces synthesis of iron-binding proteins (Figure 2-22). Consequently, the crypt cell migrates to the tip as a mature cell high in this protein. As ferrous iron enters the cell from the lumen, it is bound to the binding protein and stored. As the cell is exfoliated into the intestinal lumen from the villus tip, it takes its iron stores with it so this iron is lost to the body and not allowed to contribute to an existing high load (Figure 2-22).[48]

Figure 2-21



The ferrous form of iron (Fe^{++}) is absorbed better than the ferric form (Fe^{+++}), and some absorbed iron combines with an intracellular protein, called apoferritin, to form ferritin. The non-bound ferrous iron is transported across the serosal border of the cell through transferrin receptors and is released to the circulation.

Figure 2-22



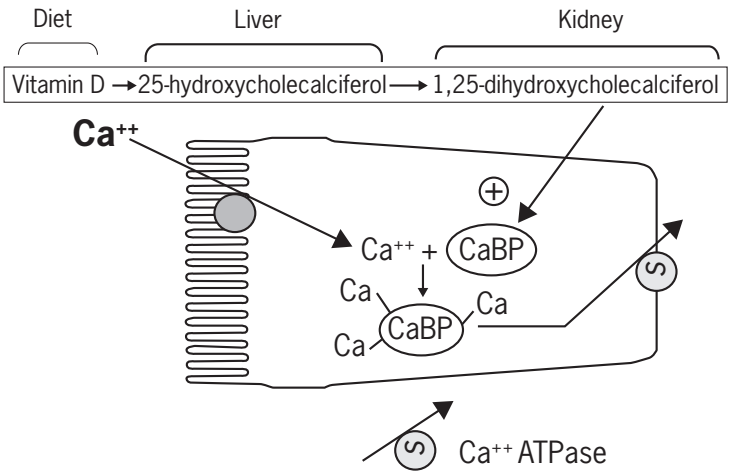
If iron stores are low in the body, little iron enters the crypt cells and little synthesis occurs of iron-binding proteins or ferritin, but the same cells will be high in basolateral transferrin receptor. Ferrous iron enters the cell from the lumen, is not bound, and is free to enter the circulation. Conversely, a large iron store in the body induces synthesis of iron-binding proteins in crypt cells and these migrate to the tip as mature cells high in this protein. Ferrous iron enters the cell from the lumen, is bound to the binding protein, and lost to the body as the cell is exfoliated from the villus tip.

Calcium and Magnesium Absorption

Lumen-to-plasma flux of calcium is highest in the duodenum, but some is absorbed in the more distal small intestine, and some endogenous calcium is passively secreted in the jejunum.[5] A high concentration of dietary magnesium can decrease calcium absorption through competition for the calcium transport site.[5] Absorbed calcium enters the cell down an electrochemical gradient from the lumen (Figure 2-23) and is transported through the cytoplasm complexed with the specific calcium-binding protein, calbindin D_{28K} (CaBP).[5] This protein is regulated by the biologically active form of vitamin D, 1,25-dihydroxycholecalciferol (Figure 2-23). Extrusion from the cell is against an electrochemical gradient mediated by the Ca^{++}–ATPase (Figure 2-23).[5]

Magnesium absorption is of interest in horses because magnesium sulfate is used as a laxative in horses, and the extent of absorption could alter its laxative effects and the risk of magnesium toxicity.[21] Mean apparent magnesium absorption is approximately 70% for supplements fed to growing foals and 40 to 60% for magnesium fed to mature ponies.[22] As in human beings,[5] most is absorbed in the small intestine, primarily the proximal small intestine, and small amounts are absorbed in the colon.[22]

Figure 2-23



Absorbed calcium enters the cell down an electrochemical gradient from the lumen and is transported through the cytoplasm complexed with the specific calcium-binding protein, calbindin D_{28K} (CaBP). This protein is regulated by dietary vitamin D that has been converted to the biologically active form by the liver and kidney. Extrusion is against an electrochemical gradient mediated by the Ca^{++}–ATPase.

Intestinal Secretion

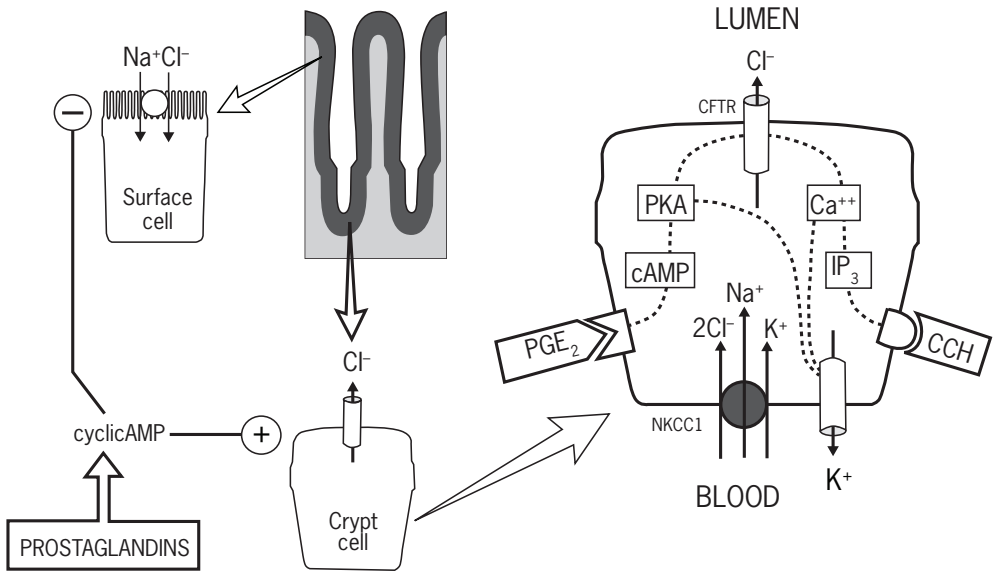
Crypts of Lieberkühn are located over the entire surface of the small intestine and they secrete an almost pure extracellular fluid that maintains chyme in a fluid state, delivers secretory IgA, and flushes crypts of noxious and infectious agents.[8] Intestinal water and electrolyte secretion are determined primarily by Cl^- movement, with movement of Na^+ and water following.

In the gastrointestinal tract, the electroneutral Na^+- K^+- Cl- (Na^+-Cl^- cotransporter or NKCC transporter; Figure 2-24) is responsible for moving Cl^- into the cell against an electrochemical potential difference.[23] The cystic fibrosis transmembrane conductance regulator is a cAMP-regulated Cl^- channel in the apical membrane of epithelial cells, and is the mechanism by which water and salts are secreted across epithelia (Figure 2-24).[9]

Intestinal secretion is under a degree of neural and eicosanoid tone, with cells of the lamina propria as the major sites of eicosanoid synthesis (Figure 2-25).[24] A dynamic interplay between mucosa, the enteric nervous system, the central nervous system, and luminal contents, regulate secretion (Figure 2-25).[8] Mediators produced by the enteric nervous system that promote secretion are acetylcholine, serotonin (5-hydroxytryptamine), substance P, and vasoactive intestinal peptide (VIP).[8,24]

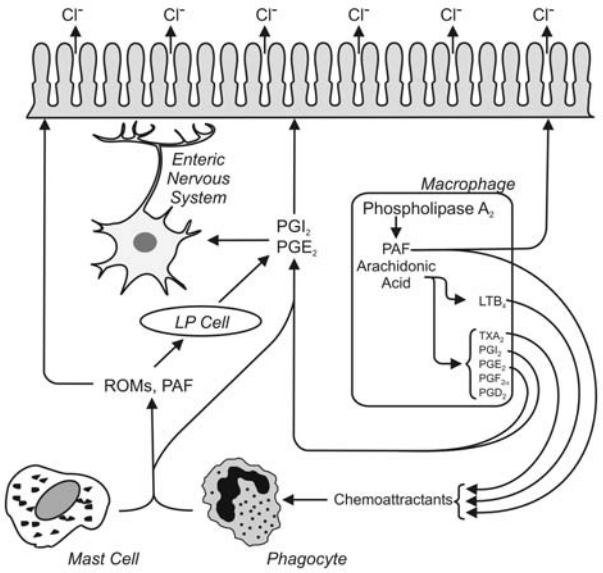
Protective mucus is secreted by Brunner's glands, which are located in the first 9.6 meters of the equine duodenum.[3] The function of mucus from Brunner's glands is to protect the duodenal wall from digestion by gastric secretions. Mucus is also secreted in large quantities by mucus cells located extensively over the surface of the intestinal mucosa and in the crypts of Lieberkühn.[3]

Figure 2-24



Effects of prostaglandins on ion transport in jejunal mucosa. Increased cyclic AMP activity in response to prostaglandin (or other agents that have the same effect) stimulates Cl^- secretion by crypt cells and inhibits the electroneutral NaCl absorption by the surface epithelial cells, and ion and water secretion are the net result. On the right is an expanded illustration of the process in a crypt cell. PGE_2 activates Cl^- secretion by cystic fibrosis transmembrane conductance regulator (CFTR) channels through cyclic AMP (cAMP) and protein kinase A (PKA). Carbachol (CCH) has the same effect through inositol 1,4,5-triphosphate (IP_3) and calcium release from calcium stores.

Figure 2-25



Proposed model for interaction between the immune system and the enteric nervous system in regulation of Cl^- secretion. Stimulation of mast cells and phagocytes (neutrophils, eosinophils, macrophages) in the lamina propria by luminal or circulating stimuli causes them to release immune cell products, such as prostaglandins, reactive oxygen metabolites (ROM), and platelet-activating factor (PAF), and the last two could stimulate other lamina propria cells (LP cell) to produce prostaglandins. Prostaglandins stimulate Cl^- secretion. The final neurotransmitters involved are unknown, but acetylcholine and vasoactive intestinal peptide are possible candidates. Modified from Bern JM, et al. Immune system control of rat and rabbit colonic electrolyte transport. J Clin Invest 83:1810-1820, 1989

Motility

Mammalian small intestine has an outer longitudinal smooth muscle and an inner circular muscle layer, and the latter is divided into a thick outer lamella and a thin inner lamella.[24] During peristalsis, rhythmic segmentation in smooth muscle and synchronous shortening of the longitudinal muscle causes aborad transit.[26] The interstitial cells of Cajal act as relays for transmission of information between the enteric nervous system and the intestinal smooth muscle and are thought to act as pacemakers[27] for the generation of electrical slow waves that propagate into the longitudinal muscle layer.[25]

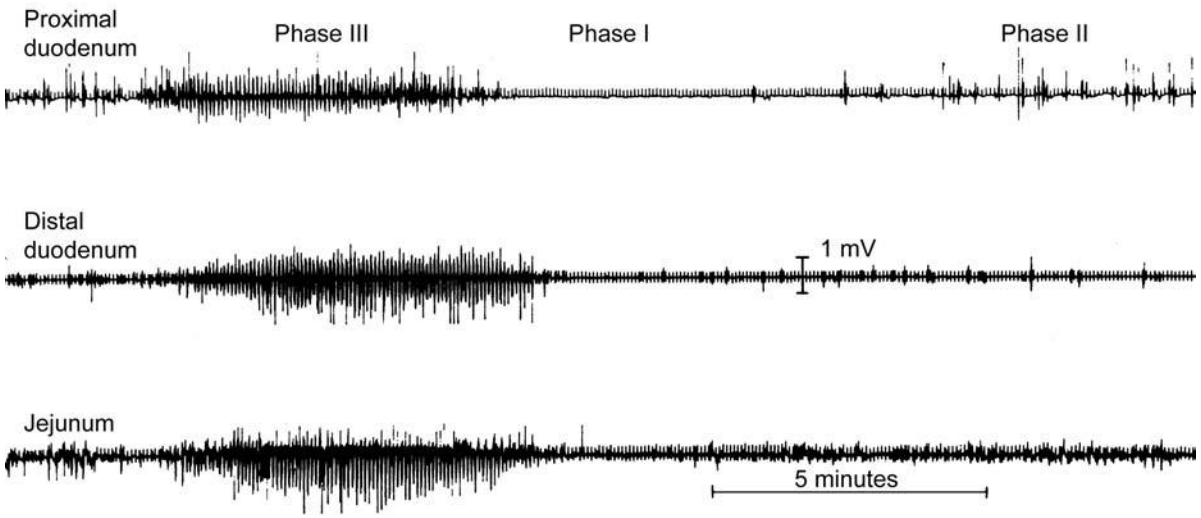
Two basic components of myoelectrical activity of gastrointestinal smooth muscle are the slow wave and the action potential, or "spike potential." Slow waves (basic electrical rhythm, or electrical control activity) are phasic oscillations of the smooth-muscle resting membrane potential that vary in frequency by site and species. They are considered responsible for the rhythmicity and polarity of intestinal contractions.[27,28] In the pony, as in other animals, slow-wave frequency is greater in the duodenum and decreases toward the ileum.[28] This determines the direction and propagation rates of associated motile events.[29]

Slow waves do not initiate contractions; instead contractions occur when slow-wave depolarization reaches the threshold for spike (action) potentials.[29] An action potential is generated if something reduces the threshold of the smooth muscle cell(s), allowing a slow-wave oscillation to reach threshold, causing rapid depolarization.[29] Mechanical (stretch), neural, and hormonal stimuli determine whether that threshold will be reached. Action potentials, therefore, are superimposed on the slow waves and trigger intestinal contractions.[27] Thus, an action potential does not necessarily occur with every slow wave, but slow-wave frequency determines maximum frequency of action potentials.[29]

These wave forms produce a distinct pattern of myoelectrical activity, called the migrating motor complex (MMC).[29] Three phases of activity occur in sequences that constitute the cyclical pattern of the MMC (Figure 2-26).[29-31] Phase I or NSA (no spiking activity) has slow waves only and no action potentials (Figure 2-26). Phase II or ISA (intermittent or irregular spiking activity) has intermittent action potentials on some slow waves (Figure 2-26). Phase III or RSA (regular spiking activity) is evident as an action potential for every slow wave and thus intense, sustained contractions (Figure 2-26).[29-31] The MMC is always present during an "interdigestive state" (for that time between meals when stomach and small intestines are essentially empty) and plays an important role in reducing bacterial colonization in the small intestine.[29] Phase II is always of the longest duration.[29-31]

Phase III is the most prominent, but often of the shortest duration.[29] After a given Phase III event begins in the duodenum, it slowly migrates aborally to the ileum, pushing any intestinal contents in front of it. Thus, it has been referred to as the "intestinal housekeeper." Phases II and III are associated with intestinal contractions that mix intestinal contents, and Phase II activity can result in two motility patterns: 1) segmentation or isolated contractions that result in mixing of intestinal contents; and 2) peristalsis that propels contents aborally.[29-31] Thus, the majority of an ingested meal is moved through the small intestine by Phase II-like activity. In the distal jejunum of the pony, as in the small intestine of other animals, regular spiking activity or Phase III is associated with the greatest myomechanical activity, and irregular spiking activity with the least.[31]

Figure 2-26



Myoelectical activity of the proximal portion of the gastrointestinal tract of a clinically normal horse, with all components of the migrating motor complex (Phases I through III) shown in the proximal duodenum. The slow wave frequency is about 14/min in all segments. From Merritt AM, Campbell-Thompson ML, Lowrey S. Effect of xylazine treatment on equine proximal gastrointestinal tract myoelectrical activity. J Am Vet Med Assoc 50:945-949,1989.

Control of Motility

Control of motor events in the small intestine is complex and involves myogenic, neural, and hormonal mechanisms. Neural control refers to an extrinsic system that involves the vagus nerve and components of the sympathetic nervous system, and an intrinsic system, called the enteric nervous system.[27] The latter consists of ganglia in the myenteric (Auerbach's) plexus and the submucosal (Meissner's) plexus, and mediates reflex behavior independent of input from the brain or spinal cord.[27] The enteric neurons also contain secretomotor neurons and can interact with both the immune and central nervous systems.[27] Myenteric neurons are the main source of innervation of longitudinal muscle and the outer lamella of circular muscle.[25] Submucosal neurons innervate the inner lamella of circular muscle.[25] One explanation for initiation of the peristaltic reflex involves mucosal pressure or mere chemical stimulation of the mucosa from an intraluminal bolus.[27,32] This mucosal stimulation causes release of 5-hydroxytryptamine from enterochromaffin cells in the epithelial lining, followed by stimulation of sensory neurons and then the myenteric plexus.[27] Hormonal control of motility involves neurotransmitters and other neural agents that act on intestinal smooth muscle.

Electrical and contractile muscle activity are influenced by input from excitatory and inhibitory junction potentials from the enteric neurons.[25] Most myenteric neurons are either excitatory motor neurons that contain acetylcholine and the tachykinins, substance P and neurokinin A, or inhibitory motor neurons containing vasoactive intestinal peptide, peptide histidine isoleucine, and nitric oxide synthase.[25,33] The latter inhibitory agents comprise the non-adrenergic, non-cholinergic component of the enteric nervous system.[25] A coordinated release of excitatory and inhibitory transmitters coordinates the peristaltic reflex responsible for propulsive activity.[25] Motilin, a peptide produced by endocrine cells in the mucosa of the proximal small intestine, is released during fasting, and regulates the interdigestive migrating motor complex.[11]

Increased sympathetic stimulation could decrease intestinal motility in equine jejunum and be relevant to development of ileus.[26] Sympathetic relaxation of ileal smooth muscle is mediated mainly by β-atypical receptor subtypes activation.[34] Whereas epinephrine decreases ileal and cecal activity, it increases ileal sphincter tone through an effect on α1 receptors.[35,36]

Nitric oxide also appears to act as an inhibitory neurotransmitter to circular smooth muscle of equine jejunum and could be released from invading macrophages in distended small intestine.[37] After small intestinal resection and anastomosis in the dog, regular spiking activity in the proximal segment tends to fade out at the anastomosis.[38] Not only are the phases reduced in number and disrupted in the distal segment, but they also seem to be delayed as they pass into the distal segment; transit time in the distal segment also is delayed.[38,39] The aboral progression of the MMC stops at the anastomotic site, but alternate pacemakers initiate regular spiking activity distal to the anastomosis.[38] Therefore, timing of the MMC appears to depend on bowel continuity and integrity of intrinsic innervation.[40] The type of anastomosis is important also, as 91% of MMCs can cross an end-to-end anastomosis in canine jejunum at 12 weeks after surgery, compared with 22% after a functional end-to-end anastomosis.[41] The latter only improves to 56% at 2 years.[41]

The mean duration of the MMC is used to evaluate small intestinal motility in horses, because myoelectrical activity is considered a valid indicator of mechanical activity.[30] Xylazine, atropine, meperidine, butorphanol, and pentazocine can increase the mean duration of MMC in pony distal jejunum, whereas flunixin meglumine, dipyrone, metaclopramide, and panthenol have no effect.[30,42] Xylazine and butorphanol as separate treatments reset the duodenal MMC in the horse, but without serious disruption of proximal gastrointestinal tract motility.[43,44] However, routine doses of xylazine, detomidine, or a combination of xylazine and butorphanol significantly reduce pressure peaks in the duodenum in that order of increasing suppression.[45] Common anesthetic regimens decrease myoelectric activity in equine ileum but the effect is short-lived (120 to 150 minutes after induction).[46] Low-dose endotoxin alters regular spiking activity in pony jejunum.[47,48] These changes can be mimicked by intravenous infusion of prostaglandin E2, they can be partly blocked by pretreatment with phenylbutazone and flunixin meglumine, and they suggest a role for endotoxin in pathogenesis of postoperative ileus.[47,48]

Function of the Ileum

The terminal portion of the ileum forms a papilla that projects into the cecum; the ileal orifice is in the center of the papilla, surrounded by the cecal musculature,[49] an annular fold of mucous membrane, and a venous network.[50,51] The lumen of the ileum decreases at the ileocecal junction[52] and forms a papilla, but not a true sphincter.[49,50] A functional sphincter does exist and appears to contract in synchrony with contractions of the cecal base.[36,52] Endoscopic studies of the cecal base of the horse have demonstrated that the ileal papilla is normally prominent and becomes even more prominent when the cecum is active.[50] The muscle of the papilla is composed of three layers, an inner circular layer, a central longitudinal muscle layer from the ileum, and an outer layer formed from the circular muscle of the cecum and arranged into two semicircular lips.[49,50] It has been proposed that the venous network and annular fold of the papilla contribute to the ileal sphincter mechanism.[49,50] However, this theory is weakened by the observation that the veins are most engorged when the ileum is discharging its contents into the cecum.[50]

The ileum appears to differ from the jejunum in its myoelectric activity and this might be related to its unique position at the junction of the small and large intestines. In the ileum of mature ponies, all phases of the MMC can be recorded, but irregular spiking activity (Phase II) predominates during the interdigestive period (time between meals).[53] The migrating action potential complex (MAPC) can be recorded in the pony ileum,[53] but not in the pony jejunum,[30,31,42] as intense spike bursts of short duration that propagate rapidly aborally.[54] Withholding food for 24 hours decreases the frequency of ileal MAPC, but has no effect on mean slow wave frequency, MMC phase distribution, MMC phase duration, MAPC conduction velocity, or conduction velocity of spike bursts in regular spiking activity.[53] Therefore, in contrast with other animals, feeding does not disrupt the MMC in ponies.[53]

The MAPC immediately precedes retrograde cecal myoelectric activity 73% of the time, indicating a possible myoelectric coupling of the ileum and cecum, and may be responsible for transit of digesta from the ileum to the cecum.[53] Also, ileal contents are discharged into the cecum in semisolid or liquid form, mostly at times when the cecum is inactive.[50] Ileal and cecal filling appear to be more important in regulating ileocecal motility events in ponies than are stimuli associated with feeding.[53]

Some evidence exists that local stimulation of chemoreceptors is important in regulation of ileal motility in the horse[35,36] and in human beings.[52] Also the human ileum, and possibly the equine ileum, acts as a reservoir, discharging contents into the cecum in response to dietary stimuli.[52] At neutral pH, tonic activity of the human ileum, but not the jejunum, is increased by intraluminal short-chain fatty acids, whereas bile acids and lipids can induce ileal relaxation.[52] Likewise, tone of the ileal papilla increases during contractions of the cecal base in horses, but not enough to prevent reflux of some cecal contents into the ileum.[35,36] In the pony, serotonin and luminal acid fatty acids increase ileal peristalsis.[36] The response to luminal acidification could be physiologically important because acidification of ileal contents by cecal reflux could stimulate ileal emptying of refluxed bacteria and cecal contents.[35,36,52] Through this response, ileal motility could augment the sphincter function of the ileal papilla[36] in preventing reflux of cecal contents.[35]

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Large Bowel Function

Marco A. F. Lopes

Unlike the more proximal segments of the gastrointestinal tract, the large bowel is not a site in which digestion by enzymes produced by glands and epithelial cells takes place. In horses and other monogastric herbivores and omnivores, the large bowel evolved to provide the ideal environment for microbial growth, where most of the fermentation and production of volatile fatty acids (VFAs) takes place. The large intestinal mucosa absorbs substantial amounts of VFAs, which serve as an important source of energy.[1] It has been estimated that, in horses, as much as 30% of the energy requirements are supplied by VFAs produced by microorganisms in the cecum.[2] Because the horse's large colon is the main fermentation chamber[1] and only about 25% of the energy requirements of horses fed a high grain diet are supplied by glucose oxidation,[3] it is likely that much more than 50% of the energy requirements in horses are supplied by VFAs. Microorganisms in the large bowel also synthesize vitamins, which are absorbed and used as nutrients.[4,7] Furthermore, the large bowel absorbs large amounts of water and electrolytes from the intestinal contents, a process that is critical for water and electrolyte homeostasis.[6] The complex functions as well as the enormous size, the high mobility, and the pronounced changes in diameter of the equine large bowel make this part of the gastrointestinal tract prone to malfunction.[7] Although many aspects of equine large bowel physiology are still awaiting investigation, some major physiologic mechanisms have already been elucidated.

Motility Patterns and Transit of Contents

Motility of the large intestine is complex, and several patterns have been identified. The purposes of these different motility patterns are to promote adequate mixing and contact of the intestinal contents with the mucosa, as well as to move the contents along slowly enough to ensure that adequate time exists for fermentation and absorption. Emptying of the large intestine is also important to provide space for additional ingesta moving in from the small intestine. Transit of ingesta through the large intestine is considerably slower than through the small intestine. In a study with ponies, the majority of the marker of the liquid phase administered via nasogastric tube took less than 2 hours to reach the cecum.[6] Conversely, in the same study and in a study with fistulated horses, it took more than 12 hours for the majority of the marker of the liquid phase to be passed in the feces.[6,8] Similarly, transit of particulate markers was considerably slower in the large intestine relatively to transit through the stomach and small intestine.[6] Within the large intestine, the large colon is responsible for most of the delay in transit of ingesta, as the majority of the marker of the liquid phase and particulate markers administered via a cecal fistula left the cecum within 8 hours. In contrast, the majority of the marker of the liquid phase and particulate markers were retained in the large colon for more than 24 hours. Passage of the marker of the liquid phase and particulate markers through the descending colon was relatively rapid.[6]

Ingesta and gas move from the ileum into the cecum through the ileocecal valve, which impedes reflux of liquid and particles back into the ileum.[6] Characteristic (tinkling and splashing) sounds produced by ileocecal flow of small amounts of ingesta can be detected by auscultation over the right paralumbar fossa as frequently as 1 to 3 times per minute.[9] Composition and volumes of ingesta and gas reaching the cecum vary considerably, depending on several factors including the diet and the size of the horse. In horses eating only roughage, the water content of cecal ingesta exceeds 90%.[10,11]

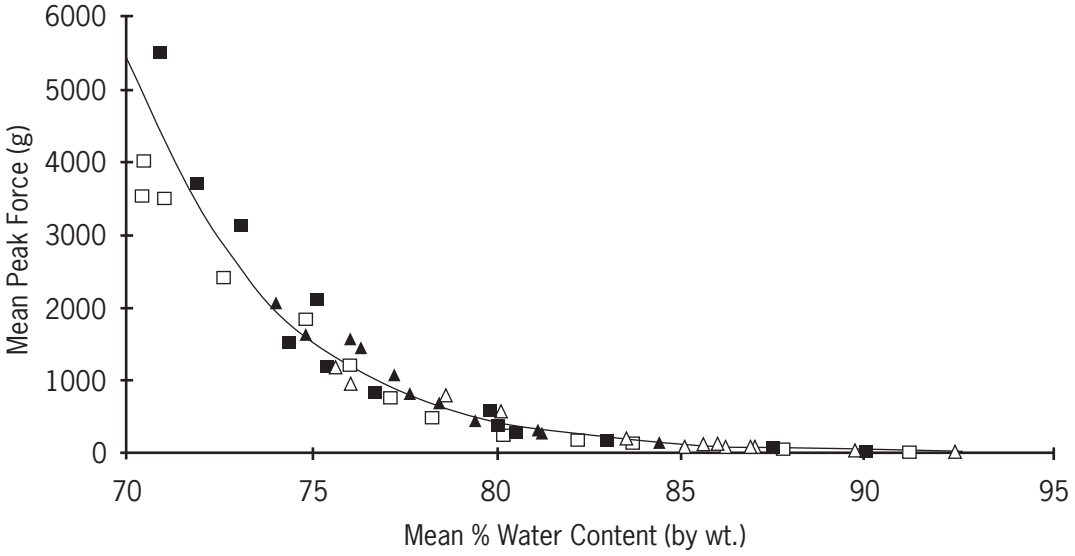
Within the large intestine, ingesta is moved aborally by peristaltic contractions of the intestinal wall. These contractions create a pressure gradient to overcome resistance to ingesta flow. Throughout the cecum and large colon, there are local haustra-to-haustra mixing movements as well as retrograde propagation of coordinated contractions, which are thought to be important for delaying gastrointestinal transit. These motility patterns have been documented by electromyography, intraluminal manometry, auscultation, radiography after administration of positive contrast media, direct observation of the large intestine in horses undergoing laparotomy, scintigraphy after administration of radiolabeled markers, and endoscopy through cecal and colonic fistulas.[12-19]

The cecum is partially filled with watery ingesta and its dorsal portion is filled with gas. Pressure within this gas cap in the cecal base is maintained slightly negative relative to atmospheric pressure. Changes in cecal shape and an effective outflow mechanism to the large colon accommodate additional ingesta and gas passing through the ileocecal valve as well as gas being produced within the cecum.[20] Cecal contents are emptied into the right ventral colon through the cecocolic ostium. Coordinated contractions originate in the cecal body near the apex as often as every 2 minutes, and move toward the base, creating a pressure gradient that moves ingesta and gas.[14,15,21] Then, muscular contractions form a constriction at the cecal base cranial to the ileocecal papilla. This constriction creates two separate compartments at the cecal base (cranial and caudal compartments), and is associated with the elevation of the floor of the cecal base and opening of the cecocolic ostium. The last event in the cecal emptying mechanism is the contraction of the cranial compartment of the cecal base.

Ingesta and gas are thus moved through the cecocolic ostium, although significant amounts of ingesta can move back to the cecal body.[22,23] Because of the sigmoid configuration of the cecocolic juction, no reflux of ingesta occurs and only minor reflux of gas from the colon to the cecum.[3,22]

Within the large colon, resistance to flow of intestinal contents is increased at the pelvic flexure, which delays emptying of the ventral colon. Although a true sphincter is not present at the pelvic flexure, physiologically the ventral and dorsal colons are distinct compartments, and no reflux of liquid or particles occurs from the dorsal colon to the ventral colon.[6,12] Passage of contents through the descending colon is rapid.[6] Intestinal contents undergo progressive dehydration while being moved aborally through the large bowel. In a study of normal horses, hydration of contents decreased from about 92% in the cecum to 88% in the large colon and to 80% in the small colon.[10] In another study with fistulated horses eating only hay, water content of the ingesta from the right dorsal colon and feces was about 90% and 80%, respectively.[8] Although viscosity of large intestinal contents has not been studied in horses, a study in pigs has demonstrated that a decrease in water content is associated with an increase in viscosity of the ingesta (Figure 2-27).[24] Furthermore, it has been clearly demonstrated in a study with rabbits that viscosity of the ingesta is a major determinant of resistance to ingesta flow.[25] Fecal balls are formed in the descending colon, thereby facilitating transit of the less hydrated intestinal contents. Secretion of large amounts of mucus in this area also reduces the resistance to transit of contents through the descending colon and rectum.[26]

Figure 2-27



Plot of mean percent water content of ingesta of pigs versus mean peak force measured with a Stevens QTS 25 Texture Analyzer (Michael G. Brown & Assoc., Newton, Pennsylvania) as an indicator of ingesta viscosity. (Modified from McRorie J, Pepple S, Rudolph C. Effects of fiber laxatives and calcium docusate on regional water content and viscosity of digesta in the large intestine of the pig. Dig Dis Sci 43:738-745, 1998.)

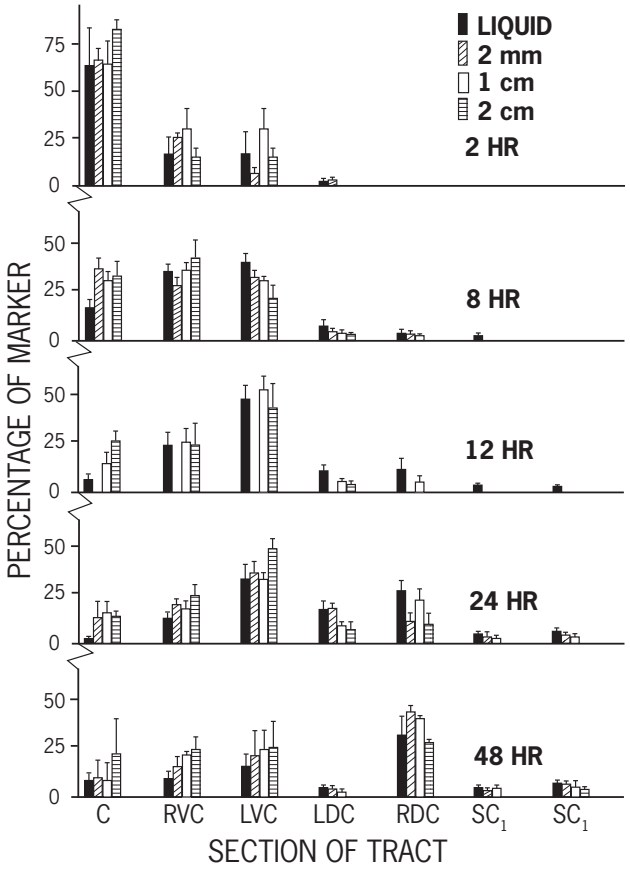
Microbial Activity and Fermentation

Relatively little has been studied about the microbiota of the equine gastrointestinal tract. Available information indicates that the microbial activity in the equine large intestine is similar to that in the bovine rumen. Several species of bacteria, protozoa, and fungi coexist in the rumen. Usually, microorganisms are present in concentrations exceeding 10 to the 9th cells/g of ruminal contents, and represent 50 to 90% of the rumen biomass. The rumen ecosystem has complex interactions between the microorganisms (e.g., competition for nutrients, predation, cross-feeding). As in any ecosystem, microbial populations are determined by the environmental conditions within the rumen, the availability of nutrients and the presence of negative interactions between organisms (e.g., predation).[27-29] The microorganisms are not evenly distributed throughout the rumen. Depending on factors such as the species, phase of the life cycle, and availability of nutrients, microorganisms can be free in the liquid phase of the ruminal contents, bound to solid particles, or attached to the ruminal mucosa. Microorganisms that utilize soluble nutrients (e.g., carbohydrates and proteins) are free in the liquid phase, while microorganisms that use insoluble nutrients (e.g., fiber) are bound to the solid particles. There are reasons other than nutrient availability for microorganisms to adhere to particles. For organisms such as some protozoa, which have a relatively long life-cycle, the turnover time of the ruminal liquid is too short, and binding to solid particles is the only way for them to stay in the rumen long enough to reproduce.[28,29]

In the bovine rumen, extracellular enzymes produced by bacteria, fungi, and protozoa degrade complex carbohydrates. Simple carbohydrates, such as oligosaccharides and monosaccharides from feed or from degradation of complex carbohydrates, are engulfed and hydrolyzed by other microorganisms. The end products are VFAs (acetic, propionic, butyric, valeric, and isovaleric acids), lactic acid, carbon dioxide, and methane. Volatile fatty acids are absorbed by the rumen mucosa and are the main source of energy for the ruminant. Rumen bacteria, fungi, and protozoa also have proteases, which rapidly degrade protein. Free amino acids and ammonia from the diet or from protein degradation are used by the microorganisms for synthesis of microbial protein and growth. In the small intestine, microbial proteins synthesized in the rumen as well as proteins from the diet that escape microbial degradation are digested and absorbed to meet the animal's need. Fats are degraded by extracellular lipases released by bacteria and protozoa. The glycerol and fatty acids produced by fat degradation have different fates: glycerol is rapidly consumed by microorganisms, while fatty acids adhere to solid particles and are degraded at a slower rate. Long-chain fatty acids, especially if polyunsaturated, are toxic to bacteria and protozoa, and high levels of intake of these compounds may reduce fiber digestion.[46,108] Besides their key role in digestion and protein synthesis, rumen microorganisms produce vitamins (i.e., vitamin K and the B vitamins), which are used as nutrients by the host.[30] Furthermore, microbial fermentation produces heat which may contribute to maintain body temperature, but may become a problem when the ambient temperature is high.[31]

Similar to the rumen, the equine large intestine is an anaerobic environment[7] where contents are held for long periods (Figure 2-28).[6] In the horse, the rich cecal and colonic microbiota are composed of large numbers of several species of bacteria, protozoa, and fungi.[32-45] Microbial activity depends on the availability of nutrients[37,39,46,47] and is reduced by fasting.[12] These microorganisms are able to ferment hydrolysable nutrients such as sugars and protein that escape digestion and absorption in the proximal gastrointestinal tract[43] as well as indigestible complex molecules including cellulose and soluble fiber.[12,32,33,36,43,45] Because the proximal gastrointestinal tract does not produce enzymes that digest fiber, it reaches the large intestine intact. In the equine large intestine, the main products of carbohydrate fermentation are VFAs (mainly acetic, propionic, and butyric acids) (Figure 2-29)[1,12,37,38,48,49] which are well absorbed by the mucosa (Figure 2-30).[1] Also in horses, VFAs produced by microbial fermentation in the large intestine provide a major portion of needed energy.[2,3,7] Small amounts of lactic acid are also produced in the large intestine.[1] Lactic acid is poorly absorbed and does not serve as a major nutrient for the horse, but would lead to intraluminal acidosis and an increase in intraluminal osmolality if large amounts were produced.[50] The ratios of VFAs to lactic acid produced within the large intestine depend on the diet (e.g., more propionic and

Figure 2-28

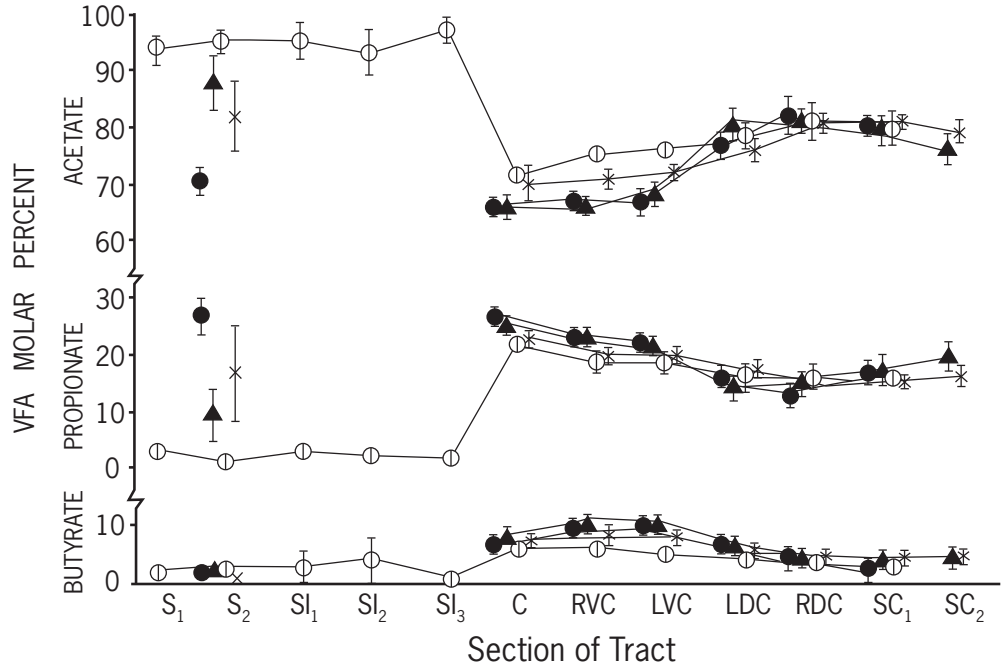


Percentage (± SE) of liquid and particulate markers (2 mm, 1 cm and 2 cm) recovered from the large intestine of ponies euthanized 2, 8, 12, 24, and 48 hours after receiving a dose of the markers via a cecal fistula. The 2-mm particulate marker was not given to animals sacrificed at the 12-hour time point. (Modified from Argenzio RA, Lowe JE, Pickard DW, Stevens CE. Digesta passage and water exchange in the equine large intestine. Am J Physiol 226:1035-1042, 1974.)

lactic acids are produced when grain is consumed)[1,37,39,46,49] and intraluminal pH (e.g., lactate synthesis is increased when intraluminal pH falls).[7] Similarly to what occurs in ruminants, evidence exists of toxicity of fat on the microbiota of the equine gastrointestinal tract. Recent studies have shown that the digestibility of fiber is decreased when horses consume large amounts of fat.[51-54] Microorganisms in the equine large intestine also produce vitamin K and B vitamins, which constitute important nutrients for the horse. It is thought that microbial synthesis and intestinal absorption of vitamin K and B vitamins are enough to supply most, if not all, of the needs of normal horses.[4,5] Furthermore, heat is produced by fermentation within the equine large intestine and may contribute to maintenance of body temperature; however, heat due to fermentation may be harmful for horses exercising under hot and humid conditions.[55,56]

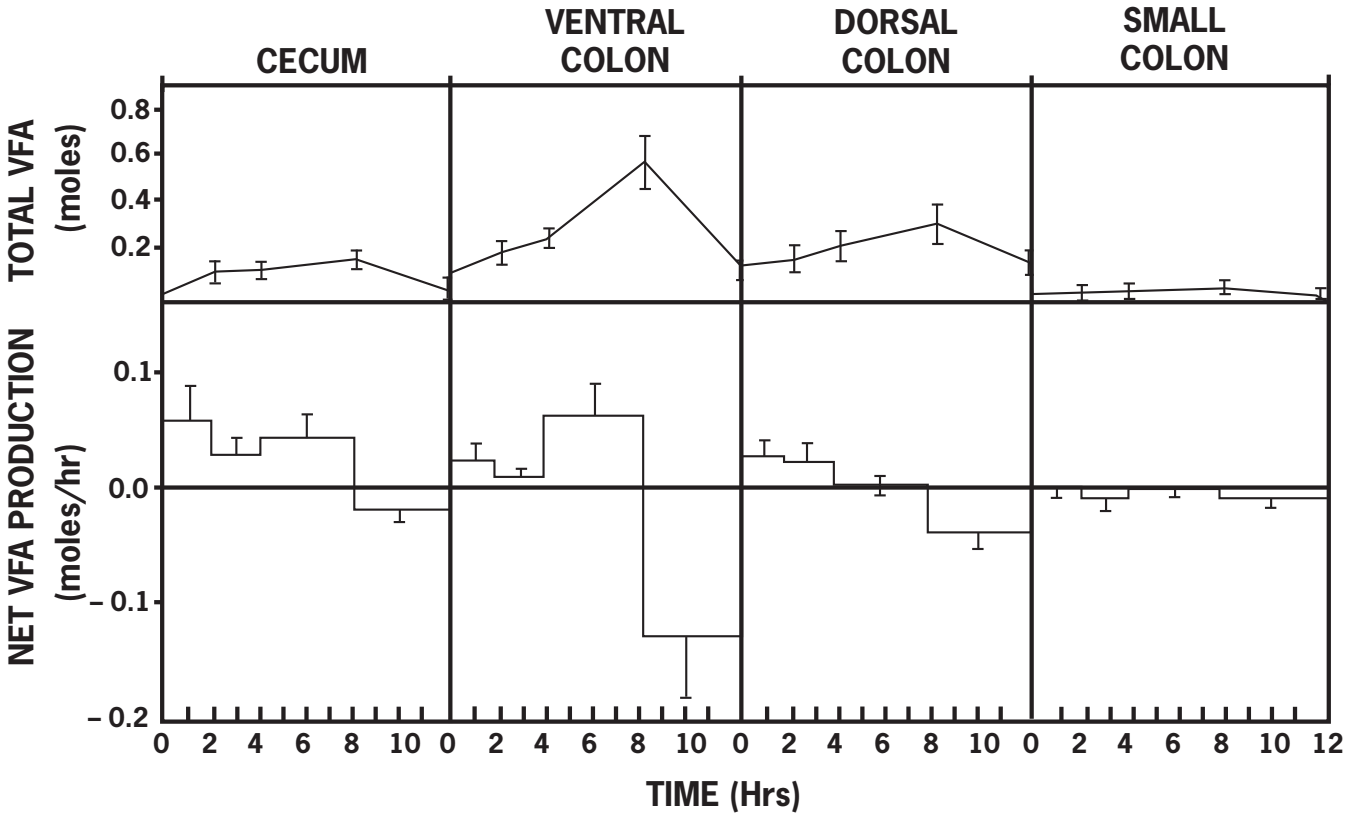
A major difference when compared with ruminants is that horses are unable to use proteins produced by the gastrointestinal microorganisms as nutrients. In ruminants, proteins produced by microorganisms in the main fermentation chambers (i.e., the forestomachs) are digested and absorbed in the small intestine.[28] In horses, proteins produced by microorganisms in the main fermentation chambers (i.e., cecum and large colon) are not usable because the mucosa of the large intestine cannot absorb significant amounts of free amino acids or peptides.[57-60] Only the practice of coprophagy would make proteins produced by the microbiota of the large intestine available for digestion and absorption in the small intestine.[61] In contrast to what is observed in other monogastric herbivores (e.g., rabbits),[62] coprophagy is not a normal behavior in horses.[63] Because significant amounts of non-protein nitrogen can be absorbed by the mucosa of the large intestine,[57] synthesis of microbial protein, a process that consumes non-protein nitrogen, has a role in nitrogen excretion. Microbial synthesis of protein traps nitrogen within the lumen of the large intestine and contributes to excretion of nitrogen in the feces.[50,61,64]

Figure 2-29



Mean relative proportions (± SE) of acetate, propionate, and butyrate in gastrointestinal contents of ponies sacrificed 0 hour (closed circle), 2 hour (closed triangle), 4 hour (open circle), or 8 hour (x) after feeding. (From Argenzio RA, Southworth M, Stevens CE. Sites of organic acid production and absorption in the equine gastrointestinal tract. Am J Physiol 226:1043-1050, 1974.)

Figure 2-30



Content and net production (± SE) of VFAs in segments of the large intestine of ponies fed twice daily and euthanized 0, 2, 4, 6, 8, 10 and 12 hours after feeding. Negative net production means absorption of VFAs. (Modified from Argenzio RA, Southworth M, Stevens CE. Sites of organic acid production and absorption in the equine gastrointestinal tract. Am J Physiol 226:1043-1050, 1974.)

Secretion and Absorption

Large amounts of water, electrolytes, and other solutes are secreted and/or absorbed by the equine large intestine.[1,6,7,65] Secretion and absorption by the large intestine have the following important roles: 1) to maintain ideal conditions for microbial growth in the intestinal lumen, which is particularly important for a monogastric herbivore such as the horse; 2) to supply the body with nutrients, such as water, electrolytes, VFAs, and vitamins; 3) to protect the mucosa against physical, chemical, and biological insults (e.g., friction of pieces of grass, acidity due to production of VFAs, and lactate); 4) to maintain low viscosity of the ingesta, and to lubricate the mucosa to facilitate flow of intestinal contents; and 5) to excrete substances such as nitrogen and potassium.

Mucus Secretion

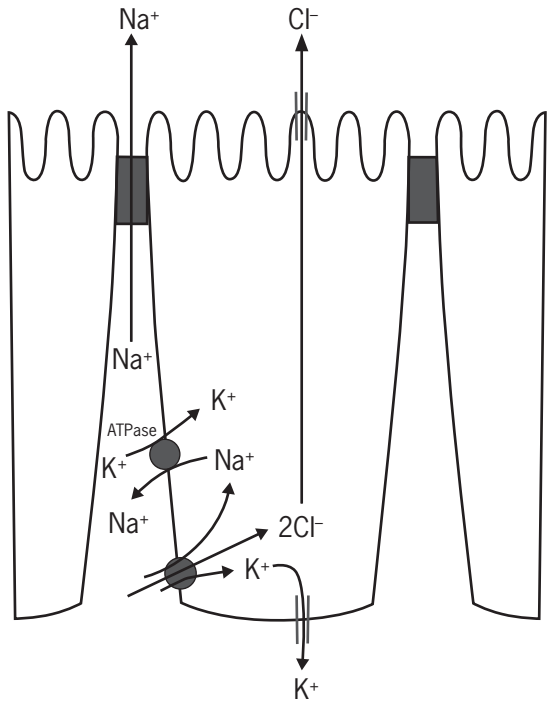
Mucus is secreted by the mucosa, which contains large numbers of goblet cells, especially in the small colon (see Chapter 1). Secretion of mucus facilitates transit of the contents of the large intestine by minimizing friction with the mucosa.[26] This is likely more important in the final segments of the large intestine, as the intestinal contents gradually become drier and more viscous as they move aborally.[10,24] Mucus also protects the mucosa against acids produced by microbial fermentation. Furthermore, mucus and other macromolecules (e.g., immunoglobulins, antimicrobial peptides) secreted by the mucosa are important to maintain the integrity of the mucosa and provide protection against pathogenic organisms and toxins.[26,66,67]

Water and Electrolyte Secretion

Large amounts of electrolytes (primarily chloride, sodium, bicarbonate, and phosphate) and water are also secreted into the intestinal lumen. Secretion of water and electrolytes is important to maintain osmolality and pH within ranges that favor microbial growth and absorption of nutrients.[50,65,68,69] Secretion of water also is important to maintain ingesta viscosity low enough to facilitate ingesta flow and avoid the formation of impactions.[10,24,25] Water secretion is a passive process driven by the osmotic gradients generated by secretion of solutes, primarily NaCl. Electrolyte secretion is initiated by an active mechanism of electrogenic secretion of chloride, which is present throughout the large intestine. This mechanism starts with chloride crossing the basolateral membrane into the cytoplasm through a Na^{+-} K^{+} 2C- cotransporter moved by the electrochemical gradient generated by the Na^{+}/K^{+} ATPase. Chloride is then secreted into the lumen through chloride selective channels

located at the apical membrane. Na^+ and K^+ cross the basolateral membrane back to the extracellular space via the Na^+/K^+ ATPase and K^+ selective channels, respectively. The electrogenic secretion of Cl^- is followed by Na^+ and K^+ secretion through the paracellular pathway (Figure 2-31).[70-73] Protein released into the lumen (i.e., mucus, sloughed cells) and non-protein nitrogen (e.g., urea) secreted into the intestinal lumen are sources of nitrogen for the microbiota and represent a secondary means of nitrogen excretion.[50,64] Secretion of potassium also occurs and functions as a secondary excretion mechanism for this electrolyte.[70,74] For some time, it has been stated that secretion of water and electrolytes occurs at the crypts where the less mature epithelial cells are located, whereas absorption is performed by more mature cells located at the surface epithelium.[50,70] The results of more recent studies suggest that this clear demarcation does not exist. Actually both crypts and surface epithelium are able to absorb and secrete electrolytes and water in the presence of the appropriate stimulus.[75]

Figure 2-31



Electrogenic Cl^- secretion by colonocytes – active Cl^- secretion is followed by passive Na^+ and water secretion. (Modified from Barrett KE, Dharmsathaphorn K. Transport of water and electrolytes in the gastrointestinal tract: Physiological mechanisms, regulation, and methods of study. In Maxwell & Kleeman's Clinical Disorders of Fluid and Electrolyte Metabolism, 5th ed. Narins RG (ed). McGraw-Hill: New York, 1994, pp. 493-519.)

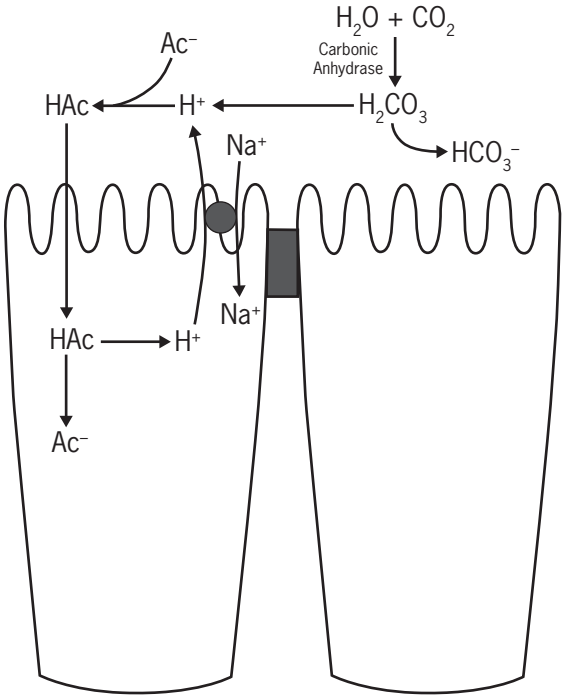
Fatty Acid Absorption

Volatile fatty acids produced by microbial fermentation are rapidly absorbed by the mucosa of the large intestine.[1] Transcellular diffusion of protonated VFAs has been proposed as the main mechanism for the absorption of VFAs in the equine large intestine. However, the pKa of the VFAs is considerably lower than the pH in the large intestine, where more than 99% of the VFAs are in their ionized forms. It was also suggested that carbonic acid produced by hydration of CO_2 within the lumen and/or the epithelium serves as a source of H^+ needed to combine with the ionized VFAs (Figure 2-32).[50,76] This same model also was used to explain the absorption of VFAs in the large intestine of other species. A modification of this model was proposed to address a major contradiction: the effective absorption of VFAs in the protonated form under conditions where almost 100% of the VFAs are ionized. According to this model (Figure 2-33), most of the VFAs are absorbed in the ionized form in exchange for bicarbonate, while only small amounts of protonated VFAs are absorbed.[75] The identification of a $VFA^-/HCO3^-$ exchange mechanism in the apical membrane of mammalian colonocytes further supports the theory that considerable amounts of ionized VFAs are absorbed via the transcellular pathway.[77] The bicarbonte ions that appear in the lumen during absorption of VFAs serve to buffer the colonic contents, counteracting the acidifying effect of the acids produced by microbial fermentation. This process is very important for prevention of mucosal damage as well as to avoid changes in the microbiota of the large intestine that would occur with intraluminal acidosis. The intensity of the alkalinizing effect of absorption of VFAs is thought to be inversely related to the electroneutral absorption of sodium through a Na^+/H^+ exchange mechanism.[50,76]

In the horse, the relative rates of transport of the absorbed VFAs through the intestinal mucosa are inversely proportional to their molecular weights (i.e., acetate > propionate > butyrate).[1] Furthermore, extraction of glutamine from the blood by the large colon is modest compared with what occurs in the small intestine[78,79] Together these findings suggest that in horses, as in other species, butyrate is the main fuel for the colonocytes.[80] The VFAs absorbed but not used by the colonic mucosa are drained to the liver via the splanchnic circulation.[81] In the liver and other tissues, VFAs serve as fuel or are used as substrates for the synthesis of other fatty acids, glucose, triglycerides, and ketone bodies.[2,82-86] Although no study on the absorption of

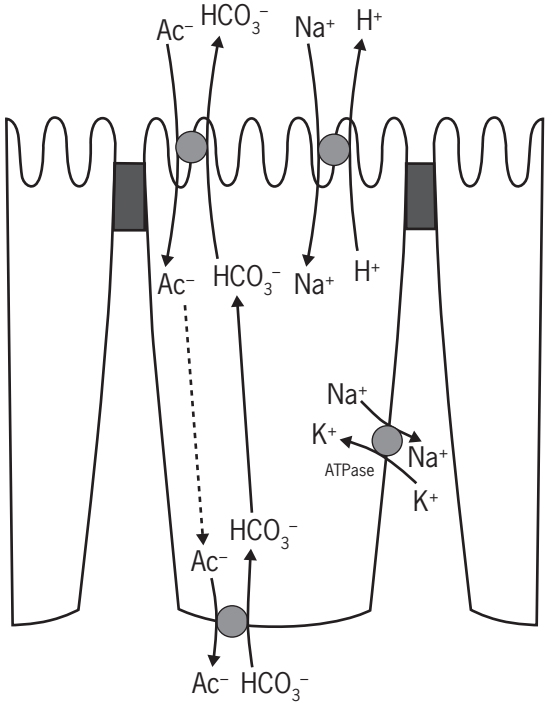
vitamins by the mucosa of the equine large intestine has been published, vitamin K and B vitamins synthesized by the microorganisms of the gastrointestinal tract are thought to be important nutrients for the horse.[4,5] Thus, the mucosa of the large intestine is likely able to absorb vitamins as the large intestine is the main site for microbial growth in horses.

Figure 2-32



Absorption of VFAs in the protonated form by colonocytes. (Modified from Argenzio RA. Physiology of digestive, secretory, and absorptive processes. In The Equine Acute Abdomen. White II NA (ed). Philadelphia: Lea & Febiger, 1990, pp. 25-35.)

Figure 2-33

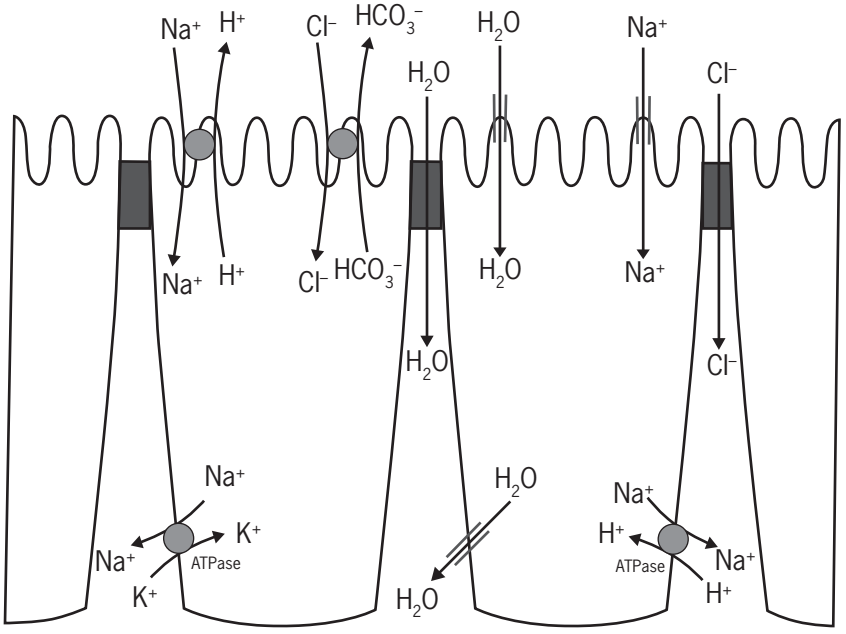


Absorption of VFAs in the ionized form by colonocytes. (Modified from Sandle GI. Salt and water absorption in the human colon: a modern appraisal. Gut 43:294-299, 1998.)

Electrolyte Absorption

In the horse, large amounts of electrolytes are absorbed by the mucosa of the large intestine, especially sodium, potassium, chloride, and phosphorus.[65,72,87] Similar to what occurs in the small intestine, sodium is actively absorbed by the mucosa of the large intestine. The electrochemical gradient generated by the Na^+ K^+ ATPase located at the basolateral membrane of the epithelium drives sodium absorption.[70] Both electroneutral and electrogenic mechanisms for sodium absorption have been identified (Figure 2-34). Electroneutral absorption of sodium involves the exchange of sodium for another cation (i.e., hydrogen). This process may be coupled with the transport of chloride that is absorbed by an exchange mechanism with bicarbonate ions.[70,71,76] Electrogenic sodium absorption occurs by uncoupled entry of sodium through specific sodium channels. This process is regulated by aldosterone and is inhibited by diuretics such as amiloride which close the sodium channels.[70,88] This mechanism makes it possible for sodium to be absorbed against a large electrochemical gradient in the last portion of the large intestine.[50,70] While electroneutral absorption of sodium predominates in the oral segments of the large intestine (i.e., cecum and large colon), electrogenic sodium absorption predominates in the small colon.[71,76,88] Potassium is also actively absorbed in the large intestine in exchange for H^+ via a H^+, K^+-ATPase.[70,89] Throughout the large intestine, chloride is passively absorbed following the absorption of cations (mainly sodium). As mentioned earlier, absorption of chloride occurs both by diffusion through the paracellular pathway and by a Cl-/HCO3- exchange mechanism through the transcellular route.[70,76,89] The mechanism for phosphate absorption is not well known. Diffusion of phosphate through the paracellular pathway is thought to be the main mechanism in the large intestine of rats.[90]

Figure 2-34



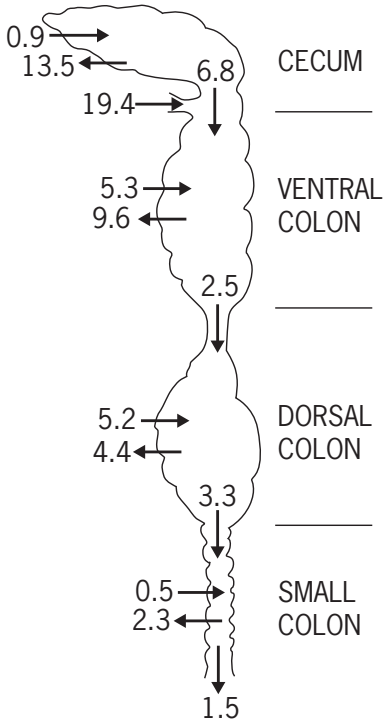
Electroneutral and electrogenic Na^+ absorption by the colonocytes – active Na^+ absorption is followed by passive Cl^- and water absorption. Water moves through via the transcelular patway (through the tight junctions) and via the transcellular pathway (through aquaporins). (Modified from Barrett KE, Dharmsathaphorn K. Transport of water and electrolytes in the gastrointestinal tract: Physiological mechanisms, regulation, and methods of study. In Maxwell & Kleeman's Clinical Disorders of Fluid and Electrolyte Metabolism, 5th ed. Narins RG (ed). New York: McGraw-Hill, 1994, pp. 493-519.)

Water Absorption

Large volumes of water are absorbed and secreted daily by the equine large intestine (Figure 2-35).[6] Bidirectional movement of water (i.e., absorption and secretion) is passive following hydrostatic, oncotic and osmotic gradients.[89] The hydrostatic gradients are produced by differences between interstitial and capillary hydrostatic pressures. The oncotic gradients result from differences between interstitial and capillary oncotic pressures, which are dictated by the concentration of macromolecules (e.g., proteins) within these compartments. The osmotic gradients depend on the concentration of all particles, including smaller particles (e.g., electrolytes, VFAs), within the various compartments (i.e., intestinal lumen, cytoplasm, interstitium, and capillaries) and are highly affected by absorption, secretion, and intraluminal fermentation.[6,73,91,92] Water moves toward the highest oncotic and osmotic pressures and away from the highest hydrostatic pressure.[91,92] Thus, during absorption, movement of solute from the intestinal lumen increases the osmotic pressure within the interstitial space. This change in the osmotic gradient leads to absorption of water, which produces an increase in the hydrostatic pressure within the interstitial compartment, leading to movement of fluid from the interstitium into the capillaries. The opposite changes

occur during fluid secretion (Figure 2-34).[73] Evidence exists that water moves by both transcellular (i.e., through cell membranes) and paracellular pathways (i.e., through tight junctions). Previous beliefs that movement of water through the gastrointestinal mucosa occurs predominantly by the paracellular pathway[70,89] are challenged by the discovery of cell membrane integral proteins, called aquaporins, which function as water channels (Figure 2-34).[93] In other mammals, several types of aquaporins (e.g., AQP3, AQP4, and AQP8) are expressed in the gastrointestinal tract, including the mucosa of the large intestine.[93] So far, few studies have been conducted, but evidence already exists of the importance of aquaporins for water absorption by the mucosa of the large intestine. In one study, stools of AQP4 knockout mice had greater water content than stools from wild-type mice, although no differences in cecal contents were detected. Furthermore, the colon of the AQP4 knockout mice was less permeable to water and the absorptive response to intravenous administration of peptide YY was reduced when compared with those of the wild-type mice. These findings strongly suggest that aquaporins have a major role in water absorption by the mucosa of the large intestine.[94] Additional studies are necessary for a better understanding of the mechanisms involved in water secretion and absorption in the large intestine, including studies in horses.

Figure 2-35



Daily net movement of water (in liters) through the large intestine of a 160-kg pony. (Modified from Argenzio RA, Lowe JE, Pickard DW, Stevens CE. Digesta passage and water exchange in the equine large intestine. Am J Physiol 226:1035-1042, 1974.)

Control of Secretion and Absorption

Control of secretion and absorption by the mucosa of the large intestine is complex. Indirect control is exerted by mechanisms regulating other functions that affect secretion and absorption by the mucosa of the large intestine (e.g., hydrostatic pressure in capillaries of the mucosa, motility of the large intestine).[70] Secretion and absorption are also regulated by direct control of the epithelial cells through autocrine, paracrine, endocrine, immunologic, or neurocrine mechanisms. Neurons, hormone-secreting and immunologic cells located in the large intestine close to the target cells (i.e., epithelial cells), cells located away from the mucosa (e.g., the enteric nervous system), and cells located outside the gastrointestinal tract (e.g., sympathetic and parasympathetic nervous systems, endocrine glands) can exert control over these mechanisms. These regulatory cells function as sensors or are connected to other cells having the capacity to respond to stimuli (e.g., intraluminal antigens, low systemic blood pressure, hyperkalemia).[70,89] The regulatory cells interact with the epithelial cells of the large intestine by releasing messengers (e.g., hormones, neurotransmitters, cytokines, nitric oxide) that bind to specific receptors in the target cells.[70,89,95,96] Receptor binding activates intracellular mechanisms, leading to the activation of secretory or absorptive pathways. Several steps in these intracellular pathways have been identified, and different extracellular messengers may trigger different intracellular mechanisms mediated by cAMP-mediated, cGMP, or calcium.[70,89]

Sympathetic stimuli have pro-absorptive effects on the large intestinal mucosa, whereas parasympathetic stimuli and locally secreted prostaglandins have the opposite effects.[70,71,88,89,97,98] Considering the importance of the large intestine for the homeostasis of sodium and water, it is not surprising that mechanisms regulating sodium and water metabolism can have direct effects on the secretory and absorptive processes in the large intestine. Activation of the renin-angiotensin-aldosterone

system decreases secretion and increases absorption of NaCl and water in the large bowel. Renin is released by the kidney in response to hypovolemia, and the renin-angiotensin-aldosterone system promotes sodium and water conservation.[88,99-101] The putative mediators of these effects on the large intestine are catecholamines, angiotensin II, and aldosterone. Catecholamines, which are co-secreted (by the adrenal glands) with aldosterone, promote water absorption in the colon.[102] The results of experimental studies indicate that angiotensin II increases electroneutral absorption of Na^+; however, a physiologic role of angiotensin II on Na^+ and water absorption independent of aldosterone release has not been proven.[100] Aldosterone increases electrogenic absorption of Na^+ by promoting the expression of Na^+ channels at the apical membrane of colonocytes.[103] Results of one in vitro study with colonic mucosa from ponies suggest that aldosterone enhances both electrogenic and electroneutral absorption of Na^+ by the colonic mucosa.[88] In another study, intravenous injection of aldosterone in horses led to a 72% reduction in fecal excretion of Na^+ at 9 hours and an increase in K^+ excretion in feces from 3 hours after treatment.[99] Another mechanism involved in controlling water and electrolyte metabolism occurs via the release of vasopressin (ADH) by the pituitary gland in response to an increase in extracellular osmolality.[101,104,105] In laboratory animals, ADH promotes water absorption in the large intestine.[106] Considering that aquaporins are expressed in the mucosa of the large intestine,[93] it is possible that ADH acts by the same mechanism operating in the kidney: by promoting the insertion of aquaporins into epithelial cell membranes.[104] Sodium and water metabolism are also affected by atrial natriuretic peptide (ANP), which may act on the mucosa of the large intestine. ANP is a hormone released by the heart in response to atrial stretching produced by an expansion in plasma volume.[110] ANP reduces sodium and water absorption in the colon of laboratory animals,[108,109] suggesting a physiologic role for ANP in the regulation of Na^+ and water by the large intestine. Currently, no studies are investigating the effects of ADH and ANP on large bowel absorption in horses.

Because of the enormous capacity of the equine large intestine and its ability to absorb large amounts of electrolytes and water, the large intestine is thought to function as a reservoir of water and electrolytes.[110,111] This reservoir can be utilized whenever necessary (e.g., to correct dehydration produced by exercise). The capacity of the reservoir depends on the diet, which may affect the water-holding capacity of intestinal contents. In one study, horses fed only hay had about 1.5 times more water in their gastrointestinal tracts than horses fed hay and grain.[110] The results of another study indicated that, after endurance exercise, horses eating only hay had lower plasma concentrations of protein and higher concentrations of potassium than horses eating hay and grain.[112] These findings suggest that feeding only hay maximizes the capacity of the large intestine to function as a reservoir of water and electrolytes.

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Liver Function

Tim Mair

The liver is one of the largest organs in the body, and constitutes approximately 1% of the body weight of the adult horse. The liver performs many essential body functions, and has a major role in the regulation of nutrient distribution. The majority of the nutrients absorbed from the gastrointestinal tract pass directly to the liver by way of the portal vein. One of the main functions of the liver is in the maintenance of homeostasis, and it acts as a filter between the gut and the systemic circulation. The liver also adjusts the carbohydrate, protein, and lipid concentrations from the gastrointestinal tract, thereby maintaining constant blood levels of nutrients and responding to special circumstances (exercise, pregnancy, disease, etc).[1]

Other major functions of the liver include:[1-7]

1. Supply bile salts and bicarbonate to assist in digestion
2. Synthesize a large number of specialized proteins, carbohydrates, and lipids
3. Excrete larger and more hydrophobic physiologic metabolites, foreign substances, and drugs (detoxification)

Bile Acid Metabolism and Excretion of Bile

Bile consists of several components, including conjugated bilirubin, bile acids, cholesterol, lecithin, water, and electrolytes. The bile released by the hepatocytes enters the bile canaliculi and is transported via the bile ducts and hepatic duct to the intestine. The horse does not have a gallbladder, and bile passes continuously into the duodenum.

Bile acids constitute 90% of the organic portion of bile. The primary bile acids, cholic and chenodoxycholic acids, are synthesised from cholesterol in the liver, conjugated with taurine to form bile salts, and then excreted by an active transport mechanism into the bile canaliculi. Once excreted into the lumen of the intestinal tract, cholate and chenodeoxycholate may be reabsorbed or degraded by bacteria, forming secondary bile acids deoxycholate or lithocholate. In the distal ileum is another active transport mechanism, which ensures the conservation of bile salts once they have fulfilled their digestive function. More than 95% of the conjugated bile acids are reabsorbed by the ileum and returned to the liver via the enterohepatic circulation. Bile acids are estimated to be recycled at least 38 times a day in healthy ponies.[3] Bile salts are powerful detergents, solubilizing lipids by enclosing them in bile salt aggregates called micelles.

Bilirubin is the breakdown product of tetrapyrroles that function as electron transport pigments. The majority of bilirubin is formed from hemoglobin and myoglobin. Macrophages (Kupffer's cells) in the spleen, liver, and bone marrow engulf the pigments and convert them to biliverdin. Biliverdin is converted to bilirubin, which is released from the cells as free, insoluble bilirubin (also called indirect reacting or unconjugated bilirubin). Uncongugated bilirubin is bound to albumin in the plasma and transferred to the hepatocytes. At the surface of the hepatocyte, the bilirubin is transferred from albumin to ligandin, which transports the bilirubin intracellularly. Within the hepatocyte, the bilirubin is conjugated with glucuronide in the endoplasmic reticulum. The conjugated bilirubin (also called direct-reacting bilirubin) is water soluble and is excreted into the bile canaliculi. Therefore, when liver and biliary tract function are normal, very little conjugated bilirubin enters the circulation. However, when biliary tract disease or obstruction is present, conjugated bilirubin is increased in the plasma.

Within the intestinal tract, conjugated bilirubin is converted by microflora to urobilinogen and stercobilin, which are responsible for causing the feces to turn yellow-brown. In horses and other herbivores, the presence of chlorophyll pigments in the ingesta masks the color of urobilinogen.[1] Urobilinogen is absorbed by the intestine and transported back to the liver as part of the enterohepatic circulation. The liver extracts most of this urobilinogen, but a small amount will be excreted in the urine, and can be detected by urinalysis.

Protein Metabolism

The liver receives amino acids from the gut (via the portal vein) and the muscles, and regulates their concentrations in the plasma by controlling the rate of gluconeogenesis and transamination.[1,2] The liver also converts ammonia to urea via the urea cycle. The liver is the major site of synthesis of almost all the plasma proteins, and for many is the principle site of their degradation. Plasma proteins synthesised in the liver include albumin, clotting factors V,VII,VIII,IX, fibrinogen, antithrombin III, protein C, transport factors (e.g., haptoglobin, transferrin, cerruloplasmin, etc.), and acute phase reactants (e.g., α- and β-globulins).

A close relationship exists between the muscles, liver, and gut with respect to amino acid flux. Muscle contributes the biggest source of protein turnover. The liver is responsible for extensively modifying the blood amino acid composition. The aromatic amino acids – phenylalanine, tyrosine, and methionine – are preferentially processed to urea, whereas the branched-chain amino acids – valine, leucine, and isoleucine – are selectively passed to the periphery, where they are predominantly metabolised by muscle. This selectivity can be lost in horses with severe liver disease, and it is possible that the resulting change in the ratio of these two groups of amino acids may alter cerebral neurotransmitter metabolism and contribute to the pathophysiology of hepatic encephalopathy.

The liver is capable of transamination of amino acids (i.e., transfer an amino group of one amino acid to an α-keto acid, thus forming a new amino acid and a new keto acid). Thus, if there is an excess of amino acids or if carbohydrates are unavailable as an energy source, the liver will deaminate amino acids to convert them to pyruvate, acetoacetate, etc, which may be oxidized for energy, or used to form glucose by gluconeogenesis. Gluconeogenesis is under endocrine control.

The liver has a major role in eliminating ammonia from the circulation. All tissues and intestinal microflora generate ammonia, which is subsequently released into the circulation. The liver is responsible for converting ammonia and glutamine into urea in the hepatocyte mitochondria via the Krebs-Henseleit cycle (or urea cycle). The urea is released into the circulation as blood urea nitrogen, which is excreted by the kidneys. Failure to eliminate ammonia from the circulation is associated with encephalopathy due to liver disease.[4]

Carbohydrate Metabolism

The liver acts as a gate for the large amounts of glucose and other monosaccharides delivered from the gut (via the hepatic portal vein) during digestion, by storing it as glycogen, and is also the main source of glucose during starvation. Initially, glycogenolysis is the principal metabolic pathway used, but as the glycogen stores become depleted, gluconeogenesis assumes greater importance. The main substrates for this pathway are lactate, pyruvate, glucogenic amino acids (such as alanine from muscle) and glycerol (from lipolysis in fat stores). The control of carbohydrate metabolism is mainly hormonal (insulin, glucagons, catecholamines, and glucocorticoids). In liver disease, the supply of glucose by gluconeogenesis is generally well-preserved, and hypoglycemia is only usually a problem in acute hepatic failure.

Lipid Metabolism

The major plasma lipids are cholesterol, cholesterol esters, phospholipids and triglycerides. These are highly insoluble in water, and are carried in macromolecular complexes of lipid and a protein carrier (apoprotein) called plasma lipoproteins. Only the intestine and liver synthesize and secrete plasma lipoproteins. The four main classes of plasma lipoproteins have different sizes and densities:

1. Chylomicrons are produced by the mucosal cells of the small intestine during dietary fat absorption, and are the main carriers of triglyceride.
2. Very low density lipoproteins (VLDL) are produced by the liver and intestine, and have a core that contains 50 to 60% triglyceride.
3. Low density lipoproteins (LDL) are formed in plasma by catabolism of VLDL. They have a higher protein content and lower triglyceride proportion than VLDL.
4. High density lipoproteins (HDL) are synthesised by the liver and intestine, and are also made in the plasma. They have the highest protein content and lowest triglyceride concentration.

Short-chain fatty acids can also be absorbed directly from the gastrointestinal tract, bound to albumin, and transported to the liver via the portal vein. The liver will also take up albumin-bound fatty acids released from adipose tissue.

The liver has several different roles in lipid metabolism, most of which are under endocrine control (principally via insulin and glucocorticoids). The primary role is to esterify free fatty acids into triglycerides for export to other tissues as lipoproteins (especially VLDLs). The liver can also oxidize free fatty acids for energy to acetyl coenzyme A via the tricarboxylic acid cycle. The acetyl coenzyme A can be used to synthesize other fatty acids, cholesterol, steroids, and ketone bodies (acetoacetate and β-hydroxybutyrate). Ketone bodies can be used by peripheral tissues as an energy source. Acetyl coenzyme A can also be synthesised by the liver from glucose and amino acids, thereby enabling lipids to be produced from carbohydrates and proteins.

Detoxification and Drug Metabolism

The liver is responsible for the detoxification (biotransformation) and clearance of many endogenous (e.g., ammonia, bilirubin, steroid hormones) and exogenous (e.g., plant toxins, insecticides, mercaptans) compounds and many drugs. In general, the more lipophilic and the higher the molecular weight, the more likely the substance is to be cleared by the liver rather than the kidneys. Such hepatic clearance usually involves metabolic biotransformation with or without conjugation. In liver disease, alterations of drug handling can induce clinically important consequences by changing drug concentrations and half life.

Storage

Several vitamins and trace minerals are stored in the liver, including vitamins A, D, and B12, and copper and iron.

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Effects of Feeding on Equine Gastrointestinal Function or Physiology

Chapter 3

Marco A. F. Lopes

The association between feeding practices and equine gastrointestinal dysfunction has been demonstrated by several epidemiologic studies.[1-6] Thus, it is interesting to review the effects of common feeding practices on equine gastrointestinal physiology.

Feeding Grain

To provide enough energy and protein to maximize performance (growth, reproduction, speed, and strength), grain is frequently added to horses' diets. Ingestion of grain has long been recognized as a potential cause of gastrointestinal dysfunction in horses,[7] however, and has been confirmed by recent epidemiologic studies.[4-6] Grains are rich in hydrolyzable nutrients[8] and may cause digestive problems in a gastrointestinal tract that evolved to digest plant material having a higher fiber content.[9] Hydrolyzable nutrients are digested by enzymes secreted by the salivary glands, stomach, pancreas, and small intestine. When large amounts of hydrolyzable nutrients are ingested (e.g., as occurs with grain meals), the digestive capacity of the gastrointestinal tract preceding the cecum may be overloaded, and large amounts of hydrolyzable nutrients can become available for fermentation in the large intestine.[10,11]

Effects on the Gastrointestinal Microbiota and Intraluminal pH

The gastrointestinal tract of normal horses constitutes a unique ecosystem inhabited by a large number and variety of microorganisms.[12-19] The resident microbiota have an important role in digestion and are essential for the health of the gastrointestinal tract. As in any ecosystem, the environmental conditions and the availability of nutrients are the main determinants of the health of the microbial populations.[20] Experiments in horses and ponies have shown that feeding grain can profoundly affect the gastrointestinal microbiota and, consequently, the concentration of microbial fermentation products, pH, and endotoxin concentration (Table 3-1). Production of lactic acid by the microorganisms that predominate after acute ingestion of large amounts of hydrolyzable carbohydrates leads to a rapid decline in pH and death of large numbers of gram-negative bacteria.[13,21] As a result of an increased availability of lactate, the number of lactate-utilizing organisms increases.[21] The effects of grain ingestion on these bacterial populations are proportional to the amount of grain fed.[22,23] Abrupt ingestion of grain produces dramatic effects, which tend to taper off after a few days even if the horse is maintained on the same high-grain diet.[21] This finding corroborates the clinical observation that horses gradually adapted to grain ingestion may tolerate considerable amounts of grain, which would produce signs of gastrointestinal dysfunction in nonadapted horses.

Table 3-1

Effects of Grain Ingestion (Acute or Chronic) in the Equine Large Intestine: Changes in the Microbiota, Concentration of Products of Microbial Fermentation and Endotoxin, and pH.

	Increase	Decrease
A few hours after acute ingestion of grain	bacterial population[22,24,25]	number of gram-negative rods[24]
	number of *Lactobacillus* sp.[13,21]	number of *Enterobacteriaceae* sp.[13,21]
	number of organisms growing in selective starch medium[21,26]	number of aerobic *Streptococcus* sp.[13,21]
	molar concentration of VFAs[22,24,27,28]	number of anaerobic *Streptococcus* sp.[13,21]
	molar concentration of lactate[22,24,27,28]	number of organisms growing in selective fiber medium[21,26]
	concentration of endotoxin[23]	number of protozoa[21]
		molar percentage of acetate[22,26,28]
		pH[13,26,28]
With chronic grain ingestion	number of bacteria growing on lactate medium[21]	digestibility of organic matter[29]
	digestibility of fiber[29]	

Effects on the Mucosal Barrier and Plasma Endotoxin Concentration

Ingestion of extremely large amounts of grain can disrupt the mucosal barrier of the gastrointestinal tract. In a study of 4 horses with cecal fistulas, administration of 17.6 g/kg of body weight of a meal rich in hydrolyzable carbohydrates (85% corn starch and 15% wood cellulose flour) via nasogastric tube caused electron microscopic evidence of damage to the cecal mucosa. Mucosal damage was thought to be caused by the increase in intraluminal acidity produced by the carbohydrate overload.[30] The same model of carbohydrate overload produced clinical signs of endotoxemia[13,23,31] and detectable concentrations of endotoxin in the plasma,[32] suggesting that endotoxin had reached the circulation after crossing the damaged mucosal barrier. The effects of ingestion of smaller amounts of grain on the gastrointestinal mucosal barrier and endotoxin absorption have not been investigated in the horse.

Effects on Gas Production and Accumulation in the Gastrointestinal Tract

Ingestion of large amounts of grain can result in gas accumulation within the gastrointestinal tract manifested as gastric dilation[33,34] or tympany of the large intestine.[33,35] Gastrointestinal dilation with gas can have serious consequences, including abdominal discomfort, gastrointestinal hypoperfusion, and respiratory distress. It has also been suggested that the reduced weight of gas distended intestinal segments can result in intestinal displacement or volvulus,[36] however, few studies have examined the mechanisms involved in tympany secondary to grain overload in horses.

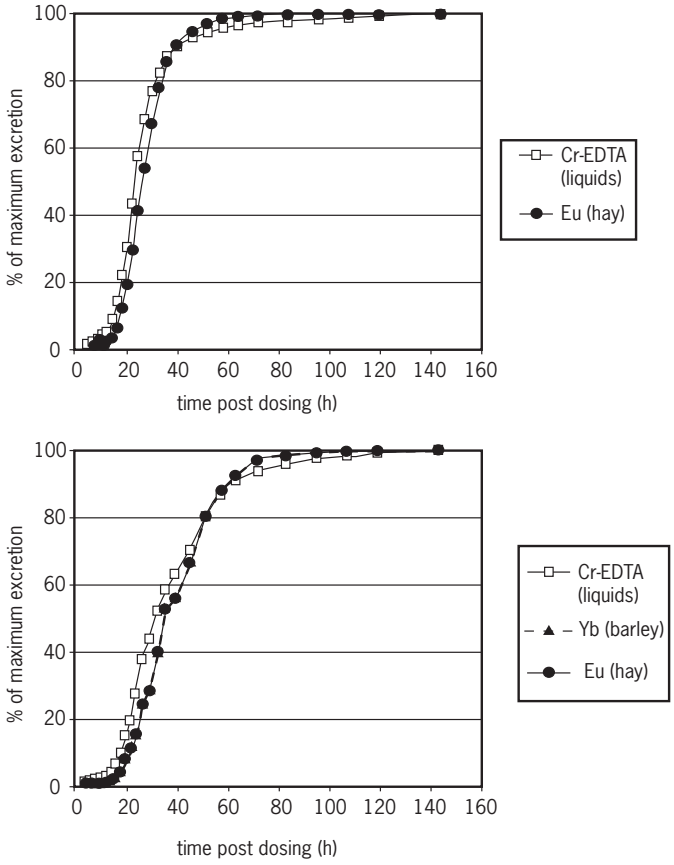
In ruminants, several aspects of the etiopathogenesis of bloat secondary to grain ingestion have been identified.[37,38] When large amounts of soluble carbohydrates reach the rumen, rapid fermentation produces large amounts of gas.[39] In addition, ruminal microorganisms synthesize substances (e.g., mucopolysaccharides) that lead to an increase in the viscosity of the ruminal fluid and, ultimately, to formation of stable froth.[40,41] Eructation, which is the main mechanism for elimination of gas from the rumen, is inhibited by froth.[39] Thus, froth accumulates in the rumen and causes an increase in intraruminal pressure and ruminal distention.[39] Inhibition of ruminal motility from luminal acidosis has also been mentioned as a factor in the pathogenesis of frothy bloat.[38] There are indications that individual variability and breed predisposition also play a role in the development of bloat. Factors such as anatomic differences in the rumen, salivary production, and appetite may explain why some individuals are predisposed.[37]

Some of the same mechanisms responsible for frothy bloat in ruminants may apply to horses with grain overload. In a study of horses with fistulas in the right dorsal colon fed free choice hay and two large grain meals (4.55 kg of sweet feed every 12 hours), colonic contents were foamy, similar to ruminal contents of cattle with frothy bloat. Colonic contents of these horses consisted of a viscous liquid and large quantities of small gas bubbles. These physical characteristics contrast with the minimal quantity of visible gas bubbles and the watery fluid phase of colonic contents when the same horses were fed only hay. Furthermore, spontaneous flow of colonic contents when the cannula was open only occurred when the horses were fed grain, suggesting that grain ingestion led to an increase in intraluminal pressure.[42] Other mechanisms described for ruminants with frothy bloat may also play a role in gastrointestinal dysfunctions in horses after grain overload despite the differences in gastrointestinal physiology (e.g., horses are hindgut fermenters, horses do not eliminate large amounts of gastrointestinal gas by eructation). Although the equine cecum is effective at handling gas, excessive amounts of gas can exceed its capacity.[43] It is also possible that intraluminal acidosis produced by grain ingestion,[13,28] could compromise gastrointestinal motility, as occurs in ruminants.

Effects on Gastrointestinal Transit

The results of several experimental studies indicate that grain ingestion delays gastrointestinal transit of liquids and solids (Figure 3-1).[29,42,44,45] Grain ingestion may affect gastric emptying, which is a major determinant of transit of gastrointestinal contents. Gastric emptying is under the control of a negative feedback mechanism to limit the availability of nutrients for intestinal digestion and absorption. Receptors sensitive to physical (e.g., osmolality) and chemical (e.g., pH, lipids) properties of ingesta located in the duodenum trigger this feedback mechanism.[46] Compared with roughage, grain contains considerably more digestible nutrients.[8] Thus, gastric emptying is slowed after grain ingestion to prevent the digestive and absorptive capacities of the small intestine from being exceeded. It has also been proposed that the slower rate of passage when horses are fed diets having a higher grain content is a consequence of a decrease in dry matter intake when compared with diets having a higher fiber content.[29,44,45] Furthermore, it has been suggested that reductions in saliva production and water intake occurring when grain is fed might contribute to slower gastrointestinal transit.[44]

Figure 3-1



Means of cumulative excretion of markers (Cr-EDTA - as a marker of the liquid phase, Ytterbium - as a marker of hay, and Europium - as a marker of barley) administered at time 0 to 6 ponies fed only hay (A) or a 50:50 hay:barley diet (B). The right shift of the curves observed when barley was fed indicates that transit of liquids and solids was slower. (Modified from Drogoul C, Fombelle A, Julliand V. Feeding and microbial disorders in horses: 2- Effect of three hay:grain ratios on digesta passage rate and digestibility in ponies. J Equine Vet Sci 21:2001, 2001).

Effects on Water Consumption

The results of several studies document reduced consumption of water by horses eating grain. In these studies, total daily water consumption was reduced 21 to 46%, while water consumption per kg of dry matter consumed fell 21 to 38%.[47-51] The fact that more water is needed within the gastrointestinal tract for the flow of gastrointestinal contents when fibrous (bulkier) feed is ingested[42,49] may explain why horses eating grain need less water. Ingestion of less bulky feed leads to reduced chewing and salivary secretion.[52] Thus, the post-prandial decrease in plasma volume and increase in plasma osmolality are likely minimized when less bulky feed is ingested. In ponies, hypovolemia and plasma hyperosmolality are the primary stimuli that induce water intake.[50]

Effects on Ingesta Osmolality and Ionic Composition

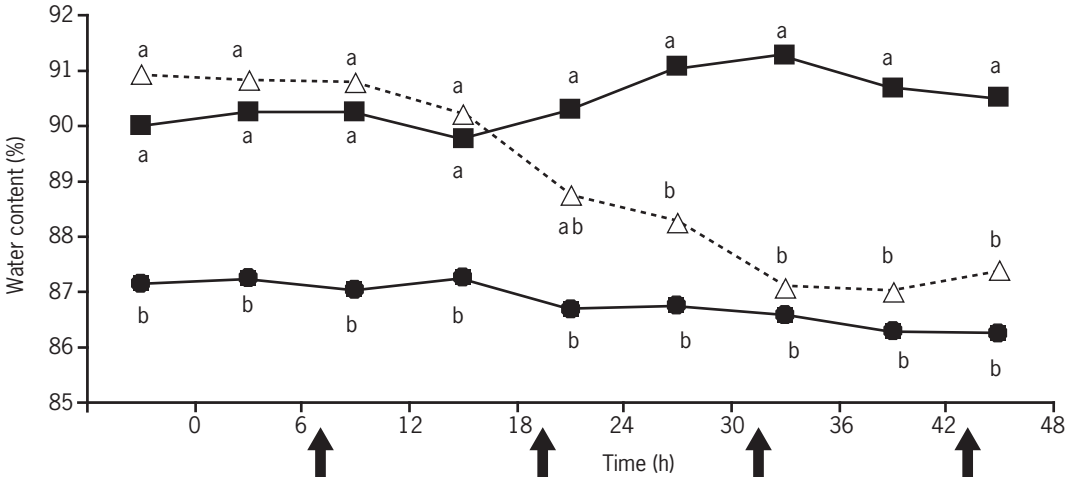
Ingesta osmolality and ionic composition can be affected by grain ingestion. When large amounts of highly digestible feed such as grain are digested and fermented, macromolecules are cleaved, producing large numbers of smaller molecules within the gastrointestinal lumen. Theoretically, unless products of digestion and fermentation of grain are rapidly absorbed or water is secreted into the gastrointestinal tract, ingestion of grain will result in post-prandial hyperosmolality of gastrointestinal contents. In horses, little has been objectively assessed about the effects of grain ingestion on the osmolality of gastrointestinal contents. In a study in ponies, hyperosmolality of the contents of the large intestine was produced by a hay-grain pelleted diet, which contrasted with the hyposmolality produced by a high-fiber-low-protein diet.[53] In one study, however, colonic contents were consistently dehydrated after ingestion of large amounts of grain when compared with the colonic contents of the same horses fed only hay.[42] This finding suggests that products of digestion and fermentation of grain are rapidly absorbed by the gastrointestinal mucosa and colonic microbiota. If this were not the case, formation of hypertonic colonic contents would retain water within the gastrointestinal tract, making intestinal contents more watery. In the only published study on the effects of grain ingestion on the ionic composition of the gastrointestinal contents, a hay-grain pelleted diet produced post-prandial changes in ionic composition of ingesta, which were not evident in ponies fed a high-fiber-low-protein diet. This result is likely the consequence of dietary electrolyte composition; the physiologic significance of this finding is not obvious.[54]

Effects on Ingesta and Fecal Water Content

Grain ingestion can produce dehydration of intestinal contents and feces. In a study in which ponies were fed either alfalfa only or alfalfa and grain, water content in the small colon was significantly lower when grain was fed (means, 82.2% versus 77.0%, respectively); however, feeding grain did not affect water content of ingesta in the stomach, small intestine, cecum, or large colon.[55] In horses, fecal hydration was lower when a low-fiber diet was fed (mean, 73.6%) in comparison with what was observed with a high-fiber diet (mean, 81.7%).[51] In horses with a right dorsal colon fistula, ingestion of 4.55 kg of sweet feed twice daily reduced water content of colonic ingesta (mean, 86.8%), but not of feces (mean, 78.9%) relative to the values measured in the same horses fed only hay (means, 90.5% and 79.1%, respectively) (Figure 3-2).[42] These findings are in agreement with the theory that ingestion of less fibrous feed requires less water to facilitate flow of contents through the gastrointestinal tract.[49]

It has been hypothesized that the less hydrated intestinal contents occurring in horses fed grain could predispose these horses to development of large-colon impactions.[9] This hypothesis contradicts the findings of a well conducted experiment in rabbits in which ingesta viscosity and not water content was shown to be the key factor responsible for intestinal obstruction.[56] The results of our study have demonstrated that ingesta becomes foamy when grain is fed, which suggests that the increased amount of gas might compensate for any trend toward an increase in ingesta viscosity produced by ingesta dehydration.[42] Furthermore, anecdotal and clinical reports have linked large intestine impaction in horses to ingestion of fibrous feeds, but not to grain ingestion. Further studies are needed to come to a definitive conclusion about the physiologic significance of dehydration of large intestinal contents in horses fed grain.

Figure 3-2



Means of water content of right dorsal colon (RDC) contents obtained from 6 horses with fistulas in the RDC that had access to hay ad libitum (diet 1; closed squares), hay ad libitum and grain (4.55 kg) every 12 hours after being adapted to hay only for at least 5 days (diet 2; open triangles), or hay ad libitum and grain (4.55 kg) every 12 hours after being adapted to this diet for at least 5 days (diet 2; closed circles). Arrows indicate the times when horses had access to grain. Within a time point, values with different letters are significantly ($P \leq 0.05$) different. (Modified from Lopes MAF, White II NA, Crisman MV, Ward DL: Effects of feeding large amounts of grain on colonic contents and feces in horses. Am J Vet Res 65, 2004.)

Effects on Systemic Hydration

Purportedly, the gastrointestinal tract functions as a reservoir of water and electrolytes in exercising horses. If this is true, a diet with less fiber may reduce the capacity of this water reservoir by reducing both the water content of ingesta and the volume of ingesta. Effects of grain ingestion on water and electrolyte balance have been demonstrated in horses undergoing endurance exercise, and these horses had higher plasma protein concentrations and lower plasma potassium concentrations relative to values obtained for the same horses fed only hay.[48] In a study comparing changes in plasma volume in horses treated with furosemide, no effect of diet (low fiber versus high fiber) could be detected.[51]

Other Effects

Intragastric administration of a carbohydrate gruel (17.6 g/kg of body weight; 85% corn starch and 15% wood cellulose flour) to horses and ponies resulted in soft feces (from pasty to liquid), increased abdominal sounds, and abdominal distention.[57] Similarly, soft acidic feces, an increase in plasma lactate concentration, and clinical signs of laminitis were observed in Standardbred horses receiving high-starch pelleted feed (85% ground maize and 13% soybean meal) ad lib. These changes were not evident when the antibiotic virginiamycin was added to the meal, although the horses ate less grain during the first 3 days that the antibiotic was added. These findings were interpreted as the result of the reduced feed intake and the prevention

of growth of lactate-producing bacteria by the antibiotic.[58] In a study in which horses with a right dorsal colon fistula were fed large amounts of grain using a regimen currently adopted for domestic horses (4.55 kg of sweet feed every 12 hours and free-choice hay), ingesta became more homogenous with less distinct separation between the liquid and solid phases. Furthermore, the liquid phase became more viscous when compared with colonic contents from the same horses fed only hay. It was also noticed that feces became softer and less formed.[42] It has also been demonstrated that the expression of monosaccharide transporters (SGLT1 and GLUT2) in the epithelium of the small intestine is increased in horses eating grain. These horses had epithelial monosaccharide transporters throughout the small intestine, whereas expression of these transporters was limited to the proximal small intestine in horses maintained on grass. These findings suggest an adaptation of the small intestine to the ingestion of large amounts of hydrolysable carbohydrates.[59]

Feeding Lush Grass

Rapidly growing pasture can have large amounts of hydrolysable and rapidly fermentable carbohydrates.[8] When lush grass is ingested, large amounts of these nutrients escape digestion in the small intestine and become available for rapid fermentation in the large intestine. Thus, ingestion of lush grass may lead to the same problems caused by ingestion of grain (e.g., diarrhea, tympany, intraluminal acidosis, mucosal damage, endotoxemia).

Replacing Grain with Fat

Although ingestion of fat may decrease digestibility of fiber in the equine gastrointestinal tract,[60-63] replacing grain with fat is likely to be advantageous. By feeding fat to horses, it is possible to increase the energy density of the diet while minimizing consumption of hydrolysable carbohydrates. Considering the deleterious effects of large amounts of hydrolysable carbohydrates on the equine gastrointestinal tract, it is thought that diets rich in fat and lower in carbohydrates may prevent gastrointestinal disorders.[64] Further studies of the effects of fat on equine gastrointestinal physiology are necessary.

Feeding Mature Grass and Poor Quality Hay

Mature grass and poor quality hay have low nutrient content and are rich in poorly fermentable fiber.[65] Ingestion of these bulky roughages increases gastrointestinal filling, which is evidenced by abdominal distention. This kind of feed may lead to gastrointestinal impaction, which is likely the result of an increased resistance to transit of rough ingesta formed by large pieces of undigested fiber. Fortunately, most horses seem to tolerate poor quality roughage and only a fraction of horses fed this diet will develop impactions. However, an abrupt change to poor quality roughage for horses adapted to good quality feed is likely to increase the risk of gastrointestinal impaction.[66]

Feeding Large Meals Intermittently and Fasting

Feeding a few large meals per day to domestic horses is a common practice because of convenience; however, this practice differs remarkably from the condition in which the horse evolved: having continuous access to grass. Therefore, episodic feeding may predispose to gastrointestinal dysfunction.[9] In the clinical setting, fasting horses for variable amounts of time is commonly adopted in many situations (e.g., preparation for general anesthesia and surgery, treatment of large intestine impaction); however, it is important to keep in mind the side effects of feed deprivation on gastrointestinal function.

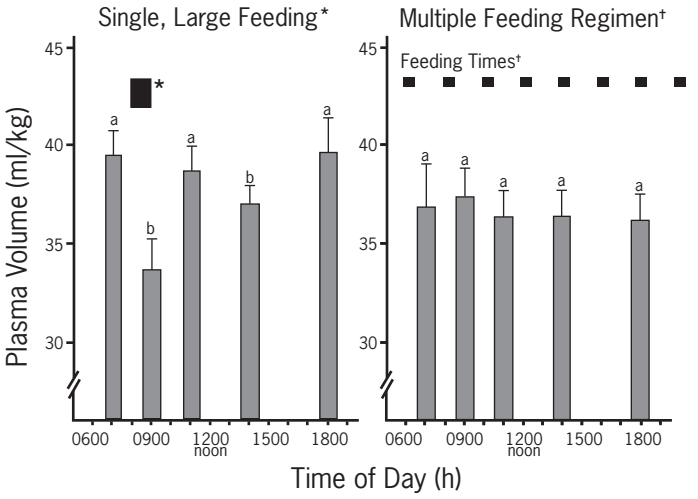
Effects on Water and Electrolyte Balance

Horses eating intermittently can develop post-prandial plasma volume contraction, electrolyte imbalances, and hormonal changes that do not occur with a more continuous eating pattern. These effects are proportional to the amount of feed ingested and are thought to be the result of post-prandial dehydration due to secretion into the alimentary tract. In one study, feeding a larger meal (2.7 kg of complete cube diet plus 5.5 kg of hay) produced more pronounced post-prandial dehydration and electrolyte shifts (a 15.8% increase in hematocrit, a 12.2% increase in plasma protein concentration, and a 16.6% decrease in plasma potassium concentration), than occurred after 2 other daily meals (each of 1.8 kg of complete cube diet).[67] Similar results were obtained in a series of experiments with ponies and horses comparing changes after a single 1-hour meal of complete pelleted feed versus the effects of 6 daily meals each containing 1/6 of the same feed. After a single meal, hematocrit, plasma protein concentration, and plasma osmolality increased (as much as 9.1%, 13.2%, and 2.5%, respectively), whereas the same parameters increased modestly (no more than 2.4%, 4.3%, and 0.7%, respectively) after one of the 6 daily meals.[68-71] In one of these studies, it was determined that the single large meal reduced plasma volume by 15% (Figure 3-3).[68] In 2 of these studies, post-prandial activation of the renin-angiotensin-aldosterone system was also demonstrated. A large meal produced an increase in plasma renin activity, which was followed by an increase in both plasma aldosterone concentration and urinary clearance of potassium and a decrease in the urinary clearance of sodium (Figure 3-4).[68,69] Post-

prandial dehydration was also documented in athletic horses fed about 7.4 kg of grass hay and 4.1 kg of grain mix divided in 2 equal meals every 12 hours. An immediate increase occurred in plasma protein concentration (3.0 to 4.7%), in plasma osmolality (1.8%), and in aldosterone concentration (up to 9%) after the large meals. These changes were not observed when the same amount of feed was divided into 6 equal meals every 4 hours.[72]

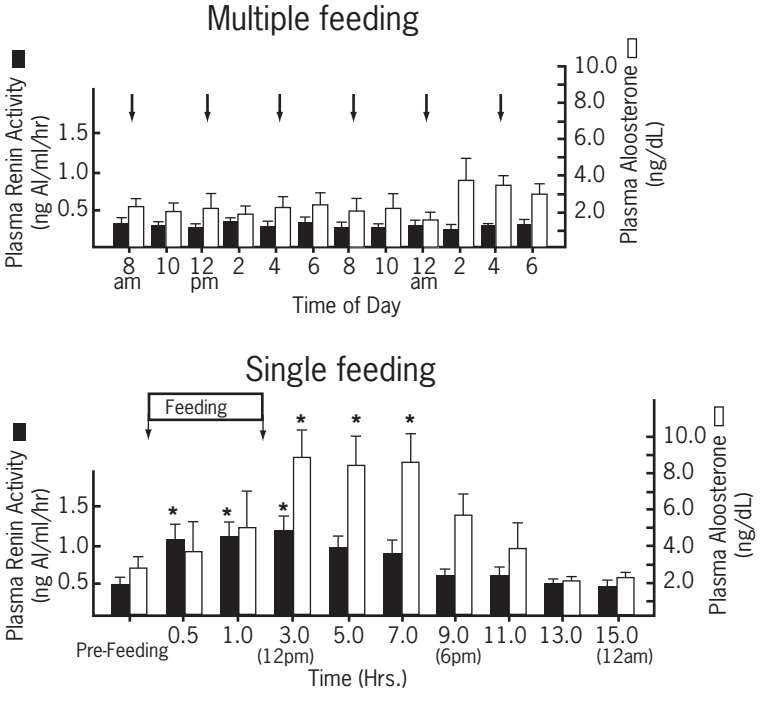
It has been suggested that the activation of the renin-angiotensin-aldosterone system produced by post-prandial dehydration after a large meal could increase water absorption in the large intestine and lead to dehydration of intestinal contents and impaction of the large intestine.[9] The fact that even with extremely artificial feeding protocols (e.g., a single 1-hour meal per day) only short-term systemic dehydration (less than 3 hours) could be produced is evidence against this theory. Furthermore, for the horse to eat a large meal in a short period of time as observed in these studies, it is necessary to add grain and limit the fiber content of the diet. These dietary changes would have additional effects on the composition of intestinal contents, which would probably reduce the risk of impaction. Thus, large meals and intermittent feeding would likely lead to gastrointestinal problems other than impactions of the large intestine.

Figure 3-3



Means of plasma volume determined by dye-dilution technique in 6 ponies fed a single large meal and multiple smaller meals. Vertical brackets represent SEM. Means with different letters are significantly (P ≤ 0.05) different.
* Represents half the daily maintenance ration given at 0800 hours.
+ Represents a twelfth of the daily maintenance ration given at 2-hour intervals on the even-numbered hours. (From Clarke LL, Argenzio RA, Roberts MC. Effect of meal feeding on plasma volume and urinary electrolyte clearance in ponies. Am J Vet Res 51:571-576, 1990.)

Figure 3-4



Means of plasma renin activity and aldosterone concentration in 7 horses fed a single large meal (SF) and multiple smaller meals (MF). Vertical brackets represent SEM. In MF, arrows indicate the times when small, equal-portion meals were offered. In SF, actual time of day is given in parentheses below horizontal axis. * Significantly (P ≤ 0.05) different from prefeeding values (mean of values from 1 hour before and immediately prior to feeding). (Modified from Clarke LL, Ganjam VK, Fichtenbaum B, et al. Effect of feeding on renin-angiotensin-aldosterone system of the horse. Am J Physiol 254:R524-530, 1988.)

Effects on other Plasma Variables

Intermittent ingestion of feed can produce other post-prandial biochemical and hormonal changes in horses, which do not occur with a more continuous eating pattern. In 2 studies (one with ponies and the other with horses), the effects of a single 1-hour meal of complete pelleted feed were compared with those of 6 daily meals consisting of 1/6 of the same feed. The single large meal produced a post-prandial increase in plasma glucose concentration (85.5%) and plasma triiodothyronine (53.8%).[71] It is likely that these changes produced by the large meal may also affect gastrointestinal function (e.g., gastric motility and emptying). In other species, higher glucose concentration after the large meal would result in higher plasma concentrations of amylin, a hormone that delays gastric emptying.[73] In humans, higher triiodothyronine concentrations in plasma after a large meal may affect gastric motility and emptying.[74]

Other Effects

Motility of the equine large bowel can be decreased by fasting and returns after refeeding;[75-77] however, likely only prolonged fasting affects gastrointestinal transit. In ponies, the gastrointestinal transit of the liquid phase of ingesta was not affected by feeding either a single daily meal or a smaller meal every 4 hours.[70] In athletic horses, feeding about 7.4 kg of grass hay and 4.1 kg of grain mix divided in 2 equal meals every 12 hours did not affect fecal output or fecal hydration when compared with the effects of the same amount of feed divided into 6 equal meals every 24 hours.[72] Conversely, in horses with a nasogastric tube, fasted and muzzled for 24 hours, the gastrointestinal transit of the liquid phase of ingesta was delayed.[78] The microbiota of the gastrointestinal tract may also be affected (reduced number and activity) by prolonged fasting because of the lack of substrate for microbial growth. Withholding food for as little as 24 hours, but especially for 48 hours, decreased the rate of digestion of cotton-threads inserted into the cecum and large colon of horses with surgically created fistulas.[75] No difference was detected in digestibility of fiber and protein in ponies allowed to consume their single daily meal in 1 hour when compared with digestibility in the same ponies fed small meals every 6 hours.[70]

Although relatively little is known about the effects of feeds and feeding regimens on equine gastrointestinal physiology, one hopes future research findings will make it possible to design feeding practices to maximize performance and minimize gastrointestinal problems in horses. Meanwhile, it is wise to feed horses using principles most compatible with the known features of equine gastrointestinal physiology: 1) minimize the total daily amount and the amount per meal of feeds rich in hydrolysable and rapidly fermentable carbohydrates such as grain and lush grass; 2) minimize the amount of low-quality roughage rich in indigestible fiber such as straw; 3) maximize the amount of high-quality roughage such as good quality hay with adequate fiber; 4) minimize meal size and maximize the number of meals per day; 5) make any change in feeding practices as smoothly as possible, allowing sufficient time for adjustment by the intestinal flora; 6) Provide continuous sources of fresh water and minerals.

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Intestinal Motility and Transit

Chapter 4

Peter C. Rakestraw

Physiology of Normal Motility

Motility of the gastrointestinal tract has two major effects. One is to facilitate the absorption of nutrients. Both retrograde and normograde flow are required to optimize the absorption of nutrients. Retrograde flow most likely occurs intermittently over short distances to aid in mixing of ingesta and exposing nutrients to the mucosa for absorption. Although little work has been done in the horse to investigate the control of these mixing patterns, most likely feedback occurs from both absorption of nutrients and afferent input by mucosal sensory receptors that control these mixing motor patterns in a similar fashion to other species. The second major effect of motility is to maintain the aboral propagation of chyme and indigestible material. Because alteration of the normal aboral movement of ingesta causes immediate clinical consequences, the majority of motility investigation in the horse has centered around the control of aboral propagation of ingesta throughout the gastrointestinal tract and the pathophysiology associated with delayed aboral propagation. This chapter will review the basic mechanisms controlling normal motility patterns, review current thoughts as to the mechanisms underlying the pathophysiology of motility disturbances, in particular postoperative ileus, and finally, review prokinetics that are available to the equine practitioner.

Gastrointestinal Smooth Muscle

The muscle layers in the intestinal tract responsible for gross motility are contained in the muscularis externa, which is divided into an inner circular muscle and the outer longitudinal muscle and separated by fascia containing the myenteric plexus. Contraction of the circular muscle narrows the intestinal lumen and, at the same time, lengthens the segment, whereas contraction of the longitudinal muscle shortens the intestinal segment and, at the same time, widens the lumen. Temporal and spatial coordination of activity of both these muscle layers is necessary for normal progressive motility. Coordination of contractile events starts at the level of the effector cell, the myocyte. Gastrointestinal smooth muscle cells demonstrate continual oscillations in membrane potential called “slow waves” (Figures 4-1 and 4-2).[1,2] These appear on intracellular recordings as rhythmic depolarizations, which are also called electrical control activity (ECA). These slow waves or ECA develop as a result of sequential opening and closing of calcium and potassium channels, with rapid changes in intracellular and extracellular ionic composition. During the slow wave, the membrane potential becomes less negative (depolarizes). This depolarization by itself does not reach the threshold for an action potential; however, at the peak of the slow wave the cell is at a state of increased excitability because it is closer to the threshold for an action potential. At this time, it requires less excitatory input to reach its activation threshold. With further excitatory (deplorizing) stimulation, which may be neural or chemical, the slow wave rises above its threshold for activation with the opening of voltage-gated calcium channels (Figure 4-1).[2] The increase in cytosolic calcium from both the influx of extracellular calcium and the release of intracellular stores activates the myosin and actin contractile proteins as cytosolic calcium binds to calmodulin and activates myosin kinase.[3] Activated myosin kinase, using energy from hydrolysis of ATP, catalyzes myosin cross-bridges attaching to actin filaments. The sequential attaching, releasing, and reattaching of the myosin bridge produces shortening of the muscle cell. These action potentials are manifested as electrical response activity (ERA) in intracellular recordings, with contraction occurring during this electrical activity (Figure 4-1). Because action potentials and the resulting contractile activity are superimposed on the peaks of slow waves, the slow waves determine the maximal frequency of contractions. Although contractions may not occur as frequently as the slow-wave oscillations if excitatory stimulation is not sufficient to depolarize the cell to the threshold for contraction, contractions cannot occur more frequently than the slow-wave frequency. For this reason slow waves are also called “pacesetter potentials,” “basic electrical rhythm” (BER), or “electrical control activity” (ECA) (Figures 4-1 and 4-2).[4,5]

Slow waves also determine the direction and velocity of propagation of contractions. Slow waves have characteristic frequencies, depending on the region of the GI tract. The frequency of slow waves is higher in the more proximal portions of each region of the GI tract and decreases moving distally.[2,4,5] The smooth muscle cells are connected to adjacent myocytes through specialized areas of cell-to-cell contact called gap junctions. These gap junctions are spanned by channel-forming protein molecules that allow ions to pass directly from one myocyte to the next, creating an electrically coupled syncytium.[6] In this manner, electrical activity in one cell spreads out through adjacent cells, allowing them to be excited or inhibited as a unit. Because of the electrical coupling between cells in the muscle layers, the slow waves are entrained (i.e., the proximal slow waves that are generated at the higher frequency spread distally and so pace the distal slow waves). Because a short lag phase occurs between the start of the proximal slow wave and the pacing of the distal slow wave, the slow waves appear to propagate distally. Also, because of the electrical coupling, slow waves occur almost simultaneously around the circumference of the intestinal segment. With excitation sufficient to cause an action potential, a ring of contraction forces luminal contents distally.[4,7]

Figure 4-1

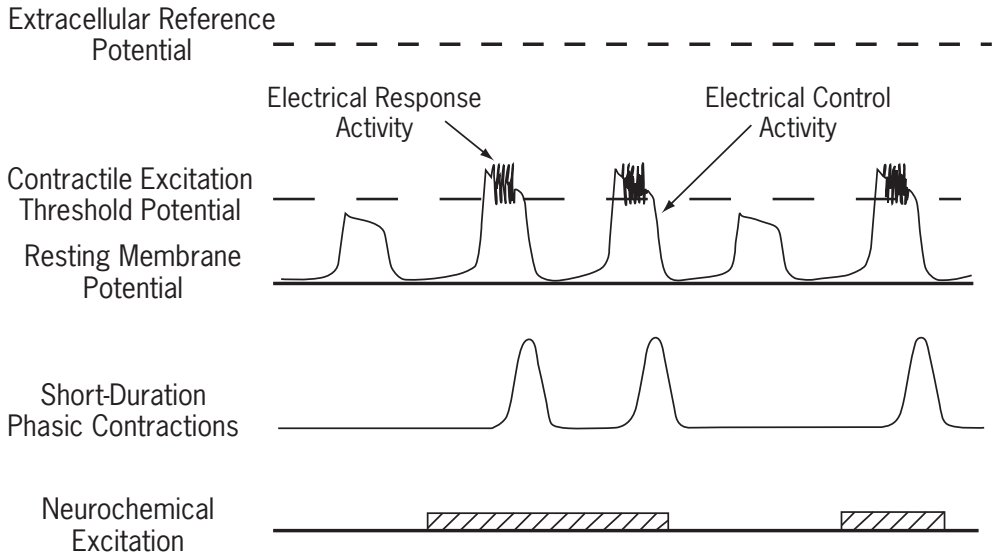
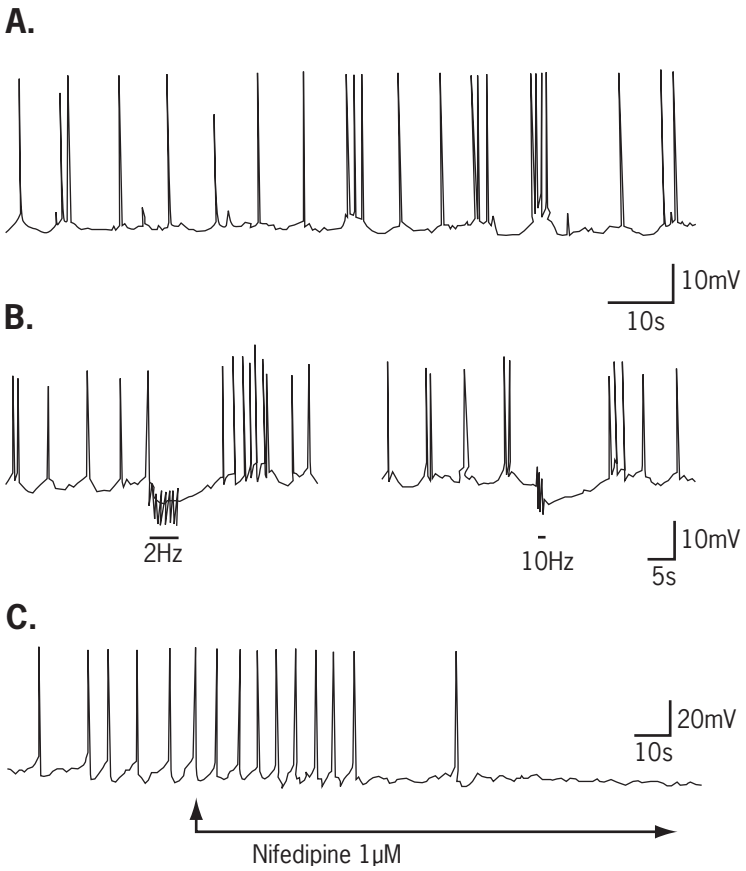


Illustration of myogenic control: type 1 for short duration phasic contractions. Figure illustrates the relationship of intracellular recorded myoelectrical activities and neurochemical excitation with contractions. The resting membrane potential is negative with respect to the extracellular reference potential. In the absence of neurochemical excitation, the ECA (electrical control activity) depolarizations do not exceed the contractile excitation threshold potential. Consequently, there is no ERA (electrical response activity) burst and no contraction (1st and 4th ERA cycles). When neurochemical excitation occurs, ECA deplorization exceeds the excitation threshold potential, an ERA burst occurs, and the smooth muscle contracts (2nd, 3rd, and 5th cycles). (Adapted from Sarna K, Otterson MF Myoelectric and Contractile Activities. In Atlas of Gastrointestinal Motility in Health and Disease. Schuster MM (ed). Baltimore: Williams & Wilkins, 1993, pp. 3-42).

Figure 4-2



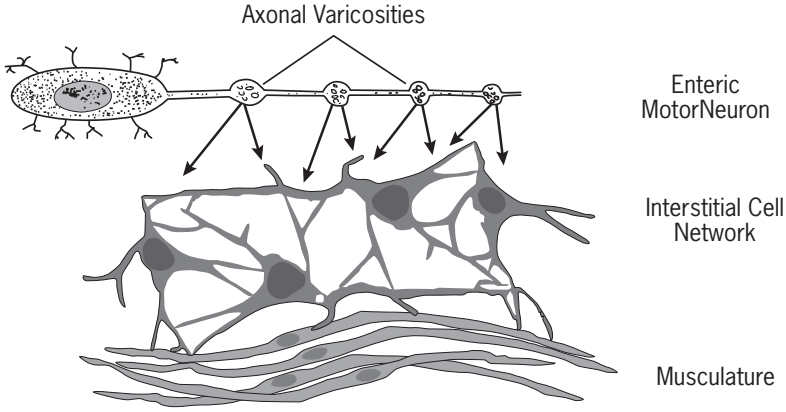
Intracellular microelectrode recording of membrane potentials associated with spontaneous myogenic activity (slow waves) in the circular muscle of jejunum in horses. All panels illustrate intracellular microelectrode recordings of membrane potentials from single circular muscle cells. **A.)** In the presence of atropine and quanethidine (2 μM each), cells had spontaneous action potentials superimposed on small amplitude membrane potential oscillations. **B.)** Stimulation of intrinsic inhibitory neurons (2 Hz and 10 Hz, indicated by bars) caused a transient hyperpolarization, an inhibitory junction potential (IJP), that temporarily inhibited spontaneous depolarization and action potential firing (arrowheads indicate stimulus artifacts). **C.)** Nifedipine (1 μM), a calcium channel blocker, abolished smooth muscle oscillations and action potentials. (Reprinted with permission. Am J Vet Res 61:362-368, 2000.)

Interstitial Cells of Cajal

The interstitial cells of Cajal (ICCs) have been shown to play a key role in the initiation of pacemaker activity.[8] Interstitial cells of Cajal are highly branched cells located in the myenteric and submucosal plexuses of the enteric nervous system. They originate from the same mesenchymal precursor cell as the smooth muscle cell.[8-10] The ICCs from the submucosal and myenteric borders surround the adjacent circular muscle cells. ICCs express c-kit, the proto-oncogene that encodes for the receptor tyrosine kinase. This finding has greatly aided in the study of ICCs by providing a method of identification either by labeling Kit receptors or c-kit mRNA.[11] Mutant mice that do not express functional Kit proteins, and so do not have ICCs, show an absence of slow-wave activity.[12] Blocking Kit function with neutralizing antibodies causes impairment in ICC development, which results in the absence of slow waves. This demonstrates that slow waves are generated by ICC pacemaker cells. The ICCs are in electrical communication with smooth muscle cells through gap junctions, allowing the electrical activity to spread passively to smooth muscle cells.[10-13] ICCs are interposed between circular smooth muscle cells and enteric motor neurons, suggesting an interaction between neural and myogenic control at the level of ICCs (Figure 4-3). ICCs amplify inhibitory nitrergic and excitatory cholinergic signals from neurons to myoctes.[8,9,14] Abnormal function or numbers of ICCs have been linked to GI motor dysfunction in humans such as in Hirschsprung disease, pyloric stenosis, chronic constipation, and pseudo-obstruction.[15,16] In a partial obstruction model, ICC networks were disrupted orad to the obstruction, resulting in loss of slow-wave activity.[17] Although several etiologies have been suggested, a reduction of ICCs has been found in horses with equine dysautonomia (grass sickness) and may contribute to the intestinal dymotility seen with that disease.[18-20] The extent to which abnormal function of ICCs contributes to other equine GI motility disturbances is not known.

Figure 4-3

Interstitial Cells of Cajal are Relays for Transmission from Entric Motor Neurons to Gastrointestinal Musculature



- Excitatory and inhibitory neurotransmitters spread diffusely from axonal varicosities to the interstital cell networks.

Interstitial cells of Cajal are relays for transmission from enteric motor neurons to the gastrointestinal musculature. (Used with permission of the AGA Undergraduate Teaching Project, Unit 36, Neurogastroenterology and Motility, Slide 15).

Myoelectrical Patterns of Activity

Slow waves do not by themselves depolarize the membrane sufficiently to initiate an action potential. Additional depolarizing (excitatory) input from humoral and/or neural sources allows the membrane to reach the threshold potential necessary to generate an action potential. This depolarization results in electrical response activity or spiking activity and is associated with contractions. The stomach and small intestine cycle through three (or four) different phases of contractile activity in the fasted (interdigestive) state. Phase I, a period of quiescence or no spiking activity (NSA), is defined as the period in which less than 5% of the slow waves (pacesetter potentials) are associated with action potentials. Phase II, a period of intermittent spiking activity (ISA), is defined as the period in which action potentials and contractions are associated with between 5% and 95% of the slow waves. Phase III, a period of regular spiking activity (RSA), is defined as the period in which action potentials and contractions are associated with 95% to 100% of slow waves (Figure 4-4). A phase IV, a short period in which action potentials and contractions subside to the quiescence of phase I, the start of the next cycle, is described by some authors. This motor pattern, which involves rhythmic activity of the enteric nervous system, is called the “migrating myoelectrical complex” (MMC) (Figure 4-4).[7,21,22]

The interdigestive motility pattern usually begins in the stomach antrum as a series of contractions, migrates through the pylorus, and travels down the small intestine to the cecum.

Figure 4-4A

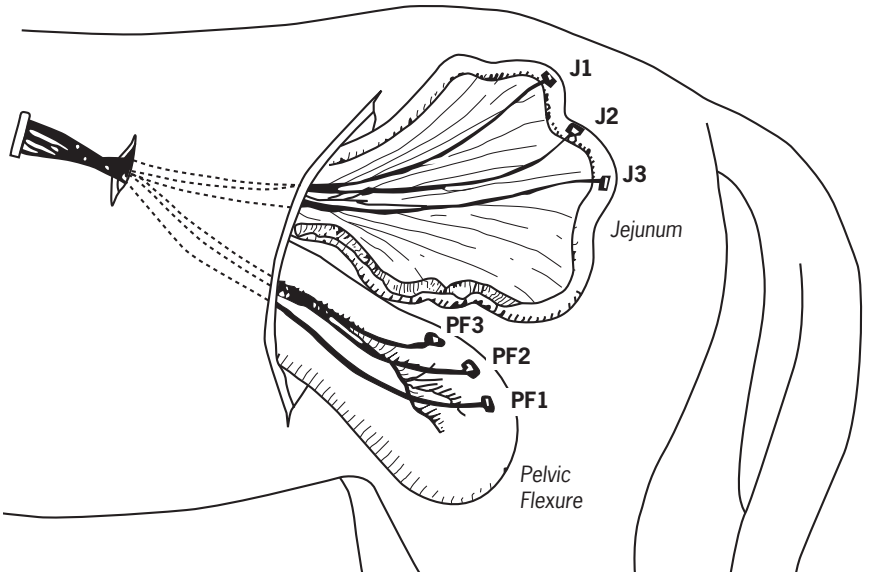
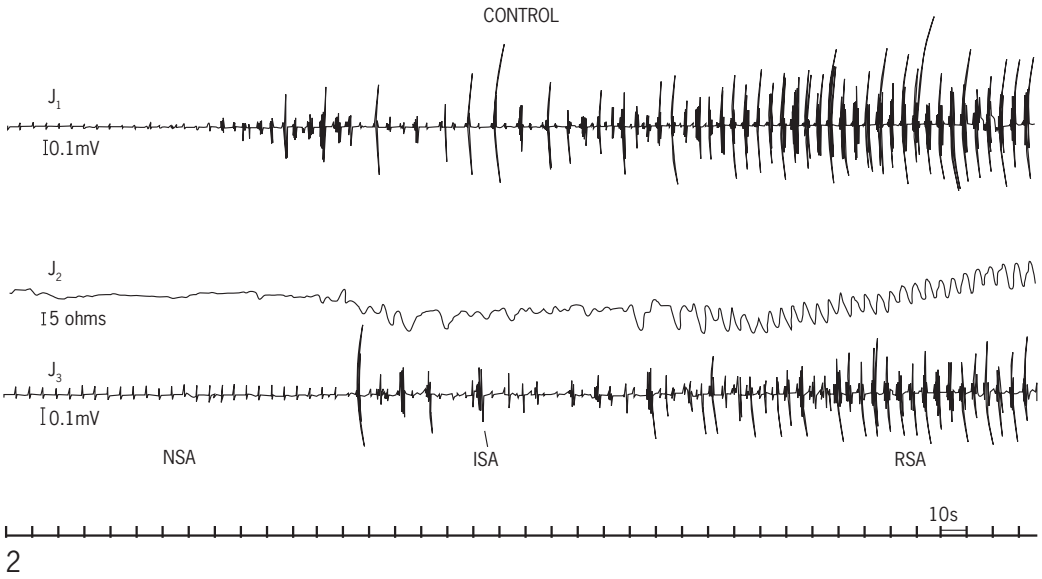


Figure 4-4B



A.) Bipolar electrodes positioned in the jejunum and pelvic flexure. J-jejunum; PF-pelvic flexure. **B.)** Physiograph tracing of myoelectrical (J1 and J3) and mechanical (J2) activity of the jejunum. NAS-No spiking activity; ISA-intermittent spiking activity; RSA-regular spiking activity. (Reprinted with permission. Am J Vet Res 45:795-799, 1984.)

The activity front has been described by various authors to include either phase III by itself or phases II and III.[23-25] It is during the activity front that coordinated contractions propel luminal contents aborally. In the horse, propulsion of ingesta has been described as occurring during phase II and phase III.[26,27] The activity front of the MMC traveling aborally is not a peristaltic wave. Peristaltic waves occur within the activity fronts of the MMC at the frequency of the slow waves, the pacesetter potentials. Each peristaltic wave begins orally within the activity front and migrates aborally, ending within the activity front. Some peristaltic waves end before they reach the aboral end of the activity front. Consequently, the recording of electrical and mechanical activity at the leading edge of the activity front first registers what is defined as phase II activity, where contractions are not seen to occur regularly with each slow wave. As the activity front migrates further aborally, a higher proportion of the peristaltic waves travels past the recording electrodes and strain gauges, now within the center of the activity front, until most or all the slow waves have associated contractions, which is defined as phase III.[25] In general, each successive peristaltic wave begins aboral to where the previous one began and ends aboral to where the previous one ended. In this way, both the activity front of the MMC and the peristaltic waves migrate down the intestinal tract. Propagation of the MMC aborally is coordinated primarily by the enteric nervous system.[5] The apparent functions of the MMC are to clear indigestible particles during the fasting state and to prevent bacterial overgrowth. Because of these functions, it has also been described as the "intestinal housekeeper."[22,25] In the fed state, the rhythmic pattern of the MMC is replaced with irregular spiking activity. Cholecystokinin and gastrin released in response to nutrients in the GI tract have been suggested as mediators of this change in myoelectrical activity from fasted to fed state.[28,29]

A temporal association exists between the appearance of the MMC and plasma motilin concentrations.[30] Exogenously administered motilin induces premature gastric and duodenal activity fronts.[31] This suggests that motilin plays a role in the initiation of MMCs. This finding has stimulated attempts to develop pharmaceutical agents that act as motilin receptor agonists to initiate premature MMCs. Because the first part of the MMC that is recognizable is the activity front, premature MMCs are theoretically associated with a return of propulsive contractile activity. As demonstrated in this example, the MMC is commonly used as a measurement to study gastrointestinal motility (Figure 4-4). In general, events that interrupt or decrease the duration of the activity front (measured as phase II and/or phase III) are considered as contributing to motility disturbances, whereas events that induce premature activity fronts or increase the duration of activity fronts are considered to contribute to restoration of progressive motility patterns. The reported mean duration of the MMC in the horse is 65.5 to 150.0 minutes.[32-34]

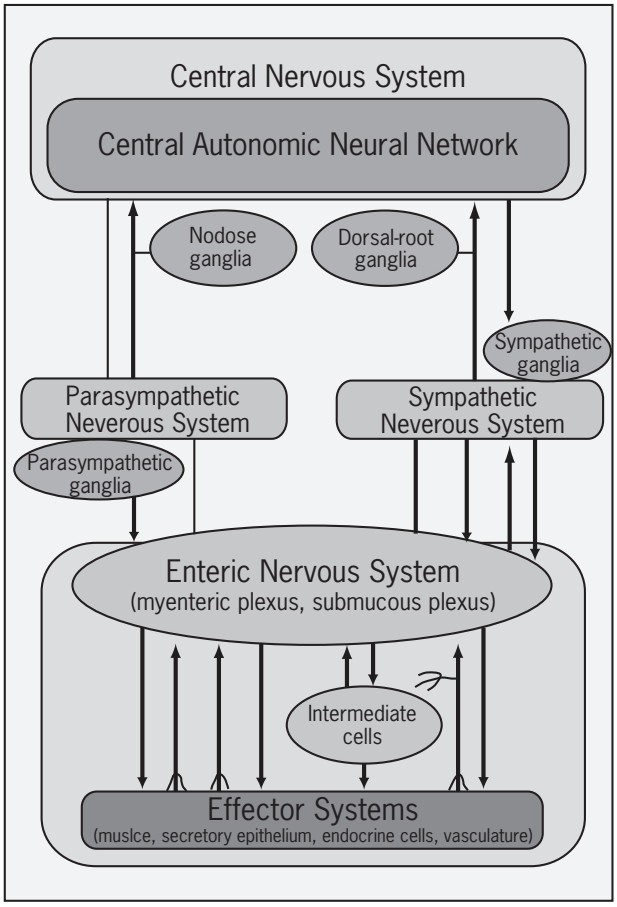
The major myoelectrical activity patterns of the equine large intestine are described as short spike bursts (SSBs) and long spike bursts (LSBs).[23,35,36] Short spike bursts, by definition, last 5 seconds or less. They are stationary and associated with segmental mixing. Long spike bursts last 10 to 20 seconds. They appear to be stronger contractions, may occur at sequential areas along the large intestine, and are associated with either retropulsion or propulsion. Several additional patterns have been described in the horse: a slowly migrating cluster of short and long spike bursts (SMC) which last 4 to 8 minutes and move aborad; and a series of high amplitude, propagated spike bursts called the colonic migrating myoelectric complex (CMMC).[27,37] Studies of the ileo-ceco-colonic area have shown multiple contractile patterns serving different functions. In the cecum, several patterns of spike bursts were seen that directed ingesta between the cranial or caudal cecal base to the apex and back. These could be described as mixing patterns. A progressive pattern was identified, which began at the cecal apex and was conducted through the cecal base and cecocolic orifice and into the right ventral colon. This appears to be coordinated with ileal contractions and continues in the colon as the CMMC.[38,39] Retropulsive and propulsive spike bursts were detected in the right ventral colon. Retropulsion is thought to prolong retention of ingesta in the cecum and colon, and so facilitate hindgut fermentation. A pacemaker in the region of the pelvic flexure is thought to coordinate retropulsion and propulsion originating at the pelvic flexure area.[40] The retropulsive spike bursts seen in the ventral colon may have originated at the pelvic flexure pacemaker. Pacemakers may also be located in the horse in the RVC and the cecal apex.[38]

Enteric Nervous System

The next level of control is the enteric nervous system (ENS) (Figure 4-5). The ENS has been described as the third division of the autonomic nervous system, with the parasympathetic and sympathetic being the other two divisions. The cell bodies of neurons in the ENS are located within the walls of the GI tract either in the myenteric or submucosal ganglia. The most basic reflex circuits consist of an intrinsic primary sensory afferent neuron, which projects circumferentially, synapsing directly on myenteric motor neurons, which in turn, synapse on muscle cells; or an intrinsic primary sensory afferent neuron that synapses on myenteric interneurons, which project orally or aborally, relaying the afferent input to myenteric motor neurons in other parts of the GI tract (Figure 4-6).[41] The enteric neurons can be classified based on electrical activity (synaptic input and after potentials).[42] S-neurons are neurons that have fast excitatory synaptic potentials (EPSPs) and short after-hyperpolarizations (AHPs). AH-neurons are neurons that do not show fast EPSPs but have prolonged AHPs. Another common classification scheme is based on morphology. Dogiel type I neurons are unipolar, whereas Dogiel type II neurons are multipolar. S-neurons are unipolar, and so classified as Dogiel type I. These have been shown to be motor neurons or interneurons (Figure 4-6). AH-neurons are multipolar and so classified as Dogiel type II.[43] Intrinsic primary afferent neurons and enteric interneurons are AH/Dolgiel type II neurons.

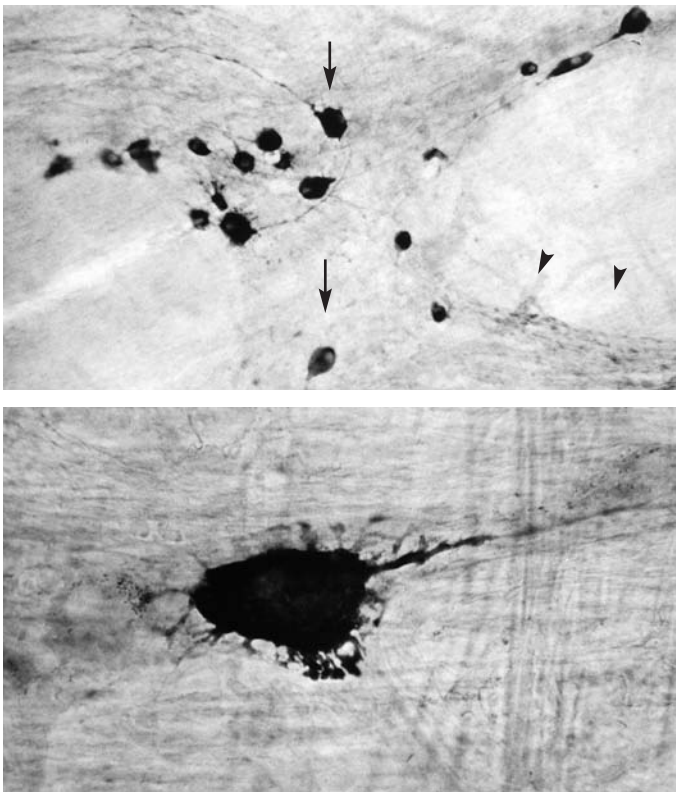
The circuitry of the ENS is responsible for many coordinated motility patterns of the GI tract. Peristaltic reflexes and other complex motor activity can occur without any extrinsic neural input (Figure 4-7). Many years ago, an enteric reflex initiated by introducing a bolus into the small intestine after severing all extrinsic neural connections was shown to be mediated by an ascending excitation (contraction of the circular muscle) and descending inhibition (relaxation of the circular muscle) with movement of the bolus aborally.[44] More recent work using intracellular recordings of circular smooth muscle indicate that distention produces ascending excitation by depolarization, called excitatory junction potentials (EJPs), of orally positioned circular muscle cells, and a descending inhibition by hyperpolarization, called inhibitory junction potentials (IJPs), of the aborally positioned circular muscle cells.[41,45,46] Mechanical stimulation of the mucosa, distention (or stretch) and chemical irritants have all been shown to stimulate this peristaltic motor pattern which is under control of the enteric nervous system (Figure 4-7). Many more complex motor patterns mediated by the enteric circuitry exist, but they are beyond the scope of this chapter.

Figure 4-5



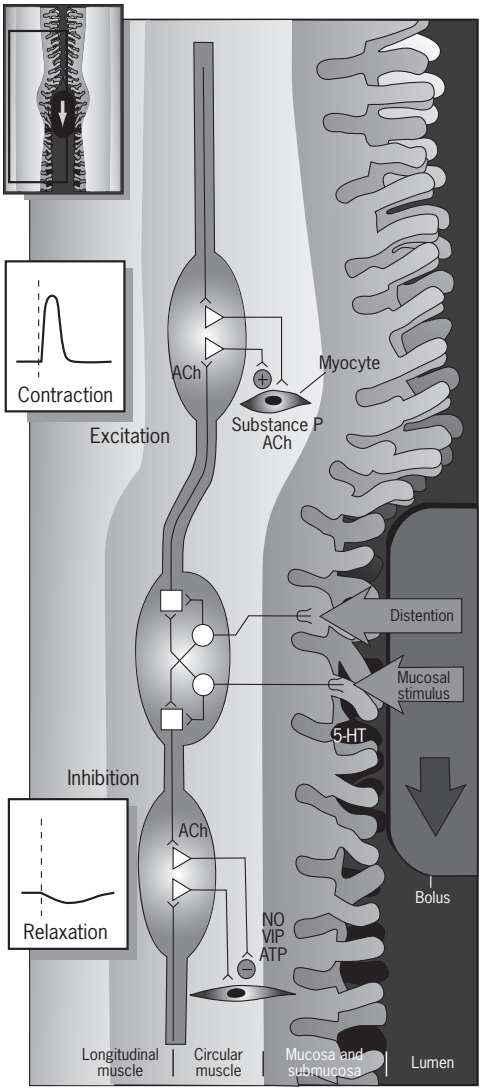
Innervation of the gastrointestinal tract. The neural plexuses in the gut represent an independently functioning network known as the enteric nervous system, which is connected to the central autonomic neural network in the central nervous system by the parasympathetic and sympathetic nerves. The enteric nervous system may influence either the effector systems in the gut directly or may do so indirectly through its action on the intermediate cells, which include the endocrine cells, the interstitial cells of Cajal, and the cells of the immune system, such as mast cells. The cell bodies of the primary vagal and primary splanchnic afferent neurons are located in the nodose ganglia and dorsal-root ganglia, respectively; each carries distinct information from the gut to the central nervous system (Reprinted with permission. N Engl J Med 334:1106-1115, 1996.)

Figure 4-6



Photomicrograph illustrating histochemistry of NADPH diaphorase (NADPH-d) activity in whole mount preparations indicating nitric oxide (NO) synthase-containing neurons in the myenteric plexuse. Top) Positively reactive cell bodies (arrows) and interganglionic fibers (arrowheads) can be identified. Bottom) Dogiel type-1 morphology in positively-reactive neuron. Notice the numerous short dendritic processes and single axonal process. (Reprinted with permission. Am J Vet Res 57:1208,1996.)

Figure 4-7



Intestinal peristaltic reflex. Peristalsis is the result of a series of local reflexes, each consisting of a contraction of intestinal muscle above an intraluminal stimulus and a relaxation of muscle below the stimulus (inset, upper-left-hand corner). The release of 5-HT by mucosal stimulation or mechanical distention of the gut lumen (main panel) triggers activity in the intrinsic afferent neurons (circles). Above the site of the stimulus, ascending cholinergic interneurons (squares) relay this signal to excitatory motor neurons (arrow heads) containing acetylcholine (Ach) and substance P. As a result, the circular muscle above the stimulus contracts. At the same time, below the stimulus site, descending cholinergic interneurons activate inhibitory motor neurons that contain nitric oxide (NO), vasoactive intestinal polypeptide (VIP), and ATP, causing relaxation. The resultant forces propel the bolus in an antegrade direction. As the bolus moves it triggers similar peristaltic reflexes at successive sites along the gut. (Reprinted with permission. N Engl J Med 334:1106-1115, 1996.)

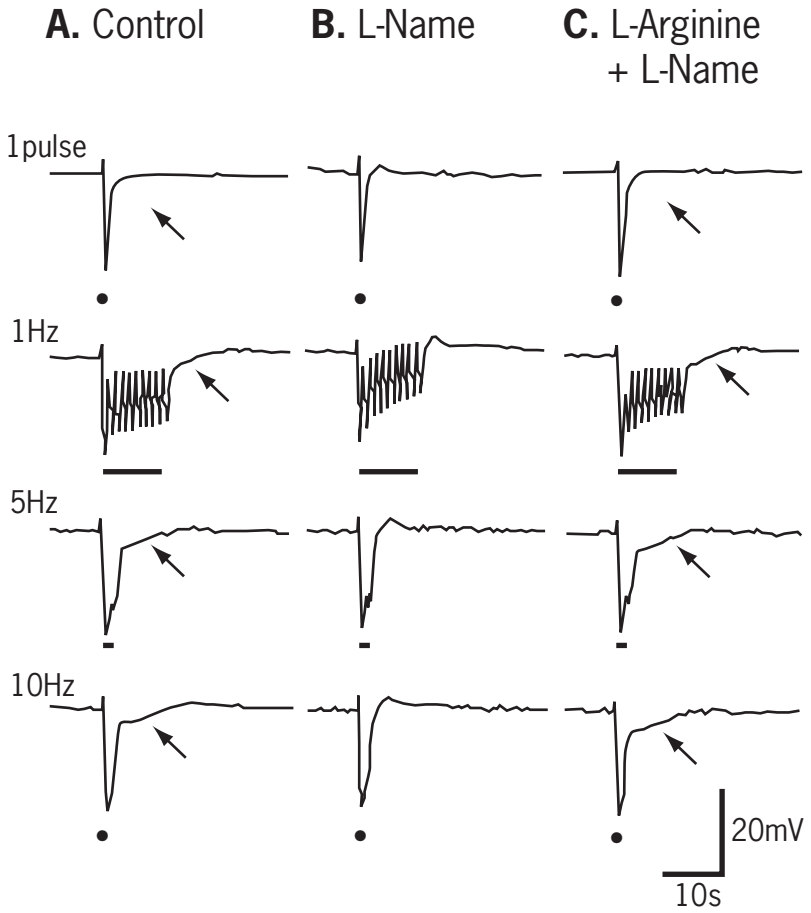
Neurons are also classified chemically, depending on the type of neurotranmitter(s) they contain. The primary neurotransmitters in the intrinsic primary afferent neurons are acetylcholine (Ach), substance P (SP), which is a member of the tachykinin family of neuropeptides, and calcitonin gene-related peptide (cGRP).[41,47] Mucosal stimulation by ingesta stimulates release of 5-hydroxytryptamine (5-HT) from enterochromaffin cells (Figure 4-6).[48] This, in turn, activates 5-HT_4 receptors on intrinsic afferents, which then synpase on ascending and descending interneurons. The primary neurotransmitter released by enteric ascending interneurons appears to be acetylcholine acting through nicotinic receptors, although ascending interneurons are also positive for SP, enkephalins (ENK), and calretinin immunostaining. The neurotransmitters released by enteric descending interneurons are acetylcholine as well as vasoactive intestinal peptide (VIP), nitric oxide (NO), somatostatin (SOM), and 5-hydroxytryptamine (5-HT, serotonin). Enteric inhibitory motor neurons release NO, VIP, and ATP at the neuromuscular junction (Figure 4-6). These are responsible for the IJPs in the aboral muscle mediating descending relaxation of the bowel during a peristaltic wave (Figures 4-2A and 4-8).[48] Other neurotransmitters found in enteric inhibitory motor neurons are neuropeptide Y (NPY), γ-aminobutyric acid (GABA), gastrin-releasing peptide (GRP), and pituitary-cyclase-activating peptide (PACAP).[41,49] The primary excitatory neurotransmitters in enteric excitatory motor neurons are acetylcholine (ACh) and substance P (SP), and possibly other members of the tachykinin family such as neurokinin A. At the neuromuscular junction, acetylcholine acts at muscarinic receptors on the enteric smooth muscle. ACh and SP are responsible for the EJPs in the muscle mediating ascending contraction during the peristaltic reflex (Figure 4-6). It should be noted that the majority of enteric neurotransmitters are neither adrenergic nor cholinergic. It is common in the literature to see the term nonadrenergic-noncholinergic (NANC) used to describe this type of neurotransmission. Neuropeptides and NO are NANC neurotransmitters.

Although species variations are likely, ample evidence exists that many of the above-described substances function as neurotransmitters in the horse. Experimental evidence supports the role of SP as an important excitatory neurotransmitter in the equine GI tract. Substance P-like immunostaining has been identified in the enteric ganglia and circular muscle in many

regions of the equine GI tract.[50-54] In vitro mechanical studies indicate that SP (as well as serotonin) increases contractile activity of the circular and, to a lesser degree, longitudinal muscle of the equine jejunum and colon.[52,55,56] In vivo mechanical studies have shown that SP increases contractile activity of the pelvic flexure.[51] In the horse, neurokinin-1 receptors have been shown to be the predominant subtype of tachykinin receptor in the smooth muscle of the pelvic flexure.[57] Co-localization of SP immunostaining and choline acetyl-transferase (ChAT) immunostaining in the equine myenteric plexus and circular muscle suggests SP and Ach can be released from the same neuron.[52] This relationship is likely important in their role mediating ascending contraction.

NANC inhibitory neurotransmitters have also been identified in the equine ENS. Several studies support a role for NO as an important inhibitory neurotransmitter in the equine intestine. Neurons with a Dogiel type-1 morphology that stain positive for NADPH-diaphorase, a marker for nitric oxide synthase (NOS), have been identified in the myentric plexus and circular muscle of the equine jejunum (Figure 4-6).[56] Intracellular recordings have shown that NO is responsible for a portion of the IJPs in the circular muscle of the equine jejunum (Figure 4-8).[58] Another portion of the IJP is blocked by apamin, a drug that may work by blocking ATP.[58] In vitro mechanical studies have shown marked inhibition of equine jejunal and colonic circular muscle contractile activity with NO donors and reduction of inhibition with NOS antagonists.[56-59] VIP-like immunostaining has also been demonstrated in the enteric ganglia and circular muscle throughout in the equine intestinal tract.[50,56] VIP has been shown to decrease in vitro contractile activity of the equine circular muscle.[56] These results suggest that NO, VIP, and ATP mediate inhibitory neurotransmission in the equine ENS as occurs in other species.

Figure 4-8



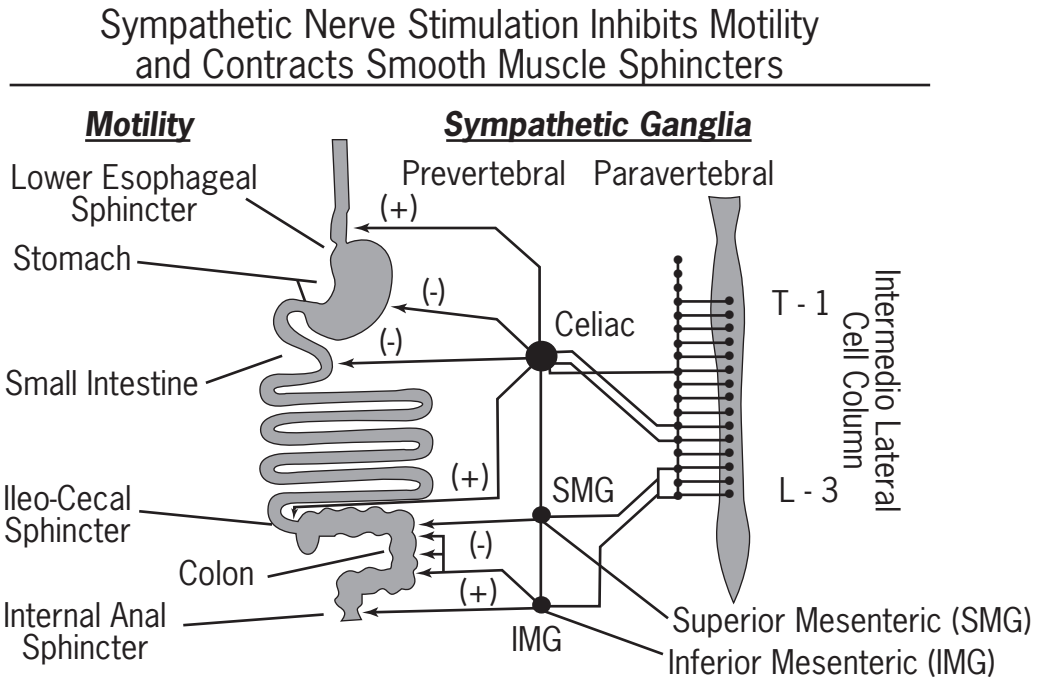
Intracellular microelectrode recording of membrane potentials in jejunal circular muscle in horses during electrical field stimulation (EFS) in absence of N-nitro-L-arginine methyl ester (L-NAME) a NOS blocker, or L-NAME and L-arginine. All panels are excerpts from a continuous recording from a single muscle cell, illustrating membrane potential changes resulting from stimulation of intrinsic (indicated by circles or bars). Left panels **A.)** illustrate control responses to a single pulse and trains of stimuli delivered at 1 to 10 Hz. The slow component of the IJP is indicated by arrows. Middle panels **B.)** illustrate responses of cells after 20-minute exposure to L-NAME (200 mM). Notice that treatment with L-NAME did not have a significant effect on IJP amplitude but blocked the slow component of the IJP. Right panel **C.)** illustrates response in presence of the nitric oxide synthase substrate L-arginine in the continued presence of L-NAME. In all tracing the upward deflections at onset of stimulus are stimulus artifacts (arrowheads at top). (Reprinted with permission. Am J Vet Res 61:364, 2000.)

Extrinsic Nervous System

Extrinsic Efferent Nerves

The next level of control is through extrinsic neural input from the sympathetic and parasympathetic divisions of the autonomic nervous system. The sympathetic division originates from thoracic and lumbar spinal cord segments T-1 through L-2 (Figure 4-9). The preganglionic efferent neuron, with the cell body located within the intermediolateral horn of the spinal cord, exits the spinal cord in the ventral roots, travels through the sympathetic chain, and synapses with postganglionic neurons in one of the prevertebral ganglia (celiac, superior, or inferior mesenteric ganglia).[60] Acetylcholine is released and acts at nicotinic receptors on the postgangionic neuron. The postganglionic neuron travels to the GI tract and synapses with enteric neurons, releasing norepinephrine that acts at presynaptic alpha$_2$ adrenoceptors (Figure 4-10). The effect is to inhibit the release of excitatory neurotransmitters such as acetylcholine at enteric synapses. In general, sympathetic stimulation depresses motility.

Figure 4-9

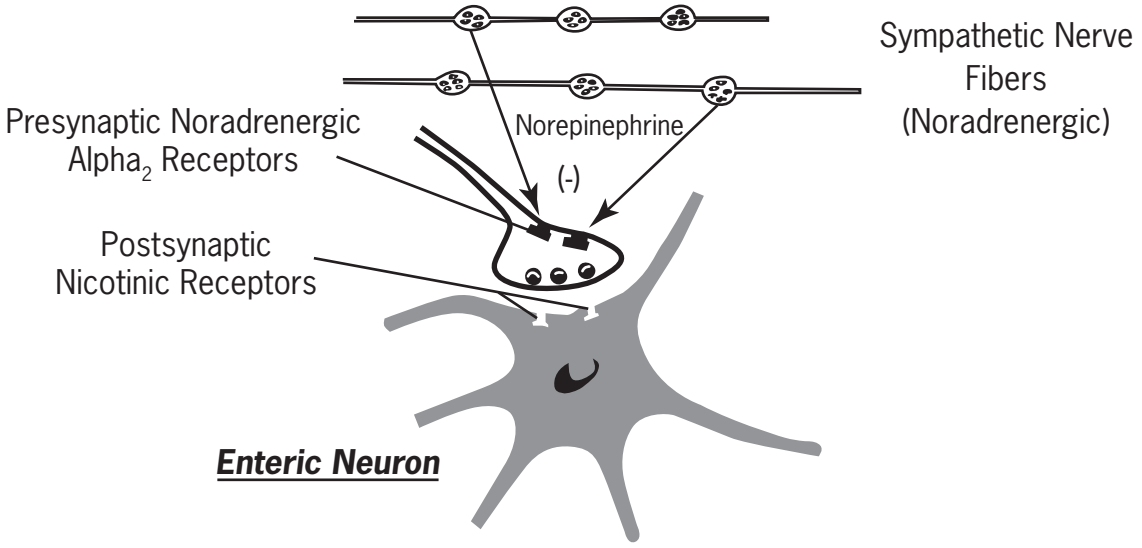


The sympathetic division of the autonomic innervation to the gut is positioned in the thoracic and lumbar regions of the spinal cord. Efferent sympathetic fibers leave the spinal cord in the ventral roots to make their first synaptic connections with the neurons in the prevertebral sympathetic ganglia located in the abdomen. The prevertebral ganglia are the coeliac, the superior mesenteric and the inferior mesenteric ganglia. Cell bodies in the prevertebral ganglia project to the digestive tract where they synapse with neurons of the enteric nervous system in addition to innervating the blood vessels, mucosa and specialized regions of the musculature. (Used with permission of the AGA Undergraduate Teaching Project, Unit 36, Neurogastroenterology and Motility, Slide 99).

The parasympathetic system is divided into the cranial and sacral divisions (Figure 4-11).[60] The cranial division supplies innervation from the esophagus to the proximal colon primarily by fibers traveling in the vagus nerve. The pelvic nerve supplies innervation to the distal colon and rectal and anal regions. The parasympathetic system is composed of preganglionic fibers the cell bodies of which are in the brainstem or posteriolateral parts of the anterior columns of the spinal cord for the cranial and sacral divisions, respectively. The preganglionic fibers synapse on postganglionic neurons the cell bodies of which are contained within the enteric ganglia in the wall of the GI tract. Presynaptic fibers release acetylcholine which acts on nicotinic receptors on postganglionic neurons. The postganglionic neurons are part of the enteric nervous system as the cell bodies are within the intestinal wall. The postganglionic neurons are either enteric cholinergic excitatory fibers or NANC excitatory or inhibitory enteric neurons described previously. Because most extrinsic efferent nerves, both sympathetic and parasympathetic, act by mediating motility synapse within the enteric ganglia and not on the enteric muscle, the extrinsic neural input in general acts not by direct stimulation of muscle but through modifying and coordinating enteric neural activity.

Figure 4-10

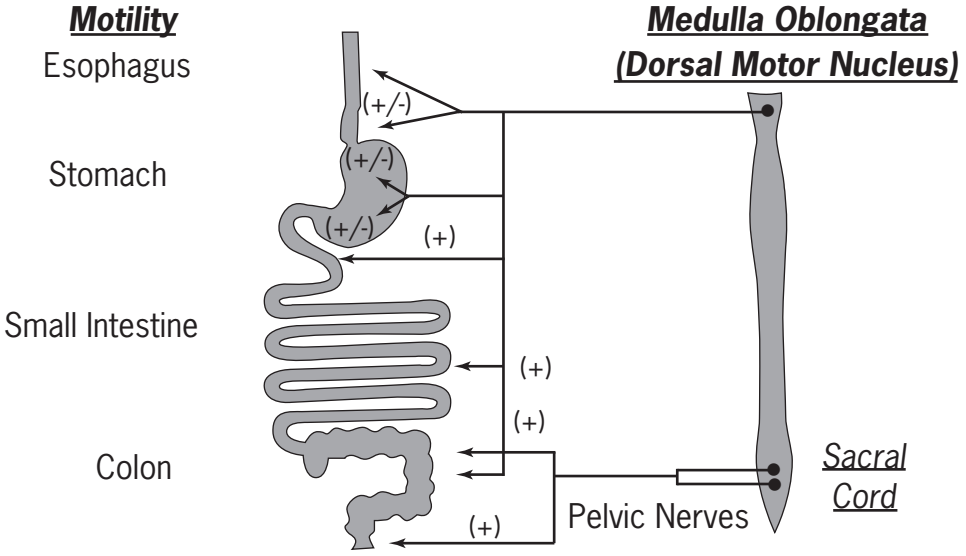
Norepinephrine Released from Sympathetic Nerves Acts by Presynaptic Inhibition to Inactivate the Enteric Neural Circuits



Norepinephrine released from sympathetic nerves acts by presynaptic inhibition to inactivate the enteric neural circuits. The synaptic interface between the postganglionic fibers of the sympathetic nervous system and the enteric nervous system is a presynaptic alpha$_2$ adrenoceptor. Norepinephrine released from sympathetic fibers suppress the release of excitatory neurotransmitters at both enteric synapses and neur-effector junctions.(Used with permission of the AGA Undergraduate Teaching Project, Unit 36, Neurogastroenterology and Motility, Slide 100).

Figure 4-11

Signals Transmitted to the Enteric Nervous System by Vagal and Pelvic Nerves may Result in Contraction or Relaxation of Digestive Musculature



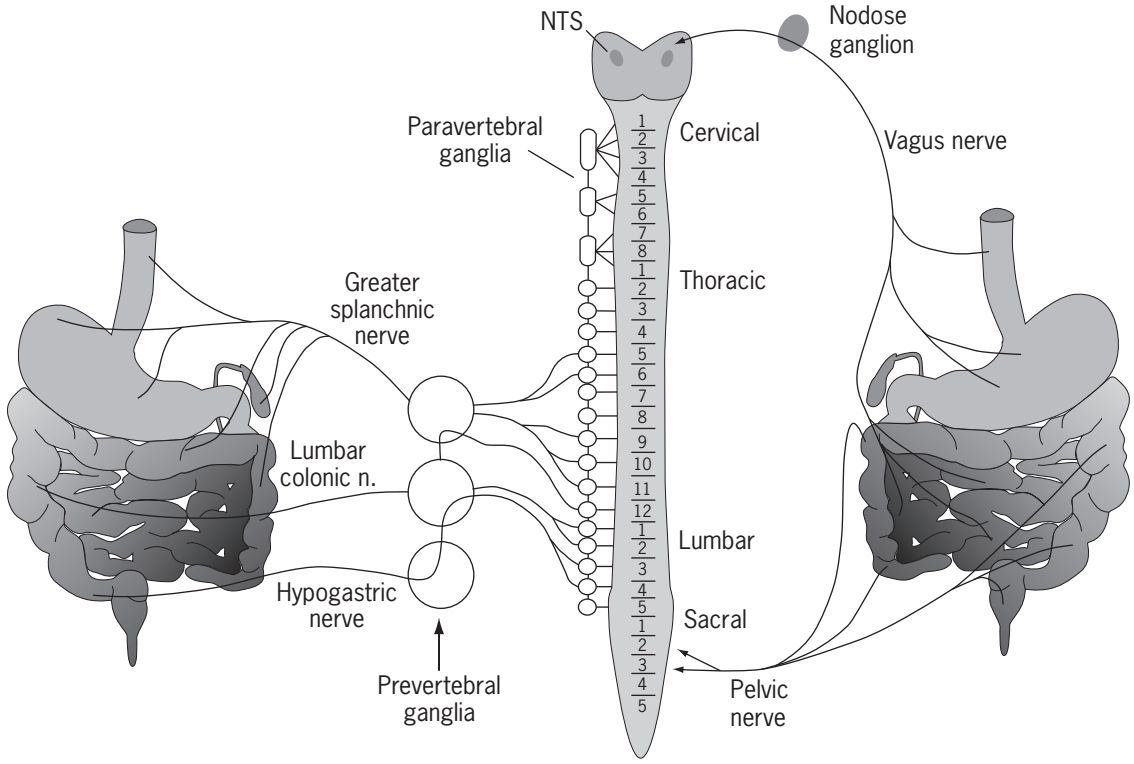
- Parasympathetic innervation of small and large intestinal musculature is predominantly excitatory.

The parasympathetic division of the autonomic innervation is subdivided anatomically into the cranial and sacral divisions. This is due to the location in the brain and spinal cord of neurons that send nerve fibers to the gastrointestinal tract. Fibers running from the central nervous system to the gastrointestinal tract are efferent fibers. The cranial division has neuronal cell bodies in the medulla oblongata of the brain, whereas the sacral division has its cell bodies located in the sacral region of the spinal cord. Axons from cell bodies located in the medulla project in the right and left vagal nerves to the digestive tract. Axons from cell bodies in the sacral region of the spinal cord project to the large intestine in the pelvic nerves. (Used with permission of the AGA Undergraduate Teaching Project, Unit 36, Neurogastroenterology and Motility, Slide 103).

Extrinsic Afferent (Sensory) Nerves

Subpopulations of afferent nerves have specialized receptors that are responsive to stimuli such as stretch, tension, or movement (mechanoreceptors); nutrients, osmolarity, and pH (chemoreceptors); luminal temperature (thermoreceptors); and pain (nociceptors), located in the wall of the GI tract. Cholecystokinin (CCK), 5-HT, noradrenaline, opioids, bradykinin, purines, and prostaglandins are local mediators that may activate these receptors.[61] As previously described, one population of afferent neurons, the intrinsic primary afferent neuron, synapses either on enteric motor or enteric interneurons (Figure 4-7). Besides these intrinsic afferents, there are two extrinsic pathways containing primary afferent neurons (Figures 4-5 and 4-12). One pathway has sensory fibers running in the vagus or pelvic nerve and cell bodies in the nodose ganglia. These have been called parasympathetic afferent nerves. The other pathway, spinal sensory afferents, have fibers running in the splanchnic or mesenteric nerves and cell bodies in the dorsal root ganglia. These have been called the sympathetic afferent nerves.[62] These fibers pass through the prevertebral ganglia and may send axon collaterals to synapse with sympathetic postganglionic neurons, establishing a reflex circuit at the level of the prevertebral ganglia. There are also sensory nerves (intestinofugal) with cell bodies in the myenteric ganglia whose fibers project with spinal afferents to the prevertebral ganglia, and sensory nerves with cell bodies in enteric ganglia of gastric and esophageal myenteric plexus (viscerofugal) whose fibers project in the vagal trunks to the CNS.[61] The extrinsic afferent neurons contain SP, cGRP, neurokinin A (NKA), and other peptides that are used as neurotransmitters.[62-64]

Figure 4-12



Represenation of sensory innervation of the GI tract. Left: visceral afferent pathways through prevertebral and paravertebral ganglia to the spinal cord; cell bodies are located in dorsal root ganglia (not illustrated). Right: vagal and pelvic nerve afferent input through nodose and dorsal root ganglia, respectively. The innervation of the viscera as illustrated is overlapping with spinal inputs to specific, but anatomically separated, spinal segments. For example, the distal colon is represented in the thoracolumbar and lumbosacral spinal segments by the least splanchnic and pelvic nerve inputs. Gastric input to the CNS is represented in the brainstem and thoracic spinal cord by vagal and splanchnic inputs. (Reprinted with permission. Current Opinion in Pharm 2:642-649, 2002.)

The function of these extrinsic sensory neurons in modulating both normal and abnormal motility patterns has been elucidated with the use of capsaicin, a sensory neurotoxin that causes functional impairment of a population of sensory nerves. Systemic administration of capsaicin causes a depletion of neurotransmitters of the sensory unmyelinated C-fibers, and perineural application of high concentrations of capsaicin has the same effect on specific peripheral nerve fibers.[65] It should be noted that perineural application of low concentrations of capsaicin causes a transient acute stimulation as neuropeptides are released. The extrinsic afferent neurons do not appear to significantly influence basal GI motor activity, but appear to mediate a number of inhibitory motor reflexes, such as inhibition of gastric emptying in response to duodenal distention or duodenal luminal contents.[66, 67] The importance of these two extrinsic sensory pathways in controlling motility is illustrated by the following study. Distention of the duodenum produces a reflex inhibition of gastric activity. Capsaicin applied to the cervical vagal trunk decreases gastric inhibition in response to low volumes of duodenal distention, but not to high volumes.

However, capsaicin applied to the celiac-superior mesenteric ganglia with ablation of spinal sensory afferents attenuates the inhibitory response to all volumes of distention.[67] The low-volume reflex may function as a normal physiologic response, coordinating the gastroduodenal motor activity involved in gastric emptying after eating through vagal afferents. The recruitment of high-threshold mechanoreceptor endings with afferent fibers in splanchnic nerves may be important in mediating reflex inhibition of gastric emptying associated with ileus in response to potentially harmful levels of distention.[67] These spinal and vagal afferents are also important in mediating sensations of fullness, satiety, nausea, and vomiting.[61] The role of the extrinsic primary neurons is discussed further under pathologic mechanisms.

Other Mediators of Motility

Opioids

Endogenous opioid peptides met-enkephalin (Met5), leu-enkephalin (Leu5), and dynorphin are present in ganglion cells of the myenteric and submucosal ganglia and in axon varicosities in both muscle layers in the small and large intestine in laboratory animals and humans.[68,69] Endogenous opioids have been shown to be modulators of GI motility. Endogenous release of opioid peptides in the canine circular muscle layer suppresses or inhibits the release of inhibitory neurotransmitters and, thereby, increases contractile activity.[70] Opioid peptides may act on prejunctional delta(δ)-opioid receptors to produce inhibition of NANC inhibitory neuromuscular transmission with a reduction in the amplitudes of the IJPs.[70,71] During the peristaltic reflex, the release of endogenous opioid peptides is decreased during the inhibitory phase and increased during the excitatory phase.[48,72] In this way, normal levels of endogenous opioids may facilitate the ascending contraction and descending relaxation. Addition of increased levels of endogenous opioid peptides or selective opioid receptor agonists decreases the velocity of pellet movement by inhibiting release of inhibitory neurotransmitters.[73] Addition of a δ-receptor antagonist increases the velocity of propulsion and has been shown to act synergistically with 5-HT. Serotonin (5-HT) acts on 5-HT_4 receptors on sensory cGRP nerve terminals, which then trigger the ascending and descending phases of the peristaltic reflex.[48,73] The opioid δ-receptor antagonist augments the peristaltic response by increasing the release of inhibitory neurotransmitters in the descending relaxation. Opioids may also act to inhibit neuronal release of excitatory neurotransmitters.[74,75]

Contrary to the importance of endogenous opioids in facilitating peristaltic activity, exogenous opioids have been shown to induce nonpropulsive contractions. The three major classes of opioid receptors, mu(μ), kappa(κ), and delta(δ) are each divided further into subtypes.[76] Morphine's activation of μ_1 receptors in the brain and μ_2 receptors in the spinal cord is responsible for its analgesic effects, whereas the decrease in gastrointestinal transit seen with systemic morphine administration is mediated primarily through μ_2 receptors located both centrally within the brain and peripherally in the myenteric nerve plexus.[76] Although central and local opioid receptors may both contribute to post-operative ileus (POI), it is likely that gastrointestinal receptors are the most important in mediating GI dysmotility.[77] Intramuscular morphine acting at peripheral receptors has been shown to enhance the delay of gastric emptying caused by intrathecal morphine. Systemic administration of morphine has been shown to induce colonic electrical response activity (ERA), causing nonpropulsive spike bursts that interrupt normal migrating myoelectrical colonic complexes.[78]

Several strategies have been developed to achieve analgesia with opioid use while circumventing the motility disturbances attributed to μ-receptor agonists. Kappa opioid agonists have been identified that may provide sufficient visceral analgesia without the unwanted motility disruption of μ agonists.[79] An alternative approach being studied in humans, which allows for the continued use of μ-receptor agonists for pain management, has been the oral administration of an opioid antagonist with poor GI absorption. The opioid antagonist blocks the GI actions of systemically administered opioids without interfering with the centrally mediated analgesic effects of the opioid.[80] GI function returned earlier in postoperative patients given the oral opioid antagonist. Although these methods show promise, opioid-sparing analgesia, where NSAIDs have been used to reduce the amount of opioids required for pain management in patients, has improved overall gastrointestinal motility in these patients and is one of the most effective ways to reduce POI in humans.[81]

Prostaglandins

Prostaglandins are synthesized throughout the gastrointestinal tract and exert a significant role in regulating gastrointestinal motility. The functional role of prostaglandins in modulating motility in the normal intestine has been studied in vitro and in vivo by recording changes in contractile activity after administration of prostaglandin synthesis inhibitors such as indomethacin, and then adding selective prostaglandins and monitoring their effect on contractile activity. Drawing conclusions concerning the role that prostaglandins have on motility is difficult because the effect of exogenous prostaglandins on motor activity varies, depending on the type of prostaglandin, the dose, and the target tissue in the GI tract.[82-86] For example, PGE_2 enhances in vitro contraction in longitudinal muscles but inhibits contraction in the circular muscle. PGI_2 usually inhibits circular muscle contractions, with variable effects on longitudinal muscle. $PGF_{2\alpha}$ increases contractile activity of both the circular and longitudinal muscles in small and large intestine in most species studied.[82,84,85,87,88]

Nonselective blockage of the cyclooxygenase enzymes in the dog ileum produces an increase in both spontaneous contractile activity and responsiveness of muscles to acetylcholine stimulation mediated through an increase in slow-wave amplitude.[84] In this model, both PGD_2 and $PGF_{2\alpha}$ were consistently shown to stimulate in vitro contractile activity of the ileal circular muscle. PGE_2 inhibited large contractions but stimulated small contractions. Prostacyclin (PGI_2) consistently inhibited contractile activity by reducing the amplitude of the slow waves and consequently reducing the ability of the muscle to respond to excitatory stimuli. The most common prostaglandin metabolite found in the muscularis externa throughout the gastrointestinal tract is 6-keto-$PGF_{1\alpha}$, the spontaneous breakdown product of PGI_2.[82] Because nonselective prostaglandin blockage enhanced contractile activity, this suggests that the dominant endogenous prostaglandin effect in the canine ileum is due to inhibitory prostaglandins, most likely PGI_2 and possibly PGE_2. In support of this, PGE_2 and PGI_2 infused into the superior mesenteric artery causes a dose-dependent inhibition of the MMC in the small intestine of dogs, whereas $PGF_{2\alpha}$ causes an increase in spiking activity[89] Blockage of all endogenous prostaglandins with indomethacin results in a marked increase in phase II and III of the MMC. The conclusion from these studies is that the net activity of the endogenous production of the prostaglandins appears to be a decrease in the excitability of the smooth-muscle membrane, resulting in inhibition of contractile activity. Other studies have contradictory findings. Prostaglandin-synthesis inhibitors have been shown to decrease peristalsis in both the guinea pig ileum and colon,[88] while in the rabbit, they have been shown to increase myoelectric activity in the ileum but decrease it in the colon.[83]

In vitro studies in the horse have been performed on the GI muscle from the large colon.[90,91] PGE_2 and $PGF_{2\alpha}$ enhanced contractile activity in the taenia coli and non-taenia coli longitudinal muscle while it decreased or had no effect on circular muscle activity. PGI_2 decreased contractile activity in the taenia coli and circular muscle while it had no effect on non-taenia coli longitudinal muscle. Of particular interest was the observation that in vitro application of anti-inflammatory drugs such as phenylbutazone, flunixin meglumine, ketoprofen, and carprofen significantly decreased contractile activity regardless of location or muscle orientation.[90,91] These results suggest that, in the equine large colon, the production of endogenous prostaglandins has a net excitatory effect on contractile activity. If this is true, nonselective blockade of prostaglandins may have an inhibitory effect on normal equine colonic motility. Anecdotal data suggest an association between use of NSAIDs and large colon or cecal impactions.[92] In vivo studies on normal horses, however, have not identified any motility disturbances, using myoelectric activity as a measurement of motility after administration of NSAIDs.[93-95] Compared with the significant inhibitory effect of prostaglandin blockade in vitro in colonic tissue, little if any effect is seen in vitro in small intestinal tissue. While not examining the activity of prostaglandins specifically, in vitro studies have failed to demonstrate any inhibition of contractile activity during nonselective blockade of prostaglandin production when indomethacin is added to tissue baths containing equine small intestine circular or longitudinal muscle.[56,58]

Pathophysiology of Ileus

Neurogenic

Numerous theories have been proposed to define factors that may contribute to ileus. The CNS, ENS, and humoral factors most likely all contribute to ileus to some extent. Surgical manipulation with activation of the sympathetic nervous system has long been recognized as one potential mechanism mediating POI. This may be explained by a neurogenic theory of ileus that states that a component of POI is mediated by mechanoceptor or nociceptor stimulation of extrinsic afferent neurons, which then activate either a peripheral or central inhibitory efferent neural pathway, decreasing GI progressive motility. One peripheral inhibitory reflex has been shown to be mediated by cGRP in spinal afferents acting at prevertebral ganglia. Immunoneutralization of cGRP, a neurotranmitter located in afferent intrinsic and extrinsic neurons, peripheral ganglia, and the CNS, partially reverses abdominal surgery-induced ileus.[64] It has been proposed that surgical manipulation may stimulate the release of cGRP which enhances nociception, possibly through potentiating SP release, with activation of the spinal afferent pathway with neurons synpasing on sympathetic postganglionic efferent nerves, resulting in reflex inhibition of motility.[64,96-98] This is supported by the finding that functional ablation of the spinal afferent pathway with capsaicin applied to the celiac/superior mesenteric ganglia partially reverses surgically induced ileus.[98]

Surgical manipulation of the intestine has also been shown to be associated with a transient increase in norepinephrine.[99,100] The increase in norepinephrine seen after abdominal surgery may be neurogenically mediated through afferent activation of the sympathetic postganglionic efferent nerves. In addition to the previously described peripheral extrinsic afferent pathway, supporting evidence also exists that a spinal afferent pathway activated by abdominal surgery sends sensory information for further processing to the CNS. Abdominal surgery and other stress-related events have been shown to neurally mediate the release of corticotropin-releasing factor (CRF) from the paraventricular nucleus of the hypothalamus and the dorsal vagal complex. The CRF functions as a central neurotransmitter that mediates the efferent limb of a gastrointestinal inhibitory reflex pathway, the afferent component being the spinal sensory afferents synapsing with ascending neurons in the spinal

cord.[101-103] It is possible that CRF may activate the sympathetic efferent pathways with release of norepinephrine that depresses gastrointestinal motility by presynpatic inhibition of acetylcholine release from cholinergic motor neurons.[99,101,103-106] In addition to activating sympathetic inhibitory pathways, CRF can also act centrally to inhibit vagally (parasympathetic) stimulated gastric motility.[107]

Based on the above-described neurogenic pathophysiology, therapies have attempted to block the efferent inhibitory pathways with sympatholytics, or to potentiate the efferent excitatory pathways with cholomimetic agents. These have met with limited success for several reasons. First, NANC inhibitory neurotransmitters, such as NO and VIP, are most likely involved in POI in addition to norepinephrine. Blocking sympathetic adrenergic pathways inhibits the ileus induced by laparotomy without bowel manipulation but only partially reverses more intense ileus induced by laparotomy and bowel manipulation.[108] Adding a NOS inhibitor completely reverses the additional inhibition induced by mechanical stimulation of bowel. The increased release of NO in response to manipulation is likely produced by constitutive NOS and NO released from enteric neurons through an inhibitory vagal neural pathway and not produced by inducible NOS as discussed later in the inflammatory model.[108] VIP has also been shown to contribute to inhibition of motility induced by manipulation.[109] Because NO and VIP have been shown to be important inhibitory neurotransmitters in the GI tract of many species, the poor results in clinical patients with therapies focused on pharmacologic manipulation of the adrenergic and cholinergic pathways might be explained by failure to block this additional inhibitory NANC reflex mediated by NO and/or VIP.[109,110] Unfortunately, pharmacologically decreasing inhibitory neural input and expecting a progressive motility pattern to return is too simplistic when dealing with the required coordination of excitatory and inhibitory activity necessary for aboral propulsion of ingesta. The complexity of interactions is illustrated by the fact that simultaneous blockade of both NO and VIP abolishes the beneficial effect of individual blockade of NO or VIP.[109] This suggests that the inhibitory effect of one of the neurotransmitters is required to maintain the descending relaxation required for propulsion.

Inflammatory

The neurogenic theory appears to explain the acute phase of ileus seen after surgery. A large body of evidence has accumulated to suggest that more prolonged motility disorders, such as POI and ileus associated with enteritis/colitis or septicemia, may be mediated by an inflammatory infiltrate into the intestinal wall.[111-114] These causes of ileus are more clinically relevant than the acute phase of ileus, especially with respect to possible therapeutic intervention. Intestinal manipulation, lipopolysaccharide (LPS) administration, and ischemia-reperfusion injury have all been shown to produce significant decreases in contractile activity of jejunal smooth muscle *in vitro*.[111,112] This reduction in motility is temporally associated with an influx of inflammatory cells into the muscularis externa. The activation and recruitment of inflammatory cells may be stimulated by bacterial products, complement, and cytokines. LPS exposure and intestinal manipulation have been shown to increase mucosal permeability leading to increased bacterial translocation and transference of bacterial products.[114] The leukocyte influx, primarily neutrophils and monocytes, peaks at 24 hours, but may last for 7 days or longer. A cause and effect relationship between the leukocyte infiltrate and motility disruption is supported by the observation that blocking the influx of leukocytes into the muscularis externa by anti-adhesion antibodies eliminates the depressed motility.[113] The infiltration of leukocytes may also result from activation of nerve fibers in the bowel wall with release of proinflammatory mediators such as substance P or cGRP, which may mediate neurogenic inflammation and/or the additional release of proinflammatory mediators.[115]

Several mediators have been demonstrated to be involved in the inflammation-associated impairment of motility. The influx and activation of inflammatory cells leads to the up-regulation of inducible nitric oxide synthase (iNOS) with the subsequent production of large quantities of NO.[111,116] As previously stated, quantities of NO has been shown to be a potent inhibitory regulator of gastrointestinal activity in the horse and many other species.[56,117,118] When the effects of iNOS are eliminated either by use of a selective iNOS inhibitor or by running the experiments in iNOS knock-out mice (iNOS KO), the impairment of contractile activity by surgical manipulation is improved (iNOS inhibition) or eliminated (iNOS KO).[116] In the iNOS KO experiments, the inflammatory infiltrate is also significantly reduced. These findings support the role of NO as one mediator in the pathogenesis of ileus, functioning to both inhibit smooth muscle contractility directly and, in a signaling role, potentiating the inflammatory response that causes ileus by recruiting more inflammatory cells into the muscularis externa.[116]

Another likely mediator involved in postoperative ileus is cyclooxygenase-2 (COX-2) and its prostanoid products. COX-2 is an inducible enzyme that can be stimulated by LPS, growth factors, and proinflammatory cytokines.[119,120] It is expressed by inflammatory cells as well as endothelial cells, neuronal cells, and vascular smooth muscle.[119] Surgical manipulation with subsequent leukocyte infiltration produces an up-regulation of COX-2 with an increased production of prostaglandins coming from inflammatory cells as well as from myenteric neurons within the muscularis externa.[120,121] A concomitant depression of

in vitro jejunal contractility and in vivo intestinal transit is seen, both of which can be alleviated by blocking COX-2 with a selective inhibitor. Leukocyte recruitment into the muscularis is also prevented with selective COX-2 inhibition. This demonstrates a role for COX-2 and prostanoid production in POI as well as a potential role in other motility disorders where inflammation is involved.

It is known that manipulation of one area of the gastrointestinal tract can influence motility in adjacent areas that have not been manipulated. In fact, early motility work in the horse described the pathogenesis of POI as lack of gastroduodenal coordination after manipulation of a more distal segment of small intestine.[122] Neurogenic theories with activation of afferent extrinsic neurons mediating efferent inhibition may account for this component of POI. One study found both inflammatory and neurogenic pathways involved in POI.[123] In this study, the infiltration of leukocytes into the small intestine after surgical manipulation was shown to activate an orad inhibitory neural pathway, which in turn, mediated a sustained decrease in gastric motility via spinal afferents activating sympathetic efferent inhibitory fibers. Adrenergic blocking agents normalized the delay in gastric emptying (the neurogenic component), but did not reverse the delay in transit in the small intestine (the inflammatory component). Another study demonstrated that surgical manipulation of the bowel produces a "pan-enteric" inflammatory and dysmotility response.[124] In addition to depressed contractile activity in the rat jejunum after surgical manipulation, the motility of both the stomach and colon is also disrupted. The molecular basis of this "pan-enteric" response is thought to be mediated through activation of the pro-inflammatory cytokines such as nuclear factor interleukin-6 (NF-IL-6) and nuclear factor κ-B (NF-κB), which in turn induce tumor necrosis factor-α, iNOS, and COX-2. These mediators of ileus are significantly elevated in the unmanipulated stomach and colon as well as in the manipulated small intestine.[124] At this time, the extent to which these inflammatory mechanisms contribute to ileus in the horse is unknown.

Treatment of Motility Disorders in the Horse

Incidence and Risk Factors for Post-operative Ileus

Ileus, the functional obstruction of aboral GI transit, is one of the most commonly encountered complications of equine gastrointestinal surgery. In horses, postoperative ileus (POI) occurs predominantly after correction of lesions involving the small intestine. POI may also be seen after correction of lesions of the ascending colon, primarily large colon volvulus. Traumatic handling of the intestine, intestinal distention, resection and anastomosis, and intestinal ischemia may contribute to ileus in these cases. Other conditions that have been associated with ileus are anterior enteritis, peritonitis, electrolyte imbalances, endotoxemia, and anesthesia. Almost all of these proposed factors contributing to sustained ileus may be explained by the previously described inflammatory pathophysiology model of POI.

Risk factors for POI identified in one equine retrospective study were the following: age older than 10 yrs, Arabian breed, PCV greater than 45%, high serum concentrations of protein and albumin, anesthesia longer than 2.5 hrs, surgery longer than 2 hours, resection and anastomosis, and lesions in the small intestine.[125] Performing a pelvic flexure enterotomy decreased the risk of POI in this study. In another report, PCV greater than 48%, high heart rate, elevated serum glucose, small intestine lesion, and ischemic small intestine were identified as risk factors.[126] The incidence of POI in horses undergoing surgical treatment of colic has been reported to be 21% and 18.4%.[125,126] In one study, survival was significantly reduced (84%) for horses that developed POI compared with survival (94%) in horses that did not develop POI.[125] In the other study, a similar trend was seen, with an 87% survival for horses with POI compared to a 93% survival in horses without POI.[126] As expected, in these studies the survival was lower for horses that developed POI compared with those that did not develop POI (87% and 84.1% survival rate in horses with POI vs. 93% and 94.1% survival rate in horses without POI). This is a significant improvement over a previous report in which 86% of horses with POI did not survive.[127] Although management of these cases has improved, postoperative ileus is still associated with 38% to 40% of all postoperative deaths after surgical intervention for conditions causing colic.[125,126]

Diagnosis

Disruption of propulsive motility results in the sequestration of fluid, gas, and ingesta in the segment of the GI tract that is dysfunctional and in the intestine proximal to that segment. This distention occurs primarily in the stomach and small intestine, but can occur in the large intestine, especially with colitis, endotoxemia, or ischemia following a large colon volvulus. The first signs associated with ileus are depression and anorexia. As the intestine distends, the horse demonstrates increasing signs of abdominal distress, such as pawing, flank watching, lying down, and rolling.[32,128,129] Borborygmi are usually decreased or absent. The heart rate is elevated, at first as a result of the pain associated with the distention. The mucous membranes become discolored and capillary refill time is prolonged. Hemoconcentration is reflected by increases in the PCV and total protein concentration. Decreases in plasma chloride and potassium are the most common electrolyte

abnormalites seen, although sodium also may be low.[32,128,129] As the severity of the intestinal distention increases, abdominal distention may become grossly visible. Rectal examination and ultrasonography aid in determining whether the small or large intestine is involved. In foals, both abdominal radiography and ultrasonography can be helpful in assessing the cause of intestinal distention. Nasogastric decompression often retrieves from 3 to 10 liters of fluid. The response to nasogastric decompression provides an important clue that the underlying problem is the result of loss of function. After decompression, the horse should show some improvement, such as decreased pain and decreased heart rate. If no alleviation of signs is observed, careful thought should be given as to the likelihood that the problem may be a mechanical obstruction and not a functional ileus.

Supportive Therapy

Although a variety of prokinetic agents have been administered in an attempt to improve GI motility in horses with ileus, the lack of consensus as to which one, if any, is effective attests to their therapeutic limitations. Consequently, the hallmark of treatment remains supportive therapy. Included in this supportive therapy are fluid, acid-base, and electrolyte replacement, which are important in any horse with colic. Antibiotics are also indicated if the intestine is compromised or the possibility of bacterial contamination exists. The primary method to treat POI in the horse remains nasogastric intubation and decompression. Questions remain regarding when to place the tube, if the tube should be kept in place, and when to start feeding. A study in normal horses indicated that leaving a nasogastric tube in place increases the rate of gastric emptying for 24 hours.[130] The clinical significance of this finding in horses after surgery involving the gastrointestinal tract is unknown. In humans, eliminating or decreasing routine nasogastric intubation[131] with early return to enteral feeding has been shown to be safe and may reduce POI.[132,133] These retrospective studies have involved human patients with colonic problems and not ileus associated with small intestinal motility disturbances. Management of pain and inflammation are also important in the treatment of affected horses.

Anti-inflammatory Therapy

As discussed in detail in the pathophysiology section, intestinal distention, ischemia, and trauma occurring during decompression and /or resection and anastomosis induce inflammation of the bowel wall with an increase in the production of inflammatory mediators such as PGI_2, PGE_1, PGE_2, and tumor necrosis factor (TNF). Endotoxemia associated with necrotic intestine or systemic infection can also stimulate production of these inflammatory mediators. Infusions of endotoxin, PGE_2, and TNF have been shown to disrupt normal motility patterns in horses.[134-137] Phenylbutazone and flunixin meglumine have been shown to significantly attenuate this disruption of gastric, small intestine, and large colon motility in the horse.[136,137] The analgesic effect of these agents should also decrease stimulation of sympathetic inhibitory reflexes. Based on these observations, nonsteroidal anti-inflammatory drugs are recommended for prevention and treatment of motility disorders associated with GI inflammation such as POI, anterior enteritis, and colitis. Although some work has indicated that selective COX-2 inhibitors are effective in reducing the surgically induced ileus in laboratory animals,[121] in an experimental distention/surgical manipulation model in the horse, selective COX-2 inhibition was not beneficial in attenuating the in vitro depression of jejunal contractions, while nonselective COX inhibition was able to attenuate the depressed contractile activity.[138] Other drugs such as polymixin B, dimethyl sulfoxide, and hyperimmune serum potentially may help if they can decrease the inflammatory response to endotoxemia.

Analgesia

Besides the NSAIDs discussed earlier, adrenergic agonists and opioids are the two classes of drugs commonly used in horses to control pain associated with colic. Xylazine and detomidine are α-2 adrenergic agonists that may inhibit presynaptic acetylcholine release in the myenteric plexus or may directly inhibit smooth muscle, thereby decreasing motility.[139] In the horse, xylazine and detomidine have been shown to decrease motility as measured by myoelectrical activity of the distal jejunum, pelvic flexure, cecum, and right ventral colon, and cecal emptying based on radiolabeled markers.[93,94,140-142] However, the results of another study suggests that, while xylazine resets the duodenal MMC in the horse, it does not seriously disrupt gastrointestinal motility.[143] Although β-adrenergic receptors are present on circular and longitudinal smooth muscle in the horse and β-adrenergic agonists cause inhibition of contractile activity,[55] their role in motility disturbances has not been demonstrated in the horse.[122] Drugs administered for reasons other than pain management that act at β-adrenergic receptors, such as dobutamine, a β-1 agonist, and terbutaline, a β-2 agonist, may depress motility.

Opioid agonists should be avoided if possible in horses with ileus as they depress motility in most species studied.[76,78,79,144] Opioids slow small intestinal transit, increase the duration of POI, and may increase chances of impaction colic by slowing progressive motility.[81,144,145] In ponies, morphine and fentanyl, μ-receptor agonists, have been shown to depresses colonic motor activity.[79,144] Naloxone, an opioid antagonist, has been suggested by some investigators to be a potentially beneficial

drug in treating equine motility disorders,[146] and some evidence exists that naloxone enhances progressive motility in the horse; however, naloxone has also been shown to cause diarrhea and colic in the horse.[147] Butorphanol tartrate, an opioid agonist/antagonist, is a strong analgesic and mild sedative used in horses with colic.[148] Butorphanol, meperidine, and pentazocine were shown to inhibit myoelectric activity in the equine jejunum while they had no effect on the pelvic flexure activity in one study.[34] Butorphanol prolonged xylazine-induced inhibition of myoelectrical activity of the equine cecum and right ventral colon in another study;[142] however, in yet another study, butorphanol was shown to reset the antroduodenal MMC without causing undesirable effects on antroduodenal motility.[149]

Prokinetics

It should be evident from the above description of the physiology of normal motility that many different factors must be precisely coordinated to produce progressive motility patterns (Figure 4-4). It is logical to assume that, during ileus in the horse and other species, an imbalance in the factors controlling excitation and inhibition of gastrointestinal tract smooth muscle contributes to the ileus. Historically, pharmacologic modulation of intestinal muscular activity in the horse has been directed at either increasing excitatory cholinergic activity with the administration of the parasympathomimetic agents such as bethanechol or neostigmine, or blocking inhibitory sympathetic hyperactivity with α-adrenergic blockers such as yohimbine and acepromazine.[122,150] A major portion of the support for the drugs discussed further on comes from experimental models evaluating the efficacy of the various pharmaceutical agents in changing motility patterns in normal horses or changing motility patterns in an acute abrasion model where a transient ileus is induced by rubbing the small intestine.[122,150] Both models have made significant contributions to our understanding of POI; however, the perceived limited efficacy of prokinetics may be a result of the inability of these studies accurately to reproduce what occurs during clinically relevant ileus in the horse.

Bethanechol

Bethanechol hydrochloride is a muscarinic cholinergic agonist that stimulates acetylcholine receptors (M_2 receptors) on gastrointestinal smooth muscle, causing them to contract.[151] Support for the use of bethanechol in the treatment of motility disorders in the horse is predicated on observations that, in normal horses, bethanechol increases the rate of gastric and cecal emptying as measured by radiolabeled isotopes, and it induces premature MMC phase III-like activity in the ileum.[94] In an equine POI model, bethanechol (0.025 mg/kg SQ at 2 and 5 hours postoperatively) shortened intestinal transit measured by passage of beads, and reduced the time until normal activity levels returned throughout the GI tract when administered in combination with the α-adrenergic receptor blocker yohimbine.[122] Bethanechol was not as effective as metaclopramide in restoring coordinated gastroduodenal motility patterns. Although its efficacy in treating motility dysfunction has been questioned in the horse and other species,[122,151] its prokinetic effects in normal horses and the clinical impression of its benefit in treating horses with ileus provides some support for its use in the treatment of certain GI motility dysfunctions such as POI and gastric and cecal impactions. The recommended dose is 0.025 mg/kg IV or SQ, every 4 to 6 hours. The most common side effect of the drug is salivation, with abdominal cramping and diarrhea occurring less frequently.

Neostigmine

Neostigmine methylsulfate is a cholinesterase inhibitor that prolongs the activity of acetylcholine at the synaptic junction. In studies on normal horses, the effects of neostigmine (0.022 mg/kg IV) varied, depending on the portion of the gastrointestinal tract examined.[93,94,150] Neostigmine was shown to delay gastric emptying and decrease propulsive motility in the jejunum, but increased propulsive motility at the pelvic flexure.[93,152] These results suggest that the drug would not be appropriate for gastric and small intestinal problems, but may be beneficial for large intestine motility dysfunction. However, neostigmine increased the amplitude of rhythmic contractions in both resting and distended jejunum in anesthetized ponies in one study,[153] and induced premature phase III-like activity in the ileum and increased the rate of cecal emptying in another study.[94] No consensus exists as to the recommended use of this drug for treatment of equine motility disorders. It is rarely used as a prokinetic in humans.[151] There is anecdotal support that neostigmine can reduce the severity of POI in horses, particularly if the large colon is involved; however, its use for impaction colic or in cases with excess GI distention has not been recommended because of the apparent force of drug-induced contractions.[94] The dose used clinically is 0.0044 mg/kg (2 mg per adult horse) SQ or IM repeated in 20 to 60 minutes. If no response occurs and the horse is not exhibiting any side effects, the dose can be increased by 2 mg increments to a total of 10 mg per treatment. The most common side effect is abdominal pain.

Acepromazine and Yohimbine

Both of these drugs are α-adrenergic antagonists. As described in the neurogenic theory of POI, afferent stimulation during surgery activates inhibitory sympathetic efferent pathways. Norepinephrine released by postsynaptic sympathetic neurons at

the enteric ganglia inhibits the release of the excitatory neurotransmitter acetylcholine by stimulating α_2-receptors located presynaptically on cholinergic neurons. Increased circulating concentrations of catecholamines, which can persist for the duration of the ileus, have been associated with increased synthesis of norepinephrine in the bowel wall in humans after laparotomy.[99,106] Acetylpromazine maleate facilitates small intestinal transit in normal ponies.[145] Based on clinical impression, acepromazine administered at 0.01 mg/kg IM every 4 hours is thought to reduce the severity of POI in horses with small intestinal lesions. Because acepromazine is a nonselective α-adrenergic blocker that can produce hypotension through α1-receptor antagonism, horses should be well hydrated before the drug is administered. Yohimbine hydrochloride (Yobine) is a competitive antagonist that is selective for α_2-adrenergic receptors. When administered at 0.15 mg/kg IV at 1, 4, 7, and 10 hours postoperatively, it reduced the severity of experimentally induced POI, especially when combined with bethanechol. Yohimbine administered at 75 μg/kg was demonstrated to attenuate some of the negative effects that endotoxin has on propulsive motility.[134] Since yohimbine is a selective α_2-antagonist, it should not produce the hypotensive response seen with acepromazine.

Metaclopramide

Metaclopramide (Reglan) is a substituted benzamide whose primary prokinetic activity is through dopamine receptor antagonism. Metaclopramide produces additional prokinetic activity by augmenting the release of acetylcholine from intrinsic cholinergic neurons by acting at 5-HT receptors and through adrenergic blockade.[122,151,154,155] Metaclopramide has been shown to stimulate in vitro contractile activity of circular muscle from the stomach and small intestine in the horse.[156] In a POI model in horses, metaclopramide was more effective in restoring gastrointestinal coordination, a measurement of motility strongly correlated to return of normal transit, than adrenergic antagonists or cholinergic agonists used individually or in combination.[122] This provided strong evidence that POI in this model was due to a disruption of gastroduodenal coordination that was mediated through dopamine hyperactivity. Although the functional role of dopamine in gastrointestinal disorders is controversial, metaclopramide does improve motility in humans regardless of its mechanism of action. In horses, the drug has been administered at a dosage of 0.25 mg/kg, diluted in 500 ml of saline, infused over 30 to 60 minutes. In a retrospective study, metaclopramide administered as a continuous infusion (0.04 mg/kg/hour) decreased the total volume, duration, and rate of gastric reflux when used prophylactically after small intestine resection and anastomosis.[157] Metaclopramide administered at a dose as low as 0.1 mg/kg may cause extrapyramidal side effects such as excitement, restlessness, and sweating, as well as abdominal cramping. For this reason a slow or continuous infusion is recommended.[157]

Cisapride

Cisapride (Propulsid), a more recently developed substituted benzamide, was one of the most effective and popular prokinetics in human medicine.[151] It functions as an indirect cholinergic stimulant by selectively enhancing the release of acetylcholine from postganglionic neurons in the myenteric plexus. Unlike metaclopramide, cisapride's main prokinetic activity appears to be mediated through 5-HT_4 receptor agonism and 5-HT_3 antagonism rather than dopamine antagonism.[158] In the horse, cisapride has been shown to act partly through a noncholinergic effect mediated by 5-HT_2 receptors.[159] In experimental studies and in clinical trials in humans, cisapride's prokinetic effects were consistently equal to or superior to those of metaclopramide and domperidone, a dopamine antagonist used as a prokinetic in humans.[151,160,161] In normal horses, cisapride augments the amplitude of gastric contractions, stimulates jejunal activity coordinated with gastric contractions, enhances contractile activity of the large and small colon, and stimulates coordinated activity in the ileocecocolonic junction.[26,146,162] In clinical trials, cisapride has been shown to be effective in preventing POI in horses.[26] There are conflicting reports on its efficacy for correcting motility dysfunction caused by endotoxemia. One study reported no benefit, while another study suggested cisapride can attenuate the motility dysfunction induced by endotoxemia.[163,164] The drug unfortunately is now difficult to obtain because of its cardiotoxic effects.[165] One report has shown that levosulpride, a new substituted benzamide with dopamine (D_2) receptor antagonist activity as well as 5-HT_4 agonist and 5-HT_3 antagonist activity, is as effective as cisapride in treating dysmotility in humans.[166] It is likely that drugs being tested or developed that have 5-HT_4 agonist and/or 5-HT_3 antagonist activity such as levosulpride, tegaserod, and prucalopride will take the place of cisapride in the near future.[167]

Erythromycin

Erythromycin is a macrolide antibiotic with recognized gastrointestinal side effects. Erythromycin is a motilin agonist that influences motility partly by acting on motilin receptors on GI smooth muscles. Motilin is a hormone that is released by enterochromaffin cells and that stimulates contractile activity in the stomach and small intestine. Motilin infusion in the horse causes strong contractions in the proximal jejunum in vivo.[168] Erythromycin also appears to act on enteric cholinergic neurons through motilin receptors and/or 5-HT_3 receptors to stimulate the release of acetylcholine.[151,169,170] Erythromycin initiates phase III of the MMC.[171] When it is administered at subtherapeutic antimicrobial levels, it has been shown to stimulate gastric

emptying, antroduodenal coordination, and phase III activity in the duodenum in humans and laboratory animals.[171] In the horse, erythromycin was effective in stimulating gastric and cecal emptying and inducing phase III activity in the small intestine.[172,173] The recommended dose is 0.5 to 1.0 mg/kg in 1 L saline infused over 60 minutes every 6 hours. Erythromycin can down-regulate motilin receptors, which may explain why the prokinetic effect diminishes with repeated treatment. At the recommended dose, which is below the effective antimicrobial dose, antibiotic-related diarrhea should not be observed; however, severe colitis associated with its use has been reported, making some clinicians reluctant to use it. Although it has been a commonly used drug to treat gastroparesis in humans, some of the therapeutic benefits that were anticipated in the human field have failed to materialize.

Lidocaine

Intravenous lidocaine shortens the duration of paralytic ileus in the colon in humans after abdominal surgery.[174] Lidocaine hydrochloride may act by 1) reducing the concentration of circulating catecholamines by suppressing the sympathoadrenal response; 2) suppressing the activity of the primary afferent neurons involved in reflex inhibition of gut motility; 3) stimulating smooth muscle directly; and 4) decreasing the inflammation in the bowel wall through inhibition of prostaglandin synthesis, inhibition of granulocyte migration and release of lysosomal enzymes, and inhibition of free radical production.[175-177] In vitro, lidocaine produces an increase in contractility of circular muscle from the proximal duodenum of horses.[156] In a clinical trial in horses, lidocaine appeared to be effective in decreasing the duration of reflux in horses with POI and in horses with duodenitis-proximal jejunitis.[178] The recommended protocol requires an initial loading bolus of 1.3 mg/kg IV administered slowly over 5 minutes followed by 0.05 mg/kg/min in saline or lactated Ringer's solution every 24 hours. Side effects include muscle fasciculations, trembling, and ataxia.

Conclusion

Based on the pathogenesis of POI, several areas should be targeted in treating POI in the horse. First, effective pain management with minimal use of opioid analgesics should reduce pain-induced motility depression mediated by afferent pathways while limiting the adverse affects opioid agonists have on motility. Preferential use of NSAIDs over opioids should help accomplish this. As stated previously, opioid-sparing analgesia, in which NSAIDs have been used to reduce the amount of opioids administered, has been shown to be one of the most effective ways to reduce POI in humans.[81] The use of NSAIDs should have the additional benefit of decreasing the inflammatory component that contributes to POI.[112] In humans, the use of epidural local anesthetics has decreased POI. Part of this effect may be mediated by blockade of inhibitory afferent reflexes.[81] Lidocaine, by blocking afferent fibers, may work in a similar manner. It appears to be the most frequently used drug to treat POI in horses. Choosing one of the other listed prokinetics seems to be based on the past experience of the individual clinician, attesting to the limited efficacy of available prokinetics. In humans, cisapride has received the most support based on clinical trials, although metaclopramide and erythromycin have also shown some efficacy in clinical trials.[81] The limited availability of cisapride and the concern of erythromycin-induced diarrhea in the horse reduces the available choices for the equine clinician. A repeat laparotomy should be considered if the horse's clinical status suggests that intestinal dysfunction is to the result of a mechanical cause rather than a functional problem.

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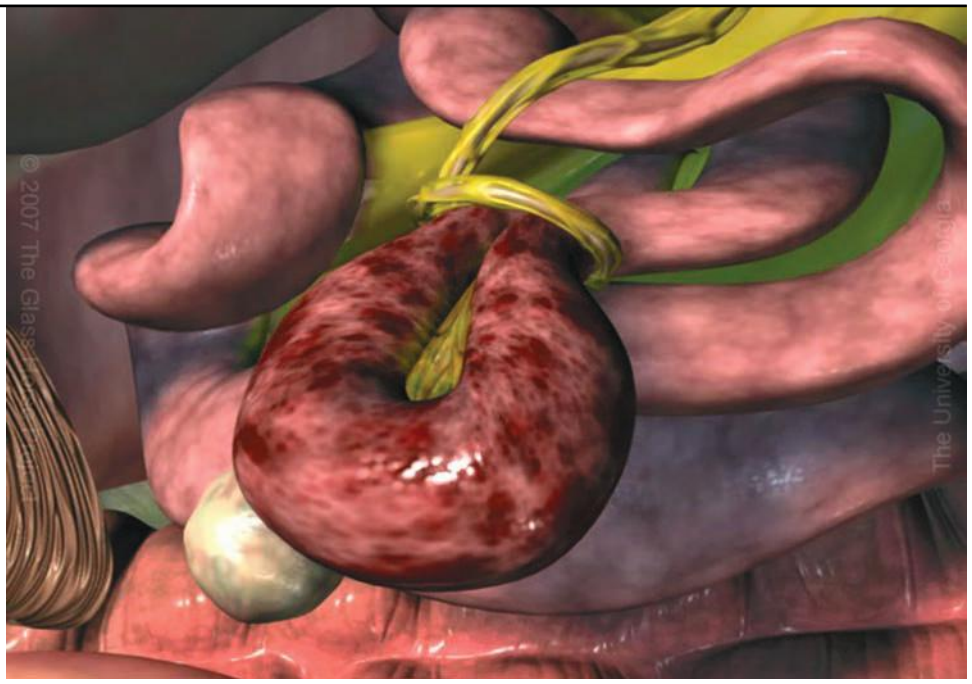
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Pathophysiology of Gastrointestinal Diseases

Part 2



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Pathophysiology of Gastric Ulcer Disease

Chapter 5

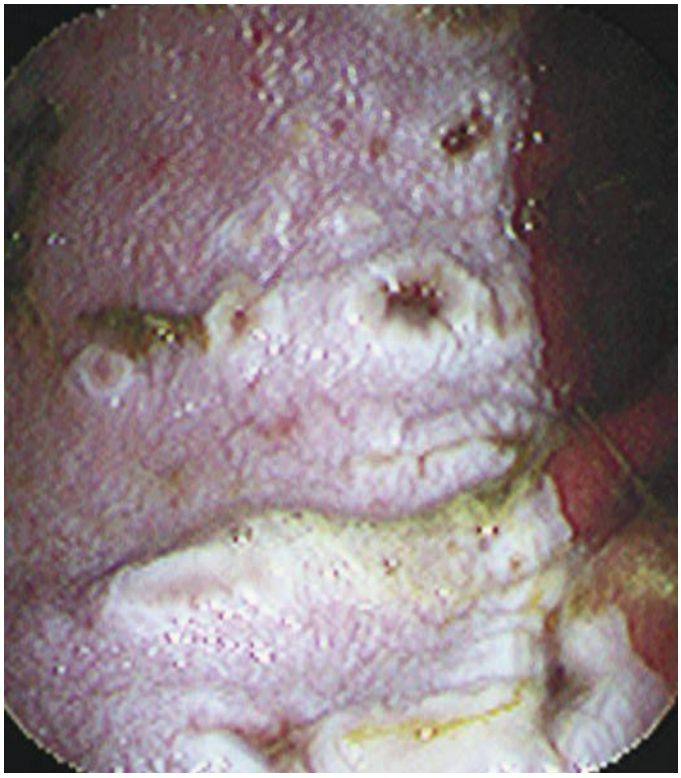
Michael J. Murray

Gastric Ulcer Disease

Gastric ulcer disease is a general term covering several different syndromes. The causes of gastric ulcers are multifactorial and differ from the squamous mucosa to the glandular mucosa. Lesions in the gastric squamous mucosa (Figures 5-1 and 5-2) result primarily from excessive exposure to hydrochloric acid (HCl).[1,2] Other factors, including short-chain fatty acids, may contribute, but HCl is believed to be the primary cause of mucosal injury.[3] The cause of ulcers in the gastric glandular mucosa is less well understood. Nonsteroidal anti-inflammatory drugs can cause gastric glandular mucosal ulcers in foals and adult horses, but the causes of spontaneous ulcers in this area of the stomach remain undetermined. Excessive acid does not appear to be a primary factor. In fact, the prevalence of ulcers in the glandular part of the stomach differs by region, from low in the oxyntic region to high in the antrum (Figures 5-3 and 5-4).[1] Lesions in the antral mucosa and associated histologic changes resemble those caused by *Helicobacter pylori* in humans. Evidence for infection of the equine gastric antral mucosa by an uncharacterized species of *Helicobacter* has come from various studies, including polymerase chain reaction data,[4] antibody data,[5] and immunofluorescence data;[6] however, no *Helicobacter* spp. have been cultured from horses and no association with clinical disease has been demonstrated to date.

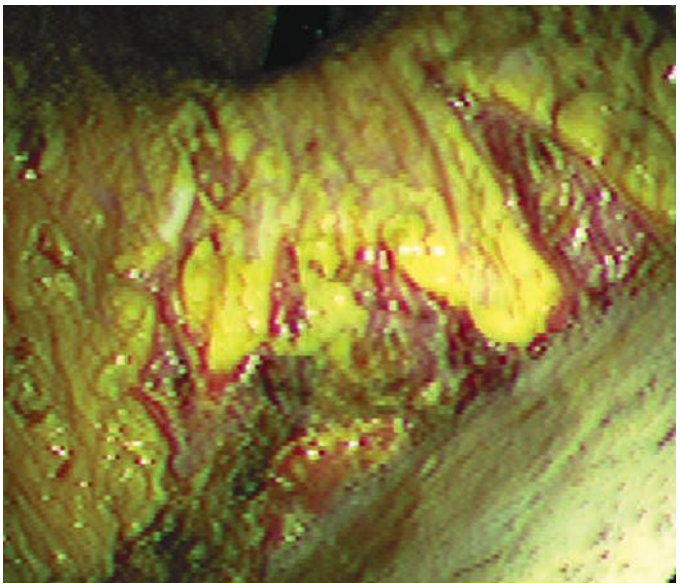
Several risk factors exist for gastric ulcers in horses. Training has a significant impact on gastric ulceration,[7] and the prevalence and severity of gastric ulceration increase with the level of training.[7-9] Gastric ulcers can be induced by treadmill training of research horses,[10] so that while many factors associated with the training of performance horses (feeding management and types of feeds, stall confinement, transportation, and undefined "stressors") have been implicated in training-associated ulcers, these are not necessarily required for ulcers to develop. Creation of increased abdominal pressure with resulting compression of the stomach and subsequent coating of the squamous epithelium with acid may explain why horses in exercise have a high rate of ulceration.[11] Risk factors for development of ulcers in foals have not been well defined. Ulcers have been associated with infection with rotavirus, but it is likely that it is not a pathogen-specific association, but rather an association with enteritis. Increased risk of ulceration of the gastric glandular mucosa has been demonstrated in foals with a variety of illnesses or painful musculoskeletal conditions.[12] Weaning and transportation may be ulcer risk factors for foals, but this has not been documented.

Figure 5-1



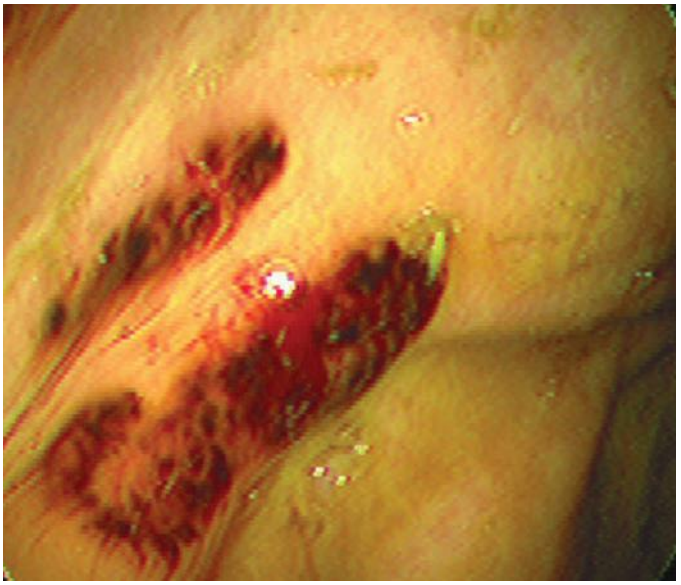
Small ulcers in the equine gastric squamous mucosa adjacent to the margo plicatus, along the right side of the stomach.

Figure 5-2



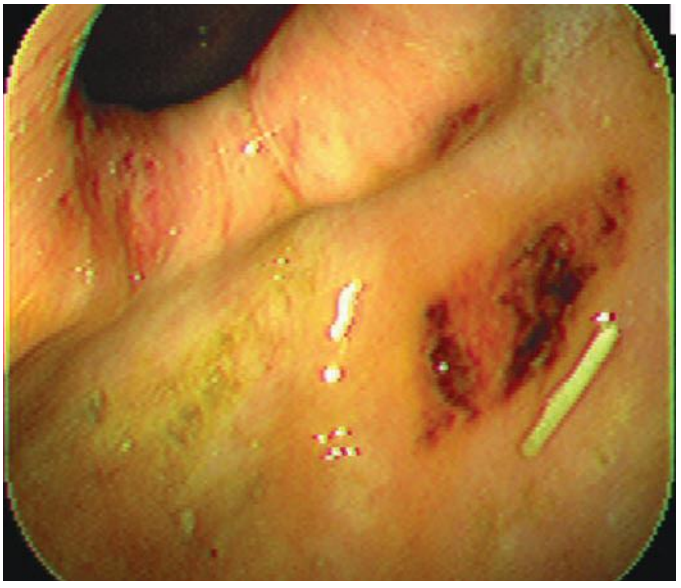
Large ulcer in the equine gastric squamous mucosa adjacent to the margo plicatus and ventral to the cardia. The adjacent mucosa is proliferative and hyperkeratotic (yellow), reflecting both healing mechanisms and continued acid injury.

Figure 5-3



Ulcer in the mucosa of the antrum, near the pylorus.

Figure 5-4



View of the antrum with thickening of a rugal fold and erosion of the mucosa.

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Pathophysiology of Gastrointestinal Disease: Obstruction and Strangulation

Chapter 6

Anthony T. Blikslager

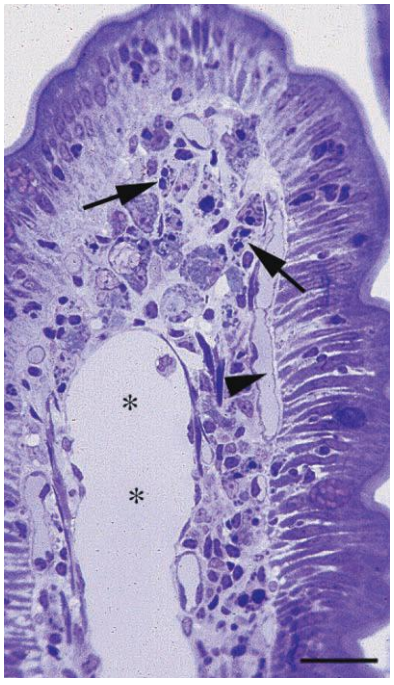
Simple Obstruction

Simple obstruction of the intestinal lumen typically involves an intraluminal obstructive mass composed of ingesta or foreign material, such as bailing twine, a piece of hay net, or rubber fencing. Additionally, endogenously formed obstructive masses, specifically enteroliths, also cause simple obstruction. All of these obstructive masses block the passage of ingesta and secreted fluid, but they do not directly interrupt intestinal blood flow, at least during the early phases of obstruction. As simple obstructive masses persist, however, fluid, gas, and ingesta accumulate proximal to the mass, resulting in increased intraluminal pressure that ultimately compresses the intestinal intramural blood supply, resulting in the onset of localized intestinal ischemia.[1,2] Furthermore, obstructive masses may ultimately directly compress the intestinal wall surrounding them, particularly as the masses are forced distally by propulsive intestinal motility into regions of the intestine having a smaller luminal diameter. For example, an enterolith formed in the distal aspect of the ascending colon may be small enough to reach the small colon, where it may fully occlude the lumen, and begin to induce mural-pressure necrosis, ultimately leading to intestinal rupture in some cases.[3]

Pathophysiology of Increased Intraluminal Pressure

Interest in the pathophysiologic role of intestinal distention was initiated by a study indicating that the prognosis for survival following surgery for intestinal obstruction was influenced by the intraluminal hydrostatic pressure. Specifically, the hydrostatic pressure was significantly increased in horses with small intestinal obstruction that did not survive compared with values for horses that did survive. In that study, intraluminal pressures greater than 15 cm H_2O correlated with a poor prognosis for survival.[4] However, it was difficult to discern from that study the exact role of intraluminal distention because most of the horses that failed to survive had a strangulating obstruction. Subsequently, studies have been conducted to assess the effects of intraluminal distention in the absence of overt obstruction of the vasculature. The results of initial experimental studies that involved 4 hours of distention at 18 cm H_2O indicated that there was no histologic evidence of mucosal epithelial sloughing, as might be expected with ischemic injury.[5] There was, however, extensive edema in the lamina propria and villous central lacteals, and accumulation of neutrophils after decompression of the distended intestine (Figure 6-1). In addition, on electron microscopy, dilatation of paracellular spaces was evident. The latter changes have more recently been shown to contribute to increased mucosal permeability, which may alter fluid flux across the mucosa and result in absorption of bacterial toxins.[6,7]

Figure 6-1

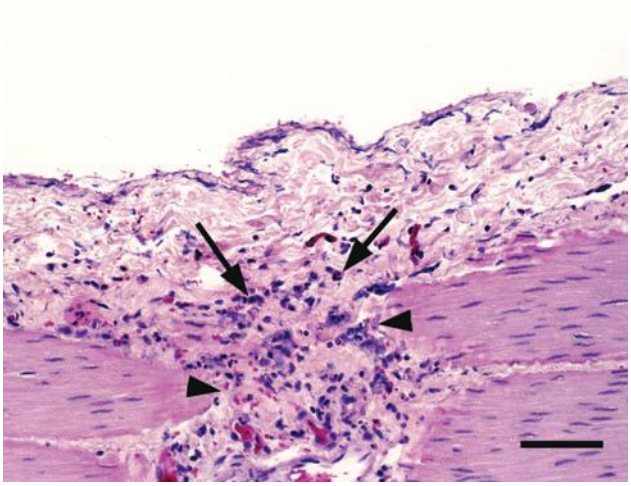


Photomicrograph of jejunal villi showing dilatation of the central lacteal (asterisks), subepithelial edema (arrowhead), and neutrophil infiltration (arrows) that occurs following decompression of dilated small intestine. Bar = 30μm

More recent studies have examined the effects of small intestinal intraluminal distention and decompression on the microvasculature. For example, distention of the jejunum to an intraluminal hydrostatic pressure of 25 cm H_2O for 120 minutes resulted in a significant reduction in the number of perfused vessels in the seromuscular and mucosal layers, and vascular perfusion remained abnormal after decompression.[1] Furthermore, during distention, blood flow to the intestine was reduced by 50%, and microvascular permeability increased after decompression, suggesting that reperfusion injury was occurring in

the intestine.[2] Interestingly, the reperfusion injury appeared to have the greatest effect on the seromuscular layer, which had evidence of mesothelial cell loss, neutrophil infiltration, and edema. This type of inflammatory seromuscular lesion has also been noted in studies of the proximal resection margins of naturally occurring small intestinal strangulating obstructions (Figure 6-2), confirming that distention leads to seromuscular injury proximal to obstructive lesions, despite the fact that this intestine may appear grossly normal.[8] Experimentally, this seromuscular injury and inflammation predisposes to adhesion formation. For instance, foals subjected to intraluminal distention of a segment of jejunum to 25 cm H_2O for 2 hours in one study developed bowel-to-bowel and bowel-to-mesentery adhesions within 10 days after the surgical procedure.[9] Similar experiments in the large colon have revealed that the colon is far more resistant to a comparable seromuscular injury than is the small intestine.[10]

Figure 6-2



Photomicrograph of the seromuscular layer of a proximal resection margin of jejunum from a horse with strangulating obstruction of the small intestine. Although the jejunal resection margin appeared grossly normal at surgery, mesothelial cell loss and infiltration of neutrophils (arrows) is apparent. In addition, neutrophils appear to penetrate the muscular tissue layers via anatomic divisions (septa) in the outer longitudinal layer (arrowheads), which may have an effect on muscular function. Bar = 100μm.

Strangulating Obstruction

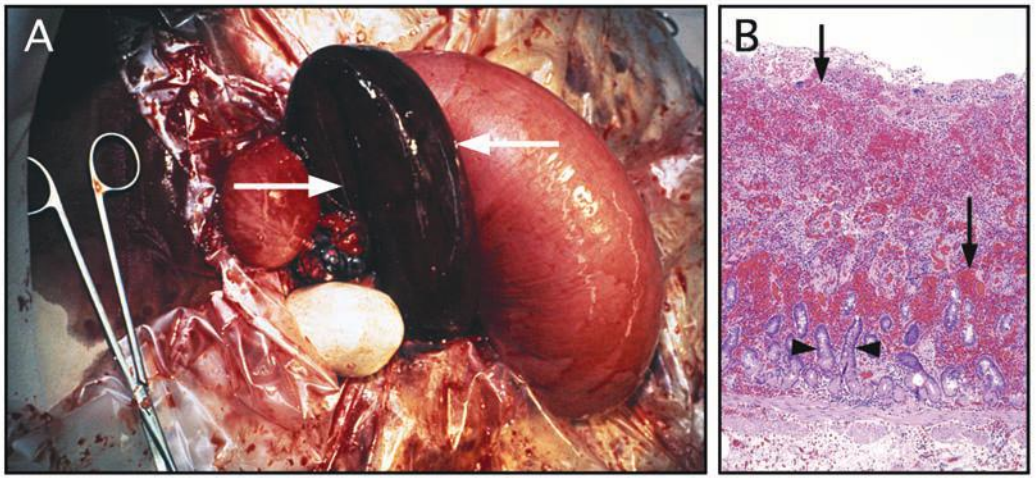
Strangulating obstruction results from simultaneous occlusion of the intestinal lumen and its blood supply. Thus, all of the pathophysiologic features of simple obstruction, including the effects of intraluminal distention, occur during strangulating obstruction, but the severity of injury induced by occlusion of the blood supply is more rapid in onset and of a greater magnitude that that caused by distention alone. Nonetheless, distention at the periphery of a strangulating lesion can induce injury that is hard to detect, and therefore, resection margins may not be as normal as suggested by gross appearance.[8] The degree of injury attributable to occlusion of the blood supply is highly variable, depending on the nature of vascular occlusion. In most instances, the veins are occluded earlier than the arteries in the course of strangulating obstruction because of their thinner, more compliant walls and the lower hydrostatic pressure in the veins. This results in a disparity in blood flow during the early phases of strangulating obstruction, with continued delivery of arterial blood into the intestinal wall, which, in the absence of patent venous outflow, causes a hemorrhagic lesion termed hemorrhagic strangulating obstruction. This results in ischemic injury, but also in tremendous congestion of the tissues (Figure 6-3). Such hemorrhagic congestion has two opposing effects: it disrupts tissue architecture, including the mucosa and its epithelium, but it continues to provide oxygenated blood to the tissues during the early stages of the ischemic episode. Alternatively, the strangulation may exert enough pressure on both the veins and arterial supply to occlude both simultaneously, resulting in so-called ischemic strangulating obstruction. This results in rapid degeneration of the mucosa.[11] For example, in experimental large-colon volvulus, near-complete mucosal degeneration developed within 3 hours after occlusion of the vasculature.[12] As compared with hemorrhagic strangulating obstruction, ischemic strangulation obstruction has a pale appearance. From a clinical standpoint, this sometimes makes it difficult to assess the degree of mucosal injury in horses with strangulating injuries, because intestine that appears nonviable (dark red) may in fact have less mucosal injury than that of ischemic strangulated intestine.[8]

Mucosal Ischemic Injury

To understand how the mucosa becomes injured during ischemia, critical anatomic features of the mucosa have to be taken into consideration. In the equine small intestine, the villus tip is the region most susceptible to ischemia, largely due to the countercurrent exchange mechanism of blood flow in the small intestinal villus.[13] This countercurrent exchange mechanism is attributable to the vascular architecture, which consists of a central arteriole that courses up the core of the villus, arborizes at the tip, and is drained by venules coursing down the periphery of the villus.[14] As oxygenated blood enters the central arteriole, oxygen diffuses across the wall of the arteriole, across the interstitial tissues, and into the peripheral venules, which are flowing in the opposite direction (Figure 6-4). This short-circuits the oxygen supply, resulting in a villus tip that is relatively

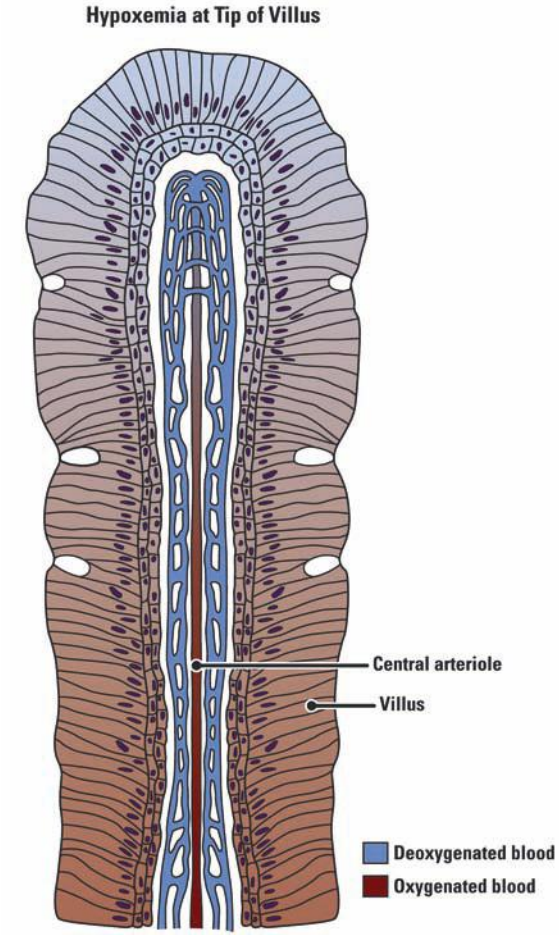
hypoxic even under normal conditions. Countercurrent exchange is exacerbated when the rate of the arterial blood flow is reduced, essentially providing more time for the oxygen to diffuse out of the arteriole across to the venules. When the arterial flow is reduced to a critically low level, the tip of the villus becomes hypoxic, with attendant epithelial injury.[13,15] This mechanism might explain why the small intestinal mucosa is more susceptible to ischemic injury, compared with the colon, which lacks villi. For example, the duration required to produce severe morphologic damage to the equine colon is approximately 25% longer than that to produce comparable damage to the small intestine.[12]

Figure 6-3A, B



Gross and morphologic appearance of hemorrhagic strangulating obstruction. **A.)** A horse with a strangulating obstruction of the jejunum, in which a pedunculated lipoma had wrapped around a segment of jejunum. Note dark appearance of the bowel (arrows) indicative of arterial blood trapped within the tissues during development of the lesion. **B.)** Photomicrograph of the mucosa from a horse with hemorrhagic strangulating obstruction. Note extensive hemorrhage throughout the tissues (arrows), with extensive disruption of mucosal architecture. Crypts remain relatively protected deep within the mucosa (arrowheads), partly as the result of the separate blood supply to this area of the mucosa. Bar = 100 μM

Figure 6-4



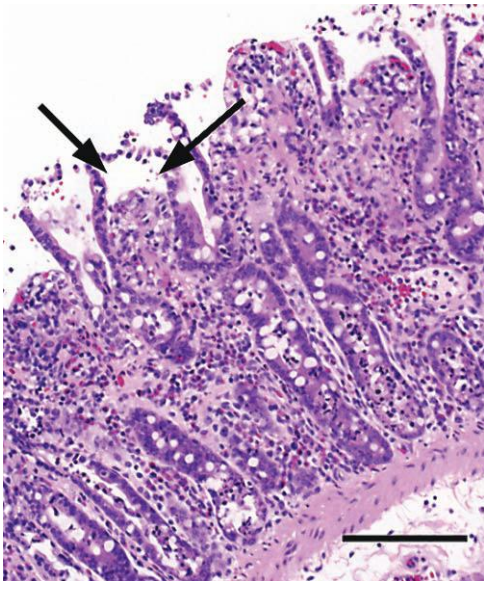
Schematic depiction of the countercurrent exchange system in small intestinal villi, during which oxygen from the central arteriole diffuses across the lamina propria to the peripheral villous venous supply, thereby depriving the villous tip of oxygen during low-flow states.

Mucosal epithelium is particularly susceptible to hypoxic injury because of the relatively high level of energy required to fuel the Na^+/K^+-ATPase that regulates epithelial ion and nutrient transport. The first biochemical event to occur during hypoxia is a loss of oxidative phosphorylation. The resulting diminished ATP concentration causes failure of the energy-dependent Na^+/K^+-ATPase, resulting in intracellular accumulation of sodium and, subsequently, water. The pH of the cytosol decreases as lactic acid and inorganic phosphates accumulate from anaerobic glycolysis. The falling pH damages cell membranes, including lysosomal membranes, resulting in the release of lysosomal enzymes into the cytosol, further damaging cellular membranes. Damage to the cell membrane allows the accumulation of high concentrations of calcium in the cytosol, which activates calcium-dependent degradative enzymes.[16] These events result in cytoplasmic blebbing of the basal membrane, with subsequent detachment of cells from the underlying basement membrane.

Studies on epithelial injury during ischemia suggest that the majority of epithelial cells undergo programmed cell death (apoptosis) during ischemia and reperfusion rather than necrosis, allowing retention of reusable components of irreversibly injured cells.[17] In one study, 80% of detached epithelial cells during small intestinal ischemia/reperfusion underwent apoptosis.[18] Although the most obvious result of apoptosis is loss of surface epithelium, a number of cells on the lower portion of the villus (in the small intestine) and cells within the crypts may also undergo apoptosis that may only become evident up to 24 hours after reperfusion of ischemic tissue.[19]

As epithelium separates from the underlying basement membrane in the small intestine, a fluid-filled space termed Grüenhagen's space forms at the tip of the villus (Figure 6-5).[15] The mechanism of fluid accumulation in this space is not entirely understood, but may result from continued epithelial absorption of NaCl and water, before the cells have fully detached. The fluid accumulation likely exacerbates epithelial separation from the basement membrane. Subsequently, epithelium progressively sloughs from the tip of the villus toward the crypts, which are the last component of the intestinal mucosa to become injured.[20-22] The relative resistance of the crypts to injury likely relates to the vascular architecture, as the crypts have a blood supply that is separate from the vasculature involved in the villus countercurrent exchange mechanism. The early morphologic changes observed in the equine large colon during ischemia are similar to those described for the equine small intestine, with initial loss of the more superficially located surface cells, followed by cellular injury and sloughing within the crypts.[12,23] The orderly progression of tissue injury has been used by one group of investigators to accurately predict survival in horses with large-colon volvulus. Biopsies were taken from the pelvic flexure, which has been previously shown to accurately reflect mucosal changes along the length of the colon,[24] and histologically examined for the width of the crypts and inter-crypt interstitial space. The latter measurements were expressed as an interstitium crypt width ratio (I:C). Nonviable colon was defined as that which had more than 60% loss of crypts and an I:C ratio greater than 3. Using this methodology, survival was correctly predicted in 94% of horses.[25]

Figure 6-5



Photomicrograph of ileal mucosa subjected to 1-hour of complete ischemia. Note the formation of Grüenhagen's space (arrows) with fluid trapped between an intact epithelial layer and the basement membrane. The formation of this space is exacerbated by active contraction of the villi. Bar = 100 μm

Reperfusion Injury

Intestinal reperfusion injury originally was characterized in a series of basic science studies performed in cat and rodent models, during which it was shown that ischemic injury was markedly worsened by reperfusion.[26-30] The concept of further injury developing during reperfusion initially seemed counterintuitive, as reperfusion with an oxygenated blood supply was predicted to rescue degenerating mucosa; however, it was the oxygen itself that was indirectly responsible for triggering the additional injury.

Events that culminate in reperfusion injury in the small intestine are initiated during ischemia when the enzyme xanthine dehydrogenase is converted to xanthine oxidase, and its substrate, hypoxanthine, accumulates as a result of ATP utilization.[31,32] However, little xanthine oxidase activity exists during ischemia, because oxygen is required as an electron acceptor. During reperfusion, xanthine oxidase rapidly degrades hypoxanthine in the presence of oxygen, which acquires a single additional electron, producing superoxide (Figure 6-6).[31] Superoxide contributes to oxidative tissue damage, but this reactive oxygen metabolite is relatively lipid insoluble, limiting the level of injury. The more important role for superoxide is in the generation of neutrophil chemoattractants.[26,27] Superoxide interacts with lipid membranes, triggering arachidonic acid metabolism in the process of seeking to couple its unpaired electron. For example, the arachidonic acid metabolite leukotriene B_4, produced by the lipoxygenase pathway, serves as a chemoattractant that also activates neutrophils. Because of the critical role of xanthine oxidase, inhibition of this enzyme in feline studies of intestinal ischemia/reperfusion injury prevented infiltration of neutrophils, and subsequent mucosal injury.[27,29] Subsequent studies demonstrated that reperfusion injury could be inhibited at several levels of the reperfusion cascade, including scavenging superoxide with superoxide dismutase, inhibiting neutrophil infiltration with monoclonal antibodies directed against neutrophil adhesion molecules, and scavenging neutrophil-released reactive oxygen metabolites.[27,31] Researchers were initially optimistic that this would provide practical therapeutic interventions, because many of the treatments tested, including the xanthine oxidase inhibitor allopurinol, could potentially be administered prior to reperfusing ischemic tissue during surgery.

Figure 6-6

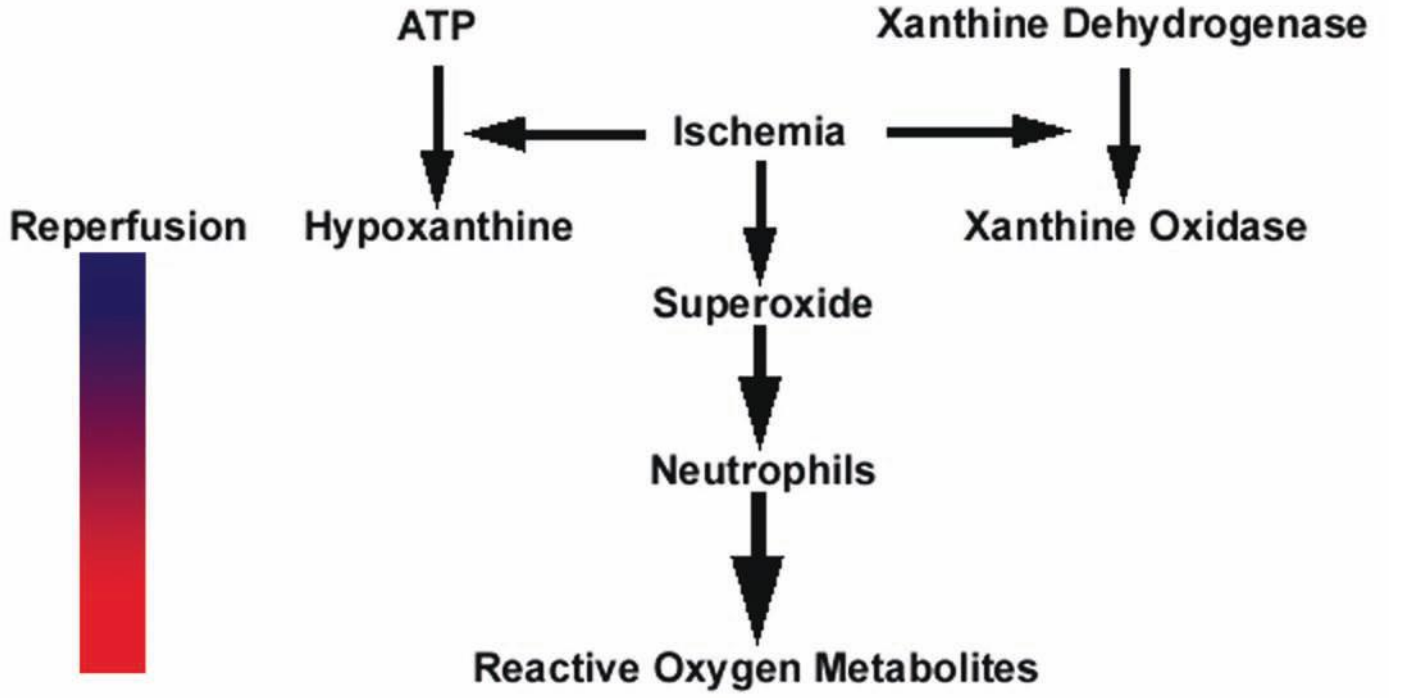


Diagram of the events that occur during ischemia/reperfusion injury, resulting in formation of reactive oxygen metabolites. As oxygenated blood is returned to tissues (depicted by the color gradient during reperfusion), reactive oxygen metabolites are generated. Neutrophils, which are attracted to the cells producing these metabolites, generate more reactive oxygen metabolites.

Unfortunately, treatment of reperfusion injury has not proven to be highly effective at reducing the level of mucosal injury in most cases of strangulating obstruction. One important reason for this is that strangulating obstruction induces maximal mucosal injury during the ischemic phase, as compared with studies in laboratory animals in which "low-flow" ischemia was used.[33] The latter involves reduction but not cessation of arterial flow, which induces relatively minor levels of injury, while priming tissues for injury during subsequent reperfusion.[28,34] Studies in horses using low-flow ischemia indicate that equine tissues are susceptible to reperfusion injury following this type of ischemia.[35-38] For example, studies in equine jejunum have

shown that capillary permeability is increased, associated with neutrophil infiltration during reperfusion.[36] Although a direct link to xanthine oxidase has not been shown, equine small intestine expresses substantial levels of xanthine dehydrogenase, which is converted to xanthine oxidase during ischemia.[39] Low-flow ischemia studies in equine colon have shown continued mucosal degeneration during reperfusion associated with marked neutrophil infiltration, despite the fact that the equine colon does not express appreciable levels of xanthine oxidase. Alternative oxidant enzyme sources such as aldehyde oxidase have been suggested as potential sources for the reactive oxygen metabolites.[37]

Having shown the capacity of equine tissues to develop reperfusion injury, additional studies have been performed to determine if reperfusion injury occurs in clinically applicable models of ischemia that simulate strangulating obstruction. In one study assessing either arteriovenous or venous occlusion in equine jejunum, a small degree of reperfusion injury was documented after 3 hours of ischemia;[40] however, the level of ischemic injury was near-maximal after 3 hours, and the additional injury that developed during reperfusion was not sensitive to allopurinol, a xanthine oxidase inhibitor, or DMSO, a reactive oxygen metabolite scavenger.[41] The likely cause of reperfusion injury in this instance was initiation of epithelial injury during ischemia, including initiation of apoptosis that could not be reversed during reperfusion.[16] Initial studies of morphologic changes occurring with total arterio-venous occlusion (including obstruction of blood flow through the bowel wall) documented initial mucosal cell loss with subsequent loss and necrosis after reperfusion. Intraluminal administration of oxygen was effective in decreasing the progressive morphologic change during the period of reperfusion.[42] More recent studies in equine small intestine,[22] and studies in equine colon[43] using ischemic models relevant to strangulating obstruction have failed to detect any level of reperfusion injury. Studies of strangulating obstruction in laboratory animals have also shown that this type of ischemic insult is less likely to develop reperfusion injury.[44,45]

Other species-specific factors also may affect the potential for equine tissues to develop reperfusion injury. For example, the foal appears to have very low concentrations of xanthine oxidase in the small intestine,[33] whereas concentrations in adult horses are much greater, particularly in the proximal small intestine.[39] In addition, horses appear to have low numbers of resident neutrophils in the intestinal mucosa,[33] and it is this population of neutrophils (rather than those recruited from the circulation) that appear to be most critical for induction of reperfusion injury.[28] The increases in neutrophils in both the mucosa and serosa in horses after ischemia reperfusion suggest that neutrophils from the systemic circulation localize in the injured tissues.[10]

In a review of the pathogenesis of intestinal reperfusion injury in the horse, the concept of a therapeutic window wherein treatment of reperfusion injury would be beneficial was suggested.[31] The basis of this concept is that there are certain conditions under which ischemic injury is minimal, and that tissues are severely damaged during reperfusion.[45] Thus, under conditions of low-flow ischemia, very little injury is demonstrated during 3 hours of ischemia, but remarkable injury occurs after 1 hour of reperfusion.[26-29] A narrow therapeutic window may exist under conditions of strangulating obstruction where severe injury occurs rapidly during ischemia, thereby limiting the prevention of further injury with treatments such as antioxidants. Nonetheless, this does not mean that treatments directed against reperfusion injury have no potential place for treatment of horses with strangulating obstruction, particularly as new treatments become more effective. Multimodal therapies involving intravascular or intraluminal infusion of solutions containing antioxidants, intestinal nutrients, and vasodilators have proven very effective in vitro and in vivo, although these treatment modalities have been used predominantly in low-flow ischemia models (Table 6-1).[46-49] It is also becoming clear that the consequences of reperfusion injury are more widespread, and involve tissues other than the intestinal mucosa. Low-flow ischemia models have demonstrated neutrophil infiltration into the serosa (Figure 6-7) that likely contributes to important complications such as adhesions.[9,57] This neutrophil infiltration appears to be relevant to strangulating obstruction, because similar neutrophil infiltrates were noted in the resection margins of resected strangulated small intestine.[8] Thus, although antioxidant-based therapies may be unable to reduce mucosal injury, because of its rapid onset during ischemia, both immediate and subsequent treatments may be able to reduce neutrophil infiltration in other layers of the intestine. In addition, once strangulated intestine has been reperfused, even if no reperfusion injury to the mucosa occurs during the early phases of reperfusion, there may be injury to the mucosa associated with inflammation that develops during mucosal wound healing. In a recent study in a porcine model of strangulating obstruction, there was no evidence of neutrophil infiltration or further mucosal injury during 1 to 3 hours of reperfusion after a 1-hour period of ischemia, but significant neutrophil infiltration occurred between 4 and 18 hours after reperfusion.[58] These neutrophils collected beneath repairing epithelium and rendered this repairing mucosa more permeable to macromolecules. Interestingly, this injury was inhibited by treatment at the time of reperfusion with superoxide dismutase (complexed with polyethylene glycol to prolong its half-life), or treatment with a monoclonal antibody directed against critical neutrophil adhesion molecules (CD11/ CD18).[58] Neutrophil infiltration of the mucosa was also reported in the horse during reperfusion after low flow ischemia (Figure 6-8).[59]

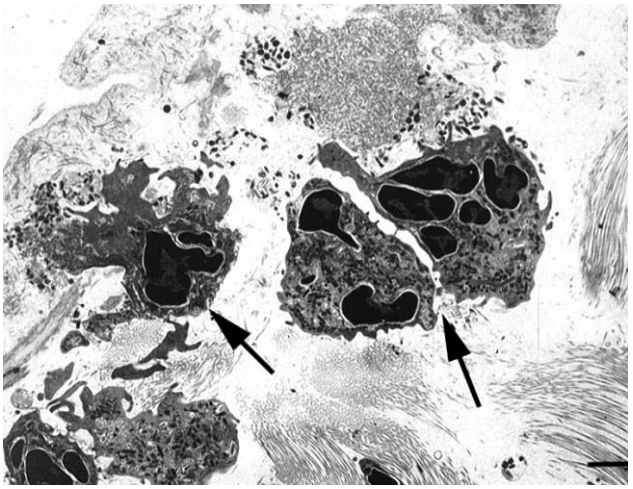
Table 6-1

A Partial List of Therapeutics that have been used Experimentally for Treatment of Ischemia/Reperfusion Injury in Horses.

Therapeutic	Segment of intestine	Type of ischemia	Time of ischemia/reperfusion	Effect of treatment on mucosa	References
DMSO	Jejunum	Arterial occlusion	1 hour/1 hour	None	20,21
Superoxide dismutase	Jejunum	Anoxia (*in vitro*)	15 min/15 min	Reduced injury	50
Allopurinol DMSO Intraluminal O_2 insufflation	Jejunum	Venous obstruction Arteriovenous obstruction	3 hours/1 hour	None (all treatments evaluated separately)	41
U-74389G (21-aminosteroid)	Jejunum	Ateriovenous obstruction Low-flow	2 hours/2 hours 2 hours/2 hours	None None	51
Carolina Rinse[a]	Jejunum	Low-flow Low-flow/no flow Distention/ decompression	1 hour/1 hour 2 hour/10 days 1 hour/1hour	Reduced microvascular injury Decreased serosal fibroplasia None	49 46
Custom solution[b]	Jejunum	Low-flow (*in vitro*)	40 min/60 min	Reduced injury	47, 48
DMSO	Large colon	Venous obstruction Ateriovenous obstruction	1 hour/1 hour	None	43
U-74389G (21-aminosteroid)	Large colon	Arteriovenous obstruction	2 hours/2 hours	Prevented reductions in mucosal surface area	52
WEB 2086 (PAF[c] antagonist)	Large colon	Strangulating obstruction (720^0 volvulus)	3 hours/3-5 hours	None	53
DMSO Allopurinol U-74389G (21-aminosteroid) Manganese chloride	Large colon	Low-flow	3 hours/3 hours	None (all treatments evaluated separately)	54
High molecular weight dextran macromolecules	Large colon	Low-flow	3 hours/3 hours	None	55
L691880 (PAF[c] antagonist)	Large colon	Low-flow	3 hours/3 hours	None	56

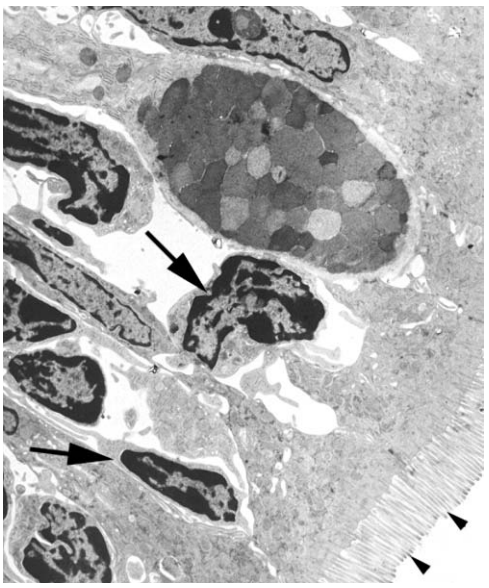
[a]Carolina rinse contained allopurinol, deferoxamine, glutathione, glucose, fructose, glycine, nicarpidine, adenosine
[b]Custom solution contained allopurinol, deferoxamine, DMSO, glutamine, dextrose, PGE1, adenosine
[c]Platelet activating factor
(Reprinted from Blikslager AT. Treatment of ischemic intestinal disease. Vet Clin North Am 19:715-728,2003.)

Figure 6-7



Transmission electron-micrograph of neutrophil infiltration into the serosa of intestine injured by ischemia/reperfusion. Neutrophils (arrows) are actively degranulating, contributing to serosal injury. Note the lack of mesothelial cells on the edge of the serosa. Bar = 5μm.

Figure 6-8



Photomicrograph of neutrophil infiltration into mucosal epithelium following ischemia/reperfusion of equine jejunum. The microvillus brush border of mucosal epithelium is marked with arrowheads. Neutrophils (arrows) physically separate epithelial cells as they infiltrate the mucosa and ultimately traverse the epithelium into the intestinal lumen. Bar = 5μm.

Intestinal Reparative Mechanisms

Mucosal Barrier Function

Before detailing mechanisms whereby intestinal mucosa is repaired, it is important to understand regulation of mucosal integrity under physiologic conditions or otherwise referred to as mucosal barrier function. Intestinal barrier function is vital because it prevents bacteria and associated toxins from gaining access to subepithelial tissues and the circulation. The mucosa has two conflicting functions: it must serve as a protective barrier while continuing to absorb solutes necessary to maintain the host. This conflict is most notable at the intercellular (paracellular) space, which allows passage of select solutes and water,[60-63] but which does not admit large molecules, including bacterial toxins.[64] The paracellular space is almost exclusively regulated by the tight junction,[65] which is the interepithelial junction at the apical-most aspect of the paracellular space. Although these tight junctions were originally viewed as inert cellular adhesion sites, it has become clear in recent years that tight junction permeability is dependent on tissue-specific molecular structure and regulated by a complex array of intracellular proteins and the cytoskeleton.[66] Tight junctions consist of a group of transmembrane proteins that interdigitate from adjacent cells, including occludin and a group of tissue-specific proteins called claudins.[67] These transmembrane proteins interact with the cytoskeleton via a series of tight junction plaque proteins, including zonula occludens (ZO)-1, ZO-2, and ZO-3.[68] In general, the relative contractile state of the actin cytoskeleton determines the degree to which tight junctions are open or closed, and this, in turn, is dependent on the activation of plaque proteins and a range of intracellular signaling molecules.[69,70] Tight junction function also is dependent on the anatomic location. For example, tight junctions in the crypts leak more than those in the surface epithelium because of fewer and less organized tight junction strands.[71,72] Conversely, surface epithelium has a greater number of well organized tight junction strands that result in epithelium with a relatively high resistance.[71] This correlates well with the absorptive function of epithelium located on the mucosal surface and the secretory

function of crypt epithelium. Structure of tight junctions also varies with the segment of intestine. For instance, tight junctions in the ileum have more strands than in the jejunum, which is reflected by a higher transepithelial resistance in the ileum.[73]

Aside from interepithelial tight junctions, the other components of the mucosal barrier are the apical epithelial membrane and an adherent layer of mucus. In the small intestine, epithelial apical membranes are far less permeable than adjacent interepithelial tight junctions. This makes the small intestine relatively "leaky". Conversely, colonic mucosa is far less permeable than the small intestine, largely because colonic tight junctions are less permeable to ions and macromolecules than are tight junctions in the small intestine.[71,74] Because of the relative impermeability of the apical epithelial membrane, an array of distinct protein transporters are present that selectively allow entry of specific ions, nutrients, and water. Although the apical epithelial membrane provides a stringent barrier against potentially harmful luminal contents, including bacteria and their toxins, some pathogenic bacteria have developed specific mechanisms for penetrating the apical membrane. For example, *Salmonella typhimurium* can penetrate the apical membrane using a type III secretion apparatus, which allows the insertion of bacterial proteins into the host cell.[75,76]

Mucus, secreted by goblet cells, adheres to the microvilli on the apical epithelial membrane, forming the so-called unstirred water layer. The most critical barrier-forming component of mucus is mucin glycoproteins, which provide the viscoelastic properties required to maintain a continuous protective layer over the mucosa during intestinal motility and secretion. This mucous protective layer prevents bacterial organisms from adhering to the apical epithelial membrane as a result of its physical properties, including electrical charge.[77] The importance of this component of the barrier is highlighted by studies showing that pathogenic bacteria are able to adhere to and invade intestinal epithelium in the absence of the unstirred water layer.[78] Perhaps the most relevant cause of diminished mucous barrier function is surgical stress, although the reasons for reduced mucus formation after abdominal surgery are not clear. Interestingly, the mucous layer can be reconstituted in surgical patients by administration of exogenous gel-forming compounds such as high molecular-weight polyethylene glycol.[79]

Villus Contraction and Restitution

In the small intestine, villi contract during injury (Figure 6-5) and during the reparative phase after injury in order to reduce the size of the epithelial defect. Villus contraction that begins during injury is mediated by enteric nerves, and the contractile element is a series of myofibroblasts situated immediately beneath the epithelial basement membrane.[80] Once the injurious event has subsided, such as correction of a strangulating lesion, villus contraction continues to a lesser degree, as a result of prostaglandin-mediated contraction of smooth muscle cells that line the central villus lacteal.[81] The initial phase of contraction that occurs during injury is very important to mucosal repair; inhibition of this process by blocking enteric nerve conduction delays repair of the mucosal defect.[80] The subsequent phase of villus contraction that continues during early mucosal repair under the influence of prostaglandins appears to have little effect on the speed of mucosal recovery. For example, treatment of acutely injured small intestinal tissues with a nonselective cyclooxygenase (COX) inhibitor prevented ongoing villus contraction, but this had no discernible effect on mucosal repair.[82]

As villi contract, assuming the basement membrane is intact, epithelial cells from the margins of the wound migrate in a centripetal direction to resurface toward the tip of the villus; a process called restitution.[80] Restitution also occurs in denuded colonic mucosa, except that it may proceed more rapidly because of the lack of villi.[83] Epithelial restitution is solely a migratory event that does not depend on provision of new enterocytes by proliferation. Cellular migration is initiated by extension of cellular lamellipodia that receive signals from the basement membrane via cell surface integrins (Figure 6-9). Intracellular signaling converges on the actin cytoskeleton, which is responsible for movement of lamellipodia. Specific components of the basement membrane appear to be critical to the migratory process. For example, application of antibodies to collagen types III and IV, which are important components of intestinal mucosal basement membrane, impedes epithelial restitution.[84,85] Other elements of the basement membrane, including proteoglycans, hyaluronic acid and noncollagenous proteins such as fibronectin and laminin may also provide important signals.[86] These subepithelial matrix components that facilitate restitution may form the basis for clinical treatments designed to speed the repair process, analogous to administration of matrix components to horses with articular cartilage damage.

The process of restitution is dependent on a group of compounds called polyamines.[87,88] The rate-limiting enzyme in the formation of the polyamines spermine, spermidine, and putrescine is ornithine decarboxylase. Polyamines are constructed of long carbon chains which are heavily protonated under physiologic conditions. The mechanism whereby polyamines stimulate epithelial restitution is not clear, although it may relate to their physical structure. Polyamines are relatively long carbon chain molecules that are heavily protonated because of their amine groups, and may, therefore, facilitate restructuring of extracellular matrix in order to facilitate cellular crawling. For example, physical extension of lamellipodia is significantly reduced in rodent IEC-6 intestinal epithelial cells depleted of polyamines.[89]

Figure 6-9

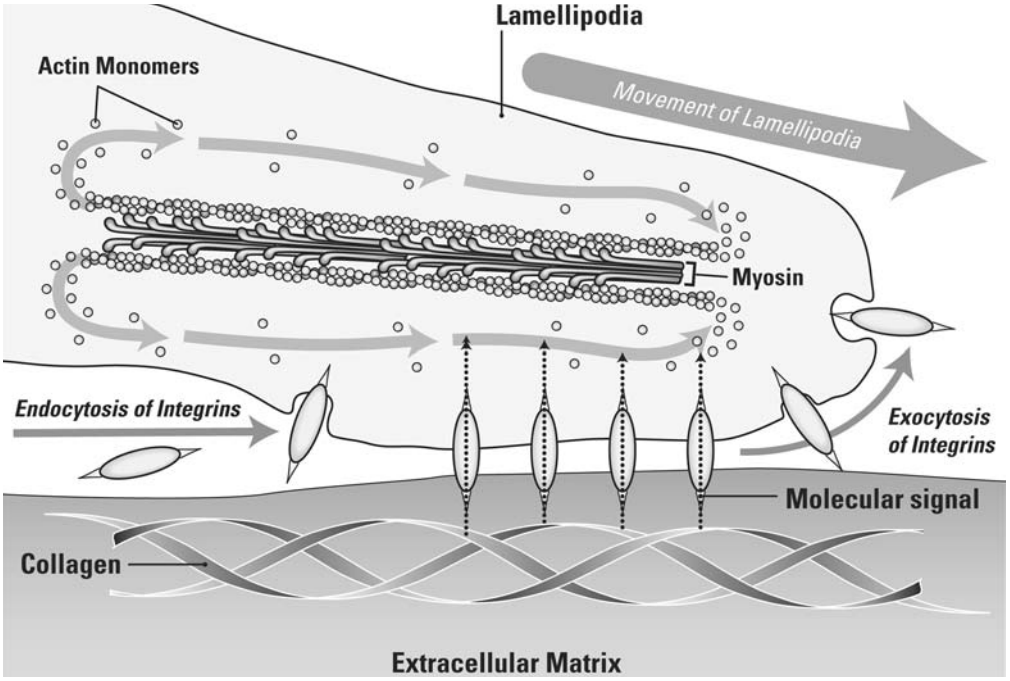


Diagram of the cellular events that occur during epithelial restitution. Note extension of a lamellipodia across denuded basement membrane, driven by "treadmilling" of the actin-myosin cytoskeleton. The signal that drives this treadmilling process is derived from basement membrane components, which convey information via integrins to the cell.

Other important mediators of restitution include growth factors, which are locally produced peptides that interact with specific cell surface markers to induce a cellular response. The most important of these growth factors in early mucosal repair events is transforming growth factor-beta (TGF-β), which is produced by gastrointestinal epithelium, and is a potent stimulus of epithelial restitution and modulator of the extracellular matrix.[90] Other growth factors with potent effects on restitution include epidermal growth factor (EGF), which is produced by the salivary glands and duodenal Brunner's glands, and the related TGF-α, produced by small intestinal enterocytes. These growth factors share approximately 30% of their amino acid structure, bind to the same receptor on the basolateral surface of enterocytes, and are not related to TGF-β.[91] The physiologic role of EGF is somewhat difficult to discern because it is present in the intestinal lumen, with no apparent access to its basally located receptor.[92] It has been proposed that EGF acts as a "surveillance agent" that gains access to its receptor during epithelial injury (when the EGF receptor would likely be exposed) to stimulate proliferation.[92] Transforming growth factor-α presumably has a similar role, but it is present in greater concentrations in the small intestine where it is produced by differentiated villus enterocytes. The mature peptide is cleaved from the extracellular component of the transmembrane TGF-α precursor and released into the lumen.[91]

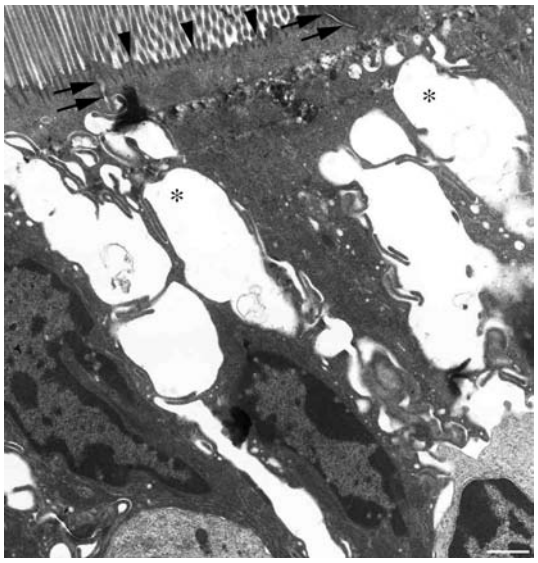
Another group of proreparative peptides that are locally produced within the gastrointestinal tract are the trefoil peptides. Under physiologic conditions, trefoil peptides are secreted by mucus-producing cells at distinct anatomic sites. For example, the trefoil peptide pS2 is produced by gastric epithelium whereas intestinal trefoil peptide is produced by small and large intestinal mucosa;[93] however, any of the trefoil peptides may be upregulated within repairing epithelium regardless of anatomic site.[90,94] Trefoil peptides are the most potent stimulants of epithelial migration *in vitro*, and their effects are independent of growth factors.[95] The importance of trefoil peptides to the mucosal repair response in vivo is illustrated by gene knockout studies, in which mice deficient in intestinal trefoil peptide have dramatically reduced ability to repair injured intestine.[96] The mechanisms whereby trefoil peptides stimulate epithelial migration are yet to be fully characterized, but appear to involve translocation of the adherens junction protein E-cadherin, thereby allowing cells to become untethered from neighboring cells.[90]

Tight Junction Closure

Although epithelial restitution results in gross closure of previously denuded regions of gastrointestinal mucosa, closure of interepithelial spaces is ultimately required to restore normal epithelial barrier resistance (Figure 6-10).[6,7,97] Because the tight junction is principally responsible for regulating the permeability of the inter-epithelial space, repair and closure of this structure is critical to restore intestinal barrier function. This tight junction closure appears to be mediated by prostaglandins, particularly PGE_2.[98] Therefore, administration of nonselective COX inhibitors retards recovery of intestinal barrier function, not as a result of

inhibition of villous contraction or restitution, but as a result of delaying recovery of normal levels of paracellular permeability.[98] This may have particular relevance to horses with colic, which are routinely treated with the non-selective COX inhibitor flunixin meglumine. In one study in which horses were subjected to 2 hours of complete jejunal ischemia, postoperative treatment with flunixin meglumine retarded recovery of mucosal barrier function for at least 18 hours.[99] We have shown that this results in significant increases in absorption of lipopolysaccharide, suggesting that these findings are clinically relevant.[100]

Figure 6-10



Electron micrograph of the mucosal epithelium showing the apical membrane (arrowheads) with its microvilli, interepithelial tight junctions (arrows), and paracellular spaces (asterisks). This section of jejunum has been subjected to ischemia/reperfusion, and is restituting; however, the paracellular spaces and tight junctions show evidence of dilatation (asterisks). Closure of the tight junctions will result in restoration of normal paracellular apposition, and recovery of mucosal barrier function. Bar = 3μm.

Mucosal Proliferation

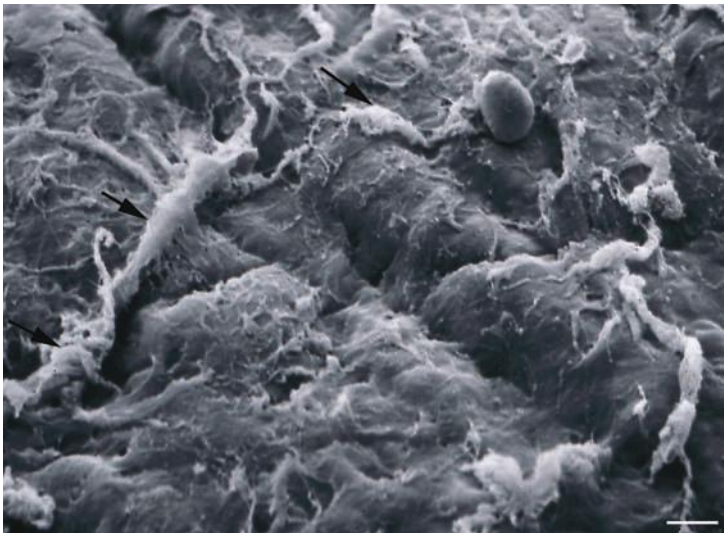
Once the epithelial barrier has been restored, normal mucosal architecture must be reestablished to allow normal gut absorptive and digestive functions. The flattened villus epithelium that characterizes restitution is replaced by newly proliferated crypt epithelium. Under normal circumstances, new enterocytes are formed by division of stem cells, of which there are approximately 4 at the base of each mucosal crypt. Newly divided enterocytes migrate from the crypt onto the villus.[101] During migration, enterocytes differentiate and acquire specific absorptive and digestive functions. Fully differentiated enterocytes reside on the upper third of the villus for 2 to 3 days, and are then sloughed into the intestinal lumen.[102] This process is accelerated during mucosal repair, which requires increased rates of proliferation. Increased proliferation may be stimulated within 12 to 18 hours by a variety of locally available gut-derived factors, including luminal nutrients, polyamines, and growth factors.[103] The return of the normal leaf-like shape of the villus occurs subsequent to the appearance of normal columnar epithelium.

Factors involved in regulating and stimulating epithelial proliferation include polyamines, growth factors, and luminal nutrients. Polyamines are produced by fully differentiated enterocytes at the villus tip, and may reach the crypt either within sloughed luminal epithelium or via local villus circulation in order to stimulate crypt cell proliferation.[104] After intestinal injury, polyamines appear to stimulate enhanced proliferation by increasing the expression of protooncogenes, which control the cell cycle.[105] The mechanism whereby polyamines influence gene expression likely relates to the cationic nature of these compounds, which may influence the tertiary structure of negatively charged DNA and RNA.[88] Of the growth factors that stimulate restitution, EGF and TGF-α also stimulate proliferation, whereas TGF-β has an inhibitory effect on proliferation. Normal intestinal nutrients also have potent effects on epithelial proliferation, suggesting that early re-feeding of patients with intestinal injury likely stimulates mucosal recovery. The principal metabolic fuel of small intestinal enterocytes is glutamine, whereas for colonocytes it is butyrate; however, recent studies suggest that glutamine and butyrate have more specific proliferative actions aside from their role as nutrients. In the piglet IPEC-J2 enterocyte cell line, glutamine enhances gene transcription by increasing mitogen-activated protein kinase activity.[106,107] Similarly, butyrate stimulates mucosal growth after infusion into the colon in the rat.[108] Due to its growth-promoting actions, glutamine prevents intestinal mucosal atrophy and dysfunction that accompanies starvation[109,110] and long-term total parental nutrition.[111,112] Intestinal nutrients may also synergize with other proliferative agents. For example, administration of glutamine and TGF-α to porcine ileum that had been subjected to 2 hours of ischemia resulted in a synergistic increase in mitogen-activated protein kinase activity, enterocyte proliferation, and villous surface area.[103] Although there has been a concern that such early return to normal surface area may result in dysfunctional mucosal digestive and absorptive function because of re-surfacing denuded mucosa with immature epithelium, nutrients and growth factors also appear to promote early differentiation. In the case of glutamine and TGF-α restoration of post-ischemic small intestine, rapid recovery of digestive enzymes was also documented.[113]

Serosal Reparative Responses

Although a lot of attention has been directed toward mechanisms of mucosal restoration, repair of injured serosal surfaces is also a critical event, particularly considering the important role of adhesions in postoperative morbidity and mortality.[114] Prior studies indicate that distention/decompression or ischemia/reperfusion resulting from vascular occlusion leads to loss of serosal mesothelial cells and infiltration of neutrophils (Figure 6-7).[10] The altered microvascular permeability and neutrophilic infiltrate results in deposition of a fibrinous exudate (Figure 6-11) that is invaded by fibroblasts. Depending on the extent of the injury, adhesion formation may result when inflamed and fibrinous serosal surfaces become adhered, and a subsequent reparative response results in a fibrous scar. Therefore, several studies have been directed toward serosal reparative responses in order to reduce the incidence of adhesions. For example, by reducing the neutrophilic infiltrate immediately after injury, the extent of adhesion formation is significantly reduced. This has been proven in experimental studies in which serosal injury was induced by distention/decompression; treatment with Carolina Rinse significantly reduced serosal fibroplasia.[46] Furthermore, application of a variety of topical agents to a site at increased risk for adhesions, such as an anastomosis, can also modulate the degree of adhesion formation. For example, application of a hyaluronate solution to the serosal surface of a jejunal end-to-end anastomosis significantly reduced adhesion formation, presumably because of decreased deposition of fibrin.[115] Similar results were obtained with application of a hyaluronate membrane,[116] which is now commercially available, making this a clinically applicable technique. Although hyaluronate may simply serve as a barrier against contact with inflamed serosal surfaces, it has also been shown to have selective anti-inflammatory properties in inflamed equine joints, which might account for these effects.

Figure 6-11



Scanning electron micrograph of the serosa following ischemia/reperfusion injury. Note deposition of fibrin (arrows) that may ultimately lead to the formation of fibrous adhesions. Bar = 4μm

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Prevention and Treatment of Postoperative Intraabdominal Adhesions in Horses

Chapter 7

P.O. Eric Mueller

Despite numerous research and clinical investigations, intraabdominal adhesions continue to present clinical challenges to the equine surgeon. Depending on the location and organization of an adhesion, it may remain clinically "silent" or be the cause of serious complications. Fibrinous and omental adhesions are normal responses to peritoneal injury and inflammation and rarely cause clinical problems.[1-3] Adhesions become clinically important when fibrinous adhesions mature to restrictive fibrous adhesions that compress or anatomically distort the intestine, narrowing the intestinal lumen and impeding the normal passage of ingesta (Figure 7-1). Adhesions may also lead to the development of intestinal incarceration, strangulation, or volvulus, predisposing the patient to intestinal obstruction and recurrent signs of abdominal pain. Treatment of mature adhesions often is unrewarding, costly, and associated with high patient morbidity and mortality. An emphasis, therefore, should be placed on preventing adhesions rather than treating adhesions once they have formed. The primary method of minimizing the development of intraabdominal adhesions postoperatively continues to be meticulous, atraumatic, surgical technique. However, the presence of preexisting peritoneal inflammation and the inherently invasive nature of surgery make it difficult to prevent adhesion formation in horses. The current pharmacologic and technical advancements for adhesion prevention are directed at minimizing peritoneal trauma and inflammation, separating potentially adhesiogenic tissues during early postoperative healing, enhancing peritoneal fibrinolysis, and promoting intestinal motility.

Figure 7-1A

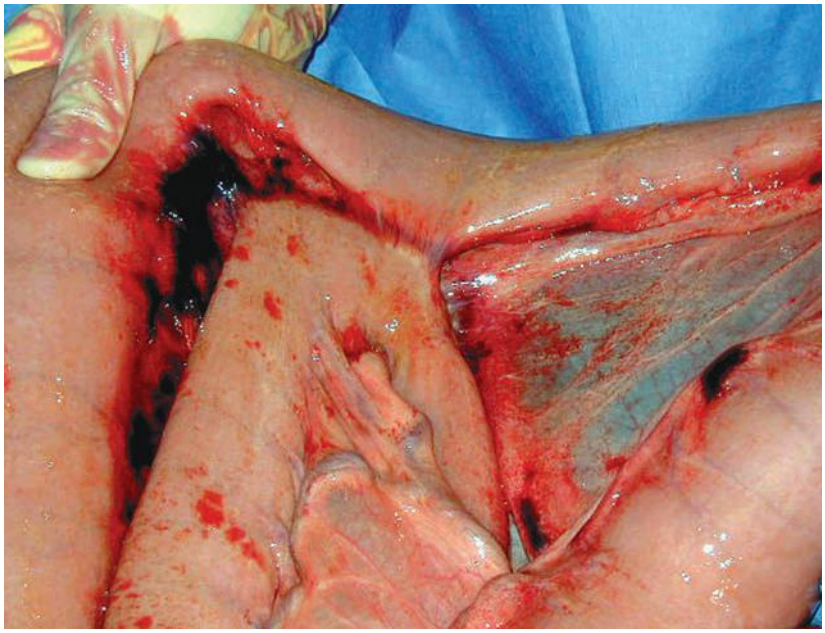
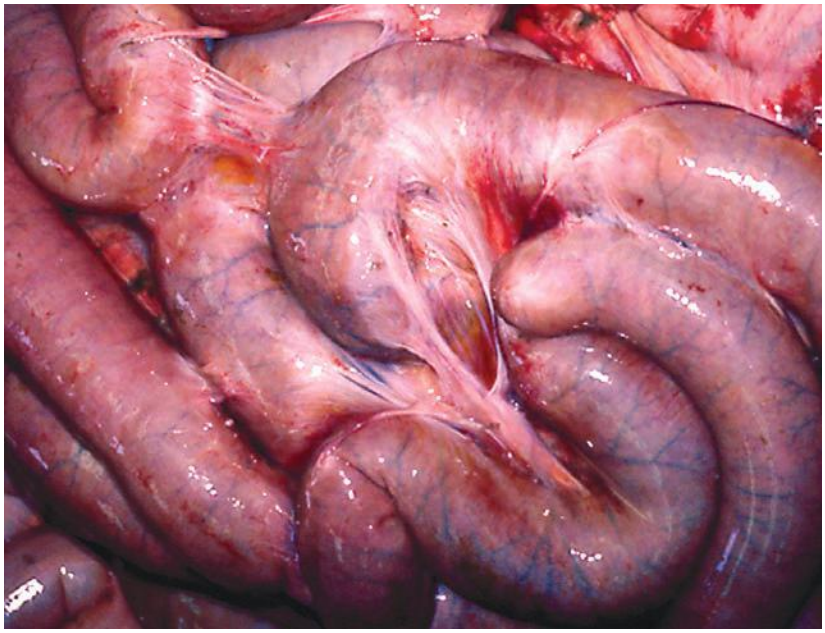


Figure 7-1B



A.) A jejunojejunal adhesion identified during repeat celiotomy for recurrent acute abdominal pain in a horse. The adhesion caused distortion and secondary luminal obstruction of the small intestine. **B.)** Small intestinal adhesions subsequent to a volvulus in which no enterotomy was performed.

Early recognition and treatment of acute abdominal pain, along with advances in anesthesia, surgery, and perioperative care have decreased the morbidity and mortality associated with surgical treatment of intestinal diseases in horses. The improved survival rate for horses undergoing exploratory celiotomy for intestinal diseases has resulted in more horse owners opting to pursue surgical treatment. Correspondingly, the clinical significance of long-term postoperative complications, such as postoperative adhesion formation, has concurrently become more apparent.[4-6]

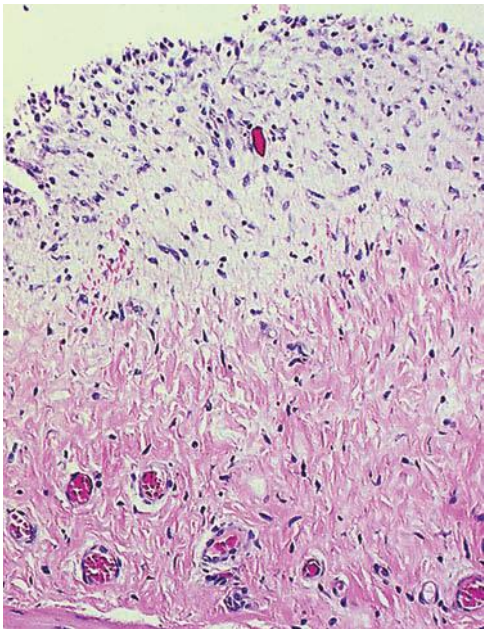
The incidence and clinical consequences of postoperative adhesions are well documented in people. A recent prospective clinical study in human patients who had previous laparotomies demonstrated a 93% incidence of adhesion formation.[7] Furthermore, intestinal obstructions due to intraabdominal adhesions accounted for more than 3% of all major laparotomies and more than 25% of all intestinal obstructions in people.[8] The economic burden of adhesion-related intestinal obstruction in the United States is enormous, with an estimated annual health care expenditure of $1.3 billion on surgical adhesiolysis and related hospital stays.[9]

The specific incidence of postoperative adhesions in horses is not known, but is most likely underestimated because most adhesions are neither severe nor extensive enough to result in clinical symptoms. Additionally, many horses with postoperative pain that may be attributed to adhesion formation respond to medical management or are euthanized without a necropsy being performed. Published incidence rates of adhesions in horses have been determined primarily by findings obtained during repeat celiotomy or postmortem examination.[10-13] In horses surviving surgery for small intestinal lesions, the reported incidence of adhesions that necessitate repeat celiotomy or euthanasia ranges from 14 to 22%.[10-13] Adhesions are the most common cause of recurrent abdominal pain in horses after small intestinal surgery and the second most common cause for repeat celiotomy in horses after abdominal surgery for any reason, with intestinal ischemic necrosis being the most common.[12] When all abdominal surgeries in horses are considered, however, the incidence of postoperative adhesions has been estimated to be approximately 5%.[13]

Current Concepts in Pathophysiology of Adhesion Formation

The abdominal parietal and visceral peritoneum is composed of loose connective tissue beneath a single layer of mesothelial cells loosely interconnected by desmosomes and separated by a basement membrane.[14] These layers provide external support to the abdominal and intestinal musculature and maintain a lubricating layer at the serosal surface.[3,15] Injury or inflammation of the peritoneal mesothelium initiates adhesion formation by stimulating procoagulant activity of the mesothelium or exposed basement membrane and which is characterized by secretion of serofibrinous exudate and deposition of fibrin (See Chapter 7).[14,16] The result is a fibrin matrix that can form fibrinous adhesions between adjacent viscera or peritoneum within hours of injury.[17] The initial fibrin matrix provides a scaffold for vascular and cellular migration, allowing tissue repair and restoration of the inflamed serosa and mesothelium.[3,17,18] As normal peritoneal healing progresses, fibroblasts and endothelial cells migrate into the fibrin to form a layer of granulation tissue that fills the original mesothelial defect. Primordial mesenchymal cells then form fibroblasts or differentiate into mesothelial cells and cover the granulation tissue (Figure 7-2).[19,20]

Figure 7-2



Photomicrograph of jejunal serosal adhesion resulting from experimental ischemia (2 hours) and reperfusion (10 days). Fibroplasia on the surface of the original serosa has created a layer of fibroblasts without regeneration of the mesothelial surface.

Local peritoneal fibrinolytic activity lyses the fibrin and fibrinous adhesions within 48 to 72 hours. Therefore, when inflammation is not excessive, adhesions are removed before they mature to fibrous tissue.[4,19,21] However, intestinal ischemia or inflammation, caused by strangulation or distention, or surgical manipulation and the corresponding incidental trauma may depress peritoneal fibrinolytic activity, thereby, predisposing to the persistence of intraabdominal fibrin and ultimately to adhesion formation.[3,4,15,22-25]

Coagulation, fibrinolysis, kinin/bradykinin, arachidonic acid metabolism, and complement activation are some of the complex biological processes that are involved in the pathogenesis of adhesion formation.[21] The fibrinolytic system is the principal modulator of adhesion formation and is responsible for lysis of fibrin into fibrin degradation products through the action of the enzyme plasmin.[17,26-28] Plasmin is stored as the inactive substrate plasminogen, which is converted to the active enzyme primarily by tissue plasminogen activator (tPA), and to a lesser extent, by urokinase-type plasminogen activator (uPA). Tissue plasminogen activator is present in virtually all tissues and is responsible for 95% of plasmin generation in the human peritoneum.[23]

Fibrinolysis is a potent process and is tightly regulated by plasminogen activator inhibitors type 1 (PAI-1) and type 2 (PAI-2). Synthesis of these inhibitors is induced by stimuli such as trauma, infection, or endotoxin.[22,29,30] These inhibitors bind and form inactive complexes with tPA and uPA. Slower acting plasma proteins, α2-antiplasmin, α2-macroglobulin, and α2-antitrypsin are also inhibitors of plasmin activity; however, their role in tissue repair and adhesions is not well delineated.[17] A decrease in plasminogen activator activity may result from decreased concentrations of plasminogen activators, and/or increased expression of plasminogen activator inhibitors.[17,24,26,28,31,32]

The difference between normal peritoneal healing and adhesion formation lies in the balance between fibrin deposition and degradation and, ultimately, fibrosis of the serosa. Peritoneal fibrinolytic activity has been hypothesized to play an important role in adhesion formation.[16,17,22,24-26,32] If local fibrinolysis is adequate, fibrinous adhesions are lysed and normal mesothelial restoration occurs. In contrast, if local fibrinolysis is insufficient, fibrin persists, becomes infiltrated with fibroblasts and capillaries, and permanent fibrous adhesions are formed. The precise role of peritoneal hypofibrinolysis in the pathogenesis of adhesion formation has yet to be elucidated.

Risk factors associated with postoperative adhesion formation include small intestinal disease,[4,10,11,13,33] intestinal resection and anastomosis,[13,34] and abdominal surgery in foals[15] or Miniature Horses.[35] It has been the author's experience that middle to aged horses (more than 15 years of age) are less likely to develop complications related to postoperative adhesion formation.

Diagnosis of Intraabdominal Adhesions

The presenting clinical signs of horses with intraabdominal adhesions are similar to those associated with acute abdominal pain secondary to small intestinal obstruction or strangulation (see Chapter 6). Consequently, a complete and thorough history, physical examination, including nasogastric intubation, transrectal examination, abdominocentesis, and laboratory examination should be performed. Information obtained in the clinical history of previous abdominal surgery or diseases causing severe intraabdominal inflammation, such as diffuse enteritis or peritonitis, should alert the clinician to the possibility that intraabdominal adhesions may be responsible for clinical signs of acute abdominal pain. Although not common, severe peritoneal inflammation secondary to enteritis and peritonitis may result in intraabdominal adhesion formation and clinical symptomatology in horses or foals that have not undergone an exploratory celiotomy.

The clinical signs associated with intraabdominal adhesions vary in relation to the degree of luminal or vascular compromise. Horses with adhesions that distort or compress the intestine without compromising vascular integrity may have clinical signs consistent with mild to moderate recurrent abdominal pain. In contrast, adhesions that result in complete luminal obstruction or secondary vascular compromise as a result of intestinal incarceration or strangulation are usually associated with clinical signs of severe, unrelenting abdominal pain. Results of cytologic examination of peritoneal fluid obtained from horses with intraabdominal adhesions usually reflect the nature of the current disease process (obstruction or strangulation) and are not specifically indicative of adhesion formation. Transrectal examination often reveals distention of the segment of affected intestine. Chronic, partial obstruction produces dilated, thickened intestine, proximal to the obstruction. If the adhesion is located in the caudal aspect of the abdomen, in rare instances it may be palpated by the examiner. Ultrasonography and laparoscopy are additional ancillary procedures that may be performed to support or confirm the diagnosis of intraabdominal adhesions (see Chapter 15).[36-39]

Current Concepts in Prevention of Adhesion Formation

An emphasis is placed on prevention of adhesion formation, because treatment of mature adhesions often is unrewarding, costly, and associated with high patient morbidity and mortality.[4,6,7,11,40,41] The primary objectives in preventing adhesions are 1) to minimize peritoneal and serosal inflammation, 2) to maintain or enhance peritoneal fibrinolysis, 3) to mechanically separate potentially adhesiogenic surfaces, and 4) to stimulate adequate intestinal motility.[3,4,31,42-44]

Perioperative Pharmacologic Interventions to Prevent Adhesion Formation

Intravenous administration of broad-spectrum antimicrobials, non-steroidal anti-inflammatory agents, and dimethyl sulfoxide (DMSO; 20 mg/kg) has been reported to minimize adhesion formation.[3,4,15,34,44-48] All of these pharmacologic agents have been shown to decrease peritoneal inflammation, thereby, minimizing fibrin production and subsequent adhesion formation. A routine perioperative pharmacologic regimen for a horse undergoing exploratory celiotomy includes potassium penicillin (22,000 IU/kg, IV, every 6 hours), gentamicin (6.6 mg/kg, IV, every 24 hours), flunixin meglumine (1.1 mg/kg, IV, every 12 hours) and DMSO (100 mg/kg in 1L 0.9% NaCL, IV, every 8 hours). If a typhlotomy or small colon enterotomy is anticipated, metronidazole (TEVA Pharmaceuticals Inc., Sellersville, PA 18960) (20 mg/kg, P.O. or per rectum, every 6 hours) is administered to provide antimicrobial activity against anaerobes. Antimicrobial administration is continued for 48 to 96 hours postoperatively, depending on the location and severity of the initial lesion, duration of surgery, and the potential for intraoperative contamination.

Heparin, a naturally occurring proteoglycan, has been reported to decrease adhesion formation in an intestinal ischemia-reperfusion model in ponies but not in foals.[43,48] Heparin acts as a cofactor of antithrombin III to increase the rate of antithrombin III inactivation of serine protease coagulation factors. The result is decreased production of thrombin, which is responsible for the conversion of fibrinogen to fibrin, and ultimately the formation of fibrous adhesions. Heparin also enhances fibrinolysis by stimulating plasminogen-activator activity. The recommended dosage and route of administration of heparin remain controversial. Systemic dosages from 20 to 100 IU/kg every 6 to 12 hours, for 48 to 72 hours postoperatively have been used.

Intraperitoneal administration of heparin has been shown to reduce adhesion prevention in laboratory animals;[49,50] however, neither experimental nor controlled clinical studies have been performed in horses. In horses at a risk of adhesion formation, the author administers 30,000 IU of heparin (Heparin sodium, Elkins-Sinn Inc., Cherry Hill, NJ 08003) diluted in 4L of lactated Ringer's solution into the abdomen before closure of the abdominal incision. Intravenous administration of heparin sulfate (40 IU/kg, every 6 hours) is continued for 48 to 72 hours postoperatively. Systemic administration of heparin results in a transient decrease in the PCV by as much as 50% after 3 to 4 days of heparin therapy.[51] This decline in PCV is due to erythrocyte agglutination and not hemorrhage or hemolysis.[51] The PCV returns to normal within 4 days after cessation of heparin therapy.

Recombinant tissue plasminogen activator (recombinant tPA) (Alteplase, Genentech, South San Francisco, CA 94080), a thrombolytic agent that binds to fibrin and activates the conversion of plasminogen to plasmin, decreases the incidence of postoperative adhesion formation in laboratory animal models.[52-55] Concentrations of 0.01 to 0.5 mg/ml have been used. The results of studies of the effect of recombinant tPA on healing of anastomosis have been controversial, with some studies indicating no effect,[52] and others indicating inferior anastomotic healing with intraperitoneal administration of recombinant tpA.[53] The intraperitoneal use of recombinant tPA in horses may not be economically practical. If adhesion prevention is demonstrated by adding lower concentrations of recombinant tPA to protective barrier solutions, such as sodium carboxymethylcellulose,[52] there may be potential benefit in equine abdominal surgery.

Postoperative ileus may increase the risk of adhesion formation by maintaining inflamed serosal surfaces in close apposition. Predisposing factors that have been implicated in the development of ileus include chronic intestinal distention, ischemia, peritonitis, excessive intestinal manipulation, electrolyte abnormalities, and sedative and anesthetic drugs[56] (see Chapter 4). Prolonged apposition of inflamed serosal or peritoneal surfaces is likely to result in the formation of restrictive, permanent fibrous adhesions between these surfaces. In addition, intestinal distention alone results in serosal injury and ischemia, and has been demonstrated to cause adhesions in foals.[15] Various gastrointestinal prokinetic agents, such as lidocaine hydrochloride, neostigmine, metoclopramide, erythromycin, and cisapride have been evaluated in experimental and clinical studies in horses.[56] The clinical benefit of these agents in horses after abdominal surgery remains controversial. Early return to enteral nutrition may be the most important factor in stimulating and maintaining intestinal motility postoperatively.

Intraoperative Considerations and Preventive Therapy

Minimizing peritoneal trauma and inflammation through meticulous aseptic surgical technique and removal of all potentially adhesiogenic tissues are the most important principles of adhesion prevention.[4,22,24,57] Strict adherence to Halsted's principles of surgery, including minimal and atraumatic tissue handling, meticulous hemostasis, minimizing tissue contamination from exposed bacteria-laden intestinal mucosa, minimizing exposure of foreign materials, and short surgery time are all essential to minimize the incidence of postoperative adhesion formation.

Starch powder present on commercially available surgical gloves incites peritoneal inflammation and significantly increases adhesion formation in a dose-dependent manner.[58-62] Simple rinsing of gloves before surgery does not effectively remove the starch powder from the glove surface; therefore, powder-free, hydrogel coated gloves (Biogel Powder Free Surgical Gloves, Regent Medical, Norcross, GA 30092) should be used when performing intraabdominal surgery.

Intestinal manipulation should be as atraumatic as possible. Serosal surfaces should be kept moist with balanced electrolyte solutions to prevent direct mesothelial damage from desiccation. Protective coating solutions such as 1% sodium carboxymethylcellulose (SCMC) (sodium carboxymethylcellulose, Aqualon Co., Wilmington, DE 19894) or 0.4% hyaluronate solution (Sepracoat, Genzyme Corp., Cambridge, MA 02139) (*see protective coating solutions*) should be applied to the surgeons' gloves and all serosal surfaces before and during intestinal manipulation to provide a protective lubricating barrier and minimize serosal friction, abrasion, and incidental surgical trauma.[5,6,63,64] Potentially adhesiogenic tissues such as devitalized intestine, or intestine of questionable viability should be resected. Inverting or appositional anastomotic suture patterns should be used to minimize peritoneal exposure of bacteria-laden mucosa and suture, and preserve normal intestinal motility and function, thereby, minimizing the incidence of adhesion formation.[65-68]

Although controversial, surgical techniques such as omentectomy have been advocated to minimize adhesion formation.[33] Omental adhesions may cause signs of abdominal pain by creating abnormal tension on the mesentery, or serving as a focus for intestinal obstruction or strangulation. Conversely, omental adhesions have also been reported to provide a vascular supply to potentially ischemic tissue, thereby, facilitating healing and potentially preventing adhesions.[2,22,42] In one retrospective study in horses, omentectomy was associated with a lower incidence of clinically significant adhesions.[33] In the author's opinion, omental adhesions rarely cause clinically significant problems. The author has been successful in intentionally suturing omentum to serosal surfaces to cover potentially adhesiogenic intestinal tissues in an effort to minimize subsequent adhesion formation. If this technique is elected, the possibility of future strangulations involving attached omentum must be weighed against the benefits of use of a vascular omental pedicle. Removal of inflamed or damaged omentum also seems logical to prevent future adhesions, although the risk of adhesion has not been documented.

Separation of Adhesiogenic Surfaces

Intraabdominal Lavage

Intraoperative abdominal lavage is advocated to prevent desiccation of serosal surfaces, minimize serosal trauma during intestinal manipulation, and remove blood, fibrin, and inflammatory mediators from the abdominal cavity.[34,57,69] Postoperative intraabdominal lavage through an indwelling tube placed at the time of surgery has been demonstrated to reduce the incidence of adhesions in an experimental serosal abrasion model of adhesion formation.[69] Ten liters of warm lactated Ringer's solution (LRS) is infused into the abdomen through a 32F fenestrated catheter (Trocar Catheter, Deknatel Inc., Fall River, MA 02720) placed in the right ventral abdomen, just cranial and lateral to the cranial extent of the celiotomy incision. The lavage fluid is then allowed to drain through a Heimlich valve (Bard-Parker Heimlich Chest Drain Valve, Benton Dickson Co., Franklin Lakes, NJ 07417). The lavage procedure is performed at 12, 24, and 36 hours after surgery and then the catheter is removed. Postoperative intraabdominal lavage is reported to decrease adhesion formation by creating a hydroflotation effect, which separates intestinal serosal surfaces, and by removing fibrin and inflammatory mediators.[69] Reported complications with this technique include occlusion of the catheter with fibrin and localized ventral edema at the abdominal catheter placement site. The author uses postoperative abdominal lavage in horses that are at a particularly high risk of adhesion formation (severe, diffuse peritoneal inflammation and/or potential intraoperative bacterial contamination). Heparin sodium (30,000 to 50,000 IU/10L LRS) is routinely added to the lavage fluid.

Protective Tissue Coating Solutions

Coating tissues with protective lubricating barrier solutions during abdominal surgery minimizes adhesion formation by reducing the extent and severity of tissue damage that occurs as a consequence of surgical manipulation.[70-73] Precoating visceral tissues involves manual application of these solutions to the serosal surface before manipulation, and is more

effective at reducing adhesion formation than intraperitoneal administration of the solutions at the end of surgery, after tissue damage has already occurred.[64,70,74] Additionally, these solutions provide a mechanical lubricating barrier between serosal and peritoneal surfaces, preventing the formation of adhesions in the early postoperative healing period.[6,75-77]

Protective tissue coating solutions commonly used in equine abdominal surgery are high-molecular weight viscous polymer solutions such as 1% SCMC and 0.4% sodium hyaluronate solution. Of these solutions, 1% SCMC has been the most popular because of its availability, ease of preparation, and relatively low cost. Administration of SCMC has been shown to prevent the reformation of adhesions after surgical lysis of existing adhesions.[64,78] Furthermore, studies have demonstrated that intraperitoneal instillation of SCMC significantly decreases experimentally induced adhesion formation in horses[75] without adversely effecting intestinal[79] or abdominal wound healing.[80] Initial studies recommended administering 7 ml/kg of 1% SCMC solution (approximately 3L/450 kg horse) into the abdomen just prior to abdominal closure.[76] Based on experience and experimental studies,[23,64,81] the author recommends using 1 to 2 L of 1% SCMC solution per 450 kg horse. The solution is applied to the surgeon's gloved hands and serosal surface of the intestine at the start of surgery. The solution is reapplied as necessary to keep the intestinal and peritoneal surfaces well lubricated, thereby minimizing incidental serosal trauma. The SCMC solution does not support bacterial growth[82] and is removed from the abdomen by peritoneal macrophages within 4 to 7 days after administration.[83]

A 1% solution of SCMC is prepared by adding boiling, sterile water to 10 g of SCMC powder to bring the total volume to 1 L. Cold filtering of the SCMC through a 0.22 micron filter increases the viscosity of the solution, but is extremely tedious and is not routinely performed in the author's hospital. The SCMC solution is then transferred into 1-L glass bottles and autoclaved at 121°C for 20 minutes. The shelf life of the solution is 60 days.

The results of a study in laboratory animals indicate that a combination of SCMC and 0.5 mg/ml of recombinant tPA is more effective at reducing postoperative adhesion formation than either agent alone.[52] This combined treatment has not been evaluated in horses but may be of potential benefit in the future.

Sodium hyaluronate, is a naturally occurring hydrophilic polymer that has been proven effective in reducing postoperative adhesions after abdominal,[70,72-74] pericardial,[84] and orthopedic operations.[85] Sodium hyaluronate readily forms tissue protective solutions and is an excellent tissue lubricant, even at low concentrations.[70,74,84] As well as having an anti-inflammatory effect, sodium hyaluronate prevents adhesions by forming a protective lubricating barrier on the intestinal serosal surface, much like SCMC, by preventing abrasive manipulative trauma and desiccation, and by preserving the integrity of mesothelial surfaces.[70-74] Concentrations of 0.4% sodium hyaluronate have been shown to maximally inhibit adhesion formation.[70,71] The 0.4% sodium hyaluronate solution is resorbed from the peritoneal cavity and excreted within 5 days of administration.[63,74] An additional benefit of sodium hyaluronate solutions over SCMC may be chemical modulation of adhesion formation by increasing tPA concentrations at the visceral peritoneal surface and promoting mesothelial fibrinolysis.[28] This profibrinolytic effect is attributed to preservation of mesothelial cell layer integrity during intestinal manipulation, thereby, retaining local concentrations of mesothelial tPA within the visceral peritoneum. Additionally, the results of recent *in vitro* studies indicate that sodium hyaluronate also enhances the fibrinolytic response of human mesothelial cells exposed to tumor necrosis factor-α by decreasing both the synthesis and release of PAI.[86] Alternatively, the sodium hyaluronate solution may act as a barrier, containing profibrinolytic enzymes such as tPA, on the intestinal serosal surface, and resulting in high local concentrations of tPA.[28,71] The result is dissolution of early fibrinous adhesions before they become mature fibrous adhesions.

The results of experimental studies in horses have demonstrated that a 0.4% sodium hyaluronate solution (SepraCoat, Genzyme, Cambridge MA 02139) significantly decreases the incidence and severity of experimentally induced intraabdominal adhesions without adversely affecting jejunal anastomotic healing.[77] Unfortunately, cost-effective commercial preparations of sodium hyaluronate in sufficient volumes are not presently available. The use of sodium hyaluronate solutions in equine abdominal surgery may hold promise in the future.

Resorbable Barrier Substances

Various resorbable barrier materials have been evaluated in laboratory animal models of adhesion formation. Such materials include oxidized regenerated cellulose (Interceed TC-7),[87-89] expanded polytetrafluoroethylene (Gor-Tex Surgica Membrane),[88,89] synthetic biodegradable polymers, fibrin glue (Tissucol),[89] and a bioresorbable hyaluronate-carboxymethylcellulose membrane (Seprafilm).[89-94]

Ideally, a barrier substance should effectively prevent adhesion formation, be highly biocompatible, be resorbable, be effective on inflamed surfaces, be applicable through a laparoscope, and cost-effective.[89] As of yet, the ideal barrier substance does not exist, however, the barrier substance that has received the most attention and use in equine surgery is a bioresorbable hyaluronate-carboxymethylcellulose membrane (HA membrane) (Seprafilm, Genzyme Corp., Cambridge, MA 02139).

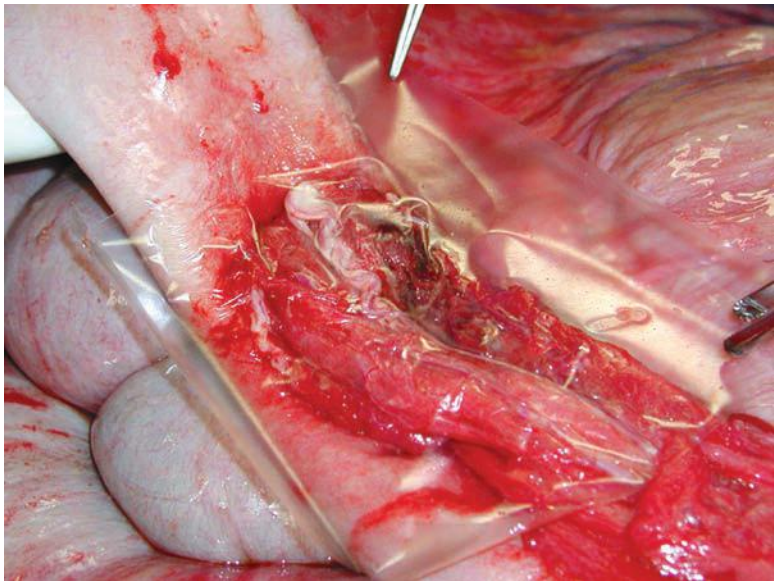
The HA membrane was developed to reduce postoperative adhesion formation in people.[94-96] In experimental models of adhesion formation in laboratory animals, the HA membrane reduced the frequency and severity of postsurgical adhesions to parietal and visceral peritoneal surfaces and the pericardium.[94,95] The flexible HA membrane is applied to the serosal surface of the intestine or parietal peritoneum, forming a temporary protective barrier against serosal-serosal or serosal-peritoneal adhesion formation during early postoperative healing (Figure 7-4).[94-98] After the membrane is applied to the tissue, the membrane hydrates to form a gel that adheres to tissues and most surfaces. This gel remains at the site of application for up to 7 days, separating potentially adhesiogenic surfaces, and is then cleared from the abdominal cavity within 28 days by peritoneal macrophages. In a prospective multicenter study, use of the HA membrane decreased the incidence of postoperative adhesions from 94% to 51% in people undergoing abdominal surgery for colectomy and diverting-loop ileostomy.[96] Similarly, the HA membrane has been shown to significantly reduce postoperative adhesion formation in horses,[97] with no adverse effects on intestinal or peritoneal healing.[77]

The HA membrane is used as an adjuvant in abdominal surgery for reducing the incidence, extent, and severity of postoperative adhesions at the site of placement. The surgical lesion is corrected and the HA membrane is applied to potentially adhesiogenic surfaces just prior to abdominal closure (Figure 7-4).

More recently, the HA membrane has been demonstrated to facilitate small intestinal anastomoses in horses. Use of an HA membrane in combination with a continuous single-layer appositional suture pattern results in an anastomosis that provides larger stomal diameters and takes less surgery time than a conventional, two-layer, inverting anastomosis.[99] This technique also minimizes the incidence of perianastomotic adhesion formation.[99]

The author routinely uses one to two HA membranes in areas of localized serosal or peritoneal trauma that are at an increased risk of postoperative adhesion formation. Such areas would include focal areas of intestinal inflammation, segments of intestine that have vascular compromise, but deemed viable by subjective or objective measures, and focal adhesion formation in which adhesiolysis was subsequently performed. Additionally, HA membranes may be used to facilitate small intestinal and small colon anastomoses in foals and adult horses.[99]

Figure 7-4



Intraoperative photograph demonstrating a hyaluronate-carboxymethylcellulose membrane covering a focal area of serosal inflammation and an omental adhesion to a segment of equine jejunum. The membrane is applied to completely cover the inflamed jejunal serosa and adjacent mesentery.

Treatment of Intraabdominal Adhesions

Treatment of horses with mature adhesions that are causing clinical problems often is unrewarding, costly, and associated with a poor prognosis for survival. In less severe cases, recurrent abdominal pain associated with postoperative adhesions may be managed successfully by feeding a low residue diet of complete pellet rations and grazing green grass. Severe restrictive adhesions that result in complete intestinal obstruction or strangulation require repeat celiotomy or euthanasia.

Surgical treatment of adhesions involves establishing a functional conduit for passage of intestinal contents and removal of any devitalized intestine. In most cases, adhesiolysis alone is associated with an unacceptable rate of repeat adhesion formation. Therefore, in such cases resection of all potentially adhesiogenic tissue should be performed. If mature, fibrous adhesions are present, an intestinal by-pass is performed without adhesiolysis to minimize the formation of new adhesions. Protective lubricating solutions should be used during intestinal manipulation, and all potentially adhesiogenic tissues that must be left in situ should be completely covered with a resorbable barrier substance. Laparoscopic adhesiolysis has been reported in humans; however, this procedure is of limited use in horses with acute intestinal obstruction and severe intestinal distention. Successful laparoscopic adhesiolysis of focal, less severe, intestinal adhesions in foals and horses has been reported.[37,39,100]

The prognosis for horses requiring repeat celiotomy due to adhesions is poor, with reported long-term survival rates ranging from 0 to 20%.[4,10,12,101] Most clinical complications in horses associated with postoperative adhesions are apparent within the first 60 days after surgery and are associated with decreased survival rates, as compared with horses in which adhesions first cause clinical problems more than 60 days after the original celiotomy.[10] In a survey of equine surgeons, 91% reported a less than 50% success rate for treating horses with adhesions that required additional celiotomies, and 25% of respondents had a less than 10% success rate in horses that required a second celiotomy.[101]

Adhesion Prevention Strategies

In the author's hospital, all horses undergoing exploratory celiotomy receive intravenous balanced isotonic fluid therapy based on their deficit and maintenance requirements (see Chapter 17), intravenous broad spectrum antimicrobials, and flunixin meglumine (1.1 mg/kg, IV) preoperatively. One percent SCMC is applied to the surgeon's hands and serosal surfaces of the intestine at the start of surgery and during all manipulations. Horses determined to be at high risk of forming postoperative intraabdominal adhesions, for example a horse with a rent in the mesentery incarcerating 15 to 20 feet of devitalized small intestine, benefit from aggressive perioperative and intraoperative anti-adhesion therapy. In these cases, additional therapies may include those targeted at severe dehydration, metabolic acidosis, electrolyte abnormalities, and endotoxemia. Intraoperatively, 1% SCMC is also applied to the devitalized segment of intestine within the rent, via a sterile stallion catheter. This reduces the friction against the surface of the entrapped intestine and facilitates reduction of the incarceration. After completion of the appropriate resection and anastomosis, lavage of the abdominal cavity is completed with 10 to 20 liters of warm sterile lactated Ringer's solution. Ten to 20 million units of potassium penicillin and/or 20,000 to 30,000 units of heparin may be added to the lavage fluid. Once lavage of abdominal cavity is complete, SCMC is reapplied to the small intestine. The anastomosis is exteriorized, and a single HA membrane is applied to the anastomotic site. Depending on the severity of peritoneal inflammation, contamination, and overall assessment of the remaining intestine, a fenestrated abdominal drain may be placed for performing postoperative abdominal lavage. Horses undergoing surgery for small intestinal lesions are placed on a constant-rate infusion of lidocaine hydrochloride immediately after surgery. In the author's experience, delayed treatment with lidocaine, once postoperative ileus is evident, has resulted in limited success at resolving the ileus. Depending on the response to lidocaine therapy, additional prokinetic agents, such as neostigmine or erythromycin may be administered (See Chapter 4).

Conclusions

The presence of pre-existing peritoneal inflammation and the inherent invasive nature of surgery limits our potential for preventing adhesion formation in horses. The surgeon's primary defense in adhesion formation continues to be proper, meticulous, atraumatic surgical technique and removal of all potentially adhesiogenic tissues, thereby reducing peritoneal inflammation and trauma. Current methodologies of adhesion prevention are directed at minimizing peritoneal trauma and inflammation, postoperative treatment with anti-inflammatory drugs such as flunixin meglumine and DMSO, enhancing peritoneal fibrinolysis, promoting intestinal motility, and separating potentially adhesiogenic tissues during early postoperative healing. No currently available treatments accomplish all of these objectives. However, through research and a more thorough understanding of the physiologic processes of adhesion formation, development of novel and innovative technologies targeted at adhesion prevention may reduce the morbidity and mortality associated with postoperative adhesions in horses.

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Pathophysiology of Peritonitis

Chapter 8

John F. Peroni

The peritoneal cavity is frequently affected by infectious, inflammatory, and traumatic processes and, rarely, neoplasia. The response of the peritoneum to these insults is predictable, resulting in inflammation, edema, and the formation of a fibrinous scaffolding of tissue that matures into adhesions between peritoneal surfaces in an attempt to isolate and contain the pathologic process.[1] This chapter will first review the anatomy and pertinent pathophysiology of peritoneal disease and will then focus on peritonitis, abdominal trauma, and hemoperitoneum.

Anatomy and Physiology of the Peritoneum

The peritoneum is a thin serous membrane, which lines the abdominal cavity and part of the pelvic inlet and covers almost all of the abdominal viscera. In the male, the peritoneum is a closed sac, whereas in the female, it has two small abdominal orifices through which the fallopian tubes communicate with the uterus. These latter orifices provide an indirect communication with the external environment.[2] The glistening peritoneal surface is composed of a layer of mesothelial cells, which share the same embryologic origin as the endothelial cells that line blood vessels. The peritoneal surfaces are constantly moistened by peritoneal fluid which minimizes friction during movement of the abdominal organs.[2] The subserous surface of the peritoneum is attached to the abdominal wall and viscera. The omenta divide the peritoneal cavity into two main regions, one bounded by the greater omentum and the other by the lesser omentum. These two regions communicate via the epiploic foramen (foramen of Winslow).

The peritoneal reflections that form peritoneal ligaments, mesenteries, and omenta, coupled with the natural flow of peritoneal fluid, influence the spread of disease processes within the abdominal cavity.[3] The flow of peritoneal fluid is directed ventrally by gravity and cranially by the negative intraabdominal pressure generated in that region of the abdomen by the action of the diaphragm during inspiration. Peritoneal fluid drains through stomata in the muscular portion of the diaphragm and accesses the lymphatic system via specialized openings called lacunae.[4] The relative porosity of the diaphragm may explain the frequent clinical finding of pleural effusion in horses with inflammatory and infectious diseases involving the abdominal cavity.

The peritoneal cavity contains cells that are active in the local defensive response against bacterial invasion and in the removal of blood components when intraabdominal hemorrhage occurs. Although mononuclear phagocytes predominate in peritoneal fluid, mesothelial cells have important roles in maintaining homeostasis by virtue of their fibrinolytic activity and ability to initiate immune responses.[5] The fibrinolytic function of these mesothelial cells involves production of plasminogen activator proteins, which activate plasmin, a polypeptide responsible for breakdown of fibrin. Under normal conditions, the mesothelial cells efficiently control the coagulation cascade within the abdominal cavity. However, during intestinal diseases characterized by ischemia, infection, or inflammation, the fibrinolytic system is overwhelmed, thereby favoring the formation of intraabdominal adhesions.

Mesothelial cells also play a central role in cell-signaling pathways and are a potent source of proinflammatory mediators, including interleukins 6 and 8, monocyte chemoattractant protein 1, macrophage inflammatory protein 1 , and tumour necrosis factor (TNF) α.[6] Through the synthesis and release of these cytokines and chemokines, the mesothelial cells have a major influence on the recruitment of phagocytes and neutrophils into the peritoneal cavity. Mesothelial cells express intracellular adhesion molecule 1, vascular cell adhesion molecule 1, and platelet endothelial cell adhesion molecule 1; expression of these adhesion molecules is increased in patients with peritonitis.[7,8] These adhesion molecules allow neutrophils to bind to peritoneal mesothelial cells, thereby facilitating emigration of the neutrophils into the peritoneal cavity. Depending on the insult, the initial influx of neutrophils is replaced by macrophages within 6 to 12 hours of the onset of peritonitis.[9]

Coupled with cellular invasion of the peritoneal cavity, complement activation is a second vital step in local peritoneal defense mechanisms.[10] Although the end result of phagocyte infiltration and complement activation is a hostile environment for invading microbes, it can also cause peritoneal damage. As an example, free radicals generated by activated neutrophils can destroy bacteria, but may also have a toxic effect on peritoneal mesothelial cells.[11]

In addition to the aforementioned cellular defense mechanisms, the peritoneal cavity responds to injury by gradually isolating the pathologic process through the formation of adhesions and abscesses. The omentum contributes to this localization process by adhering to inflamed tissues via a layer of fibrin. Once the omentum has localized the primary focus of contamination, the omentum absorbs microbes and degenerated macrophages through its stomata, and accommodates neutrophils and macrophages in specialized areas called milky spots. These are perivascular lacunae in which cells of the reticulo-endothelial system attempt to reabsorb debris and contaminants.[12] In horses, adhesions formed in response to chronic low-grade peritonitis can become restrictive as they mature, resulting in obstruction of the intestine and the development of signs of colic.

Because omentectomy has been reported to decrease adhesion formation in horses, this procedure is routinely performed by some equine surgeons.[13] This is in contrast to the limited use of omentectomy in people and dogs. The results of a large retrospective study involving 645 human patients undergoing proctocolectomy and ileoanal anastomosis, showed that omental removal increased the incidence of postoperative sepsis and the need for a second surgery.[14] Furthermore, in both humans and dogs, the omentum has been intentionally sutured over the incision line in an attempt to protect anastomoses and promote healing.[15,16]

In instances in which the degree of peritoneal contamination is low and has been handled by the animal's local inflammatory/immune response, horses may fully recover from the initial injury. If, however, the local responses were inadequate, horses may later experience signs associated with the formation of adhesions or intraabdominal abscesses despite aggressive medical and surgical treatment.[17]

Etiology of Peritonitis

Peritonitis is defined as inflammation of the peritoneum, the mesothelial cell layer that lines the abdomen and covers the abdominal viscera. Despite advances in surgical and medical treatment of equine abdominal disorders, peritonitis is associated with a very high mortality rate ranging from 30% to 67%.[18,19] The reported mortality rate associated with peritonitis after abdominal surgery is 56%, whereas the mortality rate is 43% when abdominal surgery has not been performed.[20,21]

Causes of peritonitis include septicemia, bacterial translocation during visceral ischemia, mechanical trauma (surgery, external injuries), chemical insults (bile, urine, pancreatic enzymes), parasitism, and miscellaneous factors (neoplasia, drug reactions, decreased immune resistance).[22] To provide a general framework for treatment, peritonitis can be categorized as primary, secondary, or tertiary. Primary peritonitis is a spontaneous pathologic event lacking an obvious initiating cause and is usually treated with antimicrobial agents and supportive care. In secondary peritonitis, the integrity of the gastrointestinal tract and/or the abdominal wall have been compromised, leading to contamination of an otherwise sterile peritoneal cavity. Secondary peritonitis is treated by removing the source of contamination, which usually requires surgical intervention, supportive care, and administration of antimicrobials. Tertiary peritonitis has been described as a condition in people, in which peritonitis either recurs or persists after treatment of secondary peritonitis. These cases are characterized by frequent recurrence and may need multiple surgical interventions and prolonged antimicrobial therapy.[23]

The same categorization of peritonitis appears to be well suited to the horse. Primary peritonitis in the horse is usually bacterial in origin, as determined by abdominal paracentesis, and lacks evidence of intestinal or abdominal wall damage. This includes peritonitis associated with bacteremia and *Actinobacillus equuli* infection, but may also include parasitism, uroperitoneum, and hemoperitoneum as additional causes.[18,24,25] More commonly, however, peritonitis in horses occurs secondary to a breach in the integrity of the intestine after necrosis or perforation of the bowel. Peritonitis may also be secondary to abdominal surgery as a result of leakage of an anastomosis or dehiscence of an enterotomy site.[19,26] Tertiary peritonitis in horses may appropriately characterize situations in which an exploratory celiotomy is used to treat peritoneal infection. In these cases, an accurate diagnosis can be difficult to obtain because changes in peritoneal fluid may reflect both the effects of the celiotomy and the underlying infectious process. Ample evidence exists in horses indicating that the white blood cell count in peritoneal fluid may be significantly increased by simple abdominal procedures and intestinal manipulation.[27,28]

It is important to note that the results of retrospective clinical case studies indicate that peritonitis in horses is often idiopathic. For example, in an early retrospective study of 30 horses with peritonitis, the cause was not always identified.[29] In two subsequent retrospective studies, 52% and 13.4% of horses with peritonitis were diagnosed as idiopathic.[19] In the latter study, peritoneal fluid cultures yielded *Escherichia coli, Staphylococcus epidermidis, Staphylococcus* spp., *Bacillus* spp., and *S. zooepidemicus*.[18]

Clinical Presentation

Careful scrutiny of the clinical signs can yield useful information during the diagnostic process. Most horses with peritonitis are febrile. The intensity and severity of symptoms depend on the underlying cause of the disease and on the magnitude of the infectious and inflammatory processes. Common presenting clinical signs include abdominal pain, depression, anorexia, diarrhea, and tachycardia. Horses will be more severely affected by peritonitis when the normal host defense mechanisms are compromised or when the bacterial inoculum is large or accompanied by other noxious agents such as necrotic tissue, hemoglobin, or bowel contents.[30] In the latter instances, a large shift of fluid from the vasculature to the peritoneal cavity occurs, resulting in 8% to 10% dehydration and hypovolemic shock. This compromises the cardiovascular system, leading to

hyperemia of the mucous membranes, prolongation of the capillary refill time (more than 2 sec), hemoconcentration (increased packed cell volume), and increased heart and respiratory rates. Peritonitis is often associated with endotoxemia, particularly when the abdomen is contaminated with fecal material. Abdominal infection leads to decreased gastrointestinal motility as a result of alterations in the coordinated propagation of the myogenic myoelectric complex.[31] Generalized ileus causes a reduction in fecal output, and intestinal borborygmi are decreased on abdominal auscultation.

Diagnostic Approach

A conclusive diagnosis of peritonitis can be made by demonstrating increases in total nucleated cell count (more than 5,000 cells/μL) and total protein (more than 2.5 g/dL) in the peritoneal fluid. Abdominal paracentesis is a low risk procedure and should be performed in all cases in which peritonitis is suspected. Specific techniques are described elsewhere in this book, however, in peritonitis, a few considerations deserve attention. All efforts should be made to avoid performing an enterocentesis, which would compromise the diagnostic value of the peritoneal fluid sample. To avoid this potential complication, this author prefers to perform an ultrasound-guided abdominal paracentesis when peritonitis is suspected. Using a curvilinear 3.5 mHz ultrasound probe, the ventral abdomen can be scanned for fluid "pockets" that can be safely accessed without inadvertent penetration of the abdominal viscera. The use of transabdominal ultrasound in equine gastrointestinal disease has been described and, in peritonitis, is useful in determining the extent of the disease process.[32] Infected peritoneal fluid is usually turbid and hyperechoic. In addition, peritoneal fibrin tags may be identified, along with thickened intestinal serosal surfaces. Both transabdominal and transrectal ultrasound exams can be useful in verifying the presence of abdominal masses or abscesses.

Once peritoneal fluid is retrieved form the abdomen, it should be submitted for cytology and microbial culture and sensitivity. In peritonitis, the cytologic interpretation is consistent with suppurative inflammation characterized by the presence of degenerate, toxic neutrophils and intra- or extracellular bacteria (see Chapter 15). Retrospective case reviews indicate that gram-staining of peritoneal fluid samples revealed bacteria in only 27% to 32.5% of cases.[18,19,29] Regardless, peritoneal fluid samples should be cultured for aerobic and anaerobic microorganisms given that determination of antimicrobial sensitivity is critical to the selection of the appropriate antimicrobial agent(s). Commercially available 5-ml blood culture media can be used and have been reported to yield positive culture results more often than traditional culture medium devices.[33] Peritoneal fluid analysis may not be as valuable when evaluating horses suspected of having peritonitis after abdominal surgery as total nucleated cell count and protein concentration in peritoneal fluid increase markedly after simple abdominal procedures.[27,28,34] Increases in total nucleated cell counts may, therefore, be increased as a direct result of surgery, complicating the diagnostic process. The clinician should, however, suspect a septic process when bacteria or foreign material is identified in a peritoneal fluid sample obtained after surgery; the presence of bacteria in peritoneal fluid samples after intestinal resection and anastomosis is rare.[34] In such cases, assessing other peritoneal fluid parameters may be important. Reportedly, peritoneal fluid pH less than 7.3, glucose concentration less than 30 mg/dL, and fibrinogen concentrations exceeding 200 mg/dL are consistent with a diagnosis of septic peritonitis.[35] Clinical signs such as anorexia, depression, low-grade, persistent fever, and the presence of excess peritoneal fluid on transabdominal ultrasound should also alert the clinician to the possibility of postoperative peritonitis.

Other useful diagnostic tests include abdominal palpation per rectum, complete blood count, and biochemical and electrolyte profiles. On rectal examination, crepitus may be palpated in the dorsal abdomen, along with a "roughening" of the intestinal serosal surfaces covered with fibrin tags. Masses and abscesses often can be palpated near the root of the mesentery and may be confirmed by transrectal ultrasound. In most cases of peritonitis, signs of ileus include either the presence of distended jejunum or impaction of the large colon.

In horses with acute peritonitis, complete blood count results require careful interpretation. Typical findings include leukocytosis (more than 10,000 cells/μL) and increased fibrinogen concentration (more than 400 mg/dL). In peracute cases, however, leukopenia (fewer than 4,000 cells/μL) may be present because of the extravasation of neutrophils into the peritoneal cavity. In these peracute cases, plasma concentrations of fibrinogen and total protein may be below normal range values as a result of exudation of protein into the abdomen. In contrast, plasma concentrations of fibrinogen are increased (more than 500 mg/dL) in chronic cases of intraabdominal abscessation.

Peritonitis often causes alterations in serum biochemical profiles that are consistent with azotemia. Blood urea nitrogen and serum creatinine concentrations are increased as a result of movement of large volumes of fluids into the abdominal cavity, which lead to decreased glomerular filtration rate and prerenal azotemia.[22] Along with dehydration, horses with peritonitis may have metabolic acidosis and electrolyte imbalances, such as decreased serum concentrations of potassium, sodium, and chloride.

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Pathophysiology of Enteritis and Colitis

Chapter 9

Harold C. McKenzie

Fundamentally, the pathophysiology of enteritis and colitis is inflammatory in nature, and the clinical abnormalities that we associate with these conditions, such as enterogastric reflux and diarrhea, arise from the inflammatory processes involving the affected segment of the gastrointestinal tract. The initial stages of these conditions typically involve localized mucosal inflammation, but this frequently progresses to widespread systemic activation of the inflammatory cascade. Many of the sequelae of these conditions, such as laminitis and multiple organ failure, are related to this systemic inflammatory response.

Inflammation

Inflammation represents the response of tissues either to injury or the presence of microorganisms. Inflammation serves a vital role in the host's resistance to infection, as it enhances the directed movement of phagocytic cells and defensive molecules, such as immunoglobulin and complement, from the bloodstream to the site of infection or injury. Local inflammation arises as a result of several different insults, including direct mucosal cellular injury by the pathogen, the elaboration of toxins that injure the mucosal cells, and the production of inflammatory mediators by the host tissue in response to the presence of the pathogen or its toxins. Direct cellular injury requires that the pathogens gain access to the host's intestinal tissue, either from the luminal surface or by hematogenous spread. Once an organism has gained access to the host cell, it may invade the cell and establish an intracellular infection, as is the case with *Salmonella* sp. organisms, or it may liberate enzymes, toxins, or other substances that damage the host cell. Injured cells release preformed mediators such as histamine and synthesize proinflammatory substances, including eicosanoids (prostaglandins, thromboxanes, leukotrienes) and the cytokines IL-1 and TNF-α. These mediators are responsible for the initiation of a nonspecific inflammatory response. The bacterial cellular components that are recognized by the immune system include endotoxin (lipopolysaccharide, LPS) and exotoxins from gram-negative bacteria, and peptidoglycan (PG), lipoteichoic acids (LTA), enterotoxins, or superantigenic exotoxins from gram-positive bacteria.[1,2] It is important to note that while bacterial infection may be responsible for the initiation of an inflammatory response, the inflammatory process itself results solely from the production of endogenous mediators.

The initial changes seen in an inflammatory response are primarily the result of local vasodilation and increased vascular permeability, due to the effects of vasoactive mediators released by injured or infected cells. These factors include histamine, serotonin, kinins, eicosanoids, platelet activating factor (PAF), and the complement products C3a and C5a. Changes occur in the vascular endothelium under the influence of molecules arising from the injured tissue (IL-1, TNF-α, histamine), resulting in neutrophil diapedesis and increased vascular permeability. Upon their arrival at the site of tissue injury, neutrophils and macrophages phagocytose foreign material and injured or dead tissue cells and destroy the phagocytosed material by oxidative mechanisms (neutrophils) or by both oxidative and nonoxidative mechanisms (macrophages). In addition, macrophages release several factors that augment the immune response, including the proinflammatory cytokines IL-1, TNF-α, IL-6, IL-12, and IL-18. The proinflammatory cytokines signal target cells, primarily neutrophils, to increase their production of secondary inflammatory mediators, including phospholipid derivatives (prostaglandins, thromboxane A_2, leukotrienes), and reactive oxygen species (O^-, O_2^-, $\cdot OH$, H_2O_2, NO, OCl^-), further increasing the activity of the inflammatory response.[3] The systemic manifestations of inflammation/infection (fever, lethargy, anorexia, and cachexia) are primarily due to TNF-α and IL-1.

In moderation, the changes associated with an inflammatory response are protective, resulting in enhanced killing of microbes by antigen-specific and nonspecific mechanisms, generalized immune stimulation, and increased activity of the systems required for healing of damaged tissue. The excessive, malignant form of the inflammatory response is characterized by the systemic activity of numerous proinflammatory mediators, including cytokines, phospholipid derivatives, complement components, reactive oxygen species, and vasoactive gases (NO, CO).[4] As described above, these mediators all represent components of the normal inflammatory response to a localized stimulus, but the systemic activity of these proinflammatory mediators may result in an excessive, and often detrimental, response.

Endotoxin (LPS) is commonly involved in the inflammatory responses associated with gastrointestinal disorders in the horse, due to the involvement of gram-negative pathogens in some of these conditions and the presence of large numbers of gram-negative enteric organisms within the bowel of the horse. These organisms represent a large pool of readily available LPS molecules that can be absorbed into the systemic circulation through the compromised intestinal mucosa. The frequent involvement of LPS in the development of severe systemic inflammation in the horse has resulted in severe systemic inflammatory responses observed in the horse being termed endotoxemia. Given the fact that this response can occur in the absence of LPS, it is perhaps better to describe this response as the systemic inflammatory response syndrome (SIRS).[4] SIRS is clinically characterized by the presence of two or more of the following abnormalities: fever, leukocytosis or leukopenia, tachycardia or tachypnea, and hypoxemia.[4,5] The changes associated with SIRS can lead to shock, which is characterized by severe hypotension not responsive to intravenous fluid therapy. Shock can result in hypoperfusion and

multiple organ dysfunction (MODS).[6] MODS is a progressive syndrome with initial dysfunction of the cardiovascular system, followed by involvement of the respiratory, hepatic, gastrointestinal, renal, cardiac, and neurologic systems.[7] As can be seen in severe cases of enteritis and colitis, if this process is not controlled it can result in the development of refractory hypotension, lactic acidosis, and oliguria, and may progress to death.[6] Horses that develop SIRS are at increased risk of developing laminitis, likely as a result of the effects of SIRS on digital blood flow, and some evidence suggests that vasoactive agents such as endothelin-1, which are increased in association with systemic inflammation, may be associated with alterations in digital blood flow in laminitis (see Chapter 44).[8,9] Prolonged SIRS can lead to excessive activity of the anti-inflammatory response and may result in systemic immunosuppression, which can result in the individual developing infections because of the hematogenous spread of organisms from the gastrointestinal lumen. Examples of these infections include bacterial endocarditis or fungal pneumonia.[10]

Pain

Abdominal discomfort is frequently observed in horses with enteritis or colitis, although the degree of overt abdominal pain usually subsides with appropriate supportive care in these conditions. Pain can result from the stimulation of visceral afferent neurons by local inflammatory mediators, particularly the prostanoids, produced in response to mucosal injury and inflammation. Nociceptors within the gastrointestinal mucosa detect mechanical, chemical, and thermal stimuli and relay this information to the central nervous system, with low-sensitivity fibers monitoring normal physiologic functions and high-sensitivity fibers responding only to noxious stimuli, such as severe distension.[11,12] An additional group of nociceptive fibers is composed of the "silent" fibers, the activity of which is only induced in the presence of inflammation.[11] These nociceptors are often stimulated by the plethora of inflammatory mediators associated with gastrointestinal inflammation, especially the prostanoids. In most cases of equine enteritis and colitis, however, the presence of bowel distension secondary to gas and/or fluid accumulation is likely the most potent stimulus for overt abdominal pain via the high-threshold nociceptors. The accumulation of gas occurs secondary to gas production arising from microbial fermentation of ingesta combined with impaired passage secondary to ileus. The accumulation of fluid occurs secondary to active fluid secretion into the gut lumen, impaired fluid absorption, and ileus. Control of abdominal discomfort is often accomplished by decompression of the stomach by nasogastric intubation in the case of enteritis or by the passage of diarrhea in horses with colitis. The low-grade discomfort commonly seen with enteritis and colitis following the initial acute stages is more likely associated with stimulation of the low-sensitivity receptors and induction of the silent receptors secondary to the presence of active inflammation. Control of this type of discomfort is best achieved by administration of nonsteroidal anti-inflammatory medications that suppress the production of the prostanoids or by administration of other types of analgesics, such as opiods or α-2 adrenergic agents, that alter the sensitivity of the nociceptors to stimulation or influence the sensory response to nociceptor stimulation.

Ileus

Gastrointestinal ileus is defined as a decrease in propulsive bowel activity, and is commonly encountered in horses with enteritis. Ileus occurs less commonly in horses with colitis, as hypermotility is present more often than hypomotility. The presence of ileus in combination with increased secretion of fluid into the small intestinal lumen results in the reflux of large amounts of fluid from the small intestine into the stomach. Accumulation of this fluid leads to abdominal pain and may result in gastric rupture. Ileus results from interruption of the normal rhythmic contractions of the intestine that occur primarily under the control of the enteric nervous system (see Chapter 4). The activity of the enteric nervous system is modulated by the autonomic nervous system, with parasympathetic input enhancing motility and sympathetic activity suppressing motility. Additional inhibitory input is provided by nonadrenergic, noncholinergic (NANC) neurotransmitters, which include vasoactive intestinal peptide (VIP), adenosine triphosphate (ATP), and nitric oxide (NO).[13] Increased sympathetic tone is thought to occur secondary to generalized sympathetic stimulation or reflexively by means of afferent signals from the intestine or peritoneal surface that are activated by the presence of inflammation. This increased sympathetic tone suppresses coordinated rhythmic activity of the intestine and results in functional obstruction of the intestine.

Hypermotility

Increased propulsive activity is commonly present in horses with colitis, leading to shortened intestinal transit times and increased frequency of defecation. When combined with passive and active fluid secretion into the bowel lumen, the net result is increased fecal fluid content and output associated with increased volume and frequency of defecation. The primary stimuli for hypermotility are inflammatory and consist of chemical, mechanical, and functional signals related to the injury or dysfunction of the gastrointestinal mucosa secondary to infection or irritation. The resulting increase in propulsion and decrease in transit time are primarily mediated by the enteric nervous system.[14,15]

Hypersecretion

Increased secretion of fluid into the lumen of the bowel occurs in enteritis and colitis. This hypersecretion can result from the activity of intrinsically produced inflammatory mediators or bacterial toxins. The secretory activity of bacterial enteropathogens is traditionally ascribed to one of two mechanisms. The first mechanism is the direct injury of the enterocytes by the invasive bacteria or by means of bacterially derived cytotoxins, resulting in a loss of villous surface area for absorption and a relative increase in the surface area of the secretory crypt epithelium. The second mechanism is via activation of enterocyte cyclic AMP (cAMP) and cyclic GMP (cGMP) pathways, which increase loss of sodium, chloride, and water across the intestinal epithelium.[16] This activation process can be initiated by bacterial enterotoxins, such as those produced by *Salmonella* organisms, or by inflammatory mediators synthesized within the mucosa, such as the prostanoids.[17] Recent work has demonstrated that the enteric nervous system is integral to the secretory response, as many of the prosecretory signals act by stimulation of the enteric nervous system rather than by direct enterocyte stimulation.[14,18]

Osmotic Diarrhea

The presence of incompletely digested carbohydrates can result in an increase in the osmotic pressure within the bowel lumen, leading to net fluid flow into the bowel because of increased secretion and decreased absorption.[19] The best example of this mechanism occurs in foals with rotaviral diarrhea, where the damage to the villous tips of the small intestinal mucosal cells causes a deficiency of lactase activity that leads to an impaired ability to digest the lactose ingested in mare's milk. The osmotic activity of lactose within the small intestinal lumen interferes with the normal absorption of fluid from the intestinal lumen in the terminal small intestine. Similar processes are thought to occur within the large intestine secondary to disruption of the normal fermentative processes at that site.

Decreased Absorption

The presence of inflammation within the gastrointestinal mucosa causes several changes that result in impaired absorption of fluid from the intestinal lumen.[17] Injury to the mucosal epithelium can cause loss of the normal architecture, as seen in the small intestine with rotavirus infections, where the villous tips, normally absorptive in function, are atrophied, while the crypt cells, which are normally secretory, proliferate.[20] Disruption of the normal transport mechanisms that move sodium and chloride from the lumen to the interstitium and vasculature also impairs absorption, as water normally follows these solutes along their concentration gradients. Dysfunction of the intracellular tight junctions impairs the ability of the mucosal epithelium to retain water and electrolytes after their absorption, decreasing the net absorption.[21]

Endothelial Dysfunction

Injury to the intestinal mucosa can result in a relative increase in hydrostatic pressure within the vasculature, secondary to increased blood flow, potentiating the flow of fluid from the vasculature into the interstitium and thence into the intestinal lumen.[19] The loss of albumin from the vasculature secondary to endothelial injury decreases the intravascular oncotic pressure and allows fluid to leave the vasculature and enter the interstitium. This results in increases in interstitial oncotic pressure, which augments fluid flow from the vasculature to the interstitium. The flux of fluid, electrolytes, and protein into the interstitium, in combination with damage resulting from inflammation, exceeds edema safety factors and leads to the development of interstitial edema. The fluid and protein within the interstitium may then enter the intestinal lumen by way of the damaged and dysfunctional epithelium, resulting in intestinal fluid losses and protein-losing enteropathy.

Specific Diseases

Duodenitits Proximal Jejunitis – Anterior Enteritis

Although the acute inflammatory response in the small intestine and the presence of profound hypersecretion make it likely that infectious organisms are involved in the pathogenesis of this syndrome, no definitive etiologic agents have been identified.[22] Although organisms such as *Salmonella* spp. and *Clostridium* spp., have been identified in the enterogastric reflux obtained from some horses with duodenitits proximal jejunitis – anterior enteritis, no causal relationship has been established.[22] There is some suggestion that fungal toxins may be involved in the development of this condition, as the test feeding of corn containing fumonisin B1 produced by certain strains of *Fusarium moniliforme* was associated with intestinal lesions consistent with duodenitits proximal jejunitis – anterior enteritis; however, clinical disease was not observed in those studies.[23,24] The mechanism by which this toxin acts is unknown, although disruption of sphingolipid metabolism has been used as a biomarker for fumonisin B1 activity.[24]

Clinically horses with duodenitits proximal jejunitis – anterior enteritis present most often with a history of mild colic followed by profound depression, large-volume enterogastric reflux (up to 15 to 20 liters every 2 hours), mild to moderate small intestinal distension on abdominal ultrasonography and/or rectal examination, low grade fever (101.5° to 102.5°F), clinical dehydration, tachycardia (60 to 80 bpm), decreased borborygmi and injected mucous membranes.[22,25] Severe transmural small intestinal inflammation is associated with this disease syndrome, and loss of the barrier function of the mucosa likely contributes to the severity of the systemic inflammatory responses that characterize this condition. Horses with duodenitits proximal jejunitis – anterior enteritis are at increased risk of serious secondary complications, including laminitis and cardiac arrhythmias, likely because of the presence of systemic inflammation and the associated organ and tissue dysfunction.[26,27]

Salmonellosis

The development of salmonellosis represents the interplay of several factors, including the degree of bacterial exposure, the virulence of the *Salmonella* organisms, and the susceptibility of the host. The severity of exposure is directly related to the number of bacteria ingested in contaminated feed or water, with the size of the infective dose being determined by the other factors of virulence and susceptibility. This infective dose may range from hundreds of organisms in highly susceptible individuals to millions of organisms in a healthy animal.[28] The number of organisms shed by infected individuals can vary dramatically, with chronically infected horses passing small numbers of organisms intermittently, whereas acutely affected individuals may shed very large numbers of organisms. The virulence of any particular *Salmonella* organism is determined by its invasiveness, which depends on the attachment of the organism to the mucosal epithelium and the production of enzymes and toxins (cytotoxins, endotoxins, and enterotoxins) that damage the epithelium and/or alter epithelial permeability and facilitate bacterial entry into the mucosal cells.[16] The ability of *Salmonella* organisms to cause intracellular infection allows them to evade some aspects of the immune response, such as humoral immunity and phagocytosis. Evidence exists that *Salmonella typhimurium* organisms may initially gain entry into the intestinal mucosa via mucosa-associated lymphoid tissues.[29] Host susceptibility is increased in the presence of stress, such as that associated with prolonged transport or surgery, or because of the presence of concurrent diseases resulting in impaired immune functions. The normal ability of the enteric population of commensal bacteria to resist the proliferation of pathogenic bacteria, termed colonization resistance, is impaired in the face of antimicrobial administration or gastrointestinal dysfunction, and loss of this function increases the susceptibility of the host to *Salmonella* infection.

After the establishment of a *Salmonella* infection, local and systemic inflammatory responses develop in an effort to eliminate the organism. Mucosal inflammation results in increased mucosal permeability, increased secretion of water and electrolytes, and alterations in motility due to altered enteric nervous system function. The development of this secretory response, in combination with intestinal hypermotility and decreased intestinal transit times, likely functions to decrease mucosal adherence of pathogenic organisms. Unfortunately, the loss of the normal barrier function of the intestinal mucosa, in combination with derangements in the normal flora, increases the pathogenicity of *Salmonella* organisms. The loss of fluid, electrolytes, and protein may be severe in equine salmonellosis, requiring aggressive supportive care. Severe intestinal inflammation can occur, leading to permanent dysfunction and overwhelming systemic inflammation, resulting in the death of the affected individual.

Clostridial Enterocolitis

Equine clostridial enterocolitis affects both foals and adults. The appreciation of the involvement of clostridial organisms in equine diarrheic syndromes has increased with improvements in our ability to detect and identify these organisms and their toxins in the feces of horses with diarrhea. The primary pathogens of concern are *Clostridium difficile* and *Clostridium perfringens,* with *Cl. difficile* being more commonly implicated in equine diarrheic syndromes. These organisms are strict anaerobes with fairly wide distributions in soil. They can represent a component of the normal gastrointestinal flora of horses; fecal shedding has been documented in horses showing no clinical signs of disease. Pathogenicity depends on production of bacterial toxins, with *Cl. difficile* producing primarily toxins A and B, and *Cl. perfringens* producing as many as 17 different toxins, although 4 cytotoxins (the exotoxins alpha, beta, epsilon, and iota) and enterotoxin (CPE) are most important.[30] The clinical signs associated with equine clostridiosis are not fundamentally different from any other equine enterocolitis. They consist of diarrhea, fever, depression, mild colic, and dehydration. Clostridial enterocolitis in some foals and adults is associated with hemorrhagic diarrhea, which is uncommon in most other equine enterocolitis syndromes. Consequently, the presence of this abnormality should heighten the clinician's suspicions that clostridial organisms may be involved.

Clostridium Difficile

Cl. difficile has been associated with enterocolitis in adult horses and foals in several studies.[31-38] Specific disease syndromes in which this organism is implicated include enterocolitis of foals and adult horses, hemorrhagic necrotizing enteritis of foals,

as well as nosocomial enterocolitis and antibiotic-associated diarrhea of foals and adult horses.[39] The frequent association of this organism with syndromes likely to involve disturbances in the normal enteric flora suggests that *Cl. difficile* is an opportunistic pathogen that is normally prevented from inducing disease by colonization resistance.[40] As this organism is not an invasive pathogen, the pathogenicity of *Cl. difficile* is primarily associated with the elaboration of toxin A and toxin B; these toxins exert their effects via receptor-mediated mechanisms.[41] Toxin A is commonly referred to as enterotoxin; it causes fluid secretion and inflammation.[42] Toxin B is typically termed cytotoxin, but recent work suggests that it exerts a primarily enterotoxin-like effect.[41] The net effect of the activity of these toxins is to induce a secretory diarrhea with substantial intestinal inflammation.

Clostridium Perfringens

Cl. perfringens has been associated with enterocolitis in foals and adult horses.[43-52] This organism appears to be a common member of the enteric flora in normal horses, with disease being associated only with the presence of increased numbers of the organism. *Cl. perfringens* does not invade the intestinal epithelium, but exerts its effects by means of the plethora of toxins that it produces. Alpha toxin is a phospholipase produced by all strains of *Cl. perfringens*, and is the primary lethal toxin associated with this organism.[30] The beta toxin is also capable of inducing mucosal necrosis and inflammation, and is potentially lethal.[30] A new form of cytotoxin, termed beta-2, has been identified in horses. It may prove to have a role in the development of typhlocolitis in the horse.[43] The epsilon toxin is produced as an inactive prototoxin. Following protease cleavage, the molecule becomes active and increases intestinal permeability.[30] The iota toxin increases vascular permeability and is potentially lethal.[30] *Cl. perfringens* enterotoxin (CPE) is produced by only 2% to 5% of isolates, predominantly type A, but the production of this toxin is highly correlated with the pathogenicity of isolates. CPE initially impairs fluid and electrolyte absorption, followed by increasing intestinal inflammation and injury, including villous blunting and loss of the intestinal epithelium, which lead to the development of secretory diarrhea.[30]

Equine Monocytic Ehrlichiosis

Equine monocytic ehrlichiosis (EME), or Potomac horse fever, is an ehrlichial colitis of horses. The etiologic agent of EME was originally termed *Ehrlichia risticii*, but is now named *Neorickettsia risticii*, due to the close relationship of this organism to *Neorickettsia helminthoeca*.[53-55] The clinical signs typically associated with EME include fever, depression, lethargy, anorexia, mild colic, diarrhea, dehydration, and laminitis.[56] Interestingly, only 60% of affected horses are reported to develop diarrhea,[56] and the incidence of diarrhea appears clinically to be even lower among horses that have lived for long periods of time in endemic areas. Abortion has also been reported in association with EME, both in experimentally induced EME and in natural infections.[57,58] Clinicopathologic changes that may be associated with EME include hemoconcentration, leukopenia, hypoproteinemia, and azotemia. The reported case fatality rate of horses affected by EME is 5% to 30%.[59]

The epidemiology of EME is extremely interesting, as the association between the seasonal development of this disease and exposure of affected animals to streams and rivers has been long-standing, yet no vector associated with these water sources could be identified. The seasonality of the disease, with cases occurring only during the summer months, suggested the involvement of a vector that was only active during this time of year, which fits well with an insect vector. Much work was done to identify an arthropod vector, especially ticks, as this mode of transmission is common among other ehrlichial pathogens, but no evidence supporting this mode of transmission has been found.[56,60-62] The association of this disease with natural watercourses suggested that some part of the life cycle was associated with aquatic organisms. As the close relationship between *N. risticii* and *N. helminthoeca* became clear, interest intensified in attempting to identify a trematode (fluke) vector. It has been demonstrated that several different trematodes may act as vectors for *N. risticii*, and several different species of aquatic snails appear to be intermediate hosts for these trematodes.[56,63] The route of equine exposure remained unclear until it was determined that aquatic insects (mayflies, caddisflies, damselflies, dragonflies, and stoneflies) may be infected with trematode metacercariae containing *N. risticii* DNA.[63,64] The oral transmission of EME has long been established, and work has demonstrated the induction of EME in horses fed infected aquatic insects (caddisflies).[65,66]

Cyathostominosis

As control of the large strongyles has improved in the last 20 years, the small strongyles (Cyathostominae) have assumed their current role as the primary parasitic pathogen of the horse.[67,68] The primary disease process associated with these parasites is associated with the larval stages, rather than the adult stage present within the gastrointestinal lumen. The cyathostomins have a direct life cycle, during which the adults within the lumen lay eggs that are passed in the manure, where they hatch as first-stage larvae (L1), and after maturation to the third stage (L3), they become infective.[68] After being ingested by a horse, the larvae enter the gastrointestinal mucosa, where they encyst and mature through the fourth (L4) to the fifth stage, which represents the adult form.[68] Disease is associated with parasite entry into and exit from the gastroin-

testinal mucosa, with the associated interstitial edema, along with eosinophilic and mononuclear inflammation, resulting in disruption of normal motility and, in severe cases, leading to profuse watery diarrhea and severe protein loss.[67,69-71] Larval cyathostominosis has also been associated with weight loss, colic, fever, neutrophilic leukocytosis, hypoalbuminemia, and hyperglobulinemia.[72,73] The simultaneous emergence of large numbers of larvae in the late winter/early spring, or possibly after anthelmintic administration, is a poorly understood but clinically significant problem, as this may be associated with colic, diarrhea, and severe protein-losing enteropathy.[67] Unfortunately, the difficulty in diagnosing this condition means that it is likely that many horses with cyathostominosis go undetected and untreated. Often one must assume that cyathostomins may be responsible for diarrhea and hypoproteinemia, unless another definitive diagnosis can be made. It is important to note that the presence of another etiologic agent does not preclude the presence of encysted small strongyles.

Viral Enterocolitis

Rotaviral enterocolitis is the most widespread and significant form of viral enterocolitis in the equine species and is a common cause of foal diarrhea, with affected foals ranging from 2 days of age to 6 months of age.[74,75] Younger foals are often more severely affected than older foals, with the disorder in some older foals remaining subclinical. Rotaviruses are RNA viruses of the family Reoviridae and are typically species-specific.[20] Infection follows ingestion of the organism in feces-contaminated feed or water, with subsequent attachment to the intestinal epithelium and uptake by the epithelial cells.[20] Rotavirus is highly contagious, and outbreaks may develop rapidly after the onset of clinical disease in a single foal. Clinically normal adults and foals may shed the organism, as may clinically affected foals. The amount of virus shed often increases after exposure to a clinically affected individual.

Rotavirus infects the middle and upper portions of the villous epithelium of the small intestine, resulting in villous atrophy and villous blunting, with replacement of the villous epithelium with cells from the epithelial crypts. Replacement of the normally absorptive villous epithelium with the secretory crypt cells appears to play a role in the impairment of intestinal absorption and increased secretion of fluid and electrolytes.[20] Interestingly, many of the small intestinal villi may be unaffected in the presence of infection, suggesting that absorption and secretion should not be severely affected and raising the possibility that other mechanisms may be responsible for the secretory diarrhea associated with rotavirus infection.[18] It has been demonstrated that rotaviral infection initiates a local enteric nervous system response that is responsible for as much as two thirds of the secretory response, and this response may be initiated by a "toxin-like" protein (NSP4) produced by the virus.[18] The resulting diarrhea is often profuse and watery, and the diarrheic phase may last from as little as 2 days to more than a week. Infection is ultimately self-limiting, but supportive care may be required because of substantial enteric fluid losses and associated electrolyte abnormalities. Enteral rest of 1 to 3 days' duration may be useful, as the damage to the small intestinal villi results in a relative deficiency of lactase, resulting in exacerbation of the diarrhea from accumulation of osmotically active lactose molecules within the intestinal lumen.

Protozoal Enterocolitis

The primary etiologic agent of protozoal enterocolitis in the horse is *Cryptosporidium parvum*. *C. parvum* is a fairly unique coccidial organism, which exhibits little or no host specificity, is highly resistant to antimicrobial agents, and has the potential to cause autoinfection.[76] This organism has a direct life cycle, with oocysts containing sporozoites being shed in the feces, where they represent an immediate source of infection for other animals.[77] After the oocytes are ingested, the sporozoites are released and invade the intestinal epithelium, where reproduction occurs.[77] Autoinfection occurs when oocysts just released from the epithelium into the lumen release sporozoites that infect other intestinal epithelial cells.[77] Equine cryptosporidiosis occurs primarily in young foals, with or without immunodeficiency.[74] The normal incubation period is approximately 3 to 7 days, with clinical disease persisting for 5 to 14 days in animals with normal immune function.[74] *C. parvum* infection activates mucosal cyclooxygenase expression, resulting in increased production of prostaglandin-E_2 and $-F_{2\alpha}$, and appears to induce diarrhea by impairing intestinal sodium and water absorption and increasing chloride secretion, in conjunction with alterations in mucosal barrier function, resulting in increased permeability.[14,78,79] This organism is zoonotic, with cases reported among humans handling horses and calves that are shedding cryptosporidial organisms.[80,81]

Proliferative Enteropathy

The causative agent of equine proliferative enteropathy, *Lawsonia intracellularis*, is an obligate intracellular organism that causes a similar syndrome in a wide range of mammalian and avian species.[82] Exposure alone is not adequate to achieve infection in other species, as commensal bacteria must be present for infection to occur; the role of these bacteria in the pathogenicity of *L. intracellularis* remains unclear.[83] Infection of the enterocytes with *L. intracellularis* leads to dramatic proliferation of infected immature crypt epithelium, resulting in loss of the normal villous epithelium and gross thickening of the

affected region of the small intestine.[82,84] Characteristic findings on histopathologic evaluation are the presence of numerous curved bacteria (*L. intracellularis*) within the apical cytoplasm of the infected cells and the relative absence of an active inflammatory response.[82,84] The loss of villous architecture and proliferation of the secretory crypt epithelium are likely responsible for the loss of fluid and protein into the intestinal lumen that occurs with this disease, as little or no inflammation is present within the affected intestinal segment. Hypoproteinemia and hypoalbuminemia leading to peripheral edema are characteristic findings with proliferative enteropathy. Substantial fluid and electrolyte deficiencies may also be present, requiring supportive care, typically including colloid administration (see Chapters 17 and 20).

NSAID-Associated Right Dorsal Colitis

Nonsteroidal anti-inflammatory agents are among the most frequently utilized drugs in equine medicine and surgery, and they are often administered at the owner's discretion with no specific dosage being prescribed. These compounds have toxic effects when used at dosages exceeding the label recommendations, but because of their narrow therapeutic index, some cases of toxicity occur even when the recommended dosages are given. Further increasing the risk of toxicity is the common misconception that toxicity may be avoided by combining two or more nonsteroidal drugs given at appropriate dosages, despite the fact that the toxic effects of these drugs are additive.[85] Toxicity of the nonsteroidal anti-inflammatory drugs involves the renal system as well as the gastrointestinal system, and all segments of the gastrointestinal tract can be affected. This discussion focuses on lesions occurring in the colon. The toxic potential of these drugs arises inherently from their mechanism of action, an indiscriminate suppression of prostanoid production. Most of the nonsteroidal drugs available for administration to horses inhibit the activity of both inducible cyclooxygenase-2 (COX-2), which is associated with inflammation, and constitutively expressed cyclooxygenase-1 (COX-1), which is responsible for the production of the prostaglandins required for normal tissue function. This COX-1/COX-2 paradigm remains useful, but recent evidence suggests that some crossover in functionality is present, complicating efforts to develop agents with decreased toxic potential.

The maintenance of normal mucosal function and health requires the presence of certain prostaglandins, specifically prostaglandins E (PGE), F (PGF), and I (PGI). The primary function of these compounds appears to be the maintenance of normal mucosal blood flow and tight junction functionality.[86,87] Disruption of these functions results in mucosal barrier dysfunction and mucosal injury, leading to the classic signs of nonsteroidal colitis, namely secretory diarrhea with hypoproteinemia and hypoalbuminemia, in association with mucosal ulceration, neutrophilic inflammation and colon wall edema.[88-90] These effects can be seen regardless of the route of drug administration, indicating that they do not arise solely from a topical mechanism. Impairment of mucosal blood flow and the resulting impairment of tissue integrity induced by nonsteroidal anti-inflammatory drugs is exacerbated by the presence of any type of concurrent mucosal inflammation, such as colitis, with increased tissue damage occurring as a result.[91,92] The presence of hypovolemia appears to further increase the risk of nonsteroidal anti-inflammatory drug-induced injury, resulting in toxicity despite the use of an appropriate dosage.[89] Phenylbutazone is the nonsteroidal drug that has been associated with most reported cases of right dorsal colitis,[88-90] but flunixin meglumine has been associated with most of the cases seen by the author in the last several years. This latter association between flunixin meglumine and right dorsal colitis may be a result of an increase in its use in order to avoid the well documented toxic effects of phenylbutazone.

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Malabsorption Syndromes

Chapter 10

Tim S. Mair
Thomas J. Divers

Malabsorption syndrome refers to the group of diseases with impairment of digestive and/or absorptive processes arising from structural or functional disorders of the small intestinal tract and its associated organs (including the pancreas, liver, and biliary tract).[1] These diseases can affect the absorption of carbohydrates, proteins, fats, vitamins, minerals, and to a lesser extent, water and electrolytes.[2] Infiltrative bowel diseases (i.e., diseases in which the mucosa and submucosa are infiltrated by abnormal cells - usually inflammatory or neoplastic cells) - are the most common cause of malabsorption.[2,3] In the adult horse, such diseases that are confined to the small intestine usually result in chronic weight loss, whereas chronic diseases of the large intestine result in diarrhea and protein-losing enteropathy.[2,4] However, small intestinal diseases may result in secondary large intestinal dysfunction as a result of the abnormal amounts of carbohydrates, fats, and amino acids entering the large bowel from the ileum. In addition, many of the chronic infiltrative diseases that result in small intestinal malabsorption can affect the large bowel concurrently. Thus, in clinical cases both small intestinal and large intestinal malfunction are often combined.[1,2] In people and small animals, disturbances in digestive processes (i.e., maldigestion), especially from exocrine pancreatic insufficiency or reduced intestinal bile salt concentration, are common causes of maldigestion and malabsorption. The rarity of pancreatic dysfunction and the herbivorous diet of the horse mean that maldigestion is less important and more difficult to diagnose.[2] However, maldigestion almost certainly contributes to the chronic weight loss seen in malabsorption syndromes associated with diseases that cause villous atrophy and blunted mucosa in the small intestine.[2]

The primary clinical sign associated with malabsorption syndromes in adult horses is chronic weight loss. If the disease process is limited to the small intestine, weight loss may be the only clinical sign, and it becomes important to rule out other causes of weight loss. Although malabsorption syndromes affect the digestion and absorption of carbohydrates, protein, and fat, diagnostic tests in the horse usually concentrate on dysfunction of carbohydrate digestion/absorption. Inadequate fat absorption is of limited importance in the horse, although malabsorption of fat-soluble vitamins may result in clinical conditions, such as dermatitis, neurologic diseases, and retinal dysfunction. Increased protein loss from the intestine (protein-losing enteropathy) is more commonly associated with large intestinal disease because of the larger surface area of the equine large intestine; however, concurrent small intestinal malabsorption and significant protein-losing enteropathy are likely to cause severe and rapid weight loss. Apart from weight loss, other clinical signs that may be seen in horses with infiltrative bowel diseases include colic, lethargy, diarrhea, and dependent edema.[3,5]

Causes of Malabsorption Syndrome

The important causes of malabsorption syndrome in the horse are as follows:

- Extensive small intestinal resection
- Chronic inflammatory bowel diseases
  - Granulomatous enteritis
  - Idiopathic eosinophilic enterocolitis
  - Multisystemic eosinophilic epitheliotrophic disease
  - Lymphocytic/plasmacytic enterocolitis
- Alimentary lymphosarcoma (lymphoma)
- Amyloidosis
- Enteric infections
  - *Lawsonia intracellularis*
  - Mycobacterial infection
  - *Rhodococcus equi*
  - Enteric fungal infections
- Idiopathic villous atrophy
- Congestive heart failure
- Intestinal ischemia
- Parasitism

Extensive Small Intestinal Resection

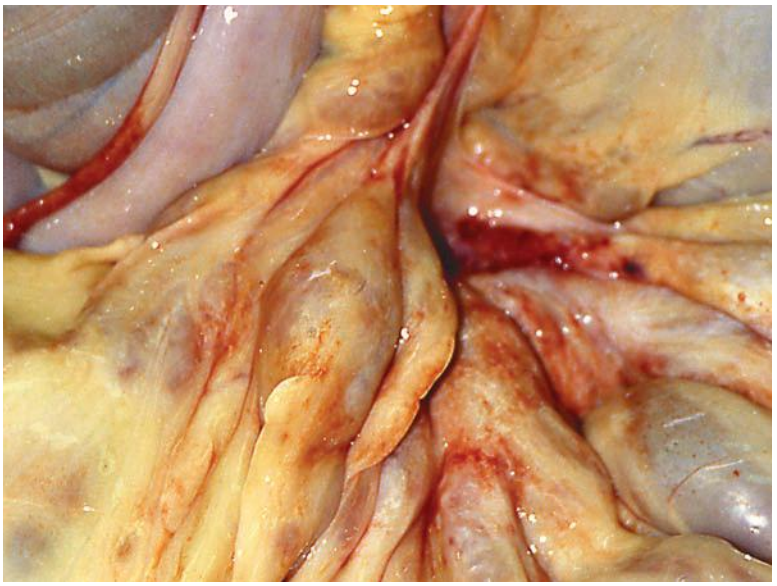
Insufficient absorptive area is a common cause of small intestinal malabsorption. This can be caused by extensive/excessive small intestinal resection after surgery for small intestinal strangulations ("short bowel syndrome"). The greater the amount of small intestine resected, the greater the risk of malabsorption of carbohydrates, lipids, and minerals. Removal of small sections of small intestine have no untoward long-term effects, but extensive resections may result in the horse becoming a "digestive cripple." Horses affected by short bowel syndrome develop weight loss and show poor performance. Other problems that have sometimes been observed following extensive small intestine resection in horses and ponies include

anorexia and liver disease.[7,8] The precise amount of small intestine that can safely be removed is still a matter of conjecture and appears to vary from horse to horse. The remaining bowel is probably capable of compensation; however, there is a limit in length of intestine required for compensation. One study suggested that no more than 60% of the small intestine could be safely resected,[7] but other studies suggest that up to 70% can be removed without causing subsequent malabsorption.[9] At the time of surgery, it should be recognised that strangulated small intestine can increase in length by up to 25%,[10] and this factor must be taken into consideration when assessing the amount of bowel that can be safely removed.

Chronic Inflammatory Bowel Disease

Chronic inflammatory bowel disease is the collective term for a group of infiltrative bowel diseases that produce similar clinical signs (primarily chronic weight loss).[3] These diseases are not as well defined in the horse as they are in other species, and their etiology is generally unknown. The small and the large intestines, the regional lymph nodes (Figure 10-1), and sometimes, other abdominal organs, may be involved. The cellular infiltrate may consist of a mixed cellular population or there may be a predominance of specific cell types such that chronic inflammatory bowel disease may be classified into a number of different disease types. Although the signalment, clinical signs, clinopathologic findings, and gross pathologic changes can sometimes be characteristic for one type of disease, in most cases, differentiation between these diseases relies on histopathologic examination of the affected portion of intestine (Table 10-1).

Figure 10-1



Gross post-mortem appearance of enlarged mesenteric lymph nodes in a horse affected by chronic inflammatory bowel disease.

Table 10-1

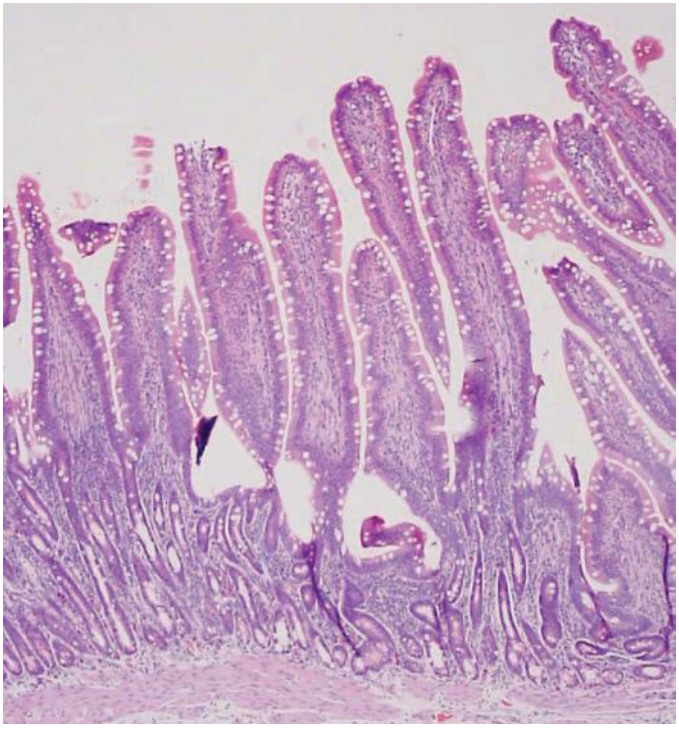
Typical Pathologic Changes in the Small Intestine in Different Chronic Inflammatory Bowel Diseases.

Disease	Pathologic changes
Granulomatous enteritis	Aggregates of macrophages and epithelioid cells Giant cells Villous atrophy
Idiopathic eosinophilic enterocolitis	Infiltration of all intestinal layers by eosinophils
Multisystemic eosinophilic epitheliotrophic disease	Infiltratrion of mucosa and submucosa by eosinophils, lymphocytes, and macrophages
Lymphocytic/plasmacytic enterocolitis	Infiltration of lamina propria with lymphocytes and plasma cells Villous atrophy

Granulomatous Enteritis

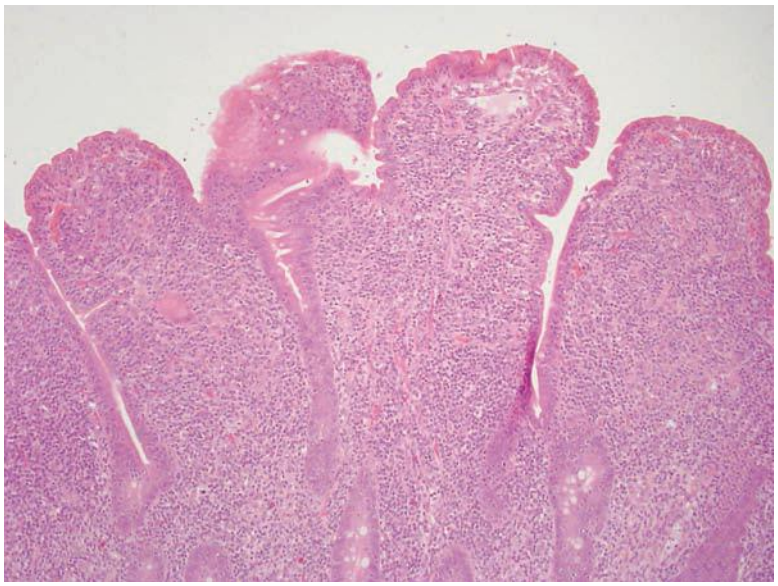
Granulomatous enteritis is characterized by diffuse granulomatous lesions, predominantly in the small intestine, with lymphoid and macrophage infiltration of the lamina propria, and variable numbers of plasma cells and giant cells.[11] Villous atrophy is marked (Figures 10-2, 10-3, and 10-4) and lesions attributable to other forms of granulomatous change (such as mycobacterial and fungal infections) are absent. No etiologic agent has been identified in granulomatous enteritis, although it has been proposed that the disease may result from an abnormal host inflammatory reaction to intestinal bacteria or dietary components. The pathology of the condition has similarities to that of Johne's disease in cattle and Crohn's disease in people. *Mycobacterium paratuberculosis* has been implicated as a possible causative factor in the development of Crohn's disease in humans, and experimental infection of horses with this organism results in microscopic granulomatous lesions similar to those seen in Crohn's disease. However, acid-fast organisms are rarely identified in Ziehl-Nielson stained sections of tissue from affected horses.

Figure 10-2



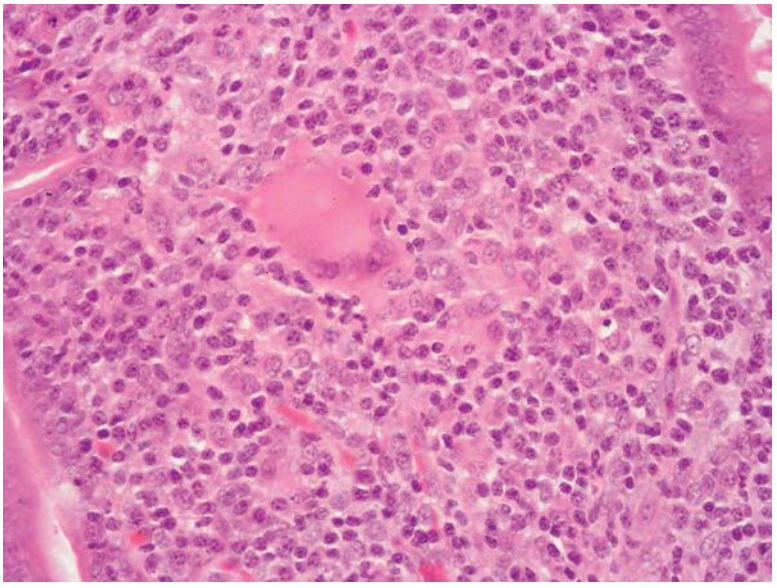
Normal mucosa of the small intestine of an adult horse showing the typical villous structure. H&E x10

Figure 10-3



Histologic appearance of the small intestinal mucosa from a horse with granulomatous enteritis: Thickening and fusion of villi with an infiltrate of mixed inflammatory cells. H&E x10

Figure 10-4



Higher power view of the lamina propria of the same horse as Figure 10-3 (granulomatous enteritis): Heavy inflammatory cell infiltrate with multinuclear giant cells. H&E x40

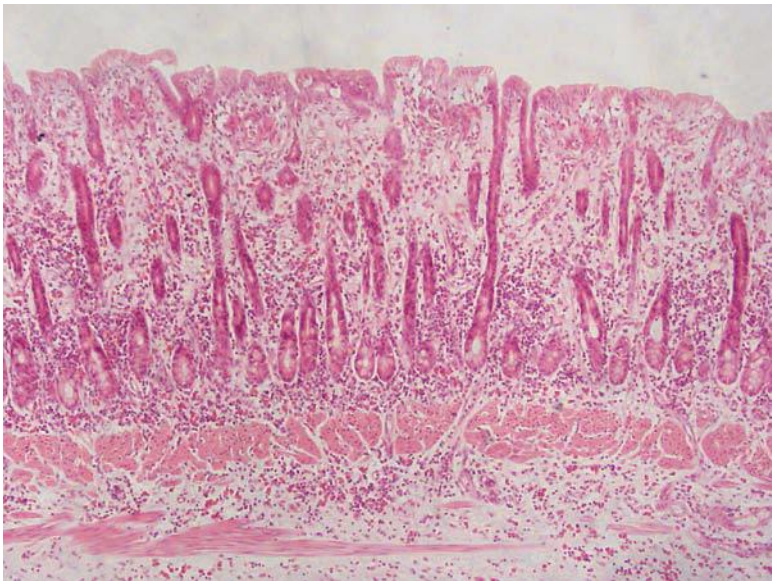
Granulomatous enteritis can occur in any age or breed or either sex, although it appears to be most common in young adult horses (less than 5 years of age).[12] It has also been most commonly reported in Standardbreds. A familial predisposition to the disease has been suggested; one report documented the occurrence of the condition in three sibling Standardbred horses. Affected horses usually present with signs of chronic and progressive weight loss and anorexia. Skin lesions, especially around the head, limbs, and coronets occur in some horses.[13] Other signs indicative of gastrointestinal disease (diarrhea and colic) are unusual. Some affected horses may respond to dexamethasone therapy.[14]

Idiopathic Eosinophilic Enterocolitis

Chronic eosinophilic infiltrates may take the form of diffuse inflammatory cell infiltration of the small intestinal mucosa with eosinophils and lymphocytes, or an eosinophilic granulomatous infiltrate (Figures 10-5 and 10-6).[15,16] Mucosal ulceration, enlargement of ileal Peyer's Patches, and mesenteric lymphadenopathy are frequently present. The etiology of the condition is unknown, but the nature of the inflammatory infiltrate has led to the suggestion that it represents an immune-mediated response to parasites.[17]

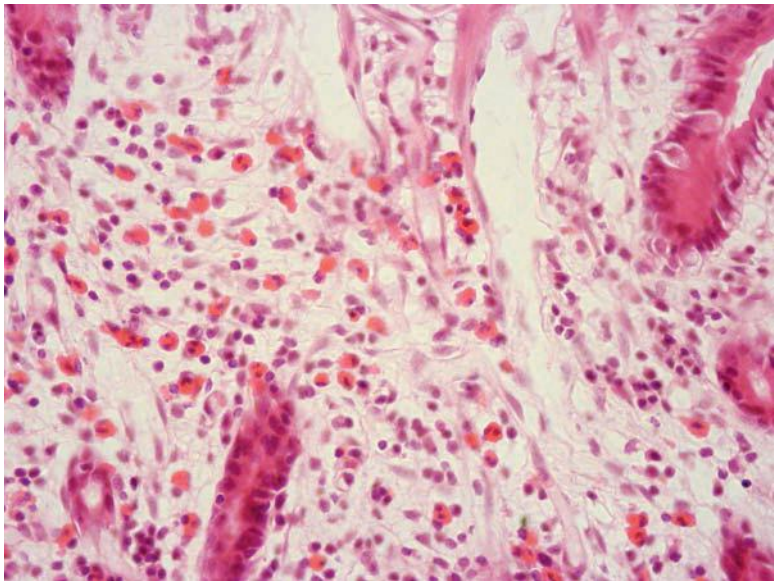
This disease may occur as a diffuse infiltrative disease of the small intestine, or as a focal infiltrative lesion. In the small intestine, the latter often cause circumferential mural bands that cause a partial obstruction of the bowel lumen and are associated with colic (often recurrent colic) (Figure 10-7).[5] These bands are thought to be caused by mural fibrosis stimulated by the eosinophilic enzymes. The diseased segments of intestine are often amenable to surgical resection.

Figure 10-5



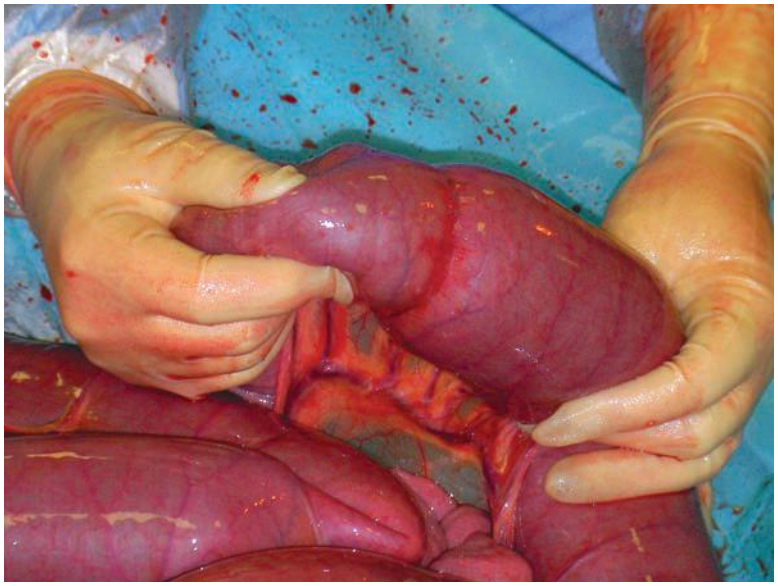
Histologic appearance of small intestinal mucosa in a horse affected by eosinophilic enteritis: Villous blunting and fusion, resulting in a flat appearance to the mucosa. H&E x10

Figure 10-6



Higher powered photomicrograph of the small intestinal mucosa of the same horse as Figure 10-5 (eosinophilic enteritis): Heavy eosinophil infiltration in the lamina propria. H&E x40

Figure 10-7



Annular constriction of the jejunum caused by focal eosinophilic enteritis. Appearance at exploratory laparotomy.

Segmental eosinophilic colitis is an uncommon disease that results in a local obstructive lesion of the wall of the left colon (Figure 10-8). Affected segments of bowel show variable mucosal necrosis, submucosal edema, and eosinophil infiltration of the lamina propria and deeper layers of the colon wall. No cause has been established although a parasite-associated etiology is suspected. Affected horses usually present with mild to moderate intermittent colic. The pain is responsive temporarily to analgesics, but recurs as the action of the analgesic wears off. There may also be varying degrees of abdominal distension for a few hours to several days. The heart rate varies depending on the duration of disease, but is usually in the range of 36 to 75 bpm.

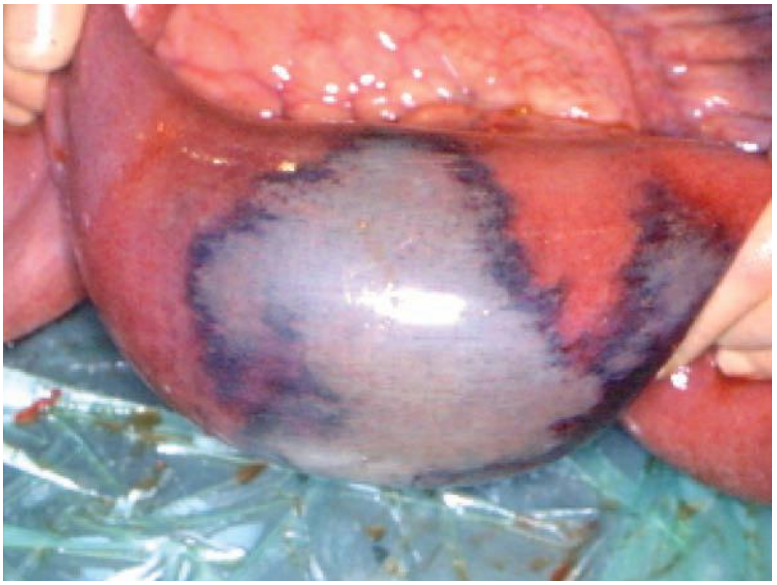
Rectal examination typically reveals varying degrees of large colon and cecal distension and a relatively soft impaction of the pelvic flexure and left ventral colon. Mural edema may be evident in the pelvic flexure and left dorsal colon, and in some cases, the corresponding mesocolon may also be edematous. This is sometimes accompanied by a segmental, firm enlargement (approximately 10 cm diameter) of the left dorsal colon. Peritoneal fluid shows evidence of nonseptic peritonitis. The fluid is usually turbid and yellow/orange, although in a few cases sanguinous peritoneal fluid is obtained. The total nucleated cell count in the peritoneal fluid is increased 0.01 to 0.250 x $10^6/\mu L$ (10 to 250 × $10^9/L$) and consists predominantly of neutrophils. The total protein concentration is also increased more than 0.3 g/dl (30 g/L).

Treatment consists of removal of the impaction, and surgical resection of the affected segment of colon. In very mild cases where the luminal obstruction is minimal, resection of bowel may not be necessary, although there is a risk of subsequent

worsening of the disease postoperatively. In cases where the segment of abnormal colon is short, a wedge resection may be performed with ligation of segmental vessels but leaving the colic artery and vein intact. When resection of longer lengths of left dorsal colon is required, the colic vessels should be ligated twice and the compromised segment of bowel transected at an oblique angle. After resection, the colon is repaired by end-to-end anastomosis. The defect in the colonic mesentery should be closed with a simple continuous suture pattern.

In one review of 22 cases of segmental eosinophilic colitis, long-term follow-up information was available for 18 cases.[18] Of these horses, 16 were alive and well, with no history of colic, 3 months to 7 years after discharge from the clinic. One horse in which resection of the colon was not performed had recurrence of colic symptoms.

Figure 10-8



Segmental eosinophilic colitis. Focal area of eosinophilic inflammation at the pelvic flexure. Appearance at exploratory laparotomy.

Multisystemic Eosinophilic Epitheliotrophic Disease

Multisystemic eosinophilic epitheliotrophic disease is characterized by cutaneous, hepatic, and pancreatic lesions as well as gastrointestinal lesions. The pathologic changes usually involve infiltration by eosinophils and lymphocytes, but in some cases basophils may be the primary inflammatory infiltrate. In some reports, the condition has been variably referred to as eosinophilic gastroenteritis, eosinophilic colitis, eosinophilic granulomatosis, hypereosinophilia syndrome, and exfoliative eosinophilic dermatitis and stomatitis. It is recommended that the terms eosinophilic gastroenteritis and eosinophilic enterocolitis should be used to describe cases in which the lesions are restricted to the gastrointestinal tract, although they may be variants of multisystemic eosinophilic epitheliotrophic disease.[3]

As with granulomatous enteritis, most reported cases of multisystemic eosinophilic epitheliotrophic disease involve young horses, especially Standardbreds.[3] A severe dermatitis resembling pemphigus foliaceus is commonly present, with skin lesions on the face, limbs, and ventral abdomen. Ulceration of the coronets and oral cavity is also commonly present.[19] Peripheral eosinophilia may be present. Involvement of the liver and pancreas result in increases in serum liver enzymes, including gamma glutamyl transferase.

Diagnosis is achieved by biopsy of skin, rectum, and/or liver. Eosinophil infiltrates in the wall of the rectum are a common finding in normal horses, but eosinophilic granulomas associated with vasculitis and fibrinoid necrosis of intramural vessels are considered pathognomic of multisystemic eosinophilic epitheliotrophic disease.[20,21]

The etiology of this disease is unknown, although immune-mediated disease and response to parasites are often assumed to be involved. Treatment of affected horses with anthelmintics, antibiotics, and corticosteroids is usually unsuccessful. Dexamethasone can sometimes effect a temporary improvement.

Lymphocytic/Plasmacytic Enterocolitis

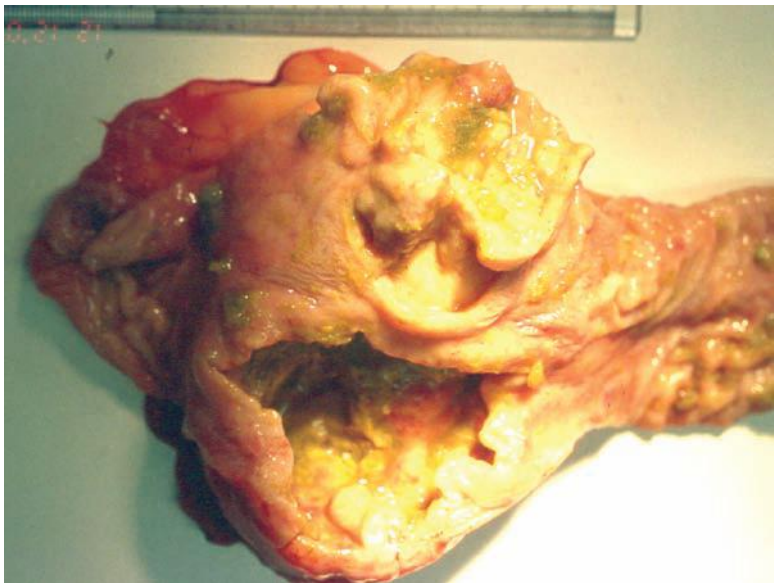
Lymphocytic/plasmacytic enterocolitis is characterized by mucosal infiltration by lymphocytes and plasma cells in the absence of granulomatous change.[22,23] The disease appears to affect horses of all ages and breeds and either sex. Clinically, most affected horses present with chronic weight loss, with or without diarrhea and recurrent colic. Some horses may respond to

treatment with parenterally administered dexamethasone. In other species, such as the dog, lymphocytic/plasmacytic enterocolitis is thought to represent a nonspecific intestinal immune response to agents that cause intestinal damage. It may represent a pre-lymphomatous change in such species; it is currently unknown if a similar progression may occur in the horse.

Alimentary Lymphosarcoma (Lymphoma)

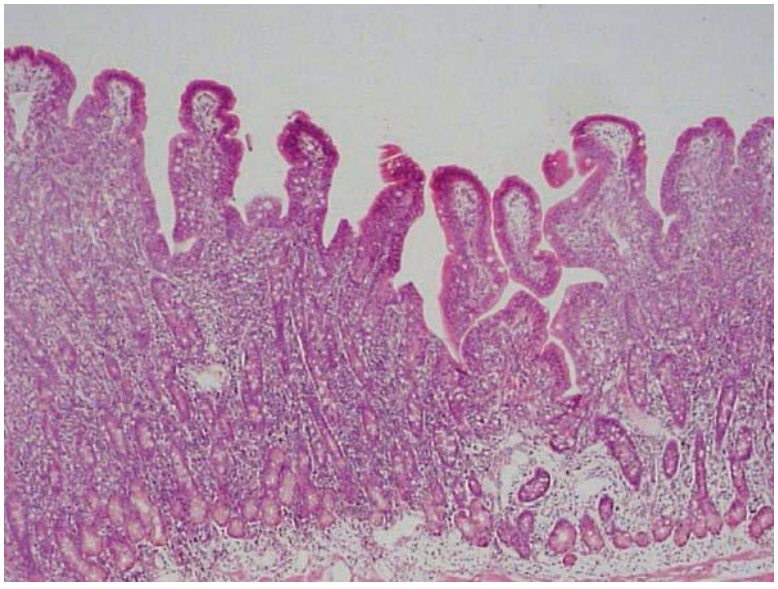
Alimentary lymphosarcoma may be a primary neoplastic disease, or it may represent part of a multicentric disease or a metastatic spread from a primary focus somewhere else in the body.[24] The disease may take the form of discrete focal tumor masses in the bowel wall (Figure 10-9) or a diffuse intestinal infiltrate of neoplastic cells that may cause malabsorption (Figures 10-10 and 10-11).[25,26] Both small and/or large intestines may be affected; mesenteric lymph nodes are also commonly infiltrated by malignant cells. Villous atrophy is commonly present in association with small intestinal infiltrates. Mucosal ulcers are also commonly present, and these can contribute to serum protein loss and the development of hypoproteinemia. Luminal bleeding can result in blood-loss anemia in addition to the typical anemia associated with chronic inflammation or neoplasia. Lesions may also be present in other organs throughout the body, and these may give rise to additional clinical signs and abnormalities of clinical pathology. Although lymphosarcoma can affect horses of any age, the disease is more commonly seen in horses over 5 years old.

Figure 10-9



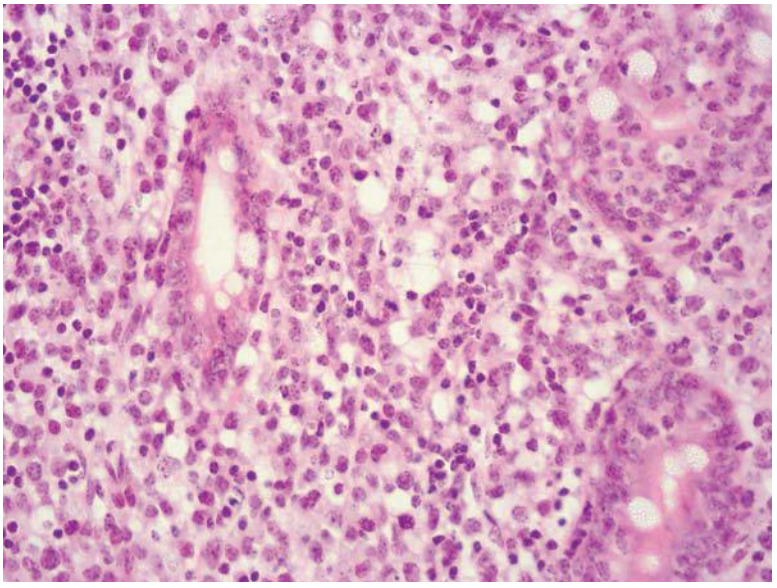
Focal area of lymphoma affecting the jejunum. The lesion has resulted in a diverticulum with ulceration of the mucosa.

Figure 10-10



Alimentary lymphoma. Photomicrograph demonstrating a sheet of neoplastic lymphocytic cells infiltrating the mucosa, resulting in blunting and fusion of villi. H&E x10

Figure 10-11



Higher powered photomicrograph of the small intestinal mucosa of the same horse as Figure 10-10 (alimentary lymphoma): A heavy infiltrate of lymphoma cells is present in the lamina propria. Mitoses are present. H&E x40

Enteric Infections

Mycobacterial granulomatous enterocolitis is rare, and is usually associated with avian strains of *Mycobacterium tuberculosis* or *Mycobacterium intracellulare*. There are also rare reports of enteric fungal infections from *Aspergillus fumigatus* or *Histoplasma capsulatum*. It has been suggested that fungal infections may be most likely in horses undergoing chronic antibiotic or corticosteroid treatments.

Clinical Signs

The clinical signs associated with chronic infiltrative small intestinal diseases are generally similar regardless of the pathologic lesion (apart from horses affected by alimentary lymphosarcoma and multisystemic eosinophilic epitheliotrophic disease which may have signs related to involvement of other body systems).

The clinical presentation is characterized by chronic weight loss. Other signs are variable and may include diarrhea, intermittent or chronic colic, variable appetite, depression, lethargy, peripheral and dependent edema, pyrexia, and skin lesions (Table 10-2). Skin lesions occurring in horses with malabsorption include thin haircoat, patchy alopecia, and focal areas of scaling and crusting. Severe, and often highly pruritic, skin lesions may be present in horses affected by multisystemic eosinophilic epitheliotrophic disease. Paraphimosis may occur in male horses associated with emaciation.[27]

Table 10-2

Clinical Signs Associated with Malabsorption Syndromes in the Adult Horse

Vital signs	Usually normal; occasionally pyrexia
Mucous membranes	Sometimes pale
Appetite	Variable – poor, normal, or increased
Body condition	Usually chronic weight loss
Demeanor	Variable – normal, dull, or depressed
Fecal consistency	Variable – normal, reduced, increased, or diarrhea
Pain	Variable – none, intermittent, or chronic low-grade colic
Edema	Variable – none or ventral/limb edema
Rectal palpation	Variable – normal, thickened intestine, enlarged lymph nodes
Skin lesions	Variable – none, generalized, exudative dermatitis, coronitis

Diagnosis

A thorough clinical and clinicopathologic examination is required in horses presenting with signs of chronic weight loss. Clinicopathologic findings in horses affected by malabsorption syndrome are nonspecific, but may include some or all of the following.[28]

- hypoalbuminemia
- hyperglobulinemia or hypoglobulinemia
- neutrophilia (occasionally neutropenia)
- eosinophilia (rare)
- anemia (normocytic, normochromic) (hemolytic and macrocytic anemia, and thrombocytopenia have been recorded in some cases of alimentary lymphosarcoma)
- hyperfibrinogenemia
- hyperlipemia
- increased serum alkaline phosphatase
- increased serum gamma glutamyl transferase (multisystemic eosinophilic epitheliotrophic disease)
- reduced glucose absorption during oral glucose absorption test[29,30]
- reduced xylose absorption during D(+)-xylose absorption test[31]
- increased serum IgA concentration
- decreased serum IgM concentration (lymphosarcoma)

Horses with chronic inflammatory bowel disease experience malabsorption coupled with enteric loss of proteins of all molecular weights. Since globulins are manufactured faster than albumin, the most consistent abnormality involving serum proteins is hypoalbuminemia. Anemia is most common in cases of granulomatous enteritis,[13] but has also been reported in some cases of lymphocytic/plasmacytic enterocolitis and multisystemic eosinophilic epitheliotrophic disease.

Enlarged mesenteric lymph nodes may be palpable per rectum in some affected horses (especially horses with alimentary lymphosarcoma). Abnormally thickened bowel wall may occasionally be palpated per rectum, and this finding can be confirmed using ultrasonography. Abdominal paracentesis frequently yields normal peritoneal fluid. Neoplastic cells are occasionally present in the peritoneal fluid of horses with alimentary lymphosarcoma.[24] Increased numbers of eosinophils may sometimes be present in peritoneal fluid from horses with eosinophilic infiltrative disease.

Diagnosis of infiltrative bowel diseases may be facilitated by histopathologic examination of rectal mucosal biopsies in some cases.[21] However, in many cases, the infiltrative disease is confined to the small intestine, and histologic examination of the rectal mucosa is normal. Lymphoidal cells and plasma cells may be found in the rectal mucosa of horses with a variety of intestinal diseases, including cyathostominosis, granulomatous disease, and alimentary lymphoma; the identification of lymphocytic proctitis in rectal biopsy should, therefore, not be interpreted as evidence of lymphocytic/plasmacytic enterocolitis. Likewise, it should be recognized that eosinophils are commonly present in the rectal mucosa and submucosa of many normal horses, and their identification in rectal biopsies is not proof of multisystemic eosinophilic epitheliotrophic disease or idiopathic eosinophilic enterocolitis. However, the presence of eosinophilic granulomas, associated with vasculitis and fibrinoid necrosis of intramural vessels in rectal tissue is considered diagnostic of multisystemic eosinophilic epitheliotrophic disease. Skin biopsies or ultrasound-guided biopsy of liver, lymph node, or lung may reveal evidence of multisystemic eosinophilic epitheliotrophic disease.

A diagnosis of small intestinal malabsorption is made using a carbohydrate absorption test such as the oral glucose absorption test or the D(+)-xylose absorption test. The oral glucose absorption test is more commonly used because of the ease of analyzing plasma glucose; however, the results of the oral glucose absorption test require careful interpretation. The immediate dietary history, gastric emptying rate, intestinal transit, age, and hormonal effects of the horse influence the glucose peak and curve shape. Higher glucose peaks are recorded from healthy horses eating hay or grass than from those eating concentrates. Recent appetite or cachexia may affect the results. In healthy horses, administration of 1g glucose per kg body weight as a 20% solution results in a maximum plasma glucose level (higher than 85% baseline) at 120 minutes.[29] Horses can be divided into three groups on the basis of the results of the oral glucose absorption test.[32]

1. Normal absorption – plasma glucose concentrations at 60 and 120 minutes are within the normal range as defined by the mean ± 2 SD of the results of Roberts and Hill,[29] and the glucose concentration at 120 minutes shows a greater than 85% increase over the resting value.
2. Partial malabsorption – plasma glucose concentrations at 60 and 120 minutes are below the normal range as defined by

the mean ± 2 SD of the results of Roberts and Hill,[29] and the glucose concentration at 120 minutes shows a less than 85% but greater than 15% increase over the resting value.
3. Total malabsorption – plasma glucose concentrations at 60 and 120 minutes are below the normal range as defined by the mean ± 2 SD of the results of Roberts and Hill,[29] and the glucose concentration at 120 minutes shows a less than 15% increase over the resting value.

Horses with total malabsorption are likely to have a diffuse infiltrative small intestinal disease. Horses with normal absorption are likely to have a histologically normal small intestine. Horses with a partial malabsorption result may have evidence of an inflammatory infiltrate, villous atrophy, or bowel wall edema, but they may also have histologically normal intestine, and further diagnostic tests should be carried out. The reason that some horses with infiltrative small intestinal diseases may have only partial malabsorption responses to an oral glucose tolerance test is likely to be the presence of focal intestinal lesions that only partially interfere with the absorptive function of the entire intestinal tract.

Unfortunately, the oral glucose absorption test is not definitive.[33] Two horses affected by weight loss have been described in which an initial flat oral glucose absorption test absorption curve subsequently improved and became more normal.[34] Intestinal biopsies were normal. It appears, therefore, that malabsorption (as determined by a history of weight loss and a flat oral glucose absorption test absorption curve) may occur in the absence of significant morphologic change in the small intestine, and the condition may be transient. In addition, abnormal oral glucose absorption test results have been recorded in a number of adult horses with chronic diarrhea, in which post mortem examination showed that the pathologic damage was confined to the large intestine.[35]

Unlike the oral glucose absorption test, the D-xylose absorption test is not affected by hormonal effects or mucosal metabolism.[31] However, gastric emptying, intestinal motility, intraluminal bacterial overgrowth, and renal clearance affect the curve shape. Healthy mares not fed for up to 96 hours had flatter curves and a slower decrease in plasma xylose than when deprived of food for 12 to 36 hours.[36] Abnormal D-xylose absorption represented by a flat curve or delayed absorption is indicative of jejunal disease, and has been recorded in horses with chronic inflammatory bowel disease, parasitism, and idiopathic villous atrophy;[1,37] however, abnormal xylose absorption curves have been detected in the absence of small intestinal histopathologic abnormalities.[1]

In one study, the diagnostic and prognostic value of nuclear scintigraphy with technetium^{99m}-labelled hexamethyl-propyleneamine oxime-labelled leukocytes was assessed in horses with weight loss due to gastrointestinal malabsorption by comparing the results with the results obtained from healthy control horses.[38] Intestinal uptake of activity was detected in some, although not all of the affected horses, but none of the control horses. The technique was therefore specific for intestinal abnormalities, but failed to detect some horses that might have had intestinal lesions. No indications of the horses' specific pathologic diagnoses were obtained, and their prognosis or response to treatment could not be predicted.

Confirmation of the diagnosis of infiltrative small intestinal diseases and villous atrophy is made by histologic examination of sections of small intestine. Full-thickness bowel wall biopsies may be obtained at exploratory laparotomy for this purpose, although horses with malabsorption states are often not good candidates for surgical exploration of the abdomen, and wound complications are common in the postoperative period because of hypoproteinemia and the catabolic state. If surgery is to be performed, biopsies should be taken from any grossly abnormal section of bowel, but if the bowel appears grossly normal then at least three small intestinal biopsies should be taken; one each in the proximal, mid-, and distal small intestine. Biopsies should also be obtained from the cecum and large colon at the same time. Biopsies of mesenteric lymph nodes often reveal similar pathologic changes to small intestinal infiltrates, and at least one lymph node should be biopsied at the same time as the bowel wall biopsies are taken. Bowel wall and lymph node biopsies can also be successfully obtained via a flank laparotomy that can be performed in the standing horse, utilizing local anesthesia. This approach greatly reduces the complications associated with healing of ventral midline incisions. Alternatively, mesenteric lymph node biopsies may be taken via laparoscopic techniques in the standing patient, thereby eliminating the necessity for general anesthesia and significantly reducing the risk of wound complications. However, the sensitivity of this approach for the diagnosis of small intestinal infiltrative disease has yet to be assessed. A noninvasive biopsy of the duodenum via gastroduodenal endoscopy can be performed. This may be diagnostic if the duodenum is involved, which is commonly the case with some of causes of infiltrative bowel disease (e.g., lymphocytic/plasmacytic enteritis). At least three samples of duodenal mucosa/submucosa should be collected. Mucosal bleeding at the site of the biopsy is an indication that an adequate sample was obtained. This procedure is most conveniently performed immediately after conclusion of the glucose or xylose absorption test.

Treatment

The prognosis for horses affected by malabsorption syndromes is generally guarded to very poor. By the time the precise diagnosis is reached, the disease is frequently well advanced. Horses affected by diffuse alimentary lymphosarcoma have a hopeless prognosis and should be humanely destroyed, although chemotherapy may prolong survival for 6 to 12 months. Treatment of horses with fungal enterocolitis with systemic antifungal drugs is usually unrewarding. Horses with diffuse eosinophilic and lymphocytic/plasmacytic enterocolitis may occasionally respond well to systemically administered corticosteroids, and on rare occasion, complete recovery may occur. Surgical resection of affected intestine in horses with eosinophilic enteritis or less commonly granulomatous enteritis may be curative.

Nutrition

Some level of digestive and absorptive capability is likely to remain in most horses with diseased small intestine. Horses with chronic inflammatory bowel disease may benefit from being fed highly digestible feeds. Provision of a palatable, easily assimilated high-energy and protein source is indicated. Supplementing the diet with electrolytes, minerals, and vitamins is also useful. Feeds with high quality fiber content (grass hay and access to pasture, complemented by commercial high-fiber diets based on beet pulp and soybean hulls) may help increase body weight by increased conversion of cellulose to volatile free fatty acids in the cecum. This high-fiber diet is especially beneficial for horses affected by chronic inflammatory bowel disease without diarrhea. Feeding more frequent meals (i.e., interval feeding) in smaller amounts may also aid in better digestion and absorption if the horse has a good appetite. Energy intake can be increased by feeding high-fat diets (5% to 10% of the diet containing vegetable oils or rice bran). Change to a high-fat diet should be undertaken slowly. Enteral feeding through an indwelling nasogastric tube is rarely indicated in view of the poor long-term prognosis. There is no justification in trying to sustain a severely debilitated horse when the prognosis is very poor.

In one study, horses with extensive small intestine resection showed weight gain when placed on interval feeding, even though the D-xylose absorption test indicated malabsorption.[9] In contrast, horses with extensive small bowel resection fed twice daily showed substantial weight loss and diarrhea in another study.[7]

Drug Therapy

Corticosteroid therapy is frequently ineffective in treating horses with chronic inflammatory bowel disease, although some cases of idiopathic eosinophilic enterocolitis and lymphocytic/plasmacytic enterocolitis appear to be responsive to corticosteroids. A minority of cases of granulomatous enteritis and multisystemic eosinophilic epitheliotrophic disease may also show a response to corticosteroids, although long-term improvement is highly unlikely.[12,13] Parenterally administered dexamethasone is likely to be more effective than orally administered corticosteroids in the treatment of chronic inflammatory bowel disease, and prolonged courses of systemic therapy are required.

Other potential treatments for chronic inflammatory bowel disease might include anabolic steroids, antibiotics, iodochlorhydroxyquin, anthelmintics, salicylazosulphapyridine and methylsulphapyridine. Currently, no evidence suggests that any of these treatments are effective. Metronidazole, which is both an antibiotic and an anti-inflammatory agent, is beneficial in the treatment of some humans with Crohn's disease, and it might have potential value in the treatment of horses with chronic inflammatory bowel disease. Hydroxyurea, an antineoplastic drug used to treat humans with hypereosinophilia syndrome, has been shown to produce a temporary improvement in a small number of cases. Other chemotherapeutic agents, including vincristine, cytosine, and cyclophosphamide, have generally failed to have any beneficial effects in horses with malabsorption.[33] As mentioned earlier, some horses with alimentary lymphosarcoma respond favorably for 6 to 12 months during chemotherapy.

Surgery

Surgical resection of limited areas of affected bowel may produce some short-term benefits, but the diffuse nature of the lesions in many of the diseases usually precludes this therapeutic option. Some cases of alimentary lymphosarcoma, granulomatous enteritis, and eosinophilic enterocolitis may affect focal areas of the intestinal wall, and these lesions may be amenable to surgical resection.

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Liver Diseases and Liver Failure

Chapter 11

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Liver disease is common in the horse, and a great many disorders can cause hepatic disease (i.e., pathologic change or damage to the liver) in both adult horses and foals. Few of these diseases, however, result in hepatic failure. The liver carries an immense reserve capacity (approximately 80%), and liver damage, therefore, must be advanced before physiologic failure occurs.[1] For example, horses with strangulating or inflammatory intestinal diseases frequently have evidence of liver disease (elevated hepatic enzymes in the serum) caused by portal hypoxia and/or increased concentrations of endotoxin in the portal circulation, but these conditions rarely progress to liver failure. The distinction between hepatic disease and hepatic failure is clinically important. In view of the large reserve capacity, many horses with mild hepatic disease will make a full recovery given time and removal of the inciting cause, provided that the diagnosis is made relatively early. If the damage progresses to cause liver failure, however, the prognosis for survival is markedly decreased.[2,3,4]

Hepatic failure is a serious condition that requires intensive therapy. If the diseased liver is capable of repair and regeneration, recovery is possible; but if the damage is irreversible (e.g., associated with severe fibrosis or cirrhosis) (Figure 11-1), death will ensue. Rarely can the diagnosis of liver disease be made purely on the results of a clinical examination, unless there is fulminant hepatic failure (as evidenced by encephalopathy and jaundice).

Many disorders that cause chronic liver disease, (e.g., pyrrolizidine alkaloid toxicosis) can present with acute signs of hepatic failure. In these cases, the underlying pathologic disease of the liver may have been present for a considerable period of time in a subclinical state; it is only when the degree of damage throughout the liver reaches a certain level that failure of liver function occurs and clinical signs become apparent.

Figure 11-1



Severe fibrosis/cirrhosis of the liver.

Causes of Liver Disease

Liver disease can arise secondary to many toxic, septic, hypoxic, neoplastic, or metabolic conditions (Table 11-1).

In ponies and miniature horses, the most common cause of acute hepatic disease and failure is hepatic lipidosis, whereas in adult horses, the most common syndromes causing both hepatic disease and failure are Theiler's disease and pyrrolizidine alkaloid toxicosis. In foals, important causes of liver disease include Tyzzer's disease, toxic hepatopathies (such as iron fumarate toxicity), hepatitis secondary to septicemia, and equine herpesvirus-1. Moderate elevations in serum gamma glutamyl transferase (GGT) can be seen in foals with significant gastroduodenal ulceration, especially pyloric outflow obstruction and stricture formation.[2] This may be due to restricted bile outflow through the sphincter of Oddi, or bile stasis and incomplete intrahepatic biliary clearance resulting from abnormal intestinal motility. A similar elevation in serum GGT (unaccompanied by other biochemical evidence of liver disease) occurs in mature horses with protracted enteritis, or postoperative ileus.[2] Elevated

liver enzymes can also occur in foals with *Rhodococcus equi* abdominal abscesses or umbilical vein remnant infection. In addition to the primary hepatic conditions listed in Table 11-1, adult horses with right-sided congestive heart failure can present with elevated liver enzymes, especially GGT and alkaline phosphatase (AP).[2]

The clinical signs of liver failure can vary, depending mostly on 1) duration – acute or chronic; 2) predominant biliary vs. hepatocellular injury; and 3) specific cause.

Table 11-1
Important Causes of Liver Disease in Horses

Toxic causes:
- Pyrrolizidine alkaloid toxicosis
- Alsike clover
- Panicum grasses
- Iron
- Mycotoxins

Infectious causes:
- Cholangiohepatitis
- Tyzzer's disease
- Hepatic abscess
- Equine herpesvirus (EHV-1)

Inflammatory, non-infectious causes:
- Chronic active hepatitis
- Neoplasia
- Granulomatous disease

Metabolic causes:
- Hepatic lipidosis
- Hyperammoninemia in horses with gastrointestinal disease (no liver disease present)
- Hyperammoninemia in Morgan foals

Obstructive causes:
- Biliary stones
- Right dorsal colon displacements
- Papillary stricture – foals with duodenal ulcers
- Neoplasia
- Hepatic torsion
- Portal vein thrombosis

Unknown causes:
- Theiler's disease
- Neonatal isoerthrolysis

Congenital:
- Portosystemic shunt

Horses with acute liver failure are more likely to have central nervous system signs as their initial and predominant finding, whereas horses with chronic liver disease leading to failure commonly (but not always) have weight loss (Figure 11-2) and/or photosensitivity (Figure 11-3) as a clinical finding.[1-5] Gastric impaction (Figure 11-4) and bilateral laryngeal paralysis are two of many complications that may be seen with equine hepatic failure.[1,3,4,6] Horses with liver disease that initiated in the biliary system are often more jaundiced (Figure 11-5), more likely to be colicky (because of biliary obstruction and possibly an enlarged liver), have photosensitivity, and are less likely to have CNS signs. Icterus, however, is not specific for liver disease, and other causes (including hemolysis and anorexia) should be ruled out.[1] Specific causes of liver failure can also result in more specific findings. These include fever with cholangiohepatitis, ventral edema with hepatic lipidosis, mild abdominal distention, and abnormally tight colonic bands with right displacement of the colon that causes biliary obstruction.

Figure 11-2



Weight loss is a common presenting sign of chronic liver disease.

Figure 11-3



Photosensitization affecting the muzzle and non-pigmented areas on the face.

Figure 11-4



Gastric impaction secondary to liver disease – appearance at post-mortem examination.

Figure 11-5



Icterus (jaundice). Yellow discolouration of the sclera.

Diagnosis of Liver Disease

The liver has a limited number of ways to respond to various insults, and, therefore, the clinical and laboratory changes tend to be similar regardless of the underlying cause.[2] In most cases, it is appropriate to first determine if the horse has liver disease, and then to attempt to identify the cause. During liver disease, some functions of the liver tend to fail before others, and this dictates the progression of clinical signs and laboratory changes.[7] In the mature horse, leakage of hepatic and biliary enzymes into the circulation, failure to convert ammonia to urea, and failure to conjugate bilirubin are generally recognized before failure to produce clotting factors or albumin.[1]

Biochemical Testing for Liver Damage

Biochemical testing is imperative in the diagnosis of both liver disease and liver failure.[1-5] Biochemical results can be helpful in narrowing the differential diagnosis for the liver failure and, when evaluated over time, can help predict prognosis. Liver-specific enzymes include sorbital dehydrogenase (SDH) and gamma glutamyltransferase (GGT) which respectively reflect hepatocellular and biliary injury. Aspartate aminotransferase (AST) and alkaline phosphatase (AP) also respectively reflect hepatocellular and biliary injury, but are not liver specific. Isoenzyme 5 of lactate dehydrogenase (LDH-5) and ornithine carbamoyltransferase are alternative indicators of hepatocellular disease, but are rarely used clinically. Sorbital dehydrogenase would be expected to increase in the serum with any mild hepatocyte injury (endotoxemia, etc.). It has a short half-life which can be very helpful in determining resolution or progression of the hepatic insult. Not all diagnostic laboratories

perform quantification of SDH, and care is required with sample handling (the enzyme is stable at room temperature only for a maximum of 12 hours). AST is the other most commonly used hepatocellular enzyme (also released in myopathic conditions), but it has a much longer half-life than SDH, and elevated blood levels may persist for well beyond a week after resolution of the inciting event. GGT is released mostly from biliary epithelium and, in the horse, often continues to elevate for a few days (presumably because of biliary hyperplasia) after the hepatic insult is no longer present. The half-life of GGT is probably similar to that of AST. Alkaline phosphatase can be released from several sites, including bone, intestine, and placenta, which limits its clinical value in assessing hepatobiliary disease. The hematocrit and serum iron are frequently high in horses with severe liver disease. Race horses may rarely have mild increases (50 to 140 IU/L) in GGT without any other evidence of liver disease. This may be a result of focal lesions in the biliary system (e.g., parasitic cysts) or drug-induced increases in GGT.

Liver Function Tests

Liver function tests only become abnormal when approximately 60% to 70% of liver function is lost. These tests include elevations in direct bilirubin, blood ammonia, prothrombin and partial thromboplastin time, serum iron, and gamma globulins (with chronic disease).[1-5] An increase in direct bilirubin is a highly sensitive and specific marker of liver failure from either hepatocellular or hepatobiliary disease; however, mild hyperbilirubinemia may occur in horses that are anorexic, regardless of the cause. Levels of both uncongugated (indirect reacting) and conjugated (direct reacting) bilirubin are helpful diagnostically. Increase in direct bilirubin of 25% or more of the total bilirubin is suggestive of a predominant biliary disease. Clinically evident jaundice associated with marked unconjugated hyperbilirubinemia but in the absence of other biochemical evidence of liver disease is suggestive of hemolytic anemia. Septic foals with intestinal ileus sometimes have elevations in direct bilirubin with minimal evidence of hepatocellular dysfunction; treatment should focus on the sepsis and intestinal ileus. Levels of BUN and albumin may be decreased with chronic liver diseases.

Serum or plasma bile acids are elevated in horses with both hepatocellular and hepatobiliary disorders, and can be an early predictor of liver failure when values rise above 30 μmol/L.[5,8] Unlike in other species, fasting samples are not required in horses to interpret bile acid results, although mild elevations of bile acids (up to 20 μmol/L) may occur as a result of anorexia.

Blood ammonia can also be used as an assessment of liver function; however, rapid and careful sample handling is required. Ideally, a control sample should be obtained from a healthy horse and measured simultaneously for comparative purposes. Dye excretion tests (such as bromosulphophthalein and indocyanine green) are now rarely used to assess liver function.

Other Biochemical Tests

Serum triglycerides are increased in equines with hepatic lipidosis. In foals with hepatic failure, hypoglycemia is often present, whereas in adult horses, blood glucose is generally normal or increased.

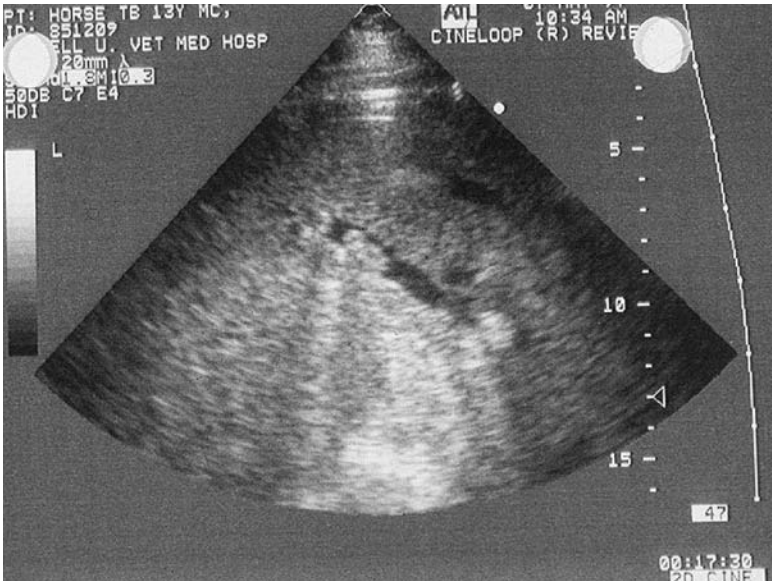
In foals, many of the standard biochemical indices of liver function and damage possess significantly different reference ranges than in adult horses. GGT, bile acids, and AP, for example, are normally higher in healthy foals than in adults.[2]

Liver Ultrasonography and Biopsy

Ultrasound examination and liver biopsy are the two most commonly used ancillary tests for detecting liver disease. Transabdominal ultrasonography is best performed with either a 2.5-MHz or 5-MHz transducer. In neonatal foals, 7.5-MHz or 10-MHz transducers are effective. The liver is best imaged from the right, immediately caudal and ventral to the lung. Typical landmarks for imaging the liver are the 6th to 15th intercostal spaces on the right, and the 6th to 9th intercostal spaces on the left. In neonatal foals, the liver can also be imaged from the ventral abdomen. In adults, the image quality and usefulness of the procedure are variable, depending on such factors as the underlying disease, normal age changes (right-lobe atrophy in old horses), extent of the lung fields, degree of gas distension of the colon, and amount of subcutaneous fat. Healthy liver tissue is less echogenic than the spleen and has a more prominent vascular pattern. The portal veins can be distinguished from the hepatic veins by the greater amount of fibrous tissue in the walls of the portal vessels. Bile ducts are not visible in the normal liver. Abnormalities that may be detected by ultrasound examination include dilated bile ducts (Figure 11-6), biliary sludge, biliary stones, hepatic fibrosis (Figure 11-7), hepatomegaly, smaller than normal liver (highly subjective), hepatic lipidosis, and hepatic masses.

Liver biopsy is best performed after the liver has been visualized on ultrasound examination on either the right or left side. Liver biopsies are best used to determine amount of fibrosis, inflammation, predominant location of disease, and for culture purposes.[9] Pre-biopsy evaluation of extrinsic, intrinsic, and common clotting function, by measurement of prothrombin time (PT) and activated partial thromboplastin time (APTT), is often recommended. Although prolonged clotting times are rare even with severe liver disease, the risk of hemorrhage is higher in adults with Theiler's disease and foals with Tyzzer's disease.[2]

Figure 11-6



Transcutaneous ultrasonogram of the right side of the liver in a horse with cholangitis, showing a distended bile duct and cholelith.

Figure 11-7



Ultrasonogram of the liver of a foal showing echogenic foci suggestive of hepatic fibrosis.

Hyperlipemia

Hyperlipemia is a disorder of lipid metabolism characterized by hypertriglyceridemia and fatty infiltration of body organs.[10-13] The disease is most common in ponies, miniature horses, and donkeys, although it occasionally affects larger horses.[14,15] The condition is usually precipitated by periods of anorexia, malnutrition, stress, and other diseases, and occurs most commonly in the winter months. The clinical signs are often vague initially, but the condition progresses rapidly and is frequently fatal unless early and aggressive therapy is instituted.

Epidemiology

Hyperlipemia is most commonly seen in small pony breeds, such as Shetland ponies and Welsh Mountain ponies, and in donkeys. Two retrospective studies from equine referral hospitals in the USA reported an incidence of hyperlipemia of 11% in miniature ponies/horses and 18% in donkeys presented to these hospitals.[14,15] The condition is uncommon in larger horse breeds, but is occasionally identified in horses affected by other diseases, including renal disease, lymphosarcoma, and pituitary adenoma (Cushing's disease or hyperadrenocorticism).

The incidence of hyperlipemia is higher in mares than in stallions and geldings. This predisposition is partly explained by the fact that hyperlipemia is common in pregnant and lactating mares; however, females also appear to be at higher risk independently of reproductive status.[16] Hyperlipemia can be seen in horses and donkeys of all ages, although it is uncommon in animals less than 18 months of age, with older animals being at greater risk (possibly because of an age-related decrease in insulin sensitivity). It is occasionally diagnosed in ill foals and has been seen as a congenital condition in foals born to hyperlipemic dams.

Hyperlipemia is often seen as a complication of other diseases, especially gastrointestinal diseases. Some of the more common diseases identified in association with hyperlipemia are summarized in Table 11-2. Many of these diseases are thought to predispose to hyperlipemia by causing inappetence or anorexia.[17] In addition to disease, hyperlipemia may be induced by periods of enforced malnutrition, such as inadequate availability of pasture or competition for food. Pregnant mares, especially in the last trimester, and lactating mares have increased nutritional requirements and are, therefore, at greater risk of developing hyperlipemia. Obesity and stress are other important risk factors for the development of the disease. Stress factors that have been implicated include transportation, change of environment or diet, inclement weather, and the stress of pregnancy, lactation, and disease.

Table 11-2
Diseases and Conditions Commonly Associated with Hyperlipemia

Intestinal parasitism
Colitis
Colonic impaction
Gastric impaction
Dysphagia and dental disorders
Esophageal obstruction
Esophageal ulceration
Lymphosarcoma
Hyperadrenocorticism (Cushing's disease)
Peritonitis
Metritis
Laminitis
Renal failure
Liver disease
Septicemia
Hypocalcemic tetany
Post-injection abscess
Subsolar abscess

Pathogenesis

Hyperlipemia represents an excessively rapid mobilization of the body's fat reserves in response to stress or failure to maintain energy homeostasis. In response to negative energy balance and after depletion of glycogen reserves, nonesterified fatty acids (NEFAs) are mobilized from fat stores and released into the circulation. The majority of NEFAs are taken up by the liver where they may overwhelm the oxidative, gluconeogenic, and ketogenic pathways and are esterified to form triglycerides. Triglycerides then accumulate in the liver and are exported in the circulation in the form of very low density lipoproteins (VLDLs). This process occurs at such a fast rate that the VLDLs cannot be utilized by peripheral tissues, and plasma levels become excessive. VLDLs are also taken up by cells of the reticuloendothelial system, resulting in fatty infiltration of many organs.

Adipose tissues represent energy stores that form as a result of esterification of free fatty acids to produce triglyceride. This esterification is promoted by the action of insulin and glucose. In the presence of negative energy balance, lipolysis takes place in adipose tissues, mediated by glucagon, which activates the enzyme hormone-sensitive lipase. This hormone is normally inhibited by insulin and glucose, but with reduced insulin and glucose levels (which occur in negative energy balance) and enhanced glucagon activity, hormone-sensitive lipase is activated. It can also be activated by hormones released in response to stress (such as adrenocorticotrophic hormone [ACTH], glucocorticoids, and catecholamines) and by hormones released in pregnancy and lactation (progesterone and growth hormone).

The lipolysis induced by hormone-sensitive lipase results in the release of NEFAs into the circulation. Nonesterified fatty acids may be used by tissues for oxidation as a source of energy; however, most NEFAs are taken up by the liver where they can be used for ketogenesis or gluconeogenesis, or they are esterified to form triglycerides. The horse has a poor capacity for ketogenesis, and most NEFAs are used to produce triglycerides. These triglycerides are exported from the liver in the form of VLDLs, which can be used as a source of energy in peripheral tissues or restored in adipose tissue. In the presence of food deprivation, plasma VLDL levels rise excessively and triglycerides accumulate in the liver.

The clearance of VLDL triglycerides from the circulation is promoted by lipoprotein lipase. It has been suggested that raised plasma triglyceride levels in hyperlipemia may be caused by reduced clearance of VLDLs resulting from inhibition of the action of lipoprotein lipase. Lipoprotein lipase activity may be inhibited by azotemia and endotoxemia; however, studies of ponies with hyperlipemia suggest that the activity of LPL is increased rather than reduced.

Insulin resistance probably plays an important role in the pathogenesis of hyperlipemia.[10,13] Tissue resistance to insulin results in a diminished ability to regulate hormone-sensitive lipase. Thus, when the enzyme is activated in response to a negative energy balance, or as a result of stress or concurrent disease, lipolysis progresses in an excessive and uncontrolled way. Nonesterified fatty acids are released in excessive amounts that overwhelm the liver's oxidative, gluconeogenic, and ketogenic capacity, so that triglycerides are produced, resulting in hypertriglyceridemia and hyperlipemia. Insulin resistance is common in ponies and donkeys, and is exacerbated by obesity and pregnancy and lactation.

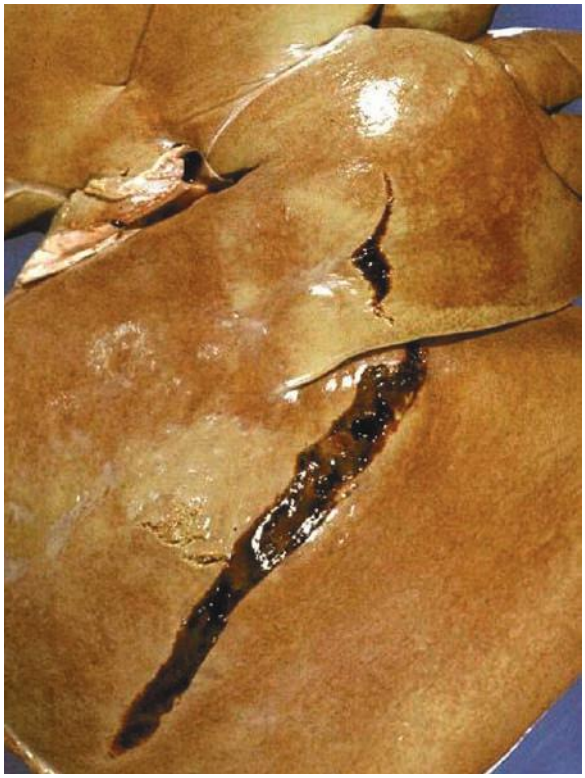
Clinical Signs

Clinical signs of hyperlipemia are compounded by the signs relating to the underlying disease or cause, such as diarrhea or dysphagia. In addition, fatty infiltration of the liver and kidneys may produce signs of hepatic and renal failure. The initial signs of hyperlipemia are often vague and include anorexia, lethargy, and weakness (Table 11-3). Rapid progression of the disease is common, with the development of ataxia, muscle fasciculations, head pressing, profound depression, recumbency, convulsions, coma, and death. Sudden death occasionally occurs as a result of hepatic rupture (Figure 11-8). Dysphagia is observed in some cases, and may result from encephalopathy or myopathy involving the muscles of mastication. Alternatively, dysphagia may be caused by an underlying primary esophageal disease such as choke. Pregnant mares may abort spontaneously or undergo premature labor.

Table 11-3
Clinical Signs of Hyperlipemia

Anorexia	Weight loss
Lethargy	Ventral edema
Weakness	Ascites
Ataxia	Abdominal pain
Muscle fasciculations	Reduced intestinal motility and fecal output
Dysphagia	Pyrexia
Sham drinking	Tachycardia
Profound depression	Tachypnea
Head pressing (Figure 11-9)	Congested mucous membranes
Circling	Icterus
Recumbency	Halitosis
Seizures	Abortion
Nystagmus	Sudden death

Figure 11-8



Hyperlipemia. Fatty infiltration of the liver with rupture of the liver capsule.

Figure 11-9



Headpressing - a common sign of hepatic encephalopathy.

Some animals demonstrate a period of rapid weight loss and development of ventral edema at the onset of the disease. This may reflect the primary underlying disease or may develop as a consequence of subcutaneous thrombosis caused by the hyperlipemia. Edema might also develop as a result of rapid fatty infiltration of the liver, partial obstruction of the portal circulation, and increased hydrostatic pressure in subcutaneous abdominal veins. Likewise, mild intermittent abdominal pain (restlessness, flank watching, and rolling) may be caused by a primary gastrointestinal disease, or may occur as a result of hepatomegaly and stretching of the liver capsule. Intestinal motility and fecal output are often reduced, and this may predispose to colonic impaction.

The clinical course of hyperlipemia is rapid in most cases. The average interval between the onset of clinical signs and death or euthanasia is 6 to 10 days. In a few cases, a more protracted clinical course may occur.

Diagnosis

Plasma Triglycerides

Gross lipemia in blood samples centrifuged or left to stand is the simplest way to diagnose hyperlipemia in practice (Figure 11-10). This is a relatively insensitive method of diagnosis, however, especially in animals with mild degrees of hyperlipemia and animals with hyperlipidemia. Accurate measurements of plasma triglyceride levels are recommended to assess the degree of hyperlipemia and to monitor the course of the disease during treatment.

Figure 11-10



Hyperlipemia. Gross lipemia of the serum.

Plasma triglyceride levels of greater than 5 mmol/L (500 mg/mL) in ponies with clinical signs of hyperlipemia are diagnostic. Triglyceride concentrations of 1 to 5 mmol/L (100 to 500 mg/mL) can be present in ponies without clinical or pathologic evidence of hyperlipemia. This has been classified as hyperlipidemia, and may sometimes progress to hyperlipemia if adequate nutritional support is not provided. Triglyceride levels in this range can sometimes be present in clinically normal pony mares during pregnancy. Normal plasma triglyceride levels in donkeys are higher than in ponies. Healthy, nonpregnant donkeys may have levels as high as 3.5 mmol/L (350 mg/mL). Triglyceride levels in suckling foals are also higher than in adults because of the relatively high daily fat intake.

Plasma concentrations of other lipids, such as cholesterol, phospholipids, and NEFAs, are also increased in hyperlipemia; however, increases in concentrations of these lipids are not as great as triglycerides, and they are not routinely assessed for diagnosis. Identification of fatty infiltration of liver biopsies is diagnostic but has no advantage over simple measurements of plasma triglycerides.

Clinical Chemistry

Monitoring of serum or plasma biochemistry panels can help to 1) detect the presence and severity of organ failure in hyperlipemia; 2) determine appropriate supportive therapies; 3) monitor the course of treatment: and 4) detect underlying primary conditions. Table 11-4 lists an appropriate chemistry panel for this purpose.

Biochemical measurements of some substances may be complicated because of interference by high triglyceride levels. This can be overcome by clearing the plasma or serum of lipids prior to analysis by ultracentrifugation or chemical precipitation.

Blood glucose concentrations may be normal, low, or elevated, depending on the duration of anorexia, previous glucose therapy, and the presence or absence of Cushing's disease. Metabolic acidosis is often present, as shown by decreased arterial pH, decreased PCO_2, decreased bicarbonate levels, and a base deficit of 0 to 24 mEq/L.

Fatty infiltration of the liver results in elevations of liver-derived enzymes, including GGT, AP, LDH, and SDH. Liver function may be impaired, as assessed by elevations of bilirubin, bile acids, and ammonia. Fatty infiltration of the kidneys can result in impaired renal function, and elevation of plasma concentrations of urea and creatinine. These metabolites may also be increased as a result of dehydration, and reassessment following hydration is required to assess the degree of renal failure. Plasma albumin concentrations may be normal, elevated (associated with dehydration), or reduced (associated with chronic hepatopathy, a primary gastrointestinal lesion, or parasitism). Serum protein electrophoresis can be helpful in assessing underlying conditions such as intestinal parasitism.

Table 11-4
Biochemistry Panel for Investigating and Monitoring Hyperlipemia in Equids[13]

Metabolic status
- triglycerides
- glucose
- hydration status – albumin
  PCV
- electrolytes – Na^+
  K^+
  Cl^-
  Ca^{2+}
- acid–base status – pH
  HCO_3^-
  PCO_2

Liver damage and function
- gamma glutamyl transferase (GGT)
- alkaline phosphatase (AP)
- bile acids
- ammonia

Renal function
- ammonia
- urea nitrogen
- creatinine

Pathology
Typical pathologic findings in ponies and donkeys affected by hyperlipemia include fatty infiltration of the tissues, especially the liver and kidneys. The liver and kidneys are enlarged, yellow, friable, and greasy. In severe cases, the surface of the liver may be fissured, or there may be capsular rupture (see Figure 11-8) and associated hemorrhage. Fatty infiltration of other organs including adrenals, skeletal muscle, and myocardium may be evident. Necrotizing pancreatitis is present in some cases. Vascular thrombosis can occur secondary to hyperlipemia and fat embolism, and can result in focal hemorrhages, myocardial infarction, and renal infarction.

Treatment
The treatment of hyperlipemia has five different objectives:[13]
1. treatment of underlying or concurrent disease
2. correction of dehydration, electrolyte, and acid-base imbalances
3. symptomatic therapies
4. nutritional support
5. normalization of lipid metabolism

Treatment of Underlying or Concurrent Disease
Intestinal parasitism is a common cause of hyperlipemia in ponies and donkeys; therefore, appropriate anthelmintic therapy is required in all cases with confirmed parasitic burdens and should be administered in all other cases where no obvious cause of the hyperlipemia is identified. Other treatments for underlying diseases should be administered as appropriate, such as pergolide therapy for Cushing's disease.

Correction of Dehydration, Electrolyte, and Acid–base Disturbances

Correction of dehydration, electrolyte, and acid–base abnormalities is essential (see Chapter 17). Intravenous fluid and electrolyte therapy are generally required. Correction of severe acidosis in the presence of liver failure may require the administration of intravenous administration of bicarbonate. Blood gas analysis should be used when available to monitor the response to bicarbonate therapy, as too rapid an increase in blood pH may exacerbate signs of hepatic encephalopathy, and overdosing with bicarbonate can lead to persistent metabolic alkalosis and respiratory depression.

Dextrose should be added to the intravenous polyionic fluids or administered as 5% dextrose solutions in animals with hypoglycemia. When 5% dextrose solutions are being administered, serum electrolytes should be monitored, and potassium chloride or calcium gluconate administered as necessary. Care must be taken to avoid overdosing with dextrose, as this can result in transient or prolonged periods of hyperglycemia with associated diuresis, dehydration, and hyponatremia.

Symptomatic Therapies

Symptomatic therapies include the use of analgesic drugs, nonsteroidal anti-inflammatory drugs, and anti-ulcer treatments. These are used as necessary on an individual basis. Therapies for hepatic encephalopathy may also be beneficial. Plasma transfusions have been used in hyperlipemic patients with hypoproteinemia and endotoxemia, and in foals with failure of passive transfer of immunity.

Nutritional Support

Nutritional support is an essential component of therapy for hyperlipemia in all cases. Affected animals should be maintained in positive energy balance in order to limit the mobilization of NEFAs from adipose tissues.

In animals that are still eating, fresh and highly palatable foods, such as grass, leafy hay, rolled grains, and high-energy feeds with added molasses, should be fed. In animals that are inappetent or anorexic, enteral feeding via a nasogastric tube should be undertaken (see Chapter 23). Even in animals that are still eating voluntarily, supplementation by enteral feeding should be considered if the plasma triglyceride levels exceed 5 mmol/L (500 mg/mL). Glucose and electrolyte solutions, commercial enteral formulations, and slurries made from hay or pelleted feeds can all be administered by nasogastric tube.

Glucose in the form of dextrose can be administered orally at a dose of approximately 100 g once or twice a day for miniature horses and small ponies. Plasma glucose levels should be monitored on a daily basis during the period of treatment. Excessive glucose administration might exacerbate lactic acidosis. To reduce this risk, it has been suggested that 100 g of galactose be substituted for the glucose on alternate days; galactose is slowly converted to glucose, thus minimizing the production of lactic acid.[18]

Nutritionally complete formulations are preferred to simple glucose solutions for enteral administration.[19,20] Commercially available formulations for use in horses can be used, or recipes of formulations incorporating water, dextrose, casein or dehydrated cottage cheese, dehydrated grass meal, and electrolyte or mineral mixtures can be used.[21] Commercial enteral formulations for use in humans have also been successfully used in ponies and donkeys with hyperlipemia,[20] but there is a risk of diarrhea and laminitis (see Chapter 23).

In affected animals with compromised gastrointestinal function, such as ileus and diarrhea, intravenous nutrition is required. In most cases, the constant intravenous administration of 5% dextrose at 1 to 2 mL/kg/hr is used. Although this will not meet the animal's total nutritional requirements, it has proven effective in clinical cases. Overdosing with glucose must be avoided as it can result in diuresis, dehydration, hyponatremia, and enhancement of hepatic lipidosis. Amino acid solutions can also be administered intravenously, but this significantly increases the cost of treatment. Plasma glucose levels should be monitored regularly, and electrolytes added as necessary. Human parenteral nutrition formulations can also be used, but these preparations are expensive and careful monitoring is required (see Chapter 23).

Anabolic steroids and multivitamin preparations are commonly administered to hyperlipemic patients to assist hepatic function. Corticosteroids should be avoided because they stimulate hormone-sensitive lipase and may induce laminitis.

The induction of abortion or premature foaling in pregnant mares has been recommended, as this significantly reduces the demands for energy. However, prematurely delivered foals have a high mortality rate because of the immaturity of body systems and susceptibility to infectious disease. A risk also exists of retained placenta and laminitis in the mare. Lactating mares that develop hyperlipemia should have their foals weaned if possible.

Normalization of Lipid Metabolism

Two approaches to modifying lipid metabolism in hyperlipemic patients are possible: 1) reducing the net release of NEFAs from adipose tissues and 2) accelerating the movement of triglycerides from plasma VLDLs to adipose tissues and skeletal muscle. The release of NEFAs from adipose tissue is promoted by the action of homone-sensitive lipase. Reducing the stimulus for lipolysis may be achieved by providing a positive energy balance, removing stress factors, and removing the hormonal influences of pregnancy and lactation.

The activity of homone-sensitive lipase is inhibited by the action of insulin, and thus exogenous insulin therapy has been recommended in the treatment of hyperlipemia. Protamine zinc insulin has been used most frequently, at dosages of 30 to 80 IU (0.1 to 0.3 IU/kg) by intramuscular injection once or twice a day. Insulin in combination with glucose and galactose administration also promotes the re-esterification of NEFAs.[18] The efficacy of insulin therapy has been questioned in view of the fact that most hyperlipemic ponies and donkeys are insulin resistant; however, this treatment is unlikely to be harmful so long as the patients are normoglycemic and are receiving glucose orally or intravenously. The following regimen has been suggested for treatment of a 200 kg pony:

Day 1 30 IU protamine zinc insulin I.M. and 100 g glucose P.O., both twice a day
Day 2 15 IU protamine zinc insulin I.M. twice daily and 100 g galactose P.O. once
Day 3 As for day 1
Day 4 As for day 2

Stimulation of lipoprotein lipase in order to increase the clearance of triglycerides from the plasma has been attempted by means of heparin intravenously, 100 to 200 IU/kg of heparin may be administered intravenously twice a day. The rationale for this therapy has been questioned because the activity of lipoprotein lipase in affected ponies has been shown to be at its physiologic maximum. Heparin therapy also poses an increased risk of hemorrhage.

Prognosis

The prognosis for animals with hyperlipemia is poor.[13] The reported mortality rate for the disease (including animals that are euthanized) ranges from 57% to 85%. In individual patients, the nature and severity of the underlying disease has an important impact on the prognosis. The degree of measured lipemia does not appear to influence the prognosis, although animals with hyperlipidemia (triglycerides less than 5 mmol/L) have a much better prognosis than those with hyperlipemia (triglycerides greater than 5 mmol/L).

Plasma triglycerides and blood biochemistry parameters should be monitored during treatment, and these results can be helpful in assessing the prognosis. In animals that recover, plasma triglycerides usually return to normal values within 3 to 10 days. Early diagnosis and prompt initiation of therapy result in the best chances for survival.

Prevention

Risk factors for hyperlipemia in susceptible classes of equids include obesity, stress, malnutrition, pregnancy, lactation, and parasitism. Avoiding these factors, therefore, will help in preventing this disease. Particular emphasis should be placed on providing adequate nutrition to susceptible animals without allowing them to become obese, and providing good routine parasite control measures. Food intake and general demeanor should be carefully monitored following periods of stress such as disease, transportation, inclement weather, and change of environment, etc. Exercise regimes may be helpful in reducing insulin insensitivity. Plasma triglyceride levels may also be measured at times of stress and during pregnancy and lactation. The early identification and treatment of hyperlipemia is far more likely to result in recovery than identification later in the course of the disease.

Theiler's Disease (Serum Hepatitis)

Theiler's disease (acute hepatic necrosis, serum hepatitis, serum sickness) is a subacute hepatic necrosis often resulting in hepatic failure and acute encephalopathy.[5] Sir Arnold Theiler first described the disease in South Africa in 1918 following the vaccination of horses against African horse sickness with live virus and equine-origin antiserum.[22] It has been termed "serum hepatitis" because often the affected horses have a history of receiving an equine-origin biologic product (now most commonly tetanus antitoxin) 4 to 10 weeks prior to the onset of clinical signs.[23,24] Cases have been reported following administration of vaccines or antisera to African horse sickness, eastern and western encephalomyelitis, anthrax, tetanus antitoxin, *Clostridium perfringens, Clostridium botulinum*, strangles, influenza, equine herpesvirus-1, pregnant mare's serum and commercial plasma transfusion.[5,23-29] In some cases, the affected horses may not have received an antitoxin, but may have been in contact with another horse that had received tetanus antitoxin. In other cases, no history exists of equine-origin biologic products being administered. The disease appears to be more common in late summer or early fall. This apparent

seasonal pattern suggests possible spread by a vector or could simply reflect the fact that many foaling mares may receive tetanus antitoxin in the spring of the year along with their newborn foal. Most commonly, only one horse on a farm is affected, although outbreaks are reported and other horses on the farm may have evidence of liver disease, e.g., elevated enzymes, without clinical signs of hepatic failure. A specific tetanus antitoxin product and/or the same batch and lot number may be found to be responsible for a high number of cases. A nearly identical clinical and pathologic syndrome has been described in pastured horses in France.[30]

The history, onset, clinical signs, and histopathologic findings of Theiler's disease are similar to hepatitis B virus in humans[5]; however, no viral etiology has ever been proven. Other suggested causes include exposure to hepatotoxic substances, such as mycotoxins (aflatoxin and rubratoxin), plant toxins, drugs, or chemicals.[5, 25,27]

Pathologic changes in Theiler's disease are limited to the liver (apart from widespread jaundice). The liver appears smaller than normal (Figure 11-11), but may be enlarged in peracute cases. Histopathologic changes include widespread centrilobular to midzonal hepatocellular necrosis with hemorrhage.[31]

Figure 11-11



Small, shrunken liver from a horse suffering from Theiler's disease (right) compared with a normal liver (left)

Clinical Signs

The clinical signs of Theiler's disease, or any severe hepatic necrosis, are attributable to the rapid loss of hepatocyte function and collapse of the liver parenchyma. The most common clinical signs seen with Theiler's disease are 1) signs of central nervous system (CNS) disorder, 2) jaundice, and 3) discolored urine. The CNS signs are variable and may range from acute depression to maniacal behavior. Affected horses may be blind and may be ataxic. Icteric membranes can be noted in most cases, although in peracute cases this may not be pronounced. The urine may be abnormally dark, indicating bilirubinuria and, in a few cases, red if a microangiopathic hemolytic process is concurrent.

Neurologic signs are frequently observed with acute hepatic failure and are referred to as *hepatoencephalopathy*. Hepatoencephalopathy is a metabolically induced, potentially reversible, functional disorder of the brain. Neurologic signs are the most pronounced and clinically troublesome signs in most cases of equine hepatic failure. Signs of hepatoencephalopathy may vary from depression to bizarre maniacal behaviour. Common signs include apparent blindness, ataxia, head pressing (Figure 11-9), propulsive circling, and frequent yawning

The pathophysiologic mechanism of hepatoencephalopathy is undoubtedly complex but is mostly a result of abnormal hepatic protein metabolism. The failing liver may be unable to sufficiently convert colonic-derived ammonia to urea via urea cycle enzymes located in the hepatocyte. The effect of excessive ammonia on the central nervous system (CNS) may include

enhancement of neurotransmitters, interference with normal neurotransmission, structural changes in the blood–brain barrier, changes in cerebral blood flow, and interference with biochemical or electrophysiologic pathways in the brain.

Cerebral edema with development of Alzheimer type II cells are characteristic of high CNS concentrations of ammonia. Alzheimer type II cells may result from hepatic failure, primary hyperammonemia, or severe uremia. In rare cases, the cerebral edema may be so severe that herniation occurs. Additionally, possible decreased hepatic extraction of gut-synthesized aminobutyric acid (GABA) may serve as a potent inhibitory neurotransmitter. The GABA-ergic neurotransmission is also closely linked to an increase in natural benzodiazepines. Furthermore, abnormal accumulation of glutamate may serve as an excitatory neurotoxin. Complex interactions of these neurotoxins may determine if the horse with hepatoencephalopathy is depressed or maniacal. The movement of GABA into the CNS may be aided by an increased aromatic-to-branched-chain amino acids ratio in the plasma, and by increased concentrations of plasma bile acids. Increased amounts of aromatic amino acids, which are normally metabolized by the liver, may also serve as false neurotransmitters. In adult horses with hepatic failure, the CNS signs of severe depression are rarely caused by inadequate hepatic gluconeogenesis and hypoglycemia.

Horses with acute hepatic failure and/or Theiler's disease generally have increases in both conjugated and unconjugated bilirubin, with the increase in unconjugated being the most pronounced in all acute diseases except biliary obstruction. The unconjugated portion becomes elevated because of lost hepatocellular function, with reduced uptake and conjugation of the bilirubin.

Intravascular hemolysis and red discoloration of the urine may be seen occasionally with equine hepatic failure. This occurs most frequently with acute hepatic necrosis, e.g., Theiler's disease, and is often, but not always, a terminal event. The cause of the hemolysis may be a microangiopathic hemolytic anemia caused by the physical damage to the red cells as they pass through the necrotic liver.

Severe bleeding problems are not commonly observed in horses with acute liver failure. When bleeding occurs, it is generally prolonged bleeding associated with hepatoencephalopathy and self-inflicted physical trauma. Hemorrhage in horses with liver failure is generally a result of failure in both the extrinsic and intrinsic pathways of coagulation, causing prolongation of both prothrombin and partial thromboplastin times. These occur because of decreased hepatic production of clotting factors. Factor VII has the shortest half-life, so prothrombin time (PT) should be prolonged prior to prolongation of partial thromboplastin time (PTT) with liver failure. In some horses with liver failure, the PTT may be prolonged beyond the normal range prior to the PT being prolonged. The reason for this is unknown. Disseminated intravascular coagulation (DIC) may be present in some horses with acute severe liver failure. The cause of this is often multifactorial and may include decreased hepatic production of antithrombin III, plasminogen, and high molecular weight proteins that inhibit excessive coagulation. Additionally, overwhelming hepatic tissue damage and/or increased circulating endotoxin may stimulate release of soluble proteins that affect coagulation. Fibrin degradation products (FDPs) are often abnormally high in horses with liver failure as the liver is the organ responsible for clearance of circulating FDPs. An increase in FDPs, PT, and PTT would be expected in horses with liver failure, and these findings should not be over interpreted as being diagnostic for DIC. If a liver biopsy is required, this can generally be performed safely in spite of the prolongation in PT and PTT, because platelet counts generally remain normal in horses with liver failure.

Diagnosis

The history, clinical findings, and laboratory confirmation are used to make the diagnosis of hepatic disease and hepatic failure. Hepatic disease can be detected most easily by measuring serum or plasma activity of liver-derived enzymes, including:

- gamma glutamyl transferase (GGT)
- aspartate aminotransferase (AST)
- sorbitol dehydrogenase (SDH)
- glutamic dehydrogenase (GLDH)
- isoenzyme 5 of lactate dehydrogenase (LDH-5)

Gamma glutamyl transferase will be elevated in all cases of Theiler's disease and is most often in the range of 100 to 300 IU/L. Aspartate aminotransferase should be measured because it may provide an indication of prognosis; i.e., those horses having values greater than 4000 IU/L have a poor prognosis. The repeated measurement of AST may also be used to monitor recovery, as the AST would be expected to decrease within 3 to 5 days if the horse is going to recover. Gamma glutamyl transferase, on the other hand, will frequently elevate further during the first 3 days of the illness in spite of clinical

improvement and eventual recovery in an affected horse. A decrease in SDH in the serum would be expected to occur more rapidly in improving horses than a decrease in AST, because of its shorter half-life, and measuring SDH can provide prognostic information more quickly than measuring AST.

Total serum bile acids may also be used to detect liver disease. In horses with Theiler's disease, the measurement of serum or plasma bile acids rarely adds further information than that provided by the measurement of hepatic enzymes. Virtually all horses clinically affected with Theiler's disease have total serum bilirubin values greater than those commonly observed with anorexia. Total bilirubin in horses showing clinical signs caused by Theiler's disease are generally in the range of 12 to 20 mg/dL (12 to 20 μmol/L). The percentage of bilirubin in the unconjugated form is almost always greater than 70%, although some increase in conjugated bilirubin occurs in affected horses. The conjugated bilirubin values are generally 1.5 to 5.0 mg/dL (25.5 to 85.5 μmol/L). The PT and PTT times are generally abnormally high in comparison with a control sample, but rarely offer information not already gathered from the measurement of direct and indirect bilirubin, bile acids, and hepatic enzyme activity in the serum or plasma. Other laboratory findings that are frequently abnormal in Theiler's disease include moderate to severe acidosis, hypokalemia, polycythemia, increased plasma aromatic amino acids, and hyperammonemia.

A more definitive diagnosis of Theiler's disease can only be made by liver biopsy. If the history, clinical findings, and laboratory findings are characteristic of Theiler's disease, a biopsy is not imperative, and in many cases, may not be easy to perform because the liver is often shrunken and may be difficult to visualize with ultrasound examination. Microscopic examination generally reveals marked hepatocellular necrosis involving the entire lobule, most severe in the central and midzonal hepatocytes. There is some fatty change and a very mild-to-moderate accumulation of lymphocytes and a few neutrophils. The degree of bile duct proliferation is often positively correlated with the duration of the disease. On necropsy examination, the liver is usually smaller than normal, tan, and may have markedly congestive centrilobular patterns. The borders of the liver are sharp.

Treatment

No specific therapy for Theiler's disease exists, although supportive therapy is often successful. The affected horse should not be stressed if at all possible. Stressful situations such as moving the animal to another facility or weaning the mare's foal often exacerbate the clinical signs of the hepatoencephalopathy. Sedation should be used only when necessary to control fulminant hepatic encephalopathy causing propulsive behavior (Figure 11-12). Xylazine (0.2 to 0.4 mg/kg) can be used to control bizarre behavior to prevent injury of the animal and to allow catheter placement. Doses of xylazine that cause lowering of the head should be avoided if possible as low-head position and hypoventilation may worsen cerebral edema. Phenobarbital can be used, but diazepam should be avoided as it may worsen hepatoencephalopathy. The benzodiazepine receptor antagonist, flumazinil (0.2 mg/kg given slowly intravenously) may be administered for uncontrolled hepatic encephalopathy, but its efficacy in both horses and humans is unproven.

Figure 11-12



Treatment of a horse affected by Theiler's disease. Intravenous fluid therapy, sedation, and the use of a head protector.

Intravenous fluids are probably the most important component of treatment for hepatic encephalopathy in horses. The intravenous fluids should consist of a balanced electrolyte solution, preferably without lactate, and should be supplemented with potassium 20 to 40 mEq/L, and 5 to 10 g of dextrose per 100 mL. Sodium bicarbonate should be given only if blood pH is less than 7.1 and/or bicarbonate is less than 14 mEq/L. Additional potassium may be given as potassium chloride mixed in molasses and administered per os via a dose syringe. Fresh frozen plasma may be used but hetastarch or stored whole blood should be avoided. Supplemental vitamins can be administered but are not necessary.

An effort should be made to decrease ammonia production in the bowel. This can be done by administering neomycin 5.0 mg/kg every 8 hours orally by dose syringe for 2 days. With fulminant hepatic encephalopathy in the horse, nasogastric intubation should be avoided if possible because nasal bleeding could occur. Nasal bleeding could exacerbate the hepatic encephalopathy if the blood is swallowed; and, because of insufficient clotting proteins, the bleeding may be prolonged. Lactulose 0.2 to 0.5 mL/kg every 8 to 12 hours may also decrease ammonia production in the bowel and can be used concurrently with neomycin. Both lactulose and neomycin may cause diarrhea if given in excessive dosages or for prolonged periods. Vinegar (acetic acid) may also be effective in decreasing blood ammonia when it is administered per os at 240 mL/450-kg horse. Affected animals should be fed high carbohydrate, high branch-chain amino acid (BCAA) feeds, with moderate to low total protein content. Sorghum and/or cracked corn mixed with molasses or commercially prepared BCAA paste are ideal. Carbohydrates should be fed frequently in small amounts. A moderate protein grass hay should be fed rather than alfalfa hay or spring-cut grass hay. Affected animals should be protected from sunlight in order to prevent photosensitization.

Antioxidant, anti-inflammatory, and antiedema therapies are indicated in acute hepatic failure. The antioxidant, antiedema treatments include dimethylsulfoxide, acetylcysteine, and mannitol given intravenously and vitamin E given intramuscularly. Anti-inflammatory therapy should include flunixin meglumine and pentoxifylline. Cases of fulminant hepatic necrosis that do not respond quickly to medical therapy usually succumb to the disease. In the future, extracorporeal liver support might be helpful in managing some horses.

Prognosis

Horses with Theiler's disease that can be maintained for 3 to 5 days without deterioration and that continue to eat often recover.[5] A decline in the SDH and PT, along with improvement in appetite, are the best positive predictive laboratory and clinical indicators of recovery. Horses that have fulminant encephalopathy that cannot be easily controlled with sedatives have a very poor prognosis, although some will recover. The degree of hyperbilirubinemia is a less powerful prognosticator than encephalopathy. Those animals that continue to eat during the first 3 days of the illness generally have a good prognosis. If the affected horse recovers, which many do within 5 to 10 days, its long-term prognosis is excellent. No evidence exists that severe hepatic fibrosis and/or neoplasia occur following Theiler's disease in the horse.

Other Causes of Acute Hepatic Disease and Failure in Adult Horses

Only scattered reports exist of other causes of acute hepatic disease and failure in adult horses. Mycotoxicosis or other hepatotoxins make up the bulk of these reports. *Fusarium moniliforme* toxins, especially fumonisin B, may cause hepatic disease and, rarely, hepatic failure in horses eating fungi-contaminated corn. Leukoencephalomalacia is the most common disease and clinical syndrome caused by this toxin. Contamination of grain by *Aspergillus flavus* and aflatoxins B_1, B_2, and M_1 may cause hepatic necrosis and fulminant hepatic failure in horses.[32] Fortunately, aflatoxicosis is rare in horses in most parts of the world. Pyrrolizidine alkaloid-containing plants may also cause acute hepatic disease and failure, although chronic disease with acute failure is most common. Septic portal vein thrombosis is rare in horses but should be considered in adult horses with acute hepatic encephalopathy.

Pyrrolizidine Alkaloid Intoxication

Pyrrolizidine alkaloid intoxication is the most common cause of chronic liver failure in horses in many parts of the world.[33-38] Pyrrolizidine alkaloid-containing toxic plants (Table 11-5) tend to be unpalatable and are generally avoided by horses. Poor pasture conditions, over grazing or herbicide treatment may contribute to consumption of these plants, however, intoxication is more likely to occur following the feeding of contaminated hay. Pelleted or cubed hay may pose a particular risk because the presence of poisonous plants cannot be detected. Not all the parts of the plants contain pyrrolizidine alkaloids, and the concentration may vary with the season. For some plants, such as *Amsinckia intermedia*, toxic alkaloids are concentrated in the seeds that may be found in screenings of grain harvested from contaminated fields. Such screenings are highly toxic, and feeding relatively modest amounts can lead to massive liver damage and functional failure within days.

The intoxication typically results in the delayed onset of chronic, progressive liver failure. The onset of clinical signs is usually delayed 4 weeks to 12 months following ingestion of pyrrolizidine alkaloid-containing plants.[3] There appear to be individual differences in susceptibility, and not all horses that consume the plants develop clinical signs.[35] Horses generally present with depression, anorexia, and weight loss for variable periods of time. Horses with areas of unpigmented skin may develop photosensitivity. The clinical course may vary from several days to several months, but when sufficient liver damage has occurred to produce functional failure, onset of profound clinical signs of hepatic encephalopathy, and in many cases, death may be abrupt. The apparent acute onset of clinical illness generally represents the end stage of a chronic, progressive disease process. Clinical signs and death may occur up to a year after the contaminated feed was eaten. Because all horses with access to a contaminated feed source are at risk, a history of other animals with progressive depression, weight loss, icterus, and death should alert the clinician to a possible common cause.

Table 11-5
Common Pyrrolizidine Alkaloid–containing Plants[34]

Botanical Name	Common Name
Amsinckia intermedia	Fiddleneck, fireweed, or tarweed
Senecio vulgaris	Common groundsel
Senecio ridelli	Woolly groundsel or Ridell's groundsel
Senecio jacobaea	Tansy or common ragwort, ragwort, or stinking Willie (Figure 11-13)
Crotalaria spp.	Rattle box
Heliotropium europaeum	Common heliotrope or potato weed
Cynoglossum officinale	Hounds tongue

Figure 11-13



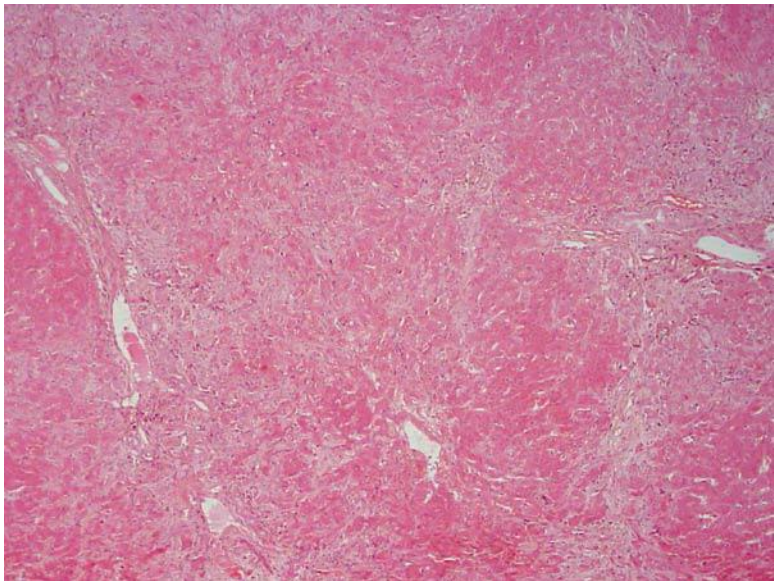
Senecio jacobea (common Ragwort) – a common cause of pyrrolizidine alkaloid toxicity in Europe.

Etiology

Pyrrolizidine alkaloid toxicity is largely determined by the total dose of the pyrrolizidine alkaloid ingested. Consumption of the plants at a dose of 2% to 5% of the body weight of the horse, fed at once or over a period of a few days, can result in acute toxicity.[39] The effects of pyrrolizidine alkaloids are cumulative, and toxicity more commonly occurs following chronic low-level exposure. The alkaloids are transported to the liver via the portal circulation, and are metabolized by the microsomal enzymes to highly reactive, unstable metabolites (the dehydroalkaloids) which are potent alkylating agents.[37] These compounds are responsible for much of the direct hepatocellular damage. Hydrolysis of the dehydroalkaloid yields the dehydroaminolcohol, which can be both antimitotic and carcinogenic. The toxic agents are capable of alkylating nucleic acids

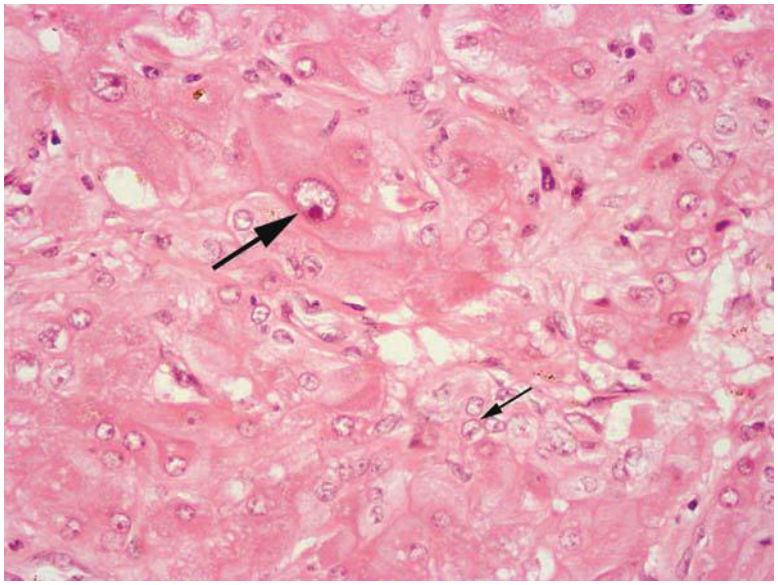
and protein, thereby inhibiting cellular replication and protein synthesis.[3] Hepatocytes surrounding the portal triads are affected first. The affected cells cannot divide, and the hepatocytes enlarge, forming megakaryocytes. These megalocytes are a characteristic histopathologic feature of this disease (Figure 11-14). When the megakaryocytes die, fibrosis follows, and the liver shrinks (Figure 11-15). Fibrosis around the portal vessels can sometimes cause portal hypertension, ascites, and diarrhea (portal hypertension is less common in horses than in cattle with pyrrolizidine alkaloid toxicity).

Figure 11-14A



Photomicrographs of the liver showing typical histologic features of pyrrolizidine alkaloid toxicity. A. The liver parenchyma is largely replaced by fibrous tissue. Surviving areas of normal hepatocytes are present. Hematoxylin and eosin stain, x4 magnification.

Figure 11-14B



Small arrow shows a normal hepatocyte nucleus. Large arrow shows the nucleus of a megalocytic hepatocyte. Hematoxylin and eosin stain, x40 magnification. (Courtesy of Dr. G.R.Pearson, Comparative Pathology Laboratory, Department of Clinical Veterinary Science, University of Bristol)

Clinical Signs

Experimental feeding studies indicate several stages in the development of pyrrolizidine alkaloid toxicity. Initially, modest characteristic liver lesions may develop along with associated biochemical evidence of liver damage without producing overt clinical signs. In a report of racing horses fed Senecio-contaminated alfalfa hay, poor performance was one of the earlier indicators of disease. Later, progressive liver damage results in compromised hepatic function, and, at this stage, clinical signs become evident with progressive development of depression, anorexia, weight loss, and variable icterus.

The final phase of the disease process occurs with the onset of failure of function and terminal hepatic decompensation. The onset of severe clinical signs may occur suddenly and represents the end stage of a disease process that may have been developing for an extended period. Vital signs (temperature, pulse, and respiratory rate) are often within normal limits unless the horse has become agitated or convulsive. Clinically detectable icterus can be variable until the final stages of the disease process when icterus may be moderate to severe. Central neurologic signs range from moderate depression to compulsive

Figure 11-15



Gross pathologic appearance of the liver of a horse affected by pyrrolizidine alkaloid toxicity. The liver is mottled brown and tan, and was firm to cut. The cut surface is a mottled pale brown/tan, and has a roughened surface. (Courtesy of Dr. G.R.Pearson, Comparative Pathology Laboratory, Department of Clinical Veterinary Science, University of Bristol)

walking, excessive yawning, ataxia, apparent blindness, and head pressing, to maniacal behavior, convulsions, coma, and death. Self-inflicted trauma may occur in horses that become oblivious to their surroundings. Intravascular hemolysis may occur in the terminal stages of the disease with resultant hemoglobinuria. Photosensitivity may be noted in nonpigmented areas of the skin. Although laryngeal paresis, edema, ascites, oral ulcers, halitosis, and diarrhea have been reported, they are not common features in horses with pyrrolizidine alkaloid intoxication.[3,37-39]

A history of exposure to pyrrolizidine alkaloid-containing plants and clinical signs compatible with progressive liver failure would allow a tentative diagnosis of pyrrolizidine alkaloid intoxication. This is particularly true in the context of previously confirmed cases from the same property or from other animals on the same feed.

Clinical Pathology

Elevation of liver-derived serum enzyme activities (SDH and AST) is associated with active liver damage, but activities may decrease toward normal until the later stages of the disease process when marked elevation may again be noted. Elevation of GGT and AP activities reflects the focus of the pathologic process in the periportal regions and the biliary system. Sustained moderate to marked elevation in these enzymes provides an early and persistent indication of liver involvement.[38] Serum bile acid concentration is generally increased. Serum bilirubin concentrations may remain within normal limits until the horse reaches a state of functional failure. Total serum bilirubin generally remains less than 10 mg/dL (170 μmol/L), and the direct-reacting bilirubin rarely accounts for more than 25% of the total. The blood urea nitrogen concentration (BUN) is generally below normal in horses with functional failure. Foodstuffs can be tested for the presence of pyrrolizidine alkaloids.

Pathology

Demonstration of typical liver lesions on biopsy or at necropsy is necessary for confirmation of the diagnosis (Figure 11-14). The liver is often small and firm and nodules of regenerating liver tissue may be noted in some long-standing cases. Typical lesions of pyrrolizidine alkaloid intoxication are megalocytosis, periportal fibrosis, biliary hyperplasia, and occlusion of the central veins. Liver lesions tend to be progressive, and as normal hepatic architecture is damaged and replaced by fibrous tissue, the prognosis becomes less favorable. Well developed lesions of veno-occlusion are also considered an unfavorable indication. Exposure to massive doses of pyrrolizidine alkaloids may produce acute centrilobular necrosis, as has been documented experimentally in a number of species.

Treatment and Prognosis

No specific recommendations exist for treatment of the damage produced by these toxic plants other than removal of the contaminated feed source. Complications associated with photosensitivity can be reduced if the horses are housed out of direct sunlight, and retention of appetite and maintenance of body weight are the most useful prognostic indicators. Even

horses with moderate histologic evidence of liver damage may survive if they maintain a normal appetite.[36] It is often recommended that horses with liver disease be put on a low protein diet. This recommendation may not always be appropriate, and it may be better to feed something that the horses will eat, alfalfa hay for example, than to offer a lower protein feed source that the horses refuse to eat. Providing adequate caloric intake of a nutritionally balanced diet of grain and forage or hay is critical. Some horses with extensive liver damage survive, but remain unthrifty and may not be able to handle the stress of active athletic training.[36] Vigorous supportive care may be unrewarding in a horse with clinical signs of advanced liver failure and histologic evidence of generalized fibrosis with loss of normal hepatic architecture.

Cholangiohepatitis and Choledocholithiasis

Cholangiohepatitis is the most commonly encountered, clinically significant form of biliary tract disease in horses.[2,40,41] Other forms of true biliary disease appear to be uncommon in horses, but biochemical evidence of hepatobiliary injury and dysfunction, including elevations in serum bilirubin, gamma glutamyl transferase (GGT), alkaline phosphatase (AP), bile acids, and prolonged exogenous dye excretion tests frequently accompany both acute and chronic hepatic diseases such as Theiler's disease, Tyzzer's disease, hepatic lipidosis, and pyrrolizidine alkaloid toxicity. Rarely, biochemical and clinical evidence of biliary tract disease may occur in association with the so-called "chronic active hepatitis," abscesses, granulomas, or infiltrative or obstructive neoplastic conditions, such as primary cholangiocarcinoma, hepatic adenocarcinoma, or metastatic hepatic tumours.

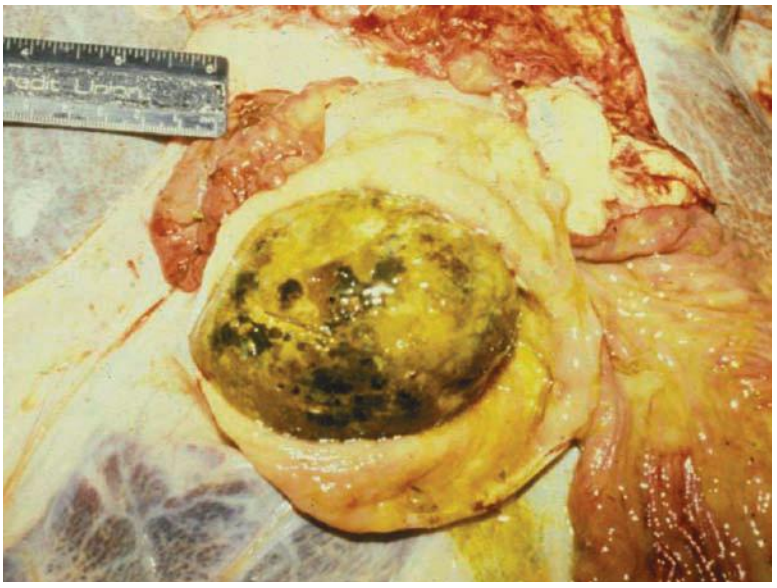
Although cholangiohepatitis probably begins as a cholangitis, the term cholangiohepatitis is appropriate because clinically significant inflammatory biliary disease in horses is extremely uncommon without extension into the periportal region of the liver. It is probable that many mild cases of cholangitis/cholangiohepatitis are undiagnosed because horses are asymptomatic, but the condition predisposes horses to chronic, active, inflammatory hepatobiliary disease and the formation of biliary calculi. Chronic cholangiohepatitis may frequently be associated with significant intrahepatic or extrahepatic calculus formation. Discrete calculi can often be visualized ultrasonographically (Figure 11-6) or at post mortem examination (Figures 11-16 and 11-17), but some horses with cholangiohepatitis develop a more sonolucent "sludge-like" material within the biliary tract. With severe suppurative cholangiohepatitis, particularly if the condition is long standing, significant periportal and bridging fibrosis can occur. Clinically significant hepatobiliary disease appears to be more common in middle-aged to older horses. Because of the absence of a gallbladder, the nomenclature surrounding biliary calculi in the horse has been confusing. The term cholelithiasis broadly refers to calculi anywhere within the biliary tract, but in humans it has come to be synonymous with calculi within the gallbladder. It is perhaps more appropriate in horses to refer to intrahepatic calculi as hepatoliths and extrahepatic calculi, usually located within the common bile duct, as choledocholiths.

Figure 11-16



Cholelithiasis. Multiple stones in the bile duct.

Figure 11-17



Complete obstruction of the bile duct by single calculus may be amenable to surgical treatment.

Etiopathogenesis

The etiopathogenesis of cholangiohepatitis in adult horses is presumed to be ascending bacterial infection from the proximal small intestine. Evidence for this comes from retrospective studies documenting the isolation of predominantly gram-negative, enteric bacteria such as *Escherichia coli, Enterobacter* spp., and *Citrobacter* spp. from clinical cases. Anaerobic enteric bacteria such as *Clostridium pefringens* are also frequently cultured. The ascending infection is believed to predispose to calculus formation by creating a nidus around which the calculus forms. The composition of calculi in horses is predominantly calcium bilirubinate and calcium phosphate, analogous to brown pigment stones in humans.

Clinical Signs and Diagnosis

Cases of cholangiohepatitis commonly present with the nonspecific clinical signs of fever, icterus, colic, weight loss, and encephalopathy. Careful history taking often reveals recurrent bouts of mild-to-moderate colic coincident with fever in the preceding days to weeks. Significant weight loss commonly accompanies more chronic cases. Occasionally, signs of hyperammonemic hepatic encephalopathy can be seen when complete calculus obstruction to biliary outflow occurs or the disease process has progressed to fulminant hepatic failure.

Serum biochemical abnormalities include large increases in the hepatobiliary enzymes GGT and alkaline phosphatase and moderate increases in the hepatocellular enzymes AST and SDH. Total serum bilirubin is elevated, frequently well above the levels typically seen with anorexia alone, with the direct-reacting or conjugated fraction representing more than 25% of the total. The ratio of direct-to-indirect bilirubin is a helpful parameter in the diagnosis of cholangiohepatitis because the proportionate increase in the direct-reacting fraction is fairly specific to this condition in horses. Bilirubinuria may also be observed. Serum bile acids are elevated in many cases of cholangiohepatitis, and can reach very high levels (more than 100 mmol/L) in cases with significant biliary obstruction. Horses with either maniacal or depressive hepatic encephalopathy in association with complete obstruction or severe, chronic cholangiohepatitis have elevated blood ammonia levels. Typically, hematologic changes are consistent with chronic, active inflammation and include neutrophilia and hyperfibrinogenemia. If the condition is more than 2 to 3 weeks in duration, hyperglobulinemia may also be documented.

Although clinical and laboratory findings can be highly suggestive of the condition, a definitive diagnosis of cholangiohepatitis requires liver biopsy. It is recommended that laboratory measurements of clotting function, specifically the prothrombin time and activated partial thromboplastin time be made prior to hepatic biopsy. Frequently, these indices are normal but they may be prolonged if the biosynthetic capacity of the liver has diminished in association with advanced post-inflammatory fibrosis. The biopsy procedure is best performed under light sedation and ultrasonographic guidance, using a 14-gauge biopsy needle. Sufficient biopsy material should be obtained for aerobic and anaerobic culture as well as for routine histopathology. Visualization of the liver via ultrasound lessens the risk of inadvertent colonic, diaphragmatic, or pulmonary injury that can occur when the procedure is performed blind using traditional anatomic landmarks. Histologically, the liver tissue should be evaluated for both the severity of inflammation and the presence and extent of any periportal and bridging fibrosis. Advanced bridging fibrosis should carry a more guarded prognosis, particularly when it is accompanied by biochemical evidence of liver

failure such as hypoalbuminemia, hypoglycemia, and altered clotting times. Bile duct hyperplasia is invariably reported but represents a nonspecific response to liver injury.

In normal horses, the liver can best be visualized between the 11th and 16th intercostal spaces on the right side, and the 9th and 11th spaces on the left side. In cases of cholangiohepatitis, the liver image can frequently be visualized over a much greater area due to hepatomegaly. The degree of hepatomegaly, bile duct dilation, and the presence of significant hepatoliths should be evaluated ultrasonographically (Figure 11-6).[42] Although it is not possible to visualize bile ducts via ultrasound in normal horses, significant bile duct dilation and discrete calculi may be detected in many clinical cases. The echogenicity of calculi and degree of acoustic shadowing vary with the extent of mineralization. With experience, it may be possible to characterize the hepatic parenchyma as being diffusely more echogenic than normal, particularly in cases where significant hepatic fibrosis has occurred.

Medical Management

Long-term antimicrobial therapy is essential in the treatment of adult horses with cholangiohepatitis and choledocholithiasis/hepatolithiasis.[43] In certain situations where biliary obstruction is complete, or the horse is in uncontrollable abdominal pain, surgery may be necessary. The choice of specific antibiotics should ideally be based on both aerobic and anaerobic cultures of liver biopsy material. If biopsy culture results are either unavailable or negative, broad spectrum antibiotics such as potentiated sulphonamides, cephalosporins, or fluoroquinolones would be appropriate choices. Although the spectrum of activity of the aminoglycosides is limited to aerobic, gram-negative bacteria, a good clinical response to this family of antibiotics is often observed. Metronidazole (7.5 to 15.0 mg/kg every 8 hours) can also be helpful, especially if penicillin is not being administered. The duration of antimicrobial therapy will vary on a case-by-case basis, but experience suggests that weeks to months of therapy are necessary. Treatment failure can commonly be associated with premature antibiotic withdrawal, and it is worth considering that both clinical and biochemical resolution should be confirmed before treatment is stopped. Many horses show substantial clinical improvement in terms of appetite, absence of fever, and weight gain while still demonstrating significant biochemical evidence of hepatobiliary disease. Antibiotic treatment is recommended to be continued until serum GGT and AP levels have been normal for 2 to 4 weeks. Repeated ultrasonographic evaluation of the liver during the course of therapy can be useful in assessing improvements in hepatomegaly, bile duct dilatation, and the resolution of any identifiable calculi. Intravenous polyionic fluid therapy can be a useful adjunct to antimicrobial therapy both in cases of acute cholangiohepatitis and during long-term therapy when an individual horse has signs of clinical deterioration.

Individuals that present with hyperammonemic hepatic encephalopathy may be treated with products to reduce both the production and absorption of ammonia in the large intestine. The oral administration of either neomycin (20 to 30 mg/kg 4 times daily) or metronidazole (10 to 15 mg/kg 4 times daily) has been recommended to alter cecal and colonic bacterial flora and thereby reduce ammonia production. Lactulose (90 to 120 mL per os 4 times daily) can be given as an acidifying agent to alter luminal pH and increase the conversion of ammonia to nonabsorbable ammonium ions. Adult horses with hepatic encephalopathy can vary from somnolent to violent and maniacal and often require chemical restraint for both their own protection and that of people around them. If hepatic encephalopathy accompanies fulminate liver failure, the prognosis is extremely guarded. Intensive intravenous fluid therapy to correct and maintain hydration and electrolyte and acid–base status are essential parts of the therapy of horses with cholangiohepatitis that present with concurrent fulminate liver failure.

Specific bile salt therapy with compounds such as ursodeoxycholic and chenodeoxycholic acid is contraindicated in horses, not only because cholesterol-rich calculi are extremely uncommon, but also because these compounds have been shown to be metabolized to pro-inflammatory hepatotoxic compounds in other hind-gut fermenters such as rabbits. Specific evidence, however, supports the intravenous use of dimethylsulphoxide (DMSO) in the medical management of brown pigment stones in people,[44] and by analogy, its use is justifiable in cases of equine choledocholithiasis and hepatolithiasis. DMSO can be administered intravenously at a dose of 1 g/kg daily for 5 to 7 days, diluted to a 5% solution in fluids. S-adenosylmethionine (SAMe) (5 g P.O SID) can also be helpful in treating cholangiohepatitis and other chronic inflammatory diseases of the liver.

Surgical Management

Surgical management of cholangiohepatitis and biliary calculi should probably be reserved for cases of complete biliary obstruction (Figure 11-17) with severe, unrelenting abdominal pain that is unresponsive to conventional analgesics. Cases of complete obstruction often present with hyperammonemic encephalopathy and, therefore, benefit from intensive supportive medical management as well as surgical relief of the obstruction. Both anecdotal and published reports claim success using surgical management by either manual lithotripsy or choledocholithomy, but bile peritonitis carries such a grave prognosis

that great care should be taken when attempting to either remove or "milk" calculi into the proximal small intestine at celiolotomy. Recurrent obstruction is likely because most horses have additional intrahepatic calculi that are inaccessible to the surgeon, and these may continue to partially or completely obstruct biliary outflow post surgically.

Other Biliary Conditions

Hepatic abscesses, neoplasia, and parasitic granulomas are documented, but rare, causes of obstructive hepatobiliary disease in horses. Cholangiocarcinoma is the most common form of primary hepatic neoplasm, but liver metastases may be seen in association with primary tumors such as lymphosarcoma, squamous cell carcinoma, and melanoma. Clinical and biochemical evidence of biliary tract disease is often absent, even with significant parenchymal infiltration, unless biliary drainage is obstructed. This is most commonly associated with space-occupying masses that impede extrahepatic biliary flow through the right and left hepatic ducts and the common bile duct.

Occasionally, elevations in GGT, AP, and bilirubin are seen in association with colonic and proximal small-intestinal disease in adult horses and foals; these changes are common in horses with right displacement and 180° rotations of the large colon.[45] Furthermore, horses with colonic displacement or volvulus may have elevations in hepatobiliary enzymes, probably because of abnormal extrahepatic biliary drainage rather than true hepatobiliary disease. It is worth remembering that donkeys, mules, and asses have a higher (up to 3 times) normal level of GGT compared with horses.

Chronic Active Hepatitis

Chronic active hepatitis is not a specific disease entity, but is a descriptive term for a group of conditions characterized by active, progressive, inflammatory liver disease of some duration.[3,4,33] The history is often one of depression, weight loss, and variable icterus. Signs are often intermittent and may be associated with fever. Some horses have a history of previous or active intra-abdominal disease. Thus far, no clear evidence exists of association with advancing age, viral disease, or drug administration. The disease can progress to the point of liver failure with major central nervous system involvement and death. Unusual cutaneous manifestations such as moist lesions at the coronary bands may be present. Liver lesions tend to be located in the periportal region and the histopathologic diagnosis is often cholangiohepatitis. The cause of chronic active hepatitis has not been determined, although autoimmune disease is possible. Alternatively, some cases may be a manifestation of chronic cholangitis.[4]

Clinical Signs

Clinical signs vary with the degree of liver damage and the presence of any underlying disease process. The onset of signs is usually insidious. Horses often present with anorexia, weight loss, variable icterus, and moderate to marked depression. Neurologic signs may progress to convulsions, coma, and death. Some horses have elevated rectal temperature, pulse, and respiratory rates. The moderate to high fever noted in some horses with chronic active hepatitis is not a common feature of many of the other causes of liver failure, unless complications have occurred. Petechial or ecchymotic hemorrhages may be noted in the visible mucous membranes. Intra-abdominal problems such as an enlarged anterior mesenteric artery, thickened bowel, or mass lesion may be noted. Some horses develop a moist exfoliative dermatitis at the coronary bands and in some cases this may be the presenting complaint.[33]

Clinical Pathology

Laboratory evaluation provides evidence of liver damage and allows an assessment of the degree of functional failure. Initially liver-derived serum enzyme activities may be slightly to moderately elevated. Later in the disease process, substantial elevation of liver-derived serum enzyme activities and of the enzymes that reflect biliary damage, GGT and AP, will be noted. Serum bilirubin may be elevated, with direct-reacting bilirubin comprising up to 40% of the total. The urine is strongly positive for bilirubin, and serum bile acids are greatly elevated. The BUN is often low, and hypoglycemia will be noted in some horses. The hemogram may show evidence of an inflammatory response with a leukocytosis, left shift, and monocytosis. Total plasma protein concentration is generally elevated, largely because of an increase in globulins. Culture of liver biopsy specimens may be rewarding because bacterial agents may contribute to hepatitis or cholangitis.

Pathology

Histopathologic lesions are most prominent in the periportal region, with hepatocyte damage and loss, variable fibrosis, and an inflammatory infiltrate. The cellular component of this infiltrate tends to be mononuclear cells, except those cases with suppurative hepatitis that may have a marked neutrophilic response. Evidence often exists of cholangitis with biliary

hyperplasia and bile stasis. Bacteria may colonize the liver during bacteremia via the portal drainage from damaged bowel or as an ascending process from the common bile duct. Viral agents or idiosyncratic reactions to drugs are thought to be major factors in the development of chronic active hepatitis in other species. The pathogenesis of the skin lesions is unclear, but these lesions appear to represent an immune-mediated vasculitis associated with liver disease.

Treatment

Intensive supportive care is indicated until horses regain their appetite. A fairly consistent favorable response to corticosteroids can be anticipated.[34] Initial treatment should consist of 20 to 40 mg of dexamethasone given by injection. This dose rate is maintained for 3 to 5 days (depending on the response) and is then gradually decreased over the next 7 to 10 days. At this time, the horse may be placed on oral prednisolone at 400 to 600 mg/day. Treatment may be necessary for 4 to 6 weeks or longer with careful monitoring of clinical signs and biochemical parameters. Bacterial infection may play a role, especially in horses with fever and a neutrophilic inflammatory infiltrate on liver biopsy, and long-term (4 to 6 weeks) systemic antibiotics are indicated. Improvement in attitude and appetite are among the earliest and most consistent indicators of response to therapy.

Klein Grass (*Panicium Coloratum*) Toxicity

Chronic liver disease has been reported in Texas in horses grazing pasture planted with Klein grass as well as horses fed Klein-grass hay.[46] Icterus, anorexia, and progressive weight loss were the principal signs, with some horses developing colic signs. Elevated GGT activity, total and direct bilirubin, blood ammonia, and Bromsulphalein (BSP) clearance times were noted. Typical liver lesions included bridging hepatic fibrosis, cholangitis, and hepatocellular regeneration. The toxic principal is thought to be a saponin. Although death losses were reported in horses with advanced liver lesions, most horses recovered after Klein grass was removed from the diet. The sporadic nature of the disease suggests individual susceptibility, variability in the amount of feed ingested, and perhaps, seasonal or maturational variation in the content of the toxic principal. A similar but more rapidly progressive disease has been seen in horses eating fall panicum hay.

Alsike Clover Toxicity

Horses grazing alsike clover or ingesting alsike clover (Figure 11-18) in hay may develop signs of liver failure, especially photosensitization, anorexia, and icterus.[47-49] Several horses on a farm may be affected at one time. Generally, these horses are on a clay-soil pasture containing large amounts of alsike clover. The disease appears to have yearly fluctuations in areas where alsike clover is common (eastern United States and Canada), suggesting that environmental factors contribute either to the toxicity of the plant or growth of a hepatotoxin on the plant. Removal of affected horses from the pasture and supportive care treatments result in complete recovery in most cases. If the horses are not removed from the alsike clover, the disease may progress to hepatic fibrosis, fulminant hepatic failure, and death.

Figure 11-18



Alsike clover.

Hepatic Neoplasia

Primary liver tumors are rare in horses. Cholangiocarcinoma occurs mainly in older horses, which may present with anorexia, weight loss, icterus, edema, and abdominal distension.[50] This tumor tends to produce multiple masses within the liver. Extrahepatic metastasis may occur with involvement of the peritoneal and pleural cavities, intestine, spleen, and lung. Cholangiocarcinoma has been reported in combination with hepatocellular carcinoma in one horse and in another horse with concurrent septic cholangiohepatitis.

Hepatocellular carcinoma (hepatoma) has been reported primarily in horses younger than 3 years.[51,52] These tumors are often solitary and may be multilobulated. Clinical signs include depression, anorexia, weight loss, abdominal distension, intermittent diarrhea, and hyperemic mucous membranes. Modest elevation of liver enzyme activity may be observed. Polycythemia or erythrocytosis as indicated by marked elevation in the hematocrit has been noted in these patients, this may be a result of secretion of an erythropoietin-like substance by the tumor. In one patient, hepatocellular carcinoma was associated with an increase in serum alpha fetoprotein, a globulin normally produced by fetal liver cells. However, it is not proven that this protein is a consistent indicator of hepatocellular carcinoma in horses.

Malignant hepatoblastoma has been rarely reported.[53,54] This is an embryonic tumor of liver with a range of histologic patterns, including epithelial and mesenchymal elements. Clinical signs include anorexia, pyrexia, and pleural effusion.

The liver is frequently involved with metastatic lesions from primary tumors arising from other sites. These tumors include lymphosarcoma, mammary carcinoma, bronchogenic carcinoma, squamous cell carcinoma, granulosa cell tumor, and Sertoli cell tumor. In most instances, these lesions do not result in massive or generalized liver damage, and the only biochemical indication in some horses may be modest elevation of liver-derived serum enzyme activities. Most horses do not manifest clinical or biochemical evidence of liver failure, although depression, anorexia, weight loss, and edema may be features of an invasive and generalized neoplastic process. Ultrasonic evaluation of the liver may provide evidence of focal neoplastic lesions within the liver parenchyma.

Hepatic Amyloidosis

The liver and spleen are the organs most commonly affected by systemic amyloidosis in horses.[55] Two forms of systemic amyloidosis exist. In reactive or secondary systemic amyloidosis, the precursor protein is serum amyloid protein AA, which is an acute-phase protein produced by hepatocytes in response to chronic infection or inflammation.[56] In systemic primary, immunocytic, or idiopathic amyloidosis, amyloid light-chain fibrils are deposited.[57]

Iron Overload, Hemochromatsis

Iron is a highly reactive element that plays an essential role in oxidation–reduction reactions. Iron balance is largely regulated by intestinal absorption as no mechanism exists for excretion of excessive iron stores. Newborn foals given an oral intestinal inoculum containing ferrous fumarate during the first day or two of life developed acute liver failure as a result of iron overload.[58] This was probably associated with an inability of the newborn animal to effectively regulate intestinal absorption of iron. Additionally, newborn foals normally have high serum iron and high percent transferrin saturation at birth, rendering them less able to deal with a sudden massive iron intake. Clinical signs developed within a few days, with rapid progression of anorexia, depression, icterus, collapse, and death. Liver lesions included massive necrosis, bile ductule proliferation, inflammatory infiltrate, and bile stasis. Deficiencies of vitamin E and selenium may play a permissive role in the tissue damage of iron toxicity. Vitamin E and selenium are thought to exert protective effects because of their antioxidant properties. Acute iron overload with liver damage has also been reported in a few adult horses given iron supplements orally.

Iron overload or hemochromatosis associated with chronic hepatic cirrhosis has been reported in adult horses.[59,60] Clinical signs in these horses included depression, anorexia, weight loss, icterus, ventral edema, and terminal hepatic encephalopathy. Liver-derived enzyme activities and serum bilirubin were increased. Histologic lesions included disruption of hepatic architecture, bridging fibrosis, and bile duct hyperplasia. Iron accumulation was noted within hepatocytes, macrophages, and Kupffer's cells as indicated by Prussian blue staining. Liver iron concentrations, measured in two horses, were high (6,700 and 18,437 ppm wet weight), some 20 to 100 times that found in the liver of control horses. Iron accumulation was not noted in other tissues in these horses. Serum iron was high in one of these horses and within the normal range in the other.

This condition in horses has some similarities to familial idiopathic hemochromatosis, an inherited disorder of humans, in which excessive intestinal absorption of iron leads to hepatic cirrhosis associated with iron accumulation in the liver and other tissues. This disorder of humans is associated with high serum iron and nearly complete saturation of transferrin. The few published reports in horses suggest a sporadic occurrence although multiple cases of liver failure in horses with high serum iron may occur on given properties. At present, no evidence exists that the disorder in horses is inherited. Because excessive dietary iron has not been a consistent feature in these horses, it has been suggested that, for unknown reasons, excessive intestinal iron absorption occurs with resultant accumulation of iron in the liver. We have noted high serum iron in some horses with chronic liver failure, although a causal relationship to liver damage could not be established. It is possible that the accumulation of iron in the liver is the result of liver failure, and may not be the cause of liver failure. Secondary iron overload occurs in humans with alcoholic cirrhosis. In one study of excessive dietary iron administration to adult ponies, the concentration of iron in the liver was increased, but this did not result in any pathologic disease.[61]

Right Hepatic Lobe Atrophy

Atrophy of the right hepatic lobe is a rare and often unnoticed condition of horses. The condition has been reported in adult horses with colic resulting from major gastrointestinal abnormalities and is also an incidental finding at necropsy.[62] Although the pathophysiology of this condition is unresolved, it has been suggested that this condition may result from compression of the liver associated with chronic distension of the right dorsal colon. High-grain, low-fiber diets may contribute to this condition.

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Systemic Inflammatory Response Syndrome: *Endotoxemia* Reconsidered

Chapter 12

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For the past three decades, signs of circulatory insufficiency in horses with a variety of gastrointestinal diseases have been linked with the term *endotoxemia.* This association between the translocation of bacterial endotoxins (lipopolysaccharides) from the gastrointestinal tract into the circulation, and the subsequent development of clinical signs referable to endotoxemia, initially was based on the detection of lipopolysaccharides in the circulation of approximately 30% to 40% of horses presented to a variety of university veterinary clinics.[1-3] The strength of this association was increased by the results of experimental studies in which the cardiovascular effects of the intravenous administration of purified lipopolysaccharides were noted to be similar to the derangements in cardiovascular function encountered in horses with gastrointestinal diseases characterized by loss of integrity of the intestinal wall.[4-6] However, differences between experimentally induced endotoxemia and the clinical syndrome of endotoxemia were recognized by veterinary clinicians. For example, the profound neutropenia and febrile responses classically reported to occur after intravenous administration of purified lipopolysaccharides often were absent in many horses described as being endotoxemic. During the same time frame, a similarly confusing situation existed in human medicine, especially when the terms sepsis, septic shock, and sepsis syndrome were used interchangeably. As a result of this confusion, in the early 1990s the term "systemic inflammatory response syndrome" was coined to account for the clinical response of human patients to a nonspecific insult (i.e., in the absence of a documented infection).[7] Whereas this systemic inflammatory response can be triggered by lipopolysaccharides, similar responses occur to other stimuli perceived to be dangerous by the host. The current knowledge regarding the systemic inflammatory response to bacterial ligands provides the basis for reconsidering the widespread usage of the term endotoxemia in equine clinical practice.

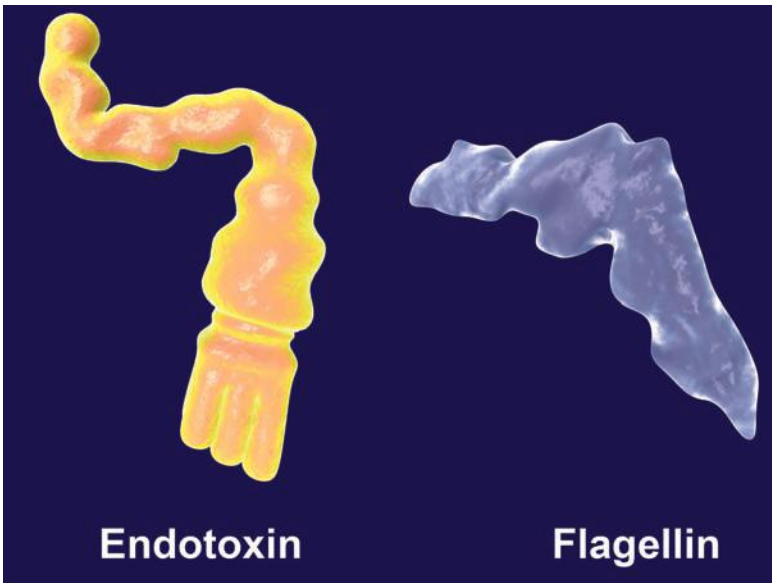
Responses to Pathogen-Associated Molecular Patterns

As Lewis Thomas wrote about microorganisms more than 30 years ago, *"It is our response to their presence that makes the disease. Our arsenals for fighting off bacteria are so powerful... that we are more in danger of them than [of] the invaders."* This observation was particularly insightful, considering what was not known at that time about the mechanisms involved in the host response to pathogens. In fact, relatively little was known until the mid- to late-1990s, when the Toll receptor protein in Drosophila was determined to be responsible for the fly's ability to respond to fungal elements.[8] Within 2 years, mammalian Toll-like proteins were identified on the surfaces of neutrophils, monocytes, and macrophages, and our understanding of the host's responses to pathogens changed seemingly overnight. Currently, 13 different mammalian Toll-like receptors have been identified, with each primarily responsible for recognizing a specific pathogen-associated molecular pattern on bacteria, viruses, fungi, or protozoa. Although much of the focus of research in this area has been on the Toll-like receptors, Nod receptors and peptidoglycan recognition receptors also are important components of the innate immune response to pathogens. Recognition of pathogen-associated molecular patterns by these receptors leads to stimulation of intracellular signaling pathways, activation of transcription factors, and the synthesis of inflammatory mediators such as cytokines. The ultimate aim of these responses is to eliminate the pathogen.

While the importance of the Toll-like receptors in the host's ability to prevent the dissemination of local infections is obvious, these receptors also are involved in the systemic response to the transmural movement of bacterial cell wall components, such as endotoxin, as well as to endogenous molecules that are released from the host's tissues during injury. An example of the latter type of endogenous stimulator of the innate immune response is the degradation products of heparan sulfate proteoglycans that are released in vivo by proteases such as elastase.[9] Because endotoxin and the degradation products of heparan sulfate are recognized by the same Toll-like receptor, the resulting systemic effects in the host are indistinguishable from those initiated by lipopolysaccharides.

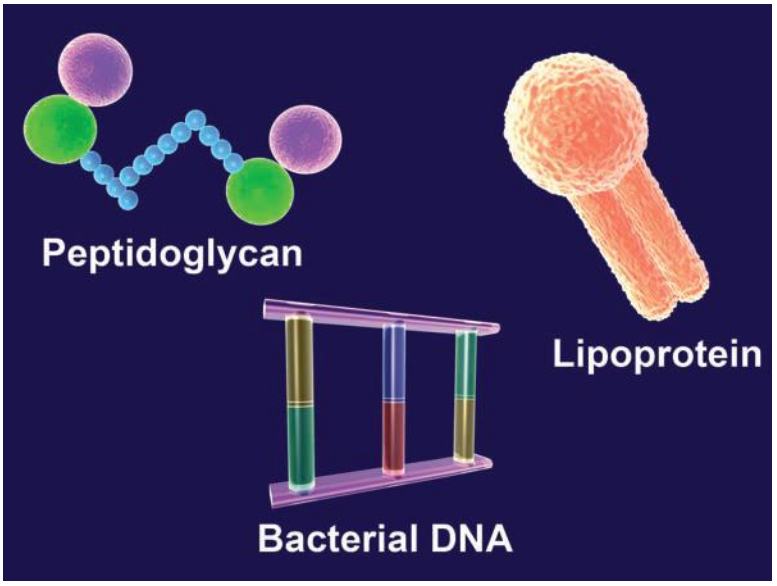
Because of the importance of bacteria in horses with gastrointestinal diseases and in neonatal foals with sepsis, a primary focus of this chapter will be on the manner in which the body senses and responds to gram-negative and gram-positive bacteria. Gram-negative bacteria generate ligands such as lipopolysaccharides, flagellin, peptidoglycan, and methylated DNA (Figure 12-1), whereas gram-positive bacteria give rise to peptidoglycan, bacterial lipoproteins, methylated DNA and lipoteichoic acid (Figure 12-2).

Figure 12-1



Two ligands commonly associated with gram-negative bacteria are endotoxin (lipopolysaccharide) and flagellin.

Figure 12-2



Structural components of gram-positive bacteria that elicit proinflammatory responses are peptidoglycan, lipoproteins, and bacterial DNA.

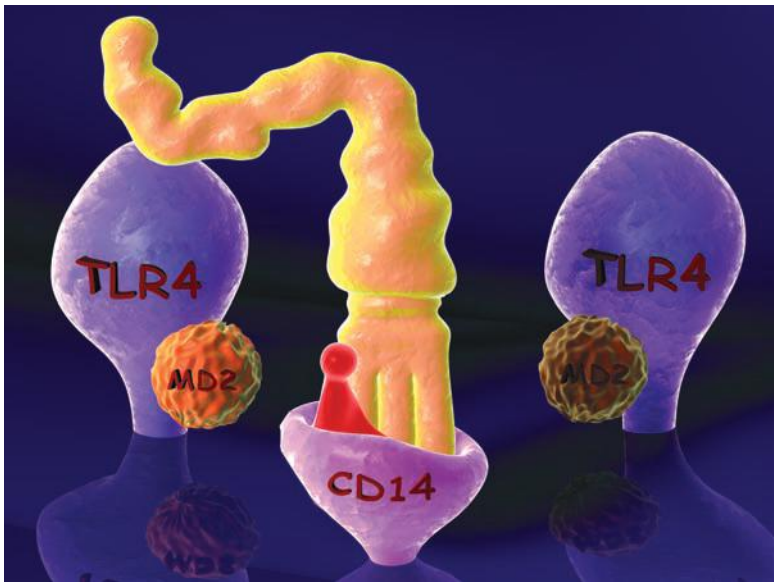
Receptors for Gram-Negative Bacteria and Bacterial Ligands

Endotoxin, the bacterial ligand commonly associated with gastrointestinal diseases in adult horses and sepsis in foals, is recognized by Toll-like receptor 4 in a large protein complex containing lipopolysaccharide-binding protein (LBP), CD14, and MD2 (Figure 12-3).[10] Toll-like receptor 4 is only expressed on the cell surface when it is bound to MD2; otherwise it is located within the cell in the endoplasmic reticulum. Endotoxin binds to LBP, which then binds to CD14. The role of CD14 and LBP is to increase the sensitivity of the cell to the presence of endotoxin by presenting the bound endotoxin to the complex consisting of Toll-like receptor 4 and MD2. At this point, endotoxin binds to MD2, thereby causing a conformational change in Toll-like receptor 4. This conformational change allows the receptor complex to dimerize with another complex of endotoxin, MD2 and Toll-like receptor 4. Dimerization of Toll-like receptor 4 initiates the intracellular signalling pathways that result in the production of proinflammatory mediators, such as cytokines, and inducible enzymes.

Because the cytoplasmic domain of Toll-like receptor 4 is similar to the cytoplasmic domain of the interleukin-1 receptor, stimulation of Toll-like receptor 4 activates many of the same intracellular signaling cascades activated by interleukin-1 through its own receptor. The finding that a single point mutation in this receptor accounts for the lack of response of the C3H/HeJ strain of mice to endotoxin highlights the importance of Toll-like receptor 4 in the response to endotoxin.[11]

Interestingly, human patients who are resistant to endotoxin have a mutation in Toll-like receptor 4,[12] and mice and people who lack Toll-like receptor 4 or whose receptors do not function normally are highly susceptible to gram-negative bacterial infections.[13,14] Of particular interest in the horse, the results of a recent study indicate that mutations identified in Toll-like receptor 4 in horses do not correlate with hyporesponsiveness to endotoxin.[15]

Figure 12-3



Endotoxin activates cellular responses by interacting with a receptor complex consisting of CD14, MD2, and Toll-like receptor 4.

One effect of the activation of Toll-like receptor 4 is phosphorylation of an intracellular inhibitory protein called IκB. Phosphorylation results in degradation of this protein, and release of the associated dimeric transcription factor, nuclear factor κB (NFκB). NF B then enters the nucleus and binds to the promoter region of genes encoding for inflammatory mediators. Although NFκB targets more than 150 genes, stimulation of Toll-like receptor 4 also activates other intracellular signalling pathways, including the mitogen-activated protein kinase pathways. The end result is the synthesis and release of a variety of inflammatory mediators, some of which have been detected in the circulation of horses administered endotoxin intravenously and in horses with naturally occurring gastrointestinal diseases. Thus, as Lewis Thomas suggested, the host's responses to recognition of pathogen-associated molecular patterns by Toll-like receptors are responsible for the deleterious effects attributed to the pathogens, or in this case to lipopolysaccharides from gram-negative bacteria.

There are major mammalian species differences regarding the response of the Toll-like receptor 4 protein complex to individual bacterial lipopolysaccharides. For example, lipopolysaccharides isolated from either *S. typhimurium* or *E. coli* are agonists in all species, whereas lipopolysaccharides and lipid A isolated from *Rhodobacter sphaeroides* are antagonists in humans and mice, but are agonists in horses and hamsters.[16-18] Although the molecular basis for the species differences in the recognition of these ligands is not clearly understood, it appears that certain regions of MD2 (e.g., amino acids 122-132) and Toll-like receptor 4 (e.g., amino acids 285-366) are important for ligand recognition.

In contrast to Toll-like receptor 4, considerably less is known about the activation of Toll-like receptor 5 and its importance in clinically important diseases. This Toll-like receptor is expressed on the surface of epithelial cells, recognizes bacterial flagellin protein,[19,20] and is likely to be one of the primary detection mechanisms for enteric infections with bacteria such as *Salmonella typhimurium.* Binding of flagellin to Toll-like receptor 5 initiates receptor dimerization and activation of an immune response (Figure 12-4). Toll-like receptor 5 seems to be less important for the response of immune cells to bacteria, but critical to the recognition of bacteria in the intestine.

Other gram-negative bacterial ligands include methylated DNA and peptidoglycan. Bacterial DNA is recognized by Toll-like receptor 9, and receptor dimerization leads to activation of intracellular signaling pathways and production of proinflammatory mediators. Although experimental evidence exists that mice lacking this Toll-like receptor are susceptible to murine cytomegalovirus infection, no information is available yet suggesting that animals or human patients with a functionally defective Toll-like receptor 9 have altered susceptibility to bacterial infection.

Peptidoglycan, or its components such as muropeptides, can also be recognized by the peptidoglycan recognition receptors and the Nod family of proteins. Although the former receptors have not been shown, as yet, to play an important role in

virulent bacterial infections, the intracellular Nod family of receptors plays an important role in a number of human diseases, including Crohn's disease (Nod-2) and Blau syndrome (Nod-2), and in recognizing *Shigella felxneri* (Nod-1). The results of early studies suggested that the Nod proteins were intracellular receptors for lipopolysaccharides, but more recent work indicates that activation of these receptors was likely a result of contamination of the lipopolysaccharide preparations with peptidoglycan. Nod-1 senses peptidoglycan molecules primarily from gram-negative bacteria (MurNAc DAP tripeptide), whereas Nod-2, primarily present in cells of myeloid lineage, detects muramyl dipeptide, which is common to gram-positive and gram-negative bacteria. These receptors are more likely to be important in patients with sepsis rather than with inflammatory responses not associated with bacterial infections.

Figure 12-4



Cellular activation is initiated when the Toll-like receptors and their bacterial ligands dimerize.

Receptors for Gram-Positive Bacteria and Bacterial Ligands

Gram-positive bacteria and their ligands, such as bacterial proteins and peptidoglycan, are detected by Toll-like receptor 2. Bacterial ligands include lipopolysaccharides derived from nonenterobacterial species, such as *Leptospira interrogans* and *Porphyromonas gingivalis*. Furthermore, bacterial extracts, such as lipoarabinomannan, and other factors from *Mycobacterium tuberculous*, *M. bovis*, and *M. avium* can activate Toll-like receptor 2. Toll-like receptor 2 is also the major receptor for lipoteichoic acid, a bacterial product associated with shock mediated by gram-positive organisms. Interestingly, cells from mice lacking Toll-like receptor 4 are nonresponsive to lipoteichoic acid, suggesting that some type of receptor co-operation is involved in the response to this particular bacterial ligand.[21] A mutation in Toll-like receptor 2 has been detected in humans who are hyposensitive to bacterial peptides and, like mice lacking Toll-like receptor 2, these patients appear to be particularly sensitive to infection with gram-positive organisms. These observations suggest that Toll-like receptor 2 plays a critical role in mediating host immunity to gram-positive bacterial infections.

Functionally, Toll-like receptor 2 can dimerize with other Toll-like receptors, such as Toll-like receptor 1 (Figure 12-5) or Toll-like receptor 6 (Figure 12-6). Association of the latter two receptors confers sensitivity of the receptor complex to modulin (a bacterial product secreted by *Staphylococcus epidermis*), peptidoglycan, the bacterial lipoprotein mycoplasmal macrophage-activating lipopeptide-2, zymosan, or Group B streptococcus, whereas dimerization of Toll-like receptor 2 and 1 occurs in response to a specific mycobacterial lipoprotein. Therefore, the ability of Toll-like receptor 2 to dimerize with other Toll-like receptor subtypes may explain how host cells are able to respond specifically to a broad range of bacterial ligands.

The current scientific literature suggests that peptidoglycan is recognized by peptidoglycan recognition receptors, Nods, and Toll-like receptor 2. The major receptor involved in circulatory shock resulting from gram-positive bacterial infections is likely to be Toll-like receptor 2, although it is unclear to what extent the other receptors are involved. Simultaneous activation of more that one Toll-like receptor, for example Toll-like receptors 2 and 4, results in a synergistic enhancement of the proinflammatory response. It is, therefore, conceivable that, in sepsis where many bacterial ligands are generated, the pronounced clinical effects may be driven by activation of more than one type of receptor.

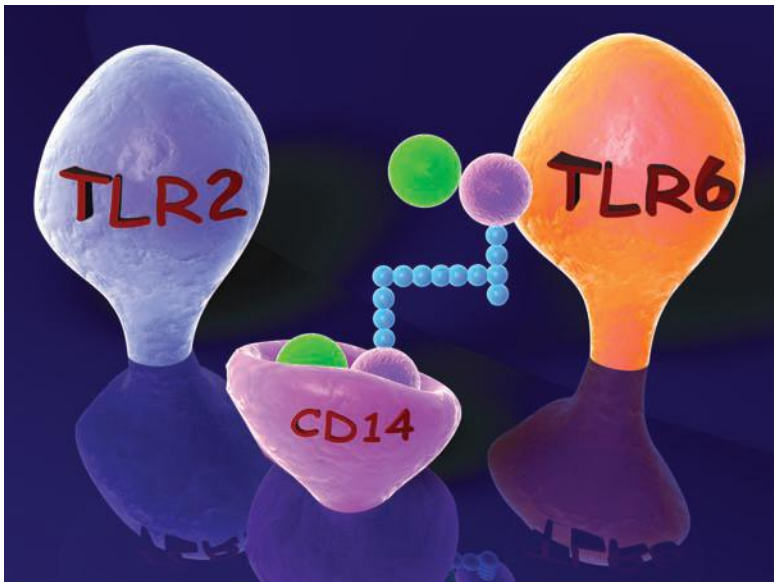
Figure 12-5



Cellular activation may be initiated when Toll-like receptors 1 and 2 dimerize; in this illustration, the bacterial ligand is a lipoprotein.

Host species differences in the response of Toll-like receptor 2 or the Nod receptors to bacterial ligands have not been described. Given the host differences documented for Toll-like receptor 4 and the range of ligands that are recognized by Toll-like receptor 2, species differences in recognition of Toll-like receptor 2 ligands are possible. Although protein sequences for human, equine, and murine Toll-like receptor 2 are similar, some differences exist in the putative binding domain for peptidoglycan/bacterial lipoprotein. Molecular studies into the biology of these receptors and their interacting ligands may lead to the generation of antagonists that may be useful in treating shock syndromes caused by gram-positive organisms.

Figure 12-6



Cellular activation may be initiated when Toll-like receptors 2 and 6 dimerize; in this illustration, the ligand is peptidoglycan.

Systemic Inflammatory Response Syndrome

Because of the aforementioned concerns regarding confusion about the classification of human patients in critical care units, the American College of Chest Physicians and the Society of Critical Care Medicine held a consensus conference in 1992 to create a common vocabulary.[7] The results of this conference were definitions for systemic inflammatory response syndrome, sepsis, severe sepsis, septic shock, bacteremia, and multiple organ dysfunction syndrome. (Table 12-1).

Because the definition for systemic inflammatory response syndrome is general, the syndrome is associated with a wide variety of conditions, and its incidence in hospitalized human patients is high. In fact, it has been estimated that more than 50% of all patients in intensive care units and more than 80% of those in surgical intensive care units meet the criteria for systemic inflammatory response syndrome.[22] The usefulness of the definition was evident in a study of more than 3,700 patients in whom it was determined that those meeting the criteria for systemic inflammatory response syndrome had a 26%

chance of developing sepsis, and those meeting more than the two required criteria had a greater chance of developing sepsis, acute renal failure, disseminated intravascular coagulation, and circulatory shock.[23] Furthermore, approximately half of the patients that met the two required criteria on admission met an additional criterion within a week of hospitalization. Interestingly, mortality rates showed little difference for patients with systemic inflammatory response syndrome or sepsis, either in this initial study or in a later multi-institutional study.[24]

Table 12-1
Definitions

Systemic Inflammatory Response Syndrome	An inflammatory response to a variety of clinical insults manifested by 2 or more of the following: temperature >38°C or <36°C, heart rate >90 beats per minute, respiratory rate >20 breaths per minute or $PaCO_2$ <32 mmHg, white blood cell count >12,000 or <4,000, or >10% immature (band) forms.
Sepsis	Systemic inflammatory response syndrome caused by infection
Severe Sepsis	Sepsis with at least one organ dysfunction or hypoperfusion
Septic Shock	Severe sepsis with hypotension that is resistant to adequate fluid resuscitation
Bacteremia	The presence of viable bacteria in the blood stream
Multiple Organ Dysfunction Syndrome	Impairment of 2 or more organ systems in an acutely ill patient in whom homeostasis cannot be maintained without therapeutic intervention

After using the classification system for a few years, some investigators noted flaws in the original definition. Specifically, the original focus on the systemic inflammatory response syndrome identified it as a condition characterized by the synthesis of proinflammatory mediators. However, the results of several clinical studies in which specific proinflammatory mediators were targeted were negative, suggesting either that the original definition was flawed or that using specific therapeutic approaches in patients with diseases having diverse causes may be the wrong way to proceed.[25-27] These concerns initiated two divergent approaches: namely, expanding the original definition to incorporate the body's anti-inflammatory response to injury, and questioning the value of grouping patients having different underlying conditions under a single heading. As an example of the first approach, the lead author on the original consensus publication altered his view of the situation to incorporate five overlapping stages representing potential progression from systemic inflammatory response syndrome to multiple organ dysfunction syndrome. In this modified classification system, the stages are local response, initial systemic response, massive systemic inflammation, excessive immunosuppression, and immunologic dissonance.[28] This classification system was based on findings that, in later stages of critical illnesses, a shift occurs in the mediators produced. The initial synthesis of proinflammatory mediators (e.g., TNF-α and interferon-γ) subsides and the patient usually survives. If the condition does not resolve, anti-inflammatory mediators (e.g., interleukins-10 and -4) predominate, the patient's ability to ward off secondary infections is impaired, and survival rates decrease.[29] As an example of the second approach, the author of a special commentary concluded that "it has not helped to lump all those conditions together... acute appendicitis is totally different from ventilator-acquired pneumonia, even though both may be called sepsis by some."[30]

To date, use of the term systemic inflammatory response syndrome in horses is in its infancy, as criteria for the syndrome have been developed only for critically ill foals, and associations for foals meeting these criteria, arterial lactate concentrations, and mortality have been identified.[31] Although it would seem obvious that the systemic inflammatory response syndrome occurs in some horses with gastrointestinal disease, a definition of the syndrome in adult horses has yet to be established.

Inflammatory Mediators and Their Source in the Horse

Whether an ill horse's responses are to endotoxin, other bacterial components, breakdown products of endogenous proteoglygans, or polypeptides arising from the intestine, the end results include deficits in tissue perfusion, depression, ileus, and an increased risk of laminitis. Several mediators have been implicated in similar responses to experimental endotoxemia and

some have been identified in the circulation of horses with naturally occurring gastrointestinal diseases. Attempts to link each mediator to specific clinical signs has not been possible because of simultaneous expression and systemic responses.

Most of these mediators are produced by mononuclear phagocytes, such as peripheral blood monocytes, peritoneal macrophages, and tissue-fixed macrophages. The association between these cells and the host's response to pathogen-associated molecular patterns, such as those occurring in the lipid A region of endotoxins, is based on the finding that mononuclear cells normally express CD14, Toll-like receptor 4, and MD2.[10] The results of other studies also implicate neutrophils, and more specifically, interactions between monocytes and neutrophils in responses orchestrated via Toll-like receptor 4.[32]

Of the numerous inflammatory mediators that have been identified, the two mediators that are most commonly monitored in studies of experimental endotoxemia in horses are TNFα and the prostaglandins. The cytokines, such as TNFα and the interleukins, are synthesized and released relatively early after exposure to endotoxins and exert their effects by altering the expression of other inflammatory genes, after first binding to specific receptors on target cells.[10] Collectively, the cytokines are responsible for initiating fever, alterations in leukocyte function, activation of coagulation, and the acute-phase-response component of the systemic response to endotoxins.[10,33,34] Serum concentrations of TNFα have been monitored in horses administered endotoxin under controlled experimental conditions as well as in horses with naturally occurring gastrointestinal diseases.[35,36] The results of these studies document that the increase in TNFα in response to administration of endotoxin occurs quickly, with peak serum concentrations detected in 1 to 2 hours.[35] While interest has been considerable in anticytokine therapy as a way of improving patient outcome, the results of studies have been mixed, at best. For example, although therapies directed against cytokines had some beneficial effects in human patients in severe septic shock, they were not effective in the majority of patients with sepsis; in fact, this form of therapy was associated with a poorer outcome in patients at low risk of death.[37] The results of studies targeting TNFα in horses also have yielded mixed results, with one study reporting that pretreatment of animals with antibody directed against equine TNFα significantly reduced the ill effects of endotoxin administration,[38] while another study reported no beneficial effects when an antibody directed against TNFα was given after initiation of endotoxemia.[4]

For more than two decades there has been convincing evidence that cyclooxygenase-derived metabolites of arachidonic acid are involved in the response of horses to experimental endotoxemia.[39-44] The results of these studies indicate that the onset of endotoxemia is associated with a rapid increase in circulating concentrations of stable metabolites of prostaglandins and thromboxanes. Furthermore, studies of experimental endotoxemia have produced convincing evidence that early administration of potent nonsteroidal anti-inflammatory drugs, such as flunixin meglumine, reduces the hemodynamic and clinical responses to endotoxin as well as plasma concentrations of arachidonic acid metabolites.[5,39,45]

The role of eicosanoids in horses with naturally occurring gastrointestinal diseases is intriguing. When flunixin meglumine was first released for use in equine practice, its efficacy in treating horses with abdominal pain was obvious. Consequently, it became the drug of choice for most practitioners called to examine a horse with colic. Clinicians at referral institutions, however, noted that an increasing number of horses was being referred after a third or fourth injection of flunixin meglumine had failed to produce the beneficial responses seen with the first or second injection. Furthermore, horses with this history had a poor prognosis for survival. These findings prompted the performance of studies designed to test the efficacy of lower doses of flunixin meglumine in experimental endotoxemia.[44,46] The findings of these studies, coupled with the aforementioned beneficial effects noted for the full dose of the drug in horses with experimental endotoxemia,[39,42,45] have led to the widespread use of nonsteroidal anti-inflammatory drugs, such as flunixin meglumine, in horses with gastrointestinal diseases. Although these drugs have become a mainstay in the treatment of horses with colic, no data have been published regarding plasma concentrations of eicosanoids in horses with naturally occurring gastrointestinal diseases. Presumably, one reason for this is the fact that virtually all horses presented to university clinics with colic have received one of these drugs before being referred, and this form of treatment is continued in the vast majority of horses, making interpretation of plasma concentrations of eicosanoids difficult, at best.

Summary

Although equine practitioners have a long history with the term *endotoxemia,* it has become increasingly important to recognize that endotoxin merely serves as a potent trigger of the horse's inflammatory response, and that it is this response that ultimately makes the horse ill. Furthermore, endotoxin contains one of many pathogen-associated molecular patterns that are recognized by the horse's innate immune system, and that have the capability of initiating a systemic inflammatory response. Equine clinicians should be encouraged to develop criteria for systemic inflammatory response syndrome in adult

horses with gastrointestinal diseases and to gather sufficient clinical data to determine whether associations can be made with development of complications and mortality rate. Although the underlying conditions may vary considerably, at least they all involve the same body system. This is quite different from the situation in human patients and may facilitate comparisons of treatment effects in horses meeting an established set of criteria. Given our history with *endotoxemia,* it will be interesting to determine whether an association exists between the presence of endotoxin in the circulation and fulfillment of the criteria for systemic inflammatory response syndrome.

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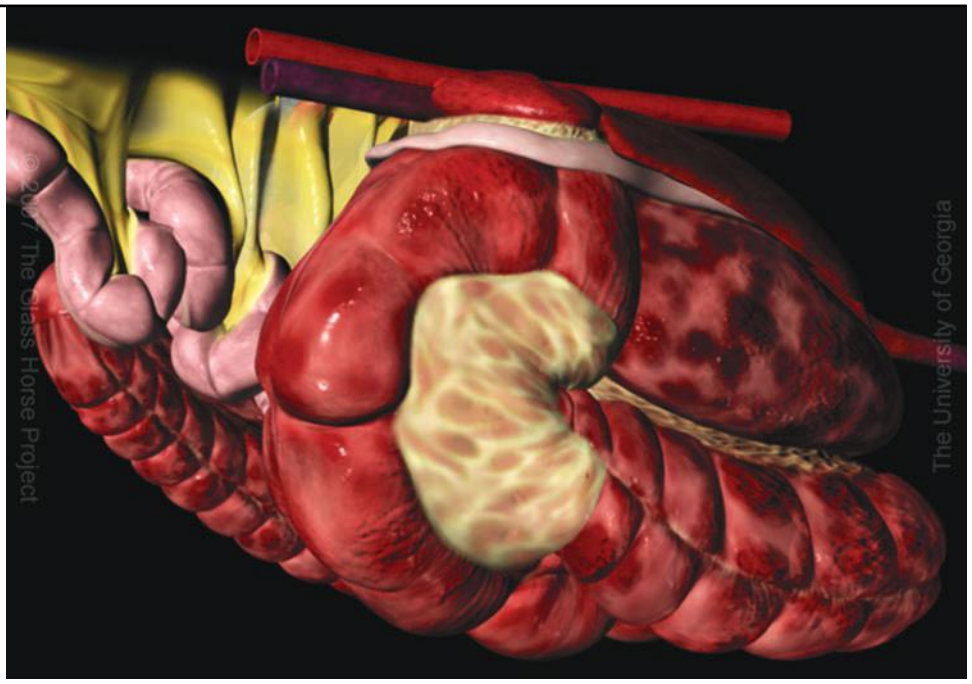
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Intestinal Parasitism

Part 3



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Intestinal Parasitism

Chapter 13

Christopher J. Proudman

Principles of Intestinal Parasitism

The common parasites of the horse's intestinal tract are widespread in their host population. The vast majority of horses harboring intestinal parasite infection suffer little or no adverse effects. So what are the determinants of parasite-associated disease? The most important is infection intensity. It is intuitive that horses with low numbers of parasites are unlikely to suffer any ill effects from their parasite burdens. A logical extension of this argument is that horses with high parasite burdens are most likely to suffer parasite-associated disease. This hypothesis is supported by numerous experimental studies, field investigations in horses and other host-parasite systems.[1,2]

A second general principle of intestinal parasitism is that not all horses are equally susceptible to infection. For reasons that are poorly understood, parasites tend to distribute in a nonrandom manner in their host population.[1] Certain individuals in the population are "predisposed" to developing high levels of infection and others are resistant to infection. This results in an asymmetrical distribution: commonly 80% of the worms are present in 20% of the hosts. In other words, a few individuals harbor high numbers of parasites, but most have modest or low levels of infection. It is these heavily infected individuals that are at risk of parasite-associated disease. The concept of predisposition is further supported by observations that, after chemotherapeutic treatment of parasite infections, it is the same individuals that become heavily reinfected and harbor large worm burdens.[3]

A third principle that is of importance when considering intestinal parasitism is age-related susceptibility to infection. Young animals are generally more susceptible to parasitism and are more likely to develop high levels of infection. Older animals develop resistance to parasite invasion, although it is unknown whether this arises from immunity or from behavioral changes that decrease exposure to infective stages.[1]

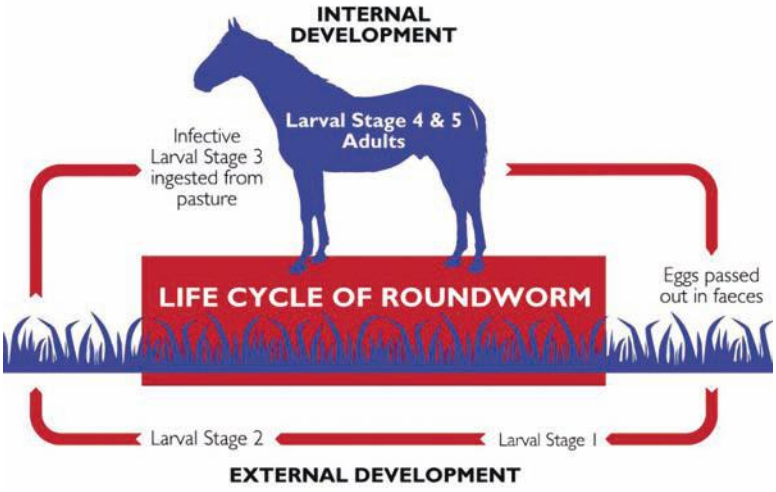
The intestinal parasites of horses with greatest relevance to acute abdominal disease are large redworms (*Strongylus vulgaris*), small redworms (cyathostomins) and tapeworms (*Anoplocephala perfoliata*).

Strongylus Vulgaris

Lifecycle

The lifecycle of this parasite involves migration of third-stage larvae through the submucosa of the cecum and colon (Figure 13-1). This is followed by further migration through the small arterioles of the intestine and into the cranial mesenteric artery. At this site, damage to the arterial intima can result in thrombus formation (Figure 13-2). Both submucosal migration and cranial mesenteric arteritis have been associated with colic in experimental models of infection.[4-6]

Figure 13-1



General lifecycle of roundworms (strongyles). (Courtesy of Virbac UK.)

Figure 13-2



Post-mortem specimen showing a large thrombus within the abdominal aorta. Note the *S. vulgaris* larvae within the thrombus.

Pathogenesis

Nonstrangulating infarction of cecum and colon (Figure 13-3) has been cited as the classic lesion associated with parasite-associated thromboembolic colic.[4] It is proposed that emboli detatch from the thrombus and are carried along the arterial tree until they become wedged in a small arteriole. This leads to physical obstruction of blood flow and to vascular spasm associated with ischemia. The net result is failure of oxygenation of tissues supplied by the arterioles and ischemic necrosis. The cecal apex, pelvic flexure, and colon are the sites most commonly involved. This lesion is rarely seen in horses at surgery or at post-mortem examination,[7] which may be explained by the marked decrease in prevalence of *S. vulgaris* since the introduction of modern anthelmintics.[8]

Figure 13-3



Nonstrangulating infarction of the left ventral colon.

Diagnosis and Treatment

The diagnosis of *S. vulgaris*-associated colic is invariably retrospective and often only possible after surgery or post-mortem examination. Horses with nonstrangulating infarction of the cecum or colon carry a guarded prognosis, as the presence of a cranial mesenteric thrombus may lead to further thromboembolic events. Spasmodic colic episodes that resolve with medical treatment in horses with a history of poor worm control may be attributable to *S. vulgaris* infection. Fecal worm egg counts will identify strongylid eggs, but differentiation between *S. vulgaris* and cyathostomin larvae is only possible by larval culture. Knowledge of poor parasite control (monitored by periodic fecal egg count) on the farm of origin may raise the index of suspicion for this disease. Treatment of proven *S. vulgaris* infection is straightforward as the parasite is sensitive to most modern anthelmintics (Table 13-1).

Spasmodic colic episodes resulting from changes in intestinal motility can usually be managed successfully with analgesics and spasmolytic drugs. Nonstrangulating infarction results in low-grade, persistent pain and changes in peritoneal fluid consistent with infarction of intestine (see Chapters 6, 15 and 38). Surgical resection of the affected bowel is indicated.

Table 13-1

Anthelmintics currently used against Equine Intestinal Helminths.

Drug	Dose	Recommended frequency of dosing	Efficacy against cyathostomes and tapeworms*.
Fenbendazole	7.5 mg/kg	6 weeks	Efficacy against benzimidazole-susceptible, adult cyathostomes and "immature" stages.
	7.5 mg/kg for 5 days	6-12 months	Ovicidal effect on nematode eggs. Five day course effective against encysted, inhibited mucosal stages of cyathostomes. No efficacy against tapeworms.
Mebendazole	5-10 mg/kg	6 weeks	Efficacy against benzimidazole-susceptible, adult cyathostomes. No efficacy against tapeworms.
Oxibendazole	10 mg/kg	6-8 weeks	Efficacy against benzimidazole-susceptible, adult cyathostomes. No efficacy against tapeworms.
Febantel	6 mg/kg		Efficacy against benzimidazole-susceptible, adult cyathostomes. No efficacy against tapeworms.
Pyrantel embonate	19 mg/kg 38 mg/kg for tapeworms	4-6 weeks	Efficacy against adult cyathostomes. No efficacy against inhibited, encysted mucosal stages. Use anti-tapeworm dose every 6-12 months. No efficacy against *A. mamillana*.
Ivermectin	200 μg/kg	6-8 weeks	High efficacy against adult cyathostomes, limited efficacy against encysted mucosal stages. No efficacy against tapeworms.
Moxidectin	400 μg/kg	13 weeks	High efficacy against adult and developing encysted cyathostomes. No efficacy against tapeworms.
Praziquantel	1 mg/kg	–	Efficacy against tapeworms, including *A. mamillana*. Available as combination anthelmintic with ivermectin. No efficacy against nematodes.

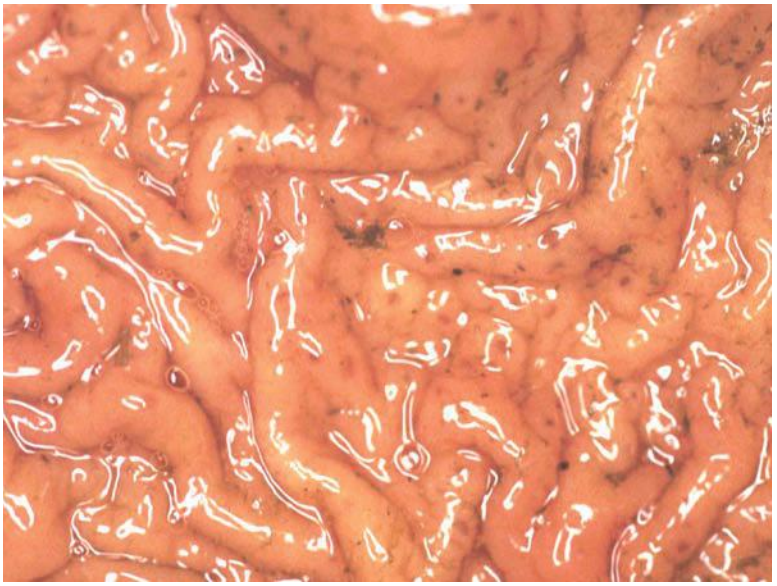
Note: *. Efficacy against large strongyles, Parascaris equorum, and Oxyuris equi, is assumed unless stated otherwise.

Cyathostomins

Lifecycle

For convenience, the many species of small strongyle parasites in the horses are considered a homogeneous group. These parasites are minimally invasive; the infective L3 stages migrating only as far as the mucosa of cecum and large colon. The lifecycle of cyathostomins differs from the general lifecycle illustrated in Figure 13-1 during the period of internal development. During larval development within the colonic mucosa, cyathostomins have the ability to go into a stage of arrested development within mucosal cysts. Such arrested encysted larvae stimulate little inflammatory response. Huge numbers of parasite larvae can inhabit the mucosa of susceptible horses (Figure 13-4). Mass emergence of these larvae as development is reactivated leads to colitis and the condition of larval cyathostominosis.

Figure 13-4



Colonic mucosa of a horse with heavy cyathostomin infection. Each black spot in the mucosa is an encysted cyathostomin parasite.

Association with Acute Abdominal Disease

Disturbance of local intestinal motility, pathology at sites of cyst reactivation, and mucosal migration are all possible mechanisms by which colic may arise. Murphy and Love observed intestinal dysfunction early in the course of experimental cyathostomin infection, suggesting a pathologic role for invading L3, not just encysted stages undergoing reactivation and emergence into the gut lumen.[9] The role of such dysfunction in the etiology of colic is not known.

An association between cyathostomin infection and colic has been demonstrated in epidemiologic studies. Uhlinger[10] demonstrated that the better the anthelmintic program being used in herds of horses, the lower the incidence of colic. The only strongyle parasites harbored by the horses in this study were cyathostomes as established by larval culture. By implication therefore, cyathostomes were associated with a significant proportion of colic cases. This observation is further supported by work that reported a reduced risk of colic in horses receiving daily pyrantel tartrate in feed[11] and a study that reported a decreased risk of simple colonic obstruction associated with the use of avermectin anthelmintics.[12]

Clinical case reports have associated cyathostomin infection with nonstrangulating infarction[13] and with cecocecal and cecocolic intussusception.[14] In both reports the authors cite clinical and pathologic evidence suggesting an association between parasite infection and intestinal disease.

Diagnosis and Treatment

Patent infection (adult parasites producing eggs) is not difficult to detect coprologically (Figure 13-5). A fecal egg count gives an indication of luminal adult strongyle burden, although it is not possible to differentiate large strongyle (*S. vulgaris*) eggs from those of the small strongyles (cyathostomins) by microscopy alone. Fecal egg counts are quantitative but may not give an accurate estimate of total worm burden. A major limitation of this diagnostic test is the inability to detect immature, mucosal infection.[15] Up to 95% of a horse's cyathostomin burden can be mucosal. Developing late-stage larvae may be observed by careful inspection of feces from horses with larval cyathostominosis, but this test is of limited sensitivity. The use of biochemical tests to detect markers for cyathostomin infection has been investigated and discounted. In particular, when the use of serum β globulins was investigated, it was concluded that total serum protein and IgG(T) responses were of limited value in the

diagnosis of parasitism.[16] At present, the diagnosis of cyathostomin infection is based on history of worm control, clinical signs, fecal examination for eggs and larvae and (after cyathostomin-associated colic) post-mortem examination.

Treatment of cyathostomin infection is not straightforward. If encysted arrested stages are present, then some anthelmintics will lack efficacy (Table 13-1). Resistance to benzimidazoles is also widespread among the cyathostomins. The current recommendation for the treatment of encysted arrested larvae is to use fenbendazole for five consecutive days in horses with benzimidazole-susceptible infections. In the face of benzimidazole resistance (which is now widespread), moxidectin is indicated.[17] Treatment is hazardous in heavily infected horses as the use of anthelmintics is associated with the development of larval cyathostominosis.[18] Preventing the accumulation of large burdens, particularly encysted arrested stages in young horses, is a safer control strategy.

Figure 13-5



Microscopic view of a strongyle egg (left) and a tapeworm egg (right) on fecal flotation.

Tapeworms

Lifecycle

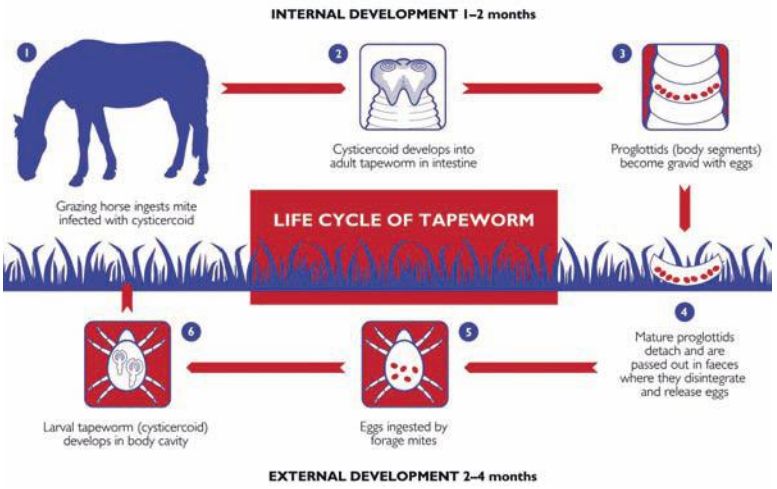
The common tapeworm of the horse in temperate climates in *Anoplocephala perfoliata*. The lifecycle of this parasite is illustrated in Figure 13-6. A fundamental difference between roundworm lifecycles and that of the tapeworm is the need for an intermediate host, in this case the ground-dwelling oribatid mite. One of the implications of this indirect lifecycle is that *A. perfoliata* is most prevalent in regions with a humid, warm climate, as this favors the intermediate host.[19] The prevalence and clinical significance of *Anoplocephala magna* and *Anoplocephaloides mamillana* are poorly understood at present.

Association with Acute Abdominal Disease

Several studies have reported the gross and microscopic pathology associated with tapeworm infection.[20-23] Mucosal ulceration, submucosal edema, and decreased distensibility of the ileocecal valve have all been reported. It is significant that this parasite chooses to aggregate around the ileocecal junction, and pathology is confined to this site (Figures 13-7 and 13-8). Intestinal disease originating at this site has been associated with heavy tapeworm infection (e.g., ileal impaction, ileocecal and cecocecal intussusception).

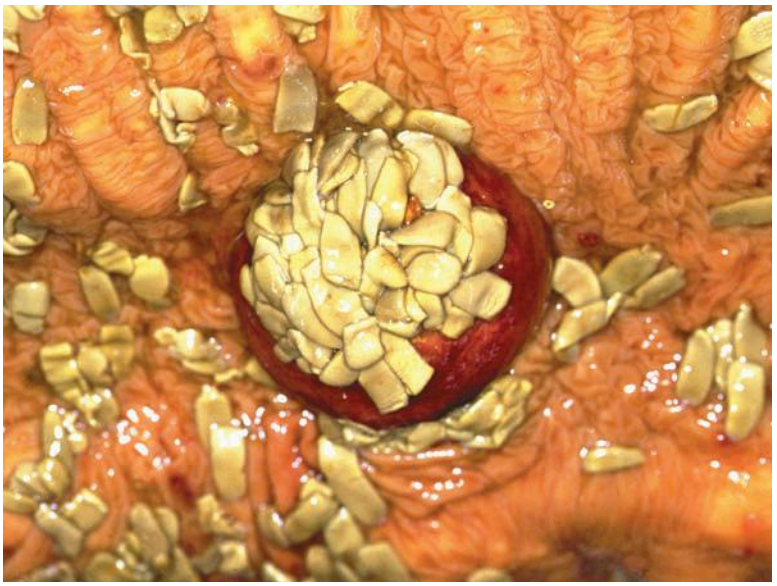
Epidemiologic studies have demonstrated an association between tapeworm *(A. perfoliata)* infection and colic. In one study, both coprologic diagnosis and a novel serologic assay were used to demonstrate an association between the parasite and spasmodic colic and ileal impaction colic.[2] Serologic data, which correlated with infection intensity,[24] were used to show a dose-response relationship between tapeworms and spasmodic colic (Figure 13-9). The greater the number of tapeworms present, the higher the risk of spasmodic colic. Slightly more than 20% of the spasmodic colic cases and over 80% of ileal impaction cases in this study were tapeworm-related. A similar study focusing on ileal impaction cases in the southeastern United States confirmed an increased risk of this disease in horses that did not receive antitapeworm anthelmintics.[25]

Figure 13-6



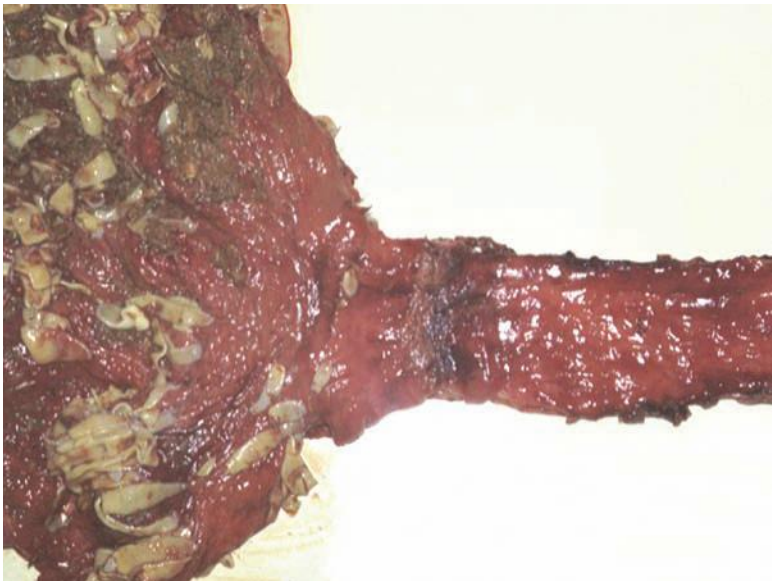
Lifecycle of the equine tapeworm *Anoplocephala perfoliata*. (Courtesy of Virbac UK.)

Figure 13-7



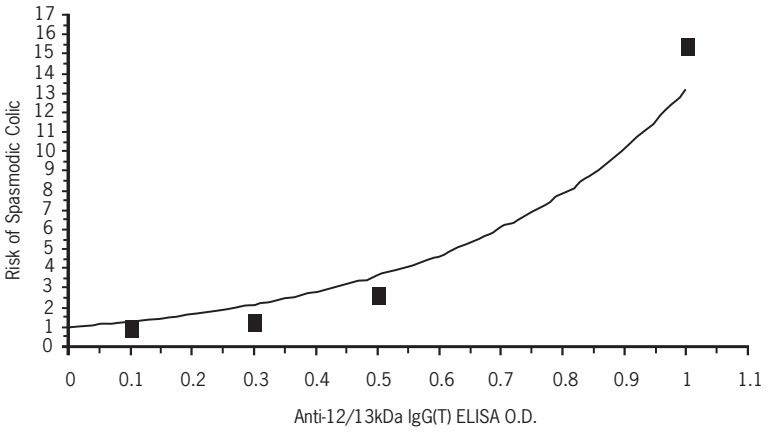
Mucosal surface of the cecum with massive edema at the site of tapeworm attachment at the ileocecal junction.

Figure 13-8



Mucosal surface of the ileocecal region of a horse with heavy tapeworm infection. Tapeworms removed from the junction revealing mucosal ulceration and edema.

Figure 13-9



Relationship between tapeworm infection intensity (measured by ELISA) and the risk of spasmodic colic. Squares represent categorized data, solid line represents the relationship for continuous data (conditional logistic regression model).[2]

Diagnosis and Treatment

Diagnosis of tapeworm infection is by coprologic or serologic methods. Tapeworm eggs can be detected microscopically after flotation in a high specific-gravity solution (Figure 13-5). Tapeworm eggs are heavy and do not float reliably on saturated salt solution used for strongyle eggs. Coprologic identification is messy, time-consuming, lacks sensitivity, and lacks correlation with infection intensity.[26] A serologic method for tapeworm diagnosis has been described, using the IgG(T) response to tapeworm antigens.[24] This ELISA test has the advantage of good correlation of test results with infection intensity, making this test useful for monitoring the risk of clinical disease in infected horses.

Treatment of tapeworm infection can be achieved by using anthelmintic-containing praziquantel or pyrantel (Table 13-1). Pyrantel has good efficacy against *A. perfoliata* when used at twice the nematocidal dose. It should be noted that this anthelmintic has no efficacy against *A. mamillana*; praziquantel should be used.

Parascaris Equorum

This ascarid parasite of the small intestine of the horse occasionally causes acute colic in young animals. The median age of horses with ascarid-related colic was 5 months in one report.[27] Large numbers of adult parasites can occlude the lumen of the small intestine (Figure 13-10), leading to intestinal distension and strangulating obstruction of the small intestine. Surgical relief of the impaction is indicated in most cases, but a poor prognosis for such cases is reported with long-term survival around 45%.[27] The reasons for this are unclear, but it is suggested that somatic antigens from the parasite may lead to ileus, which may compromise post-operative recovery. Affected animals that do not undergo surgical treatment are likely to develop intestinal rupture and fatal peritonitis.

Detection of *P. equorum* infection is by coprologic means. Infected horses usually have large numbers of eggs in their feces (Figure 13-11) but correlation between egg count and infection intensity has never been quantified. A further problem with diagnosis is that many horse owners do not consider their young stock to be at risk of disease so early in life, so feces are rarely submitted for testing. Anthelmintic therapy in the presence of heavy infection is controversial. A slow kill of parasites with benzimidazoles, pyrantel, or ivermectin has been advocated to avoid release of somatic antigens.[28] It should also be noted that apparent resistance of *P. equorum* to ivermectin has been reported.[29,30] As is so often the case, little scientific evidence is available on which to make a rational decision.

Figure 13-10



Ascarid worms in the small intestinal lumen of a young horse.

Figure 13-11



Microscopic view of a strongyle egg (left) and an ascarid egg (right).

Other Intestinal Parasites

No evidence exists to suggest that bots (*Gasterophilus intestinalis*), *Oxyuris equi*, or *Strongyloides westeri* are associated with any acute acute abdominal diseases. *O. equi* may be observed in the feces of horses or in intestinal contents removed from a colon enterotomy. Their presence should be regarded as a marker for poor parasite control.

Prevention

The successful prevention of all parasite-associated disease depends on the design and execution of a "custom-made" worm control program. Unfortunately, the concept of a "one-size-fits-all" approach to this problem is simplistic and does not work. Veterinarians should discuss with their clients worm control measures that are appropriate to each farm and, with the aid of diagnostic tests, design, implement, and monitor an appropriate control policy.

Managemental Control

Good pasture management is inexpensive, environmentally friendly, and a highly efficient method of preventing transmission of intestinal parasites. The collection of feces from the pasture twice weekly is optimal, but even weekly collection will significantly decrease the infectivity of pasture (Figure 13-12). Rotation of pastures, mixed species grazing and maintaining low stocking density are all practices that minimize parasite spread.

Figure 13-12



Removal of feces from pastures is an effective worm control option. Mechanical removal is an effective option for larger horse farms.

Anthelmintics

Numerous anthelmintic products are readily available to help with parasite control. These are listed in Table 13-1 and the spectrum of activity of each drug is given. The different ways of using these drugs are as follows:

- **Interval treatment** involves the administration of anthelmintics to all horses on the premises at periodic intervals.
- **Strategic dosing** is the use of anthelmintics at times of the year critical to parasite transmission. The exact timing of doses varies with differing climates around the world.
- **Targeted dosing** is the use of anthelmintics on just those horses demonstrated to have significant parasite burdens by diagnostic testing.

Over-dependence on anthelmintics should be avoided as intensive use of these drugs is likely to hasten the onset of resistance within parasite populations.[31] Benzimidazole and pyrantel resistance have been reported in horses worldwide.[32,33] Resistance to ivermectin has been reported in *P. equorum* in the Netherlands[29] and the United States.[30] Currently, rotation of anthelmintics is not recommended to avoid creation of resistant parasites. Strategic dosing with routine herd or individual horse evaluation for parasites is recommended for optimal parasite control.

Diagnostic Testing

Diagnostic testing in equine intestinal parasite control has three important uses. The first is to guide the targeted use of anthelmintic drugs. Second, whatever the control program used, is to monitor effectiveness of control programs by periodic testing for strongyle eggs in the feces and for tapeworm infection (coprologic or serologic tests may be used). The third indication for diagnostic testing is the investigation of colic episodes. Veterinarians are frequently asked about the cause of a colic episode after it has resolved. Strongyle and tapeworm infection status can be tested easily and treated readily if found to be present.

Occasionally, veterinarians are asked to investigate the cause of a high incidence of colic in a group of horses. Evaluation of parasite status is worthwhile in such cases, but because of the nonrandom distribution of parasites in the horses, it is not satisfactory to sample a selection of affected animals; as many horses as possible should be sampled. Such investigations have been successful in identifying and preventing parasite-associated colic problems.[34]

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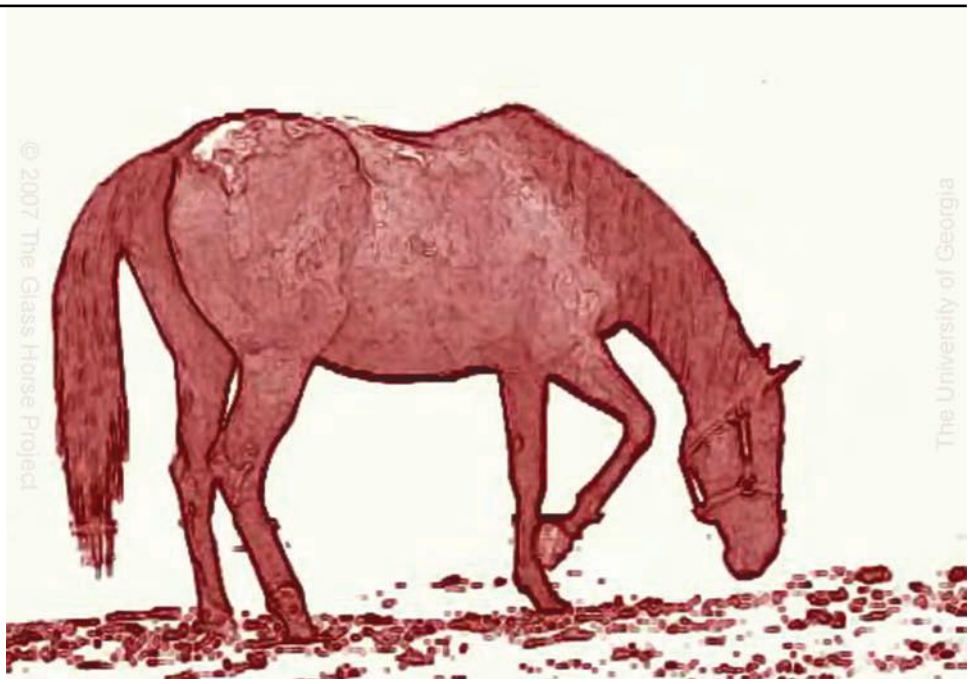
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Epidemiology

Part 4



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Epidemiology of Colic

Chapter 14

Noah D. Cohen

General Epidemiologic Considerations

Importance of Epidemiology

Epidemiology is a science concerned with the distribution of disease and the determinants of disease in populations. Although rooted in the field of public health, epidemiologic principles and the practice of epidemiology pertain directly to the care and management of individual patients. Epidemiology is quantitative. Quantification of observations and experiences is necessary to address many vital questions about a disease or group of diseases (such as colic). Epidemiologic studies enable us to address more accurately vital clinical questions relevant to managing horses with colic. These questions include: a) how often do horses experience colic? b) what factors predispose to colic? c) are certain diagnostic procedures superior to others? d) what is the most appropriate treatment for a given type of colic? and, e) what is the prognosis for a horse with a given type of colic? Answers to these and other important questions are derived from experiences or studies from individual cases or a series of cases. Information that is derived from studies in which there is a comparison (control) population is generally deemed to be superior to that derived from uncontrolled studies. Controlled studies include observational (i.e., primarily case-control and cohort [prospective] study designs) and experimental (i.e., randomized, controlled clinical trials) epidemiologic studies.

An important benefit of well designed epidemiologic studies is that the results are directly relevant to populations similar to those horses included in the study; put another way, results are directly applicable to the "real world" from which they were derived. Another advantage of the epidemiologic approach is that no unnecessary disease or exposure to factors predisposing to disease is necessary to conduct epidemiologic research. This is because epidemiologic methods entail study of spontaneous disease and exposures or characteristics that occur under what can be considered to be natural/normal conditions. From a humane standpoint, epidemiologic research is appealing.

Although epidemiologic studies possess the aforementioned advantages, epidemiologic studies do have limitations. Generally, the problems with epidemiologic studies pertain to potential problems with interpreting results derived from the "real world." The tremendous amount of variability among horses, and among veterinarians in the way they interpret findings and manage horses, results in a great deal of variability in the recorded observations. This variability cannot be eliminated, but its impact can be assessed, limited, and addressed by appropriate design, conduct, analysis, and interpretation of epidemiologic studies. Some examples of these limitations will be presented in the ensuing text. It is important to remember that the variation among individual horses and in the care they receive when they experience colic does not vitiate the value of epidemiologic studies. It does, however, require that readers of equine epidemiologic studies be familiar with certain key principles of the design and interpretation of epidemiologic studies.[1]

Selected Epidemiologic Principles

It is imperative that veterinarians be familiar with selected epidemiologic principles so that they can be better able to assess results of studies of horses with colic. In this section we consider the principles of epidemiologic design, confounding, effect modification, and biases.

Study designs

Epidemiologic study designs continue to emerge, including such examples as case-crossover, case-cohort, and case-only designs. The primary designs employed for epidemiologic studies include **cross-sectional, case-control, cohort (prospective),** and **clinical trial designs.** The principal difference among these study designs pertains to the time-points when disease status (e.g., colic versus noncolic control) and exposure status (i.e., presence or absence of a possible determinant of disease) are determined or established.

In a **cross-sectional** design, a group of horses is examined at a given point in time, and both disease status and exposure status are determined at the same time. For example, one might determine the heart rate of horses with and without colic and compare the distributions of heart rates for the two groups. The principal limitation of cross-sectional designs is that little information exists about the temporal relationship of the disease(s) and exposure(s) of interest. It is unlikely that we would interpret the finding that horses with higher heart rates are at increased risk of developing colic, because it is at least equally plausible that the higher heart rates among horses with colic are a result of the colic.

In a **case-control** design, disease status (case or control) is first determined, and then exposure status is determined for both cases and controls. For example, one might compare the dietary history of horses examined for colic with the dietary history of horses examined for lameness problems. Case-control studies are relatively easy and inexpensive to conduct, they

allow investigators to consider a wide range of possible exposures associated with disease, and are particularly useful for studying rare diseases; however, case-control studies also have a number of disadvantages. As with any epidemiologic study, a clearly specified definition of cases is required; it is imperative that the cases selected for study are representative of cases of disease in the more general population to which results are to be applied. Selection of control patients can be difficult. Because of inherent biases in selecting controls, inappropriately selected control populations can skew results of case-control studies. For example, if one compared dietary histories of horses from a wide variety of breeds and activities with colic to those of lame horses that were primarily racing Thoroughbreds in active training, one might obtain biased results because of the skewing effect of environment or management of the racehorses used as controls. Because of the inherent problems with selecting control populations, it is not unusual for investigators to consider multiple control populations: if results are consistent among comparisons using different control populations for the association of a given factor (e.g., recent increase in the amount of concentrate fed) with a disease (e.g., colic), we have more confidence in the association. Case-control studies require collecting historical data about exposures of interest. The retrospective nature of data collection may result in a number of problems related to incomplete or missing data and quality of data resources, and these problems can bias the results of such studies.

Risk is defined epidemiologically as the number of cases of a disease (or other health-related outcome) that occur during a specified period of time. By design, case-control studies cannot be used to determine risk. Rather, one can determine the odds of exposure in cases and the odds of exposure in controls. Under certain circumstances, the ratio of the odds of exposure in cases to that of controls (i.e., the odds ratio or **OR**) approximates the relative risk (**RR**).

In a **cohort study** design (sometimes also referred to as a prospective study), exposure status is defined first and then the experiences of exposed and unexposed horses are followed over time. Exposure is self-selected (i.e., not determined by the investigators). For example, one might identify a group of horses that have limited opportunity to graze and another population of horses that receives almost continual opportunity to graze. One would follow the experiences of the groups of horses over time and compare the frequency with which colic developed in the horses with restricted grazing to that of horses with constant grazing; if the frequency of colic is less in the latter group, we might conclude that grazing reduces the risk of colic. Cohort studies obviate many of the limitations of case-control studies. In cohort studies, information about exposure and disease can be ascertained better, particularly with respect to the temporal relationship of the exposure and disease. By design, risk can be determined directly from cohort studies, and the relative risk of disease in exposed and unexposed populations can be determined. Cohort studies enable investigators to consider multiple health outcomes other than the primary disease of interest. Cohort studies require a clear specification of both disease (or other outcome of interest) and exposure, can be expensive and time-consuming to conduct, can be subject to various biases, and can limit the scope of exposures that can be associated with the disease(s) of interest. Nevertheless, well designed cohort studies often yield results similar in quality and interpretation to those from clinical trials.

Clinical trials are essentially epidemiologic experiments. The investigator enrolls horses and assigns the exposure of participating horses. For example, the investigator might assign some horses in active training to receive a treatment for gastric ulcer prophylaxis and some other horses to receive a placebo. The horses are followed over time, and the investigators monitor the horses closely by physical examination, body weight, gastroscopy, etc. The frequency of primary outcomes (development and severity of gastric ulcers) and secondary outcomes (changes in body weight, changes in amount of feed consumed, etc.) can be compared between the two groups to establish the effectiveness of the treatment. Generally and preferably, exposure (treatment) status in clinical trials is established by random assignment, and those monitoring the horses for the outcome of disease are blinded to the treatment status of the horses. The conditions of exposure(s) and disease(s) can be specifically assessed in a clinical trial. Though this design is clearly superior to the aforementioned designs for assessing the impact of a given exposure (such as a treatment or intervention) on a disease, conducting such studies is generally expensive and labor-intensive.

The hierarchy of epidemiologic studies is based on the extent to which the design is subject to bias. Cross-sectional, case-control, and cohort studies are **observational** epidemiologic studies: exposure is determined by the choices of owners or care-providers of horses or the horses themselves, and the investigator is merely observing the occurrence of spontaneous events. Because of the inherent variability among individuals and groups in nature, the observational design of these studies introduces more uncertainty and imprecision. Cohort studies are generally superior to case-control studies, which are generally superior to cross-sectional studies. As such, clinical trials (**experimental** epidemiologic studies) are considered the superior study design. Nevertheless, well designed cohort studies can yield results similar in quality to those of clinical trials, and much important health information has been derived from case-control studies (for example, the association of smoking

with lung cancer). In interpreting results of epidemiologic studies of colic, the design of each study and its associated strengths and limitations should be considered.

Confounding

A confounder is a factor that is associated both with the disease of interest and the exposure of interest.[2] Confounding is the phenomenon whereby failure to account for a confounder masks the true association of an exposure with disease, or makes the confounder appear to be associated with disease. For example, consider the situation if Thoroughbred racehorses were known to be fed more concentrate relative to horses of other breeds and activities, and if feeding a large amount of concentrate were associated with development of colic. Now consider that we were to conduct an observational study of the association of horse breed with risk of colic. If we fail to account for the hypothetically "known" effects of the amount of concentrate fed to horses in the study, we might expect to find a **spurious** association of Thoroughbred breed with colic; breed is acting as a confounder for diet (and probably for activity level that often results in feeding a large amount of concentrate). Confounding can be positive or negative. Positive confounding can be considered to occur when an apparent association with disease occurs because of failure to account for confounding (as in the aforementioned example of concentrate feeding and breed or activity level). Negative confounding is said to occur when a real association is missed by failure to account for the effects of a confounder.

Confounding is usually dealt with by accounting for the factor in analysis. This can be done by stratifying analysis. For example, we might consider the association of Thoroughbred breed versus other breeds with colic stratified by the amount of concentrate being fed. That is, we might examine the association of colic and Thoroughbred breed among those horses receiving large amounts of concentrate and among those horses receiving amounts other than a large amount (Table 14-1). Accounting for confounding can also be accomplished by appropriate application and interpretation of multivariable statistical modeling, such as the commonly used multiple logistic regression model. Accounting for confounding is one of the principal reasons that multiple logistic regression is used so commonly for studies of risk factors for colic.

Although statistical methods can account for confounding factors, they can only examine the effects of factors that investigators have considered and for which data have been collected. When interpreting results of epidemiologic studies of colic, veterinarians should consider whether observed associations might have been confounded by factors that the investigators failed to include in their analyses. Moreover, we should always consider whether an observed association of a factor with colic has accounted for known predisposing factors.

Effect Modification

Effect modification is said to occur when the association of a given factor (e.g., feeding practice) with disease (e.g., colic) varies by the level of another associated factor (e.g., activity level).[2] Hypothetically, the effect of feeding a large amount of concentrate might not be associated with colic among horses that are training intensively and consistently, but might be strongly associated with colic among horses that have only intermittent exposure to intensive or extended exercise. Effect modification is also sometimes referred to as interaction. As for confounding, the presence of effect modification can be detected by stratification. Effect modification can be detected and accounted for in multivariable models using so-called interaction terms. Interpretation of interaction terms in models can be confusing, and their modeling entails important statistical considerations that are beyond the scope of this chapter.

Biases

The term bias has a number of meanings in biomedical research. In epidemiologic terminology, bias generally is interpreted to mean any systematic error in the design, conduct, or analysis of a study that results in a mistaken interpretation of the estimated impact of an exposure (or risk factor) on the risk of disease.[1] Causes of bias are legion, and describing all possible causes of bias is beyond the scope of this chapter. For purposes of illustration, examples of bias in determining exposure status and disease status are provided.

A recall bias is said to occur when there is differential recall of exposure between cases (horses with colic) and controls (horses without colic). For example, an owner of a horse that has recently had an episode of colic may be more likely to recall events such as deworming that they think may be associated with colic than the owner of a control horse that is healthy or examined for a problem which the owner does not deem to be associated with the exposure of interest.

Bias in determining disease status can occur in many ways, including bias resulting from ascertainment of disease status because of surveillance, diagnosis, referral, or selection. For example, if Arabian horses are more likely to have abdominal

Table 14-1

Hypothetical Example of Confounding in a Case-Control Study of Colic

All horses (unstratified analysis)

	Cases of Colic	Controls	Total
Thoroughbreds	100	100	200
Other Breeds	100	300	400
Total	200	400	600

Odds of being a Thoroughbred among cases = 100/100 = 1
Odds of being a Thoroughbred among controls = 100/300 = 1/3
Odds ratio of association of Thoroughbred breed with colic = 1/1/3 = 3

We interpret this to mean that the odds of colic are approximately 3 times greater among Thoroughbreds relative to other breeds

Stratification by concentrate consumption (large amount versus not)

Horses eating a large amount of concentrate

	Cases of Colic	Controls	Total
Thoroughbreds	80	80	160
Other Breeds	100	100	200
Total	180	180	360

Odds of being a Thoroughbred among cases = 80/100 = 8/10
Odds of being a Thoroughbred among controls = 80/100 = 8/10
Odds ratio of association of Thoroughbred breed with colic = 8/10/8/10 = 1

We interpret this to mean that the odds of colic are approximately equal among Thoroughbreds relative to other breeds for horses eating a relatively large amount of concentrate.

Horses eating a small amount of concentrate

	Cases of Colic	Controls	Total
Thoroughbreds	20	20	40
Other Breeds	100	100	200
Total	120	120	240

Odds of being a Thoroughbred among cases = 20/100 = 2/10
Odds of being a Thoroughbred among controls = 20/100 = 2/10
Odds ratio of association of Thoroughbred breed with colic = 2/10/2/10 = 1

We interpret this to mean that the odds of colic are approximately equal among Thoroughbreds relative to other breeds for horses eating a small amount of concentrate

AFTER ACCOUNTING FOR CONCENTRATE CONSUMPTION (BY USING STRATIFICATION), THOROUGHBRED BREED NO LONGER APPEARS TO BE ASSOCIATED WITH COLIC

radiography performed than horses of other breeds, identification of enteroliths may be more likely among Arabians than other breeds, potentially inflating the apparent risk of enterolithiasis in this breed.

In addition to bias in ascertainment of status of exposure and disease, another form of bias in epidemiologic studies is misclassification. This occurs when the disease or exposure status of a horse is misclassified. For example, an owner may inadvertently misrepresent the frequency of deworming or history of previous surgery for colic, perhaps because he was not aware of the entire life experiences of the horse. Disease status also can be misclassified in studies. For example, among horses that do not undergo celiotomy or necropsy, diagnosis of duodenitis/proximal jejunitis (DPJ, also commonly known as anterior enteritis) is based on physical and laboratory findings. Because of the inherent inaccuracy in a clinical diagnosis of DPJ, even the most experienced clinician may misdiagnose a horse with another condition as having DPJ. Consequently, case-control studies of DPJ must be interpreted with the understanding that some horses diagnosed with DPJ may not have the condition, and some horses classified as controls that have signs similar to those of DPJ (e.g., ileal impaction) may actually be cases of DPJ. If misclassification of disease status is unbiased (nondifferential) with respect to exposure status, the impact of the misclassification is often not severe in terms of interpretation of findings, and some simple adjustments for misclassification can be made; the same is true with respect to misclassification of exposure, if it is unbiased with respect to disease. When misclassification is more likely among exposed horses (e.g., a diagnosis of DPJ is more likely to be made if a horse is fed a high concentrate diet), the impact of misclassification can be important.

When reading results of case series and epidemiologic studies, it is imperative that readers consider possible sources of bias with respect to exposure status and disease status. Failure to consider these sources of bias may result in misinterpretation of findings and conclusions that can be drawn from studies. Conversely, presence of bias does not invalidate all results of a study. Although observational studies may have flaws or uncertainties because of natural variability, the end result of critical appraisal should not be to discount or reject all findings of any study that has flaws.

Incidence of Colic

Reports of the incidence of colic are relatively rare.[3-8] Generally, reported risks have ranged ranged from 3 to 10 episodes of colic per 100 horse-years of observation (i.e., 10 cases of colic in 100 horses observed for 1 year); however, the incidence can vary significantly among farms and even within farms over time. In a study of 3 horse farms in North Carolina, the reported incidences ranged from 5 to 46 episodes per 100 horse-years.[8] The incidence of colic is likely strongly influenced by management practices that occur at the farm level. Variability is likely greater in the incidence of colic among farms than among horses. Thus, colic incidence should be considered both within and among farms (or other housing facilities such as training centers, racetracks, etc.), and estimation of the incidence of colic should consider farm-level clustering. Moreover, comparisons in incidence among regions, studies, years, etc. should account for this farm-level clustering in the incidence of colic.

Factors that Predispose to Colic

In this section we attempt to summarize what is known about factors that predispose to colic as a general diagnosis (Table 14-2). In some instances, risk factors for specific forms of colic are discussed; however, a review of factors that predispose to the wide array of specific types of colic is beyond the scope of this chapter.

Factors Related to Signalment

No clear evidence exists that any traits included in a horse's signalment predispose colic. No breed has been unequivocally demonstrated to be at increased risk of colic. A descriptive report of horses with colic failed to identify any breed as overrepresented.[9] It has been proposed that miniature horses are predisposed to fecalith development.[10] Arabians have been identified as being at increased risk of colic in several studies.[11-15] Other reports have suggested that Thoroughbred horses may be at increased risk of colic.[7,16] Standardbred horses have been suggested to be either at increased risk of colic[17] or decreased risk for surgical colic.[15] Differences in study design, region, and horse populations may explain the discrepancies among studies. Considering only a single factor such as breed without accounting for other factors that may be related both to breed and to colic (e.g., activity level or diet) may result in spurious associations because of confounding.

Sex of the horse has not been clearly established as a risk factor for colic. Stallions were found to be at increased risk in one study,[4] and geldings were at increased risk for recurrent colic in another study.[18] Other studies have not found any association of sex with colic.[6,14] Risk of colic may vary by sex for specific types of colic; for example, male horses have been identified as being at increased risk of entrapment of small intestine in the epiploic foramen.[15]

Results of the association of the risk of colic with age have been variable among studies. Some reports indicate that horses younger than10 years are at increased risk of colic.[19,20] One report indicated that foals (horses younger than 6 months) were at decreased risk.[7] Evidence exists that the risk of colic increases with increasing age.[4,14,21] Differences among these studies in study design, population of horses studied, and methods of data analysis likely explain these conflicting results. Moreover, the relationship of age with risk of colic appears nonlinear,[22] and this complexity, though often overlooked, should be accounted for in analysis. Finally, association of age with colic can vary according to the lesion: older age has been identified as a risk factor for colic associated with strangulating lipoma but not epiploic foramen entrapment.[23]

Table 14-2
Factors that Predispose to Colic (see text for details)

Factor	Citation(s)
Breed	7,11,13-17
Older age	4,14,19-22
History of previous colic	11,16,20-24
Cribbing/crib-biting	24,26,27
Change in weather	16
Diet change	11,14,16,19-21
Feeding large amounts of concentrate	14,16,20
Round bale hay	16
Reduced availability of potable water	11,14
Change in activity or stabling	11,21
Activity level	3,4,11,20,21,24
Reduced time at pasture/Increased time in box stall	11,16,21,24,25
Recent transport	24
Absence of regular deworming	8,14,16,21,24
Tapeworms	37
Absence of regular dental examinations	24

Factors Relating to Anamnesis

Both a history of colic and a history of surgery for colic have been demonstrated to be associated with horses being at increased risk of colic.[11,14,20,24] Although these are not alterable risk factors, these findings are important information for veterinarians to share with owners of horses that experience colic or undergo surgery for colic. Some common forms of colic have been demonstrated to have a high prevalence of recurrence.[25]

Cribbing (crib-biting) has been associated with simple colonic obstruction or distension, epiploic foramen entrapment, and gastric ulceration.[24,26,27] Physiologic explanations have been offered for these associations, such as aerophagia leading to increased intraintestinal gas and changes in intraabdominal pressure. It may be that cribbing is a marker for some other factor (such as being predominately stalled, lack of turn-out, etc.).

The results of two studies have indicated that horses are at reduced odds of colic when owners provide care for horses, relative to horses cared for by someone other than the owner.[3,14] This finding is plausible because owners may provide better health care for their horses. Alternatively, it is possible that the density of horses (i.e., number of horses per acre) or activity level is generally less for horses that are cared for by their owners relative to horses cared for by someone other than their owner. Another possible explanation for this association would be that caretakers other than owners monitor horses more closely or have greater contact with horses on a daily basis such that signs of colic are more likely to be detected by caretakers other than owners.

Many equine veterinarians and horse owners perceive that the incidence of colic is increased with certain patterns of or changes in weather. Several studies have failed to identify an association between weather conditions or changes in weather and colic.[19,28,29] A seasonal pattern in the incidence of colic has been described by some studies.[3,30,31] One study documented an increased risk of colic among horses that experienced a significant change in weather conditions during the 3-day period prior to examination;[16] however, the specific climatic changes were not determined, and this association could have resulted from a recall bias. Thus, epidemiologic evidence of an association between weather and colic is conflicting.

Determining feeding history is important for evaluation of horses with colic. Changes in the type of concentrate or the type or batch of hay or pasture grass have been associated with increased risk of colic.[11,14,16,19-21] Horses fed relatively large amounts of concentrate also appear to be at increased risk for developing colic.[14,16,20] Feeding hay in round bales has been identified as a risk factor for colic.[16] Coastal Bermuda grass hay has been associated with ileal impactions in areas of the United States where it is fed.[32] Provision of fresh, potable water is important to prevent colic. Surprisingly, evidence documenting this importance is exiguous.[11,14]

The way horses are housed can influence the risk of colic. Several studies have demonstrated that the amount of time horses have to graze is inversely related to the risk of colic. Studies indicate that the duration of hours stabled is associated with greater odds of colic.[11,21,24] A number of markers for exposure to pasture grazing (e.g., the number of acres used for horses and the percent of time spent at pasture) have been demonstrated to increase the odds of colic.[11,16,21] Although not a controlled study, Dabareiner and White documented that a large proportion of horses with large-colon impaction had a history of being removed from pasture and confined to a stall prior to developing impaction.[25] Evidence exists that prevalence of gastric ulceration is lower among horses maintained in pastures than in horses maintained in stalls.[33] Clearly, grazing pasture is not without risk. Horses turned out into lush pastures are at increased risk of colic.[19] Some diseases such as grass sickness result directly from pasture grazing.[34] In a study of training yards in the United Kingdom, it was observed that the risk of colic was greater on premises with a larger number of horses.[3] The reason for this association was not determined, but it is possible that access to pasture or grazing was less for horses from yards with large numbers of horses, or that the density of horses increased the risk of colic.

Changes in stabling/housing management have been associated with increased risk of colic;[11,21] unfortunately, these studies did not examine which specific stabling changes predisposed horses to colic. Change in stabling is often closely related to changes in level of activity.

Activity level has been demonstrated to be associated with colic in a number of studies, although the specific type of activity or change in activity has varied among studies.[3,4,11,20,21,24] This may be partially explained by the fact that a variety of activity levels and changes in level may contribute to increased risk of colic.

Evidence exists that recent (within the previous 24 hours) transport increases the risk of simple colonic obstruction or distension.[24] Although a study in Texas found no association between colic and either history of recent transport or the number of miles transported,[11] it is plausible that transport may predispose to colic when horses become dehydrated, immobile, and possibly stressed during transport.

Preventive Health Care

Although it is intuitive that parasites that infect the gastrointestinal tract can cause colic, results of studies of colic and parasite control programs have yielded conflicting results. Some studies have failed to document an association between parasite control programs and colic.[3,11] Several studies have documented a reduction in colic for horses receiving regularly administered anthelmintics or, specifically, anthelmintics to eliminate tapeworms.[8,14,16,21,24,35-38] Some studies have associated increased risk of colic among horses receiving recent deworming,[21] increased number of dewormings,[4] or rotation of anthelmintics.[7]

Although these conflicting results may seem confusing, each of the results is plausible. Lack of association between colic and anthelmintic administration might occur because anthelmintics were regularly administered to most horses in these studies. An association of reduced occurrence of colic with anthelmintic administration would be expected because of intestinal pathology associated with parasite infestation. Increased risk of colic among horses receiving anthelmintics is biologically plausible because killing intraluminal parasites can trigger problems such as obstruction with ascarids in older foals or emergence of encysted small strongyles.[39-41] Such associations, however, could also be spurious. People whose horses have colic might be

more likely to recall events such as administration of an anthelmintic than owners of horses that are healthy or have a problem that they might not associate with deworming (e.g., skin laceration). Alternatively, it is possible that horses with colic received anthelmintics as a treatment for colic, such that the anthelmintic was an effect rather than a cause of the disease.

Poor dentition might be expected to predispose to colic. Surprisingly, data documenting an association between dental care and reduced risk of colic are lacking. In one study, no association between frequency of dental care and colic was observed;[11] however, most horses in that study received dental care at least annually. More recently, risk of simple colonic obstruction or distension was inversely related to the frequency of dental examination.[24]

Factors Indicating the Need for Surgical Management of Colic

Rapid and accurate assessment of whether horses with colic need surgical management is an important and often difficult decision facing equine practitioners. Interpreting diagnostic findings and predicting therapeutic plans and responses for individuals are largely based on projecting findings derived from groups of similar patients. Thus, epidemiologic principles and methods for studying groups of patients have great application to improving clinical decision-making. Attempts have been made to predict the need for surgery among horses admitted to referral hospitals by studying patient populations.[42-46] Models to predict the need for surgery based on data from horses admitted for the treatment of colic to teaching hospitals have been developed by a number of investigators. Discriminant analysis was used to derive a decision-tree (similar to an algorithm) for determining the need for surgery among horses with colic.[43-44] Factors included in the decision-model were the extent of abdominal distension (none or mild versus moderate or severe), rectal examination (no anomalies, impaction, or other problems versus distension of small or large intestine), and color of abdominal fluid (normal/cloudy versus serosanguinous). This study was noteworthy because the variables considered in the model were based on findings of physical examination or visual inspection of peritoneal fluid. Usefulness of the model suffered from a specificity of 55%, indicating that about 45% of horses that did not require surgery would be subjected to surgery.

Reeves et al used logistic-regression modeling to derive a predictive model for the need for surgery in horses with colic.[45] Variables selected for the predictive model were age, breed, sex, rectal findings (normal versus abnormal), intermittent signs of pain (yes or no), continuous signs of pain (yes or no), strength of peripheral pulse (normal or weak), and increased abdominal sounds, decreased abdominal sounds, or absence of abdominal sounds. The model was developed by analysis of data from 640 horses with colic from 10 veterinary teaching hospitals in the United States; the model was then validated by application to another 629 horses from these same hospitals. The model also was independently evaluated by the authors using horses from 5 teaching hospitals, 5 private referral hospitals, and 10 equine ambulatory practices that had not participated in the original study.[46] Results of validation indicated that the model tended to overestimate the need for surgery.

Attempts to apply models for predicting the need for surgery (or survival) developed at specific referral centers to other populations, particularly to general private practices, is problematic and generally unsatisfactory. Several reasons exist for this. First, the positive predictive value of a test (probability that a positive test result is from an animal with the disease) is strongly influenced by the prevalence of disease. Thus, applying models for determining the need for colic surgery that have been developed in settings where the prevalence of surgical colic is relatively high (referral centers or teaching hospitals) to settings with lower prevalence of surgical colic will result in poor performance of the model. Moreover, techniques for medical and surgical management vary among regions and change over time. Similarly, types of colic may vary by region (e.g., enteroliths are more prevalent in California than in many other states). These temporal and geographic differences may reduce the accuracy and performance of such models.

The site and type of intestinal lesions causing colic often influence the decision for surgery. Blikslager and Roberts studied the accuracy of interns and residents in predicting the site and type of lesion in horses with colic admitted to a teaching hospital.[47] Results indicated that interns and residents could more reliably identify small intestinal disorders than large intestinal disorders (i.e., more false-positive results predicted the large intestine as the affected segment of the intestinal tract). Horses with devitalized bowel are more likely to need surgery. With regard to predicting whether intestinal obstruction was accompanied by devitalized bowel, the accuracy of interns and residents was less than that for predicting the affected site (small versus large intestine). When site and presence of devitalized bowel were considered concurrently, prediction of large intestinal obstruction without devitalized bowel had the poorest overall accuracy; predicting large intestinal obstruction with devitalized bowel had a positive predictive value of 27%, indicating that many horses were incorrectly predicted to have devitalized bowel. These findings underscore the difficulty in determining viability of the affected portions of the intestinal tract in horses with large colon obstruction, particularly when based on clinical impression alone.[48]

Several studies have examined values measured either in serum or peritoneal fluid to predict the need for surgery (and to predict survival). To date, however, none of these tests has been documented to be sufficiently sensitive, specific, or available to render it widely useful. Serum and peritoneal fluid concentrations of phosphorous were significantly higher among horses that had extensive intestinal lesions that required resection or euthanasia than among horses with colic that underwent laparotomy without resection, horses with colic that were managed medically, or horses that were apparently healthy.[42] The sensitivity and specificity of the tests were less than 80% in the population studied, and the predictive value of using phosphate concentration as a test to differentiate between these groups would vary with prevalence of extensive intestinal lesions. The prevalence of severe lesions requiring resection would be much lower in general practice than at the referral center where the study was performed, such that many horses predicted to have severe intestinal lesions requiring resection or euthanasia by this test would not, in fact, have lesions requiring resection or euthanasia.

Another study examined the sensitivity, specificity, and predictive values of various parameters of peritoneal fluid (specific gravity, RBC concentration, color, and turbidity) for predicting the need for surgical treatment (and lesion type and patient outcome).[49] None of the parameters proved clinically useful for predicting the need for surgery.

Concentrations of nucleated cells and neutrophils in peritoneal fluid were significantly lower in horses with colic that were managed medically than in horses that were managed surgically and did not survive, but these concentrations did not differ significantly between the former group and horses with colic that underwent surgery and survived.[50] Activity of trypsin in peritoneal fluid was significantly higher among horses with strangulating small intestinal lesions when compared with horses with nonstrangulating lesions of the large intestine (in which activity was uniformly absent).[51] Currently, availability of trypsin assays and the small number of horses studied (N=35) render these findings of limited clinical usefulness.

It is generally considered that reddish-colored (serosanguinous) peritoneal fluid in horses with colic indicates a lesion with vascular compromise and that this finding is an indication to consider exploratory surgery. Because visual inspection may not be as sensitive as chemical analysis for the presence of hemoglobin for detecting red cells in peritoneal fluid,[52] the sensitivity and specificity were determined for a spectrophotometric assessment of hemoglobin in peritoneal fluid for differentiating horses with colic that required surgical treatment from those that were treated medically. Using a cut-off value of 0.01 mmol/L of hemoglobin, the test had a sensitivity of 80% and specificity of 82% among 35 horses with colic that underwent surgery and 39 horses with colic that were treated medically. Given that the prevalence of surgical lesions was almost 50%, the positive predictive value of the test would not be expected to be high for horses with colic seen in general practice where the prevalence of surgical lesions likely would be less than 5%.[4,6,7]

Frequency of and Factors Associated with Survival from Colic and Colic Surgery

Survival of horses with colic and colic surgery is difficult to summarize because survival is influenced by many factors, including the type of lesion. Among horses with colic seen in general practice and those with medically managed colic, the proportion that survive is generally greater than 85%, with some reports indicating proportions of horses recovering of more than 95% for colic cases seen in general practice.[3,4,6-8,11,19,21,25,28,43] For horses that undergo surgery for colic, short- and long-term survivals have been reported. The proportions surviving from colic surgery generally have been considered as either overall survival or survival among horses that have recovered from anesthesia. With respect to the latter, short-term survival proportions have ranged from 36% to 91%, depending on lesion location.[53-61] Many recent reports indicate that short-term survival for horses undergoing surgery for colic is greater than 80% for both small intestinal and large intestinal lesions, including large colon volvulus.[23,59] There are few reports of long-term survival (1 year or more) for horses undergoing surgery for colic, but cumulative probabilities of survival have ranged from 34% to more than 90%, depending on the the age of the horse and the type and location of the lesion.[53,57,59,61-63] Long-term survival is generally worse for horses with strangulating small intestinal obstruction (particularly epiploic foramen entrapment), horses undergoing resection and anastomosis, and horses that undergo more than one surgery for colic.[53,59,60]

Determining the prognosis for survival among horses with colic is important because of the financial and emotional cost of treatment and the desire to minimize unnecessary suffering in horses with colic. Several studies have identified individual factors that differ significantly between survivors and nonsurvivors of colic. Duration of clinical signs of colic, temperature, heart rate, skin tenting, absence of intestinal motility, PCV, serum protein concentration, white blood cell count, concentration of white blood cells or protein in peritoneal fluid, gross appearance of peritoneal fluid, activities of ATIII and trypsin in blood or peritoneal fluid, procoagulant activity in blood, fibrinolytic activity in blood and peritoneal fluid, serum lactate concentration,

and anion gap are examples of factors found to differ significantly between colic survivors and nonsurvivors.[41,42,44,59,64-69] For many of these variables (e.g., heart rate and PCV), some studies have yielded conflicting results. Survival from colic also has been described to vary by anatomic site of the intestinal lesion and whether the lesion is strangulating or nonstrangulating. Horses with small intestinal lesions tend to have a poorer prognosis than do horses with large intestinal lesions, and horses with strangulating obstructions are less likely to survive than are horses with nonstrangulating lesions.[13,41,47,49,67,69,70] Among horses undergoing surgery, significant prognostic factors associated with surgery include the time from onset of signs until surgery, duration of surgery, the amount of small intestine resected, and the type of anastomosis performed.[67,71]

Multivariate predictive models have been developed to estimate the probability of survival for horses with colic.[13,46,69-72] The rationale for developing these predictive models is so that they can be applied as a diagnostic or prognostic test, whereby the probability of survival can be calculated by a clinician and used by clinicians and clients for making clinical decisions.

Reeves et al developed a multivariate prognostic model for horses with colic, using data from 1,279 horses with colic examined at 10 referral centers from 1985 and 1986.[45] A statistical model for prognosis was developed using the following variables: age, sex, breed, strength of peripheral pulse (normal or weak), pulse rate, treatment (medical or surgical), PCV, self-inflicted trauma (present or absent), and capillary refill time. The model was validated by application to 335 horses derived from the same reference population during the same time period. The model was shown to fit the original data set well, but fit the validation set poorly. The same model was subsequently validated using horses from 5 university hospitals, 5 private equine referral practices, and 10 equine ambulatory practices that had not participated in the original project;[46] results of this study indicated a good fit for the prognostic model.

Using data from 165 horses with colic admitted to a teaching hospital, Furr et al developed a severity score for predicting the outcome of colic.[72] Variables used to determine the severity score were those that best predicted survival, using logistic-regression methods. The variables used for determining the severity score for a horse were pulse rate at admission, concentration of protein in peritoneal fluid, blood lactate concentration, and appearance of mucous membranes. The model was validated in a second group of 71 horses. In the validation group, the test had a sensitivity of 67%, specificity of 100%, a positive predictive value of 100%, and negative predictive value of 92%. These results indicated that the test performed well in a similar population of horses to that for which the model was developed and where the mortality proportion was about 21%. The large proportion of false negative results indicated that some horses predicted to live had, in fact, died. Prognostic factors were studied using survival analysis methods in a prospective study of 341 horses that recovered from colic surgery at the University of Liverpool.[59,60] This model identified epiploic foramen entrapment, PCV, length of intestine resected, time from onset of signs to surgery, and duration of surgery to be associated with survival from surgery. A noteworthy finding was that horses with epiploic foramen entrapment have poorer survival. This finding underscores the difficulty in predicting outcome prior to knowledge of the specific lesion. Some of the variability in performance of prognostic models may be attributable to variation in the prevalence of certain types of lesions among populations of horses.

The quality and objectives of studies to develop predictive models for prognosis (and need for surgery) for horses with colic are excellent; however, these models have limitations. The principal limitation is that it may not be possible to apply a given model to other populations of horses where the prevalence of severe colic is different, because the difference in prevalence will affect performance (i.e., the positive predictive value) of the test. Moreover, the best-fitting variables derived from the study of horses examined at a teaching hospital may differ from those identified by similar study of horses examined in general practice. Thus, application of these models by many equine practitioners may yield disappointing results. Use of these models requires familiarity with the components of the model and calculation of probabilities using mathematical equations. Often, persons examining horses with colic are not familiar with the models or how to calculate the predicted probabilities. Simple programs to perform these calculations that run in personal digital assistants (PDAs) or laptop computers might increase the use of such models. Owners and veterinarians are either unfamiliar or uncomfortable with probability theory and computation of prognosis. Furthermore, methods for diagnosis and management of colic continue to evolve such that the variables selected in 1986 may differ from those that would be important in 2008; predictive models must be continually evaluated for accuracy. Despite these limitations, the concept of seeking predictive models for survival from colic is worthwhile. Quantifying our clinical observations will almost invariably improve our knowledge and assessment of our performance.

Study of Colic Problems in Individuals and Herds

Epidemiology is a population-based science, and it is often considered to be a basic science of primary importance for preventive medicine and public health. Increasingly, epidemiology is recognized as a basic science of clinical medicine. Primary activities as clinical veterinarians include interpreting findings of anamnesis, physical examination, other diagnostic testing, and determining treatment and prognosis for our patients. In doing so, we rely on epidemiologic principles (such as understanding the principles of sensitivity, specificity, and predictive values in assessing accuracy of diagnostic tests). Moreover, we rely on information and evidence derived from epidemiologic studies. The latter is often referred to as evidence-based medicine.[1] The primary goal of evidence-based medicine is to integrate individual clinical expertise with the best available external clinical evidence. Individual clinical expertise is considered to be the proficiency and judgment that results from practice experience. The best available external clinical evidence refers to clinically-relevant findings that are primarily derived from research. Patient-centered research studies (i.e., epidemiologic studies) are considered to be the most relevant and important source of evidence.[1] Although a wide-range of valid and useful sources of clinical evidence exist, including experiences of our teachers and coworkers, textbooks, continuing education seminars, journal articles, websites, etc., not all these sources of information are considered to be of equal value. Controlled studies are preferable to uncontrolled studies. For example, a case-control study is generally considered superior to a case series. Furthermore, patient-centered research is preferable to studies involving experimental disease, particularly when experimental studies are conducted in species other than the horse. Thus, patient-centered epidemiologic studies provide the best source of evidence for making clinical decisions about colic. For example, our assessment of prognosis for a particular horse with colic should be based on our previous experiences with similar patients and epidemiologic studies of prognosis.

Epidemiologic principles and methods also apply to investigation of outbreaks of colic at farms.[73] As mentioned, the incidence of colic is probably best considered at the level of individual farms because considerable variability exists among farms in the incidence of colic and in the distribution of predisposing factors for colic. Although a review of methods for outbreak investigation is beyond the scope of this report, the topic has been reviewed.[73]

When initiating a study, it is important to verify the diagnosis of colic, to establish that the colic cases are similar, and to determine a case definition (Table 14-3). Case definitions should be based on clinical signs and, whenever possible, additional diagnostic information such as clinicopathologic or pathologic data. One should determine the magnitude of the problem (number of cases among horses at risk). When available, it is helpful to have information about the cumulative incidence of colic at a farm. An apparent outbreak may represent a clustering of rare events that appear to be temporally related simply by chance. Alternatively, the frequency of colic events may be in excess of what would be expected at the farm.

It is helpful to consider the temporal and spatial pattern of colic episodes to determine probable sources of exposure. Investigation of outbreaks generally entails investigation to determine characteristics that distinguish affected horses from unaffected horses. Attack rates can be determined for various exposures (number of cases of colic per number of horses exposed), along with temporal and spatial analyses. It is generally useful to collect samples of concentrates, hay, and water as soon as possible. Similarly, it is ideal to collect information about exposures (e.g., pasture exposure) as close as possible to the time of the outbreak. Collecting samples and data retrospectively can result in loss of critical sources of information.

It is important for veterinarians and farm owners to recognize that not all outbreak investigations will be rapidly or definitively resolved. It can take years of extensive and expensive investigation to solve the reason for outbreaks (consider the experiences with Legionnaires disease, or the mare reproductive-loss syndrome[74]). Despite considerable efforts, one may not be able to definitively determine the cause(s) of an outbreak. Nevertheless, investigation of farm outbreaks is often necessary and can successfully determine a cause or identify methods of preventing recurrences.

Table 14-3
Factors to Consider During a Farm Outbreak

1. Case definition: what form(s) of colic are observed?
    a. Clinical and, when applicable, laboratory findings

2. Determine the attack rate: number of horses affected/number of horses at risk
    a. Is this above what might be expected?
    b. Past records may be useful for comparative purposes

3. How are the cases clustered in time and/or space?

4. Determine dietary/feeding practices:
    a. Types, sources, and amounts of concentrate and hay
    b. When possible, collect specimens of feedstuffs

5. Examine watering practices/sources

6. Examine characteristics of individual affected horses:
    a. Compare with similar information about unaffected horses to identify incriminating factors
    b. Factors should include the following:
        i. Age
        ii. Breed
        iii. Sex
        iv. Duration of residence at farm
        v. Stabling (where, how long stalled, changes, etc.)
        vi. Feeding practices (what fed, how much fed, changes, supplements, etc.)
        vii. Source(s) of water
        viii. Deworming practices
        ix. Cribbing/crib-biting status
        x. Climatic conditions
        xi. Activity/use of horse (including frequency, recent changes, etc.)
        xii. History of previous colic and colic surgery
        xiii. Recent transport
        xiv. Any other changes at the farm or in the farm environment

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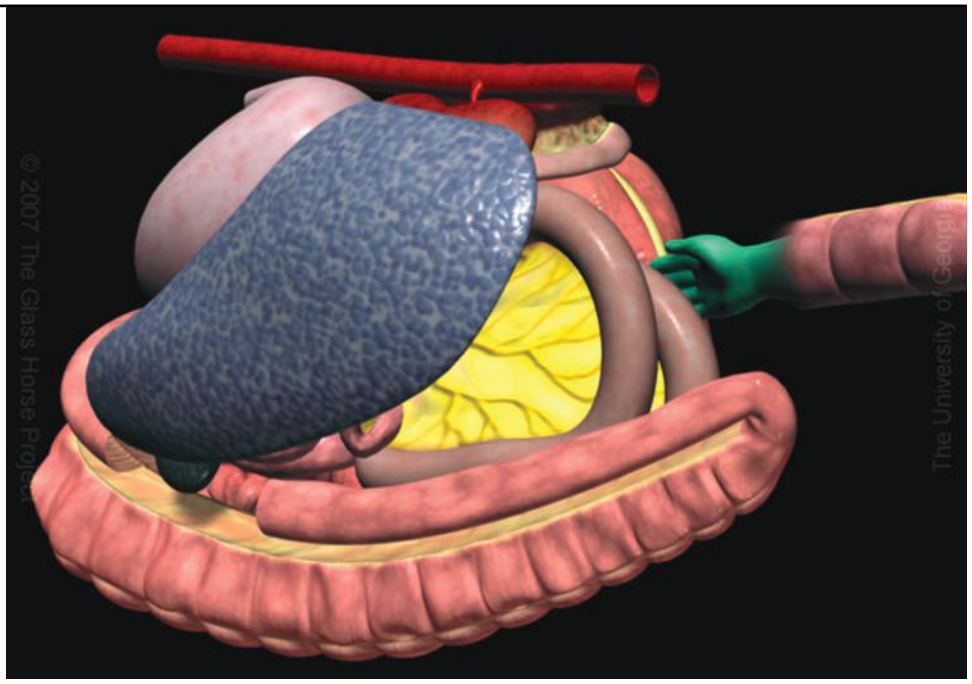
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Diagnosis

Part 5



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Diagnosis of Gastrointestinal Disease

Chapter 15

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Colic is one of the most common emergencies faced by veterinarians. Because it can be a life-threatening emergency, affected horses must be treated promptly, both for the welfare of the animal and to ease the owners' distress. It can be difficult to reach a definitive diagnosis, especially at the first examination; however, a thorough examination should be performed in every case to determine what emergency treatment should be initiated and to decide whether the horse requires surgery or intensive care. A great many horses recover spontaneously or respond to the first treatment. A cross-sectional study of colic in Thoroughbred horses revealed that of all the colic episodes recorded at training premises, spontaneous recovery occurred in 28.7% of the cases and medical recovery in 63.1%.[1] Some horses, however, will require surgery, which may be the optimal or the only possible treatment. A timely decision increases the chance of a successful outcome, minimizes patient morbidity, and potentially decreases complications.[2] Early identification of the horse that requires surgery and rapid assessment of the necessary treatments are paramount in salvaging the critically ill horse.[2] Cardiovascular parameters indicate an increased risk for several post-operative complications after an acute abdominal crisis, possibly in response to endotoxemia.[3] Thus, early referral of colic cases before endotoxic shock develops may minimize the risk of post-operative complications.[3]

During the examination for colic at the farm or stable, the veterinarian must decide if appropriate treatment can be completed on the premises, or if the horse needs to be transported to a hospital facility for further diagnostic procedures or treatment. A definitive diagnosis simplifies the decision for surgery or referral, however determining a diagnosis can be difficult when conflicting clinical signs are present. Determining which disease category exists based on clinical signs helps to make the decision.[4] If the horse is in severe pain and endotoxic shock, the examination may have to be shortened and prompt emergency medical treatment initiated to stabilize the horse for possible transport to a referral hospital. Even in the patient with mild signs, a thorough examination is vital so that a more serious disease is not overlooked as some horses may be stoic and with certain advanced diseases, such as those involving the small intestine or small colon, depression may replace pain as the primary sign. The following list of disease categories should be used when assessing the equine acute abdomen (Table 15-1).

Once the category of disease is established, the veterinarian can decide on immediate treatment, transportation to a referral facility if necessary and whether surgery is required.[5] If there is uncertainty about the horse's condition or the need for surgery, the horse should be referred to a hospital facility where the decision for surgery can be made by a veterinarian who makes these decisions frequently.[5] There has been a significant improvement in the survival rate after colic surgery over the past 20 years, and whilst this can be regarded as the natural result of the advancements in all aspects of colic management, early referral is one of the most important determinants of outcome.[6]

Table 15-1
Classification of Disease Categories Causing Equine Colic.

1. Idiopathic colic (mild abdominal pain with no distinguishing features)
2. Tympany
3. Nonstrangulating/simple intestinal obstruction
4. Strangulating intestinal obstruction
5. Nonstrangulating infarction
6. Peritonitis
7. Enteritis
8. Ulceration
9. Pain from another organ system (e.g., musculoskeletal, pulmonary, urogenital)

Signalment

Signalment may be helpful in identifying certain problems. A horse more than 10 years of age with small intestinal distention has a high risk of having a strangulating lipoma,[7] whereas a foal between 2 and 4 months of age with small intestinal distention is likely to have a volvulus.[8] The commonest cause of colic in the neonate is meconium impaction. Ileocecal intussusceptions are most common in horses 6-18 months old. Arabian,[9] Arabian crosses,[9] Morgans,[9] American Saddlebreds,[9] and miniature breeds[10] have an increased risk of developing enteroliths. Female ponies and American miniature horses are more predisposed to small colon impaction compared with other breeds in one population.[11] Standardbreds and some warmblood breeds have an increased risk of inguinal/scrotal hernias.[12] Paint foals, from a dam and sire which both carry the Overo lethal white syndrome gene, will be born with ileocolonic aganglionosis and functional obstruction of the intestine.[13]

History

It is essential that the veterinarian asks the owners or employees of a farm looking after the horse direct questions to obtain accurate information. Information may be withheld if a mistake has been made in the management, therefore the veterinarian should interpret answers carefully when taking the history.

The three general areas of the history that need to be collected include (1) the general history of the husbandry and management, (2) the recent husbandry and management, and (3) the individual history of the case in question[5] (Table 15-2).

Table 15-2
Historical Information for the Horse with Colic.

General Historical Data

1. Habitat
2. Feed
3. Daily Routine
4. Horse Use
5. Medical History
6. Parasite Control
7. Dental Care
8. Crib biting/Windsucking

Recent Historical Data

1. Duration of Colic
2. Last time fed
3. Consumption of feed and water, composition of diet
4. Recent change in feed, water, medication, housing, bedding, travel, exercise routine, horse companions, weather.

Disease Related Historical Data

1. Degree and change in pain
2. Last defecation
3. Sweating
4. Clinical signs seen-pawing, rolling, kicking abdomen, turning to flank, staying recumbent, rolling on back, depression, grinding teeth
5. Whether relief is gained from walking
6. Response to treatment
7. Previous colic episode or abdominal surgery

The general history is related to the conditions on the farm where the horse is kept. This information may already be known by the veterinarian if he or she visits the farm regularly. The horse's environment also is important. For example, if the horse has been moved to a new pasture, gas production in the large intestine may have been increased, resulting in tympany or displacement, or the horse may have been exposed to foreign objects such as rubber or bailing twine that may cause an obstruction in the small intestine or small colon. A horse that is on sandy soil may ingest large quantities of sand, especially during the summer or during low rainfall months when the pasture is short or scarce. Horses in this environment are at risk of developing sand colic. Information about poisonous plants present on the property should be investigated because certain conditions (e.g., overgrazing, drought, specific herbicide use, or masking of plants in hay, silage, or grain) may have favored ingestion of toxic plants.[14] Certain environmental conditions may also have altered toxin concentrations in plants, such as soil type and content, use of herbicides,[15] over-watering or drought, use of fertilizers, and sunlight.[14,16] The time of year in conjunction with access to certain fruits or plants within the environment may be important. For example, horses in specific geographic areas that have access to persimmon fruit may develop intermittent signs of mild to moderate abdominal pain associated with ingestion of persimmons in the fall after the ripe fruit falls to the ground.[17] In addition, certain geographic regions of the United States, for example California, and throughout the world have a high prevalence of intestinal obstruction caused by enteroliths.

Information on whether the horse is housed with other horses, and the persons responsible for the primary care is important. Interesting associations have been found between the horses' environment and the number of episodes of colic (see Chapter 14). An investigation into colic in horses in Thoroughbred training premises in the British Isles found a significant association

between the number of episodes of colic and the number of horses on the premises.[1] After correcting for the number of horses, an increased risk of colic was associated with premises that were training establishments for flat racing. In contrast, a decreased risk of colic was associated with the owner being the sole person caring for the horse rather than having a horse housed at a combined breeding and training establishment. Information acquired in the history may not lead to the diagnosis, especially in the case of a simple obstruction or displacement, but it must be recorded, because of the possibility that a problem may exist that affects other horses on the premises.

The horse's day to day routine should also be recorded, as certain feeding and housing patterns have been associated with an increased risk of colic. Recent changes in the batch of hay being fed, decreased exposure to pasture, recent changes in the type of grain or concentrate fed, feeding more than 2.7 kg of oats per day, and feeding hay from round bales have all been found to be associated with an increased risk of colic. Stabling for 24 hours a day has also been shown in the United Kingdom to increase the risk for simple colonic obstruction and distention in horses.[18] Horses spending more than 50% of their time indoors and horses fed alfafa hay have an increased risk of developing enterolithiasis.[10] The feeding of Coastal Bermuda hay and the quality of this particular hay has been suggested as a cause of ileal impaction.[19] Any changes in the horse's routine should be recorded, including exercise, feed, travel, and medications. Medications include anthelmintics and drugs, such as nonsteroidal anti-inflammatory drugs or antibiotics, which may have toxic side effects. Administration of anthelmintics may reduce the overall frequency of colic episodes; however, administration of anthelmintics has been shown both to predispose some horses to colic[20] and to decrease the risk of colic.[21] The type of anthelmintic administered is also important. For example, horses that have not been treated with a pyrantel salt that is efficacious against tapeworms may be at an increased risk for ileal impaction, especially if also fed Coastal Bermuda hay.[19]

A recent history, including any previous colic episodes, colic surgeries, illnesses, prolonged treatments, vices, and pregnancy should be noted. The specific patient history may help determine the list of differential diagnosis. The following is a list of questions that should be asked during the examination[5]:

1. When was the last defecation and what was the character of the feces?
2. Has the appetite been normal, and when did the horse last eat?
3. How much water has the horse been consuming recently?
4. How severe has the pain been, and has it increased, decreased, or stayed the same, and for how long?
5. Has the horse had a specific behavior such as playing in its water or lying on its back?
6. Could the horse have ingested anything unusual such as too much feed, chemicals, or toxic plants?
7. Has the horse been treated with anything recently either for colic or another disease?
8. Has the horse had colic previous to this episode?
9. Does the horse have any vices such as cribbing?

The information gleaned from the answers to these questions will allow the veterinarian to judge the duration of the colic, severity of symptoms, hydration status, and possible events that may have led to the episode. This may not lead to a specific diagnosis, but it can help the veterinarian to decide the most appropriate treatment. For example, acute, severe pain of short duration in a dehydrated horse may indicate a severe lesion such as a large colon volvulus, whereas mild to moderate pain over several hours or days in a dehydrated horse may be indicative of a large colon obstruction. Descriptions of the risk factors and related historical information on the specific diseases can be found in Chapter 14.

Physical Examination

The majority of decisions regarding disease severity, prognosis, and treatment are made on the basis of clinical signs. Table 15-3 outlines the steps of the physical examination and the order in which they are normally performed.

Pain

When first seen, especially in hospital settings, many horses with colic are restrained or walked by a handler. This can make it difficult to assess the level of pain because the horse is not familiar with the surroundings and may be more concerned with the new environment than with its pain. If evidence of pain is not present, the horse can be placed in a stall or paddock without restraint and observed. This should be done prior to administering analgesics or at the end of the examination to assess the level of pain. In some cases, previously administered medications will have not been metabolized and this may make accurate assessment of the animal's current status difficult. For example, if the horse is still sedated, depression and bradycardia may be present, which are not representative of the disease process.

Table 15-3

Sequence of the Physical Examination for the Horse with Colic.

1. Pain-severity; continuous, or intermittent
2. Attitude-depression, alertness, pain
3. Physical Condition-body condition and evidence of trauma
4. Temperature-hyperthermic, normal, hypothermic
5. Pulse-quality and rate
6. Respirations-rate and effort
7. Mucous membranes-color and capillary refill time
8. Nasogastric intubation-gas, fluid reflux, color and pH
9. Auscultation-borborygmi, intensity and rate, tympany
10. Percussion-ballottement of gas
11. Rectal Examination-bowel distention or displacement, peritoneal surface, mesenteric pain, masses, urogenital abnormalities
12. Abdominal Ultrasound-motility, distended small intestine, presence of excessive peritoneal fluid, presence of sand, bowel wall thickness, etc
13. Abdominocentesis-color, turbidity, cell count, protein, presence of bacteria

A fractious young horse or one in a great deal of pain may need to be sedated to complete the examination, but this horse must be observed for some time after the effects of the sedative have dissipated to assess the recurrence of pain. Breed and age can also affect how readily a horse demonstrates pain. For example, a very young horse may not be as stoic as a much older horse; a Thoroughbred in training may demonstrate severe pain in the presence of only a mild lesion; whereas a well-trained, experienced horse with a strangulating lesion may exhibit few signs of pain. Thus, the observer must be careful to assess the entire horse and look for any subtle signs.

Horses with abdominal pain express variable signs, including pawing (Figure 15-1) , turning the head toward the flank (Figure 15-2), kicking at the abdomen with the hind feet, crouching or attempting to lie down (Figure 15-3), repeatedly stretching as if to urinate, behaving restlessly such as repeatedly backing into a corner of the stall, lying in sternal or lateral recumbency for prolonged periods (Figure 15-4), rolling on the ground (Figure 15-5), dropping to the ground, assuming a dog sitting position (Figure 15-6), bruxism (grinding of the teeth), dunking the nose into the water bucket, drinking excessive amounts of water, and sweating.[5] Quivering of the upper lip or demonstrating the Flehmen response (Figure 15-7) is another sign of colic that should be considered as a sign of pain.

Figure 15-1



Pawing with the front foot is a common sign of colic.

Figure 15-2



Turning the head toward the flank appears as if the horse is pointing at the site of pain. This sign does not relate to a specific disease.

Figure 15-3



Colic causes horses to circle and crouch as if to lie down. This may be repeated several times before the horse actually lies down.

Figure 15-4



Horses with colic may stay recumbent.

Figure 15-5



A weanling with colic rolling from side to side and staying in dorsal recumbency.

Figure 15-6



Although horses rarely assume a "dog sitting" position, this may be indicative of excessive pressure on the diaphragm due to a distended stomach.

Figure 15-7



Curling the upper lip can be a sign of colic.

Pain has previously been classified into five categories based on severity: no pain, mild pain, moderate pain, severe pain, and depression.[5] Mild pain is evidenced by occasional pawing, turning to look at the flank, stretching out, bruxism and lying down for longer than normal.[5] Horses with this type of pain usually respond to analgesics for 8 to 12 hours[2] and are usually easily distracted from the pain by external stimuli such as walking. Horses with mild pain may not have signs of discomfort unless left alone in the paddock or stall. Moderate pain manifests as pawing, cramping, attempting to lie down, kicking at the abdomen, lying down, rolling, turning the head to the flank, and dog sitting,[5] and is usually controlled by analgesics for 2 to 4 hours.[2] Horses with moderate pain are more difficult to distract with walking, and analgesia is usually required. Signs of severe pain include sweating, dropping to the ground, violent rolling, continuous movement, or any of the previously mentioned signs.[5] During severe pain, the horse will often be difficult to control and may only respond to analgesics for several minutes or not at all. Depression can occur before or after an acutely painful crisis. It is usually recognizable because the horse is overly quiet, is not interested in food or water, hangs its head low, and may be reluctant to move, and has a "tucked up" appearance. Depression may be the first sign recognized by the owner at the beginning of a colic episode. Alternatively, the horse may be exhausted from a period of colic, as occurs when a horse has been in pain for some time before the abdominal pain is discovered. Horses in shock are often depressed because of acidosis. Acute rupture of the stomach or intestine can cause a dramatic shift from severe pain to depression.

The horse's signalment and personality are very important, and two different horses with the same lesion may exhibit completely different grades of pain. For example, a horse with a low threshold for pain may roll and paw continuously with a simple obstruction and mild gas distention, whereas a stoic horse may stand quietly, be inappetent, and paw intermittently. Every disease has an observable a range of pain, and all diseases can cause depression before or after a painful stage.[5] Simple obstructions are usually characterized by mild to moderate intermittent pain, initiated by cyclic intestinal contractions oral to and around the obstruction, and distention of the intestine by accumulated gas and fluid. Most simple obstructions are not complete, and some gas and fluid will pass around the obstruction. However, the pain may become more persistent or severe as the obstruction begins to completely occlude the lumen, causing significant stretching of the intestine or mesentery. Acute severe pain is often caused by strangulation or severe tympany.[5]

The horse that has mild, intermittent pain or no pain at all but significant depression may have a primary inflammatory disorder such as peritonitis or enteritis.[5] Therefore, the absence of severe pain does not indicate that the horse does not have a severe illness; a depressed, quiet horse with peritonitis may be in a life-threatening condition.

Manifestations of pain may be specific for certain diseases. For example, a neonatal foal straining to defecate or urinate most likely has a meconium impaction or ruptured bladder (Figure 15-8). A foal lying on its back for long periods suggests gastric ulceration (Figure 15-9).[5] A gelding straining to urinate may have a urolith. Although rare, a horse assuming a dog-sitting position may have gastric distention secondary to gastric impaction or obstruction in the small intestine (Figure 15-6).[5] Horses with sand impactions of the large colon tend to stand stretched out for several minutes (Figure 15-10), although this can be seen with other diseases as well.[5] Even though some behavior or body position may indicate a particular disease, the association is not always accurate.

Figure 15-8



Foals with meconium impactions or a ruptured bladder often strain with a raised tail.

Figure 15-9



Foals with colic often lie in dorsal recumbency. This foal had a meconium impaction.

Figure 15-10A



Standing in a stretched position is characteristic of mild colic.

Figure 15-10B



Stretching in a "camped out" position is a sign of colic. Horses may assume this position for several minutes.

The physical appearance of the horse may provide some clues as to the severity of its condition. During violent bouts of pain, horses can cause trauma to themselves, resulting in contusions, abrasions, and swelling around the eyes and head (Figure 15-11). If the horse is quiet or depressed when examined, but has evidence of previous trauma and severe pain, one must be alerted to the likelihood of stomach or bowel rupture. Sweating can also be a sign of severe pain as a result of stimulation of the sympathetic nervous system or from endotoxic shock.[5]

A bloated appearance indicates marked distention of parts of the intestine such as the large colon or cecum, or possibly, the entire small intestine (Figure 15-12). Cecal distention or displacement may result in a bloated right side; a left dorsal displacement of the large colon may result in a bloated left side of the abdomen. Bloating on both sides is usually indicative of severe distention of the large colon secondary to large-colon volvulus or of the entire small intestine secondary to small intestinal volvulus.[5] A miniature pony with a distended abdomen may have a distended large colon secondary to a complete small-colon impaction. A wide stance with a "tucked up" appearance may indicate pleural or abdominal pain consistent with pleuritis and peritonitis (Figure 15-13). Intestinal incarcerations and subsequent strangulating obstruction through the umbilicus in a young animal or into the scrotum in an older animal can be externally visible as a large swelling in those respective regions (see Chapter 36). Although the severity of pain is not diagnostic for specific conditions, it may narrow the differential diagnosis into a disease category (Table 15-1).

Figure 15-11



Abrasions on the head indicate previous trauma caused by rolling or recumbency from moderate to severe colic. If pain is replaced by depression, a gastrointestinal rupture or severely compromised bowel should be suspected.

Figure 15-12



Abdominal distention frquently indicates excessive intestinal distention, which can often be confirmed by rectal examination or abdominal ultrasound.

Figure 15-13



Abdominal splinting is frequently the result of peritonitis or pleuritis. This horse is walking with a stilted gait due to pleural pain.

Temperature, Pulse and Respiration

The temperature, pulse, and respiration are helpful in determining the category or severity of the colic. The rectal temperature should be taken before the rectal examination is performed; once air enters the rectum, the temperature measurement becomes inaccurate. Temperature may be increased slightly in horses that have had physical exertion such as rolling or pacing because of moderate to severe pain; however, the temperature does not usually exceed 101.5°F (38.6°C). Generally, horses with simple obstructions or displacements of the large colon do not present with an increased temperature. In some cases, however, the environmental temperature or the hydration status, which can both impede heat loss, may increase the temperature higher than expected.[5] Infectious agents and circulating endotoxins can cause fevers, usually of 102°F (39°C) or higher. For example, horses with peritonitis, duodenitis-proximal jejunitis, impending colitis, or endotoxemia usually have a fever. An increased temperature may help differentiate duodenitis-proximal jejunitis, which can be treated medically, from a strangulating lesion such as a pedunculated lipoma that requires surgery. In most cases, a fever is present with duodenitis-proximal jejunitis, whereas a horse with a strangulating lesion usually has a normal temperature (< 101.5°F). In Potomac

Horse Fever, the horse usually has a high temperature (105 to 107°F or 40.5 to 41.5°C) before the onset of the colic signs.[22,23] When a strangulating lesion has resulted in a severely devitalized bowel, the temperature may be increased because of the circulating endotoxins, but this is often countered by cardiovascular compromise and reduced tissue perfusion, resulting in a normal or only slightly increased temperature.

The heart rate is an indicator of the severity of the disease as well as of the degree of circulatory shock.[24] Heart rate has been shown to be an important prognostic indicator for survival[25,26] and for complications after colic surgery[3]. However, heart rate can be unreliable in individual cases: it may be decreased during the onset of life-threatening conditions such as a large-colon or small-intestinal volvulus, or it may be increased in a horse with a simple obstruction. Heart rate should, therefore, always be interpreted in conjunction with the other clinical signs. Although heart rate is dependent on the degree of pain and activity of the sympathetic nervous system, the vascular volume and cardiovascular status determine the heart rate. Cardiovascular status may be affected by endotoxemia (see Chapter 12) or other conditions causing massive intestinal distention and decreased venous return. A high heart rate should alert the veterinarian to a serious problem, such as a distended stomach, which is close to rupture, or severe intestinal distention which impairs venous return to the heart. Horses with simple obstructive diseases usually have a heart rate between 40 to 70 beats per minute (bpm); those with early strangulating lesions, 50 to 90 bpm; those with late strangulating lesions, 70 to 120 bpm; and those with enteritis or peritonitis, 40 to 100 bpm.[5] Although the heart rate is an indicator of condition severity, it can increase in the absence of compromise of the cardiovascular system as a result of pain and excitement. Therefore, tachycardia cannot be relied on as the sole index of condition severity.[27]

Dehydration and hypovolemic shock cause a compensatory increase in the heart rate to maintain cardiac output in the presence of a decrease in blood pressure. The pulse quality can be assessed by palpating the facial artery. A weak pulse may indicate low blood pressure secondary to hypovolemic or endotoxic shock. An irregular heart beat may indicate a dysrhythmia caused by an electrolyte imbalance, such as low ionized calcium or magnesium. Decreases in these electrolytes usually result in tachycardia and may contribute to the development of ileus. An ECG may be helpful as serum concentrations of magnesium and calcium (total and ionized) have been correlated with abnormal PR, QRS, QT, and corrected QTc intervals.[28] Other abnormalities, such as atrioventricular block, may also be evident on the ECG; for example, a horse with a low heart rate may have a second-degree heart block secondary to administration of α-2 agonist drugs.

The respiratory rate is consistently increased during abdominal pain. The increased rate allows for more shallow breaths and thus reduced work and movement of the diaphragm and chest muscles. Tachypnea also may be evident, with respiratory distress secondary to restriction of lung expansion, as occurs with pneumothorax or diaphragmatic hernia. With diaphragmatic hernia, the horse may be in severe respiratory distress, which can be mistaken for pain. Cyanosis with rapid respiratory rate can also occur when there is excessive pressure on the diaphragm and vena cava from large colon or cecal distention, or when endotoxemia is present with secondary pulmonary changes.[5] Metabolic acidosis, as may develop in horses with devitalized intestine, endotoxemia, and reduced tissue perfusion, may result in a high respiratory rate in an attempt to remove excess CO_2 to compensate for the metabolic acidosis (see Chapter 17).

Tissue Perfusion and Hydration Status

The color and moistness of the oral mucous membranes are used to assess perfusion and relative hydration. The conjunctivae can also be used for this purpose, but are sometimes inflamed from recent trauma such as rolling, transport, or recumbency.[5] The mucous membranes are usually pale pink (Figure 15-14),[29-31] but care must be taken in this assessment as lighting may affect the appearance. Tungsten light may enhance a red color, whereas fluorescent light can give the mucous membranes a slight blue-gray cast when compared with their appearance in daylight.[5] The appearance of mucous membranes in dehydrated horses can range from pale pink to brick red if venous congestion is present (Figure 15-15). Endotoxemia is characterized by a congested appearance of the mucous membranes, with a dark blue "toxic" line around the teeth (Figure 15-16).[32]

The capillary refill time is also a good indicator of tissue perfusion and, therefore, cardiovascular function. The test for capillary refill time is performed on the mucous membranes above the incisor teeth. It involves pressing on the mucous membranes to blanch the underlying tissue, and then recording the time it takes for the color to return. In a normal horse, the capillary refill time is 1 to 2 seconds. Skin tent is a measure of hydration status and is closely associated with the prognosis in equine medical and surgical colic.[26] The skin on the neck or upper eyelid can be pinched, and the time in seconds it takes for it to return to its previous position is the measure of the skin tent. With mild dehydration (5%), the skin tent is 1 to 3 seconds, mucous membranes are moist or slightly tacky, and the capillary refill time is normal; with moderate

Figure 15-14



Normal mucous membranes vary from pale pink to bright pink.

Figure 15-15



Brick red mucous membranes are associated with the early stages of endotoxic shock. Horses with enteritis or peritonitis may have this membrane color during the disease.

Figure 15-16



Cyantic mucous membranes indicate poor perfusion from shock.

dehydration, the skin tent is 3 to 5 seconds, the mucous membranes are tacky, and the capillary refill time is variable but may be 2 to 3 seconds; with severe dehydration, the skin tent is 5 or more seconds, the mucous membranes are dry, and the capillary refill time is variable but often longer than 4 seconds (Figure 15-17).[33] Care must be taken to consider the subcutaneous fat content as this affects skin tent retraction. Horses with normal hydration and minimal fat content can appear to be dehydrated based on skin tent retraction time.

The packed cell volume (PCV) and plasma total solids are the most commonly used laboratory tests to evaluate hydration. Both values often increase simultaneously, with a decrease in blood volume as fluid leaks into an extravascular space or is not replaced after obligatory loss in urine, feces, or respiratory gases. Increases in the PCV without a concurrent increase in the plasma total solids, may occur with splenic contraction. A PCV exceeding 50% usually indicates hypovolemia and dehydration.[33] If protein loss occurs as part of the disease process, it may result in a low or normal plasma protein concentration despite dehydration.[33] Increased protein concentrations with normal or decreased PCV may indicate an increased globulin concentration or anemia. Classifying hydration status can be estimated using the values in Table 15-4.

Figure 15-17



Capillary refill time is increased because of poor perfusion from hypovolemia and is seen in the late stages of endotoxic shock.

Table 15-4

Estimate of the Degree of Dehydration using PCV (%) and Total Plasma Protein (TPP; g/dL).

PCV	43-50	Slight dehydration
TPP	7.0-8.0	6%
PCV	50-57	Moderate dehydration
TPP	8.1-9.0	8%
PCV	>57	Severe dehydration
TPP	>9.0	10%

Nasogastric Intubation

A nasogastric tube should always be passed during every examination for abdominal pain. If the horse is in mild pain with a normal heart rate, the tube does not need to be passed immediately; however, if the horse is in moderate to severe pain and has tachycardia, the tube should be passed immediately to avoid possible gastric rupture. Horses with gastric distension are usually in moderate to severe pain. Gas within the stomach is easily relieved with a nasogastric tube, but fluids sequestered in the stomach are more difficult to remove, and usually do not spontaneously flow from the tube. A large-bore tube should be used as large particles within the fluid may block a small tube. For a 450-kg horse, a tube with a 1.25 cm (1/2 inch) inside diameter and a 1.8 cm (3/4 inch) outside diameter is preferred; a single opening at the end is best, as side openings may become blocked with gastric contents and are not easily cleared with retrograde flushing.[2] If gastric fluid does not flow freely, enough water (approximately 500 mL) should be used to fill the nasogastric tube through a pump or funnel. The end of the tube is first elevated and then lowered so that the end is lower than the stomach (Figure 15-18). This maneuver creates a siphon, to allow flow of sequestered fluid.

If no fluid is immediately retrieved, attempts at creating a siphon while changing the position of the tube in the stomach should be repeated until a fluid pocket is located or the veterinarian is convinced that no fluid is retained in the stomach. Even with a full stomach it can take multiple attempts to start a siphon or to locate the fluid. Suction on the end of the tube in the form of a large-volume syringe or stomach pump in reverse may be useful but can also cause ingesta to block the tube.[5]

Normally, fluid from the stomach is green, sweet smelling, consists predominantly of food particles, and has a pH in the range of 3 to 6 (this can be measured with standard pH paper).[5] Fluid that has refluxed from the small intestine is yellow-brown from the bile, and has a fetid odor from the fatty acids produced during stasis (Figures 15-18C).[5] Small intestinal secretions are intended to buffer acid, and therefore, the pH of fluid refluxed is most often neutral or slightly alkaline (pH 6 to 8).[5] If pyloric obstruction is present, the reflux fluid obtained may remain acidic even though the volumes of fluid are massive because of the retention of acid in the stomach. The volume of fluid accumulated in the stomach is greatest with a pyloric or proximal duodenal obstruction, which may create as much as 40 to 80 L in 24 hours (Chapter 36).

Draining a large volume of fluid from the stomach indicates that there is physical or functional obstruction of the small intestine and is a sign that the horse may require surgery. Large volumes of reflux are obtained in cases of duodenitis-proximal jejunitis, which is often hard to differentiate from a strangulating obstruction (Chapter 36). Gastric reflux may also occur with diseases of the large colon such as a large-colon displacement, as the duodenum is attached to the large colon at the duodenocolic ligament, creating small-intestine obstruction during abnormal large-colon positions.

The passage of a nasogastric tube can save a horse's life as well as being diagnostic for a small-intestinal problem, especially when distended small intestine in the cranial abdomen is not palpable on rectal examination. Other diagnostic tests may be performed on the fluid, such as detecting microbes by culture and sensitivity or testing for toxins.

Figure 15-18A

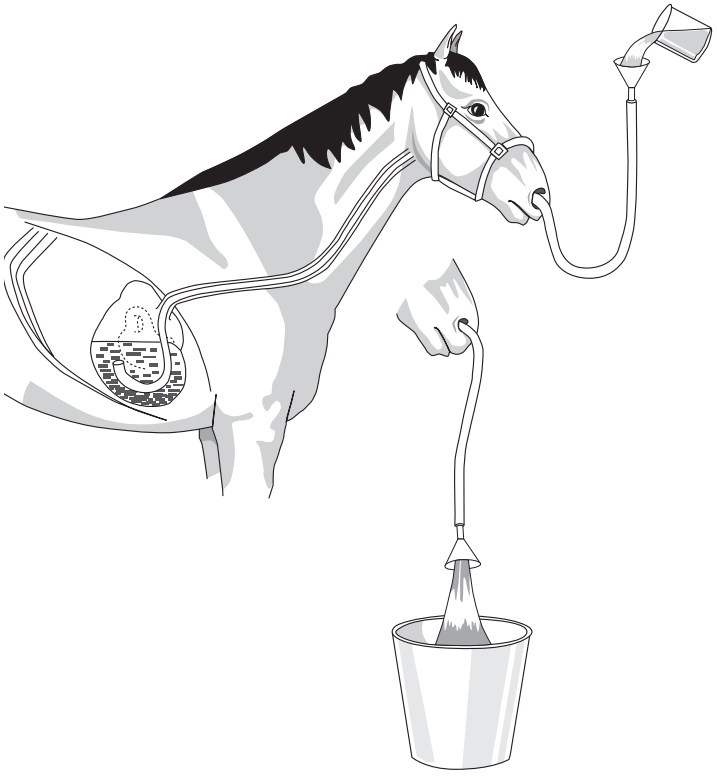


Figure 15-18B



Figure 15-18C



Once a stomach tube is in place, it should be filled with water and the end of the tube lowered to establish a siphon.

Auscultation

To auscultate the abdomen, the stethoscope is placed on four major sites: the left and right lower and upper paralumbar regions (Figure 15-19). The ventral midline of the abdomen should also be auscultated, especially in regions where sand colic is prevalent. Sounds will be heard on both sides of the abdomen both high and low. The characteristic sounds of the colon mixing can be heard low along either side of the abdomen.[5] The characteristic borborygmi, sounding like fluid gurgling, are produced by the interface and mixing of gas and fluid in the large colon and cecum. The small intestine can be highly motile but may not create referred sounds, thus the borborygmi auscultated are a good indication of large-bowel motility but not always of small-intestinal motility.

The amplitude of the borborygmi vary markedly among horses,[34] but the frequency is more consistent, with mixing sounds normally occurring regularly 2 to 4 times a minute.[5] Progressive sounds can be heard once every 2 to 4 minutes when the horse has not eaten recently. These sounds become more intense with eating as both amplitude and frequency increase, resulting in borborygmi that are a long progressive rush of gurgling heard on both the left side (left dorsal and ventral colon)

and right side (cecum) for 6 to 10 seconds.[34,35] The propulsive sounds are different from the mixing sounds; they have a different cyclic pattern and intensity and a longer duration (see Chapter 2).[34,35] Certain motility-altering drugs such as atropine,[36,37] xylazine,[38] romifidine,[39] detomidine,[40] and butorphanol[38] will temporarily reduce or abolish these propulsive sounds.[34,35] When administered together, xylazine and butorphanol can decrease intestinal sounds for about 1 hour at standard dose rates, whereas atropine can cause long-term ileus, bowel stasis, and subsequent distention, resulting in colic.[36]

In most cases of abdominal pain, the propulsive sounds are decreased, and in cases of severe intestinal disease such as strangulated bowel, the borborygmi are absent. Even with small-intestinal disease, the propulsive motility of the large colon and cecum is usually decreased or absent because of the sympathetic response to pain and the inflammatory response affecting the entire intestine. In horses with sand accumulation, a pouring or hissing sound, almost like the wind blowing through a shell if held to the ear, may be auscultated along the ventral midline during colon movement.

Movement of the horse may cause fluid and gas interfacing sounds of bubbling or pinging within the intestine. This does not represent propulsive motility but rather is indicative of a static, distended large or small intestine. In spasmodic colic, excessive borborygmi are heard and are suspected of being a result of intestinal spasms from irritation, ischemia, parasite irritation, or contraction against an impaction.[5] Borborygmi may also increase after a period of ileus or after resolution of tympanic or simple obstructive colic (resolution may occur after treatment, a trailer ride, walking, or spontaneously).[5] With resolution of ileus and the return of borborygmi, the horse usually has no pain but may appear to be tired or depressed.[5] Increased borborygmi can occur with hypermotility associated with impending diarrhea. In this early stage before the diarrhea has started, the horse may be in pain. Foals are especially subject to pain with the onset of enteritis/colitis; the intestinal sounds are "fluid" on auscultation with a lot of "sloshing" and increased frequency.

Figure 15-19A

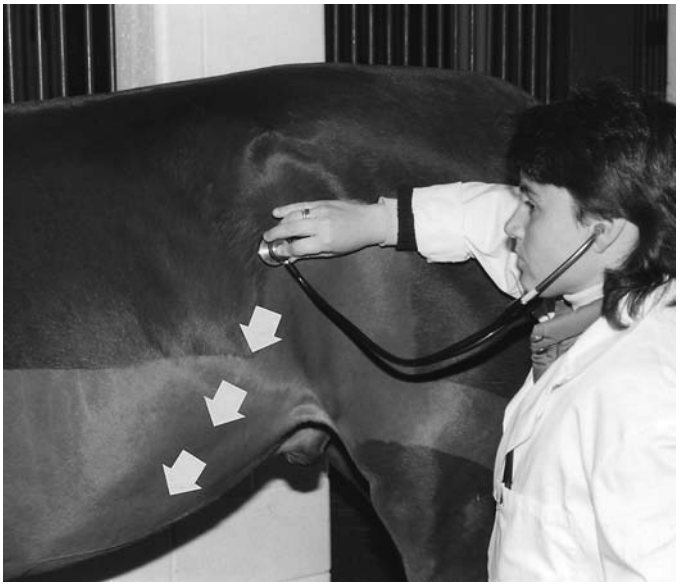
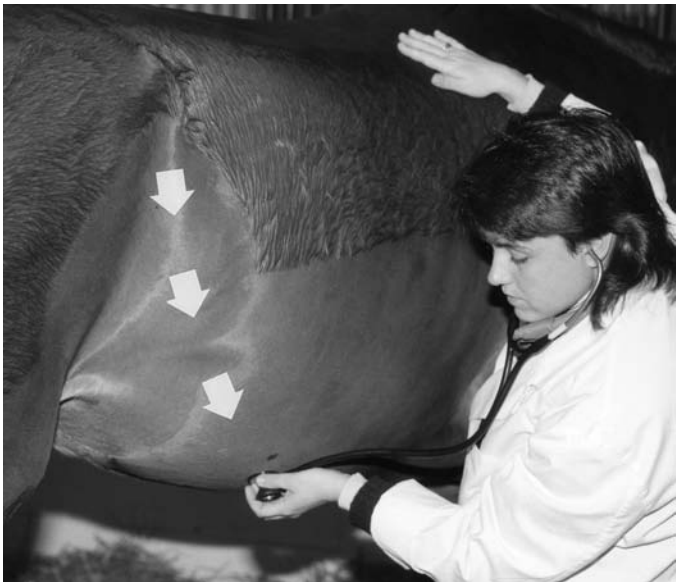


Figure 15-19B



Ascultation over the abdomen is completed by moving the stethoscope down each flank to the ventral abdomen.

Percussion

Percussion of the abdomen is usually performed along with auscultation by using the fingers to tap the area of interest while carefully auscultating the abdomen adjacent to the tapping (Figure 15-20). Percussion is useful in locating pockets of gas. For example, a gas-distended cecum can be located by hearing a ping on the right paralumbar fossa, whereas a ping in the left upper paralumbar fossa may indicate large-colon distention or displacement.[5] Percussion is not normally performed with a pleximeter and hammer as these have limited usefulness over the horse's abdomen, however they may be used to identify the splenic margins. The other parts of the intestinal tract vary in their fluid and gas content and thus are difficult to identify.[5] Ballottment, which routinely is performed in cattle, is rarely performed in the diagnostic work-up for the equine acute abdomen; a fetus or a large impacted viscus or heavy organ may rebound against the abdominal wall during ballottment,[41] however the horse often does not tolerate this maneuver. Constant pressure applied to the flank or lower abdomen may be useful in differentiating visceral pain (i.e., pain originating from the intestine) from parietal pain (i.e., pain originating from the abdominal wall or parietal peritoneum).[41] This pressure exacerbates parietal pain, causing splinting of the abdomen in horses with peritonitis; but no response occurs in horses with purely visceral pain.[5]

Figure 15-20



Percussion over the right flank in the area of the cecum is used to identify cecal tympany.

Rectal Examination

The rectal examination is one of the most important diagnostic procedures in evaluating the acute abdomen to determine the location and severity of disease and to help make the decision for surgery.[5,42-48] It may not be necessary to perform a rectal examination at the first visit for colic if the horse's physical examination parameters are within normal limits and there is no evidence of abdominal pain at that time. However, this procedure can provide vital information for the early diagnosis and treatment of intestinal conditions in horses with a history of colic. The rectal examination should always be performed when colic is observed or if pain persists, particularly if subsequent examinations are necessary.

Only the caudal 30% to 40% of the horse's abdomen can be palpated because of the size and depth of the peritoneal cavity.[49] It may not be possible to definitively diagnose a problem, and some abnormalities within the abdomen may be missed, but even determining that the rectal findings in some way are abnormal is important. A multicenter survey of 1,965 colic cases from 10 equine referral centers in the United States determined that the most important factor in deciding the need for surgery was distinguishing abnormal from normal rectal findings.[50] Although important, rectal findings should always be considered in conjunction with the results of the physical examination, nasogastric intubation, abdominocentesis, and laboratory evaluation.[51]

The value of the rectal examination should be considered in relation to the risks involved.[5] The rectal examination must be able to be performed safely for the horse, the veterinarian, and others present. Adequate restraint is of paramount importance to avoid iatrogenic perforation of the rectum during the examination and to avoid injury to the veterinarian performing the procedure. If possible, the horse should be restrained in stocks, however, if stocks are not available, positioning the horse in a stall is preferred. A twitch should be applied to the upper lip and chemical sedation administered in the form of xylazine (0.3 to 0.5 mg/kg intravenously) or detomidine (7 to 10 μg/kg intravenously).[51] A broodmare that is used to the procedure may not require sedation. Intrarectal administration of 2% lidocaine (50 to 60 mL via syringe) after removing the fecal material will promote relaxation of the rectal muscles. Alternatively, hyoscine N-butylbromide (Buscopan® at 0.3 mg/kg) helps to facilitate the rectal examination. Rarely, in a very young or fractious horse, an epidural may be required. An epidural should be performed if the horse has a suspected rectal tear (Chapter 40).[51]

Adequate lubrication of the examiner's hand in the form of KY jelly or hydrated methylcellulose is also necessary to prevent irritation to the rectal mucosa and to improve the ease of the procedure. Long plastic sleeves are used and usually are turned inside out to avoid the glove's seam irritating the mucosa. If a rectal tear is suspected, a rubber obstetrical sleeve with a surgical glove attached will provide the best sensitivity without irritating the mucosa. The rectal examination should be performed slowly, as most horses will resist the procedure if they are not accustomed to it. The examiner should stand to one side of the horse to begin the examination if the horse is not restrained in stocks. The anal sphincter is usually tight and some force is required to push the hand past this constriction, which should be opened slowly and evenly with the thumb and fingers together in a narrow configuration. Once the hand is passed through the sphincter, the examiner can move to the back of the horse and advance the hand slowly to remove the feces. The feces should be examined for consistency: hard,

dry fecal balls covered with mucus could indicate the presence of an impaction or lack of normal fecal transit (Figure 15-21); watery fetid feces may be indicative of colitis; worms within the feces indicate a heavy parasite burden; and sand seen or felt within the feces indicate sand colic.

Figure 15-21



Horses with increased transit time due to an impaction often have dehydrated feces coated with mucus.

Once the feces are removed, more lubrication should be placed on the hand, and the hand advanced slowly to the arm's length if the rectum and small colon allow. The veterinarian should never forcefully advance; if the small colon and rectum are tight and contracted, the arm should remain still or should be withdrawn and replaced. The examiner should never push against rectal or small colon contractions; if the intestine contracts, the examiner should remain still and allow the contraction to push the hand and arm out to the anal sphincter. If there is resistance, the hand should be withdrawn to avoid perforation of the rectal mucosa and wall. Once the arm is in as far as comfortably possible, the examiner should wait approximately 15 to 30 seconds while the rectum, small colon, and anal sphincter relax.[5] Initial examination of the caudal abdomen with the arm inserted halfway is frequently not productive, as it may result in straining and excessive peristaltic contraction of the rectum.[49]

Examination of the abdomen should be performed in a systematic manner. The exact sequence varies among veterinarians, but a common approach is to divide the abdomen into quadrants and examine the abdomen in a clockwise fashion, starting from the left dorsal aspect, then proceeding to the right dorsal, right ventral, and left ventral regions. This approach is thorough and avoids missing abnormalities. In addition, dividing the abdomen into quadrants may help describe structures or abnormalities palpated during the examination.

Starting in the left dorsal quadrant, the spleen is located with its caudal edge palpable against the left body wall (Figure 15-22). The renosplenic ligament, renosplenic space, and the caudal pole of the left kidney can be palpated by moving the hand up from the caudal edge of the spleen. Normally, 3 to 4 fingers can be placed in the renosplenic space,[51] but in some horses, especially in large breeds, this region is difficult to reach, and it may not be possible to palpate the kidney or the renosplenic space. From the kidney, the hand is moved to the right, forward along the midline, and again to the right where the aorta and root of the mesentery can be palpated (Figure 15-23).[51] In larger horses, the mesentery may not be able to be reached or can only just be touched with the tips of the fingers.[5] The aortic pulse is easily palpable, but the pulse in the mesenteric stalk may only occasionally be palpable.[51] The right upper quadrant is then palpated by moving over to the right. The duodenum, located dorsal to the base of the cecum, is rarely palpable but sometimes can be felt distending during a peristaltic wave or if it is distended. The hand is then moved to the base of the cecum. The ventral and medial cecal bands (taenia) are palpated and traverse in a dorsocaudal to ventrocranial direction. This palpation is facilitated by moving the hand in a lateral and caudal direction to hook the tips of the fingers into the cecal bands, which are normally relaxed and movable when gently manipulated. (Figure 15-24).[51] A large amount of the cecum is not palpable, but ingesta can often be palpated in the right ventral quadrant and may be followed forward on the ventral midline on the floor of the abdomen.[5] The examiner then moves caudally and to the left ventral quadrant where the pelvic flexure and left dorsal colon may be felt if each contains enough ingesta within its lumen (Figure 15-25). If the large colon is relatively empty, the pelvic flexure is often out of reach and cannot be palpated. The left dorsal colon is identified by the fact that no haustra or taeniae are palpable, there is only a mesenteric taenia, whereas the adjacent left ventral colon has two free taenia (running cranial to caudal) and haustra.[51] The

small colon, usually containing formed fecal balls, can be palpated in various regions of the abdomen, but is often palpated in the left quadrant (Figure 15-26).[5] The normal small intestine can sometimes be palpated as it moves when a peristaltic contraction occurs when it is touched, but usually it cannot be distinguished from other structures unless it is abnormal.

At the completion of that systematic examination, the caudal abdomen should be palpated, concentrating on the reproductive structures and pelvic rim. The bladder should be palpated for thickening or calculi. Sometimes, the bladder is very full and distended, which may prevent palpation of the rest of the abdomen. In this case, the horse should be encouraged to urinate by terminating the exam and placing the horse in a stall or catheterizing the bladder, if necessary. In the mare, the ovaries, uterus, and cervix, and in the stallion or gelding, the internal inguinal rings, must be carefully palpated. The inguinal rings can be found by palpating the pelvic rim and then feeling cranial and just ventral and lateral to the cranial edge of the pelvis (Figure 15-27). In some stallions, a finger can be inserted into the inguinal ring and the vas deferens is palpable in the caudomedial aspect of the vaginal ring. In geldings the inguinal ring is much smaller and decreases in size with age and the vas deferens is not usually palpable.[52]

Although a specific diagnosis cannot always be made in horses with colic, usually a distended or abnormally posititioned segment of intestine can be identified. The diseases described in Part 2 of this book contain detailed descriptions of rectal findings specific to each disease. The typical abnormal findings are discussed here.

Figure 15-22A

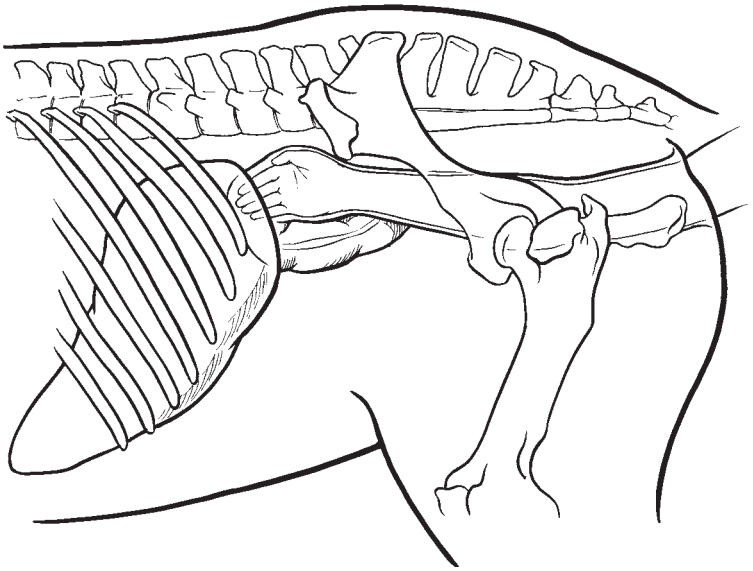


Figure 15-22B

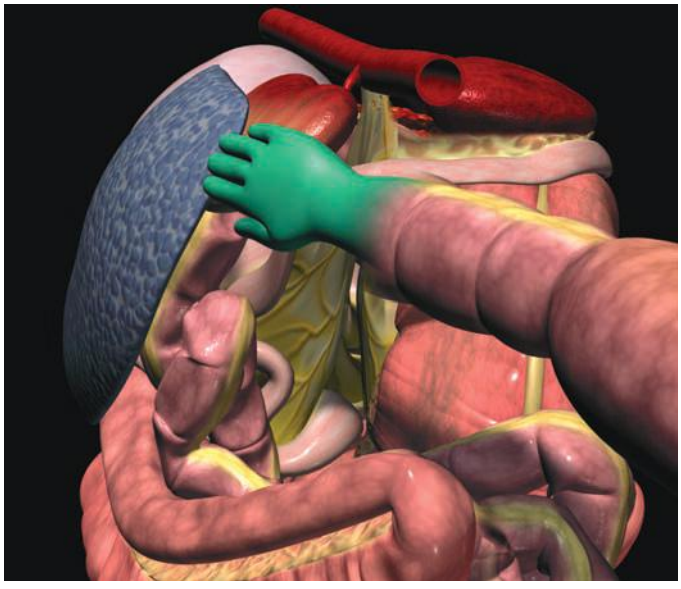


Figure 15-22C

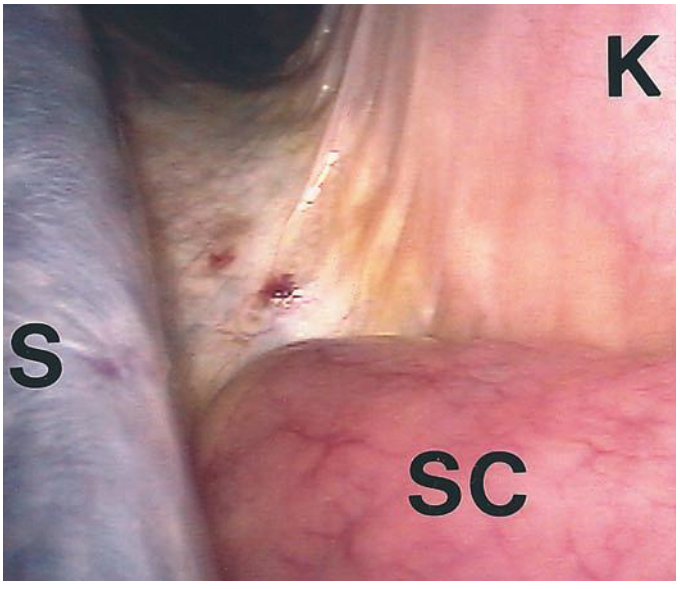
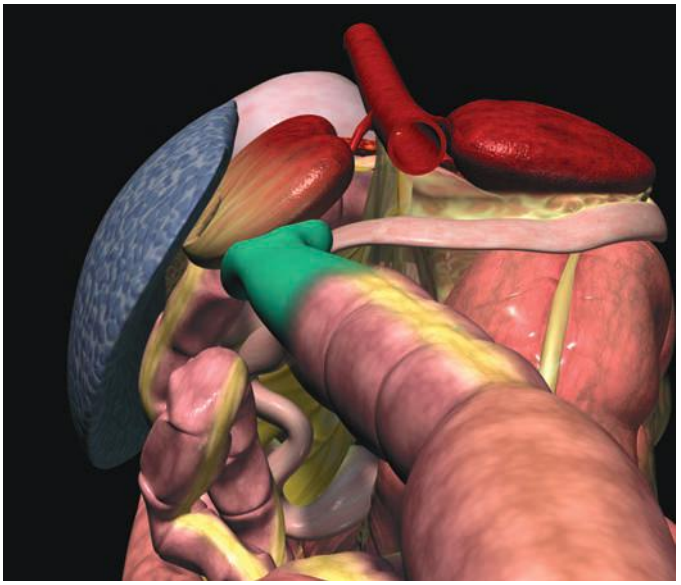


Figure 15-22D



Figure 15-22E



A.) The spleen should be identified in the left dorsal quadrant of the abdomen (From Current Techniques in Equine Surgery and Lameness, White NA, Moore JN (eds). Philadelphia: WB Saunders, 1998, pp 262-270). **B.)** The edge of the spleen can be palpated in almost all horses using the tips of the fingers (Courtesy of The Glass Horse, University of Georgia, Athens, 2008). **C.)** The spleen and fingers within the small colon can be visualized using the laparoscope (S=Spleen; SC=hand in small colon; K=kidney).**D.)** Moving to the right just inside the spleen, it is often possible to feel the renosplenic space (Courtesy of The Glass Horse, University of Georgia, Athens, 2008) and **E.)** the caudal pole of the left kidney (Courtesy of The Glass Horse, University of Georgia, Athens, 2008).

Figure 15-23A

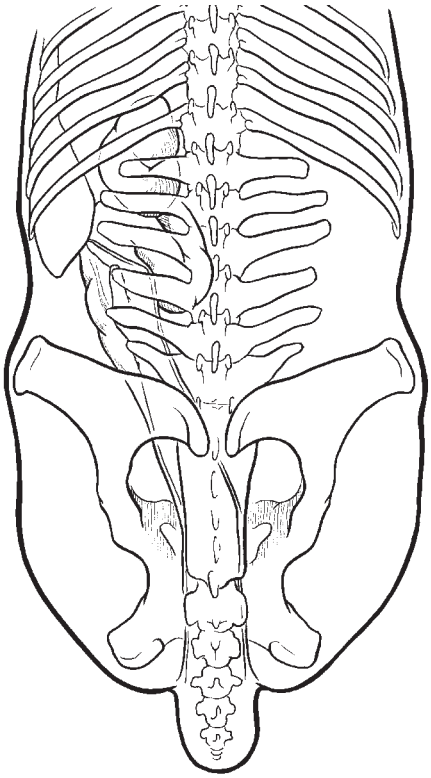
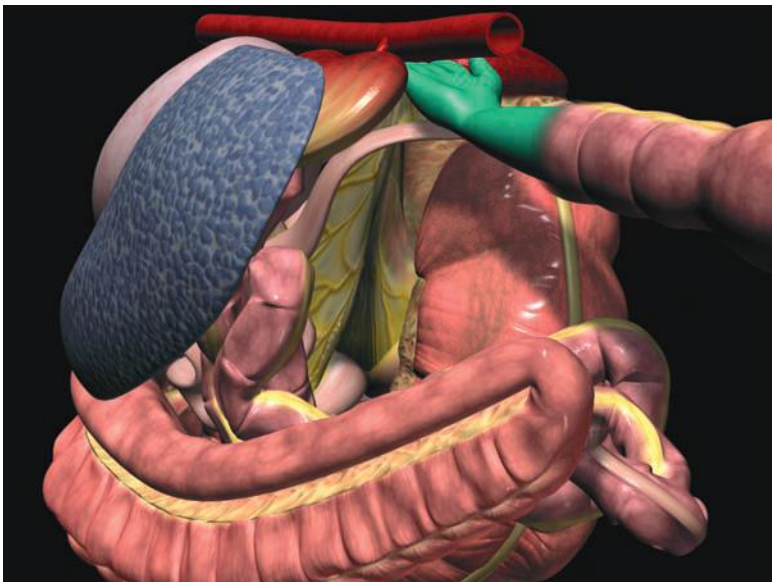


Figure 15-23B



A.) Extending the arm to the right of the left kidney and cranial (From Current Techniques in Equine Surgery and Lameness, White NA, Moore JN (eds). Philadelphia:WB Saunders, 1998, pp 262-270), **B.)** the mesenteric root can often be felt as a curtain of tissue (Courtesy of The Glass Horse, University of Georgia, Athens, 2008).

Figure 15-24A

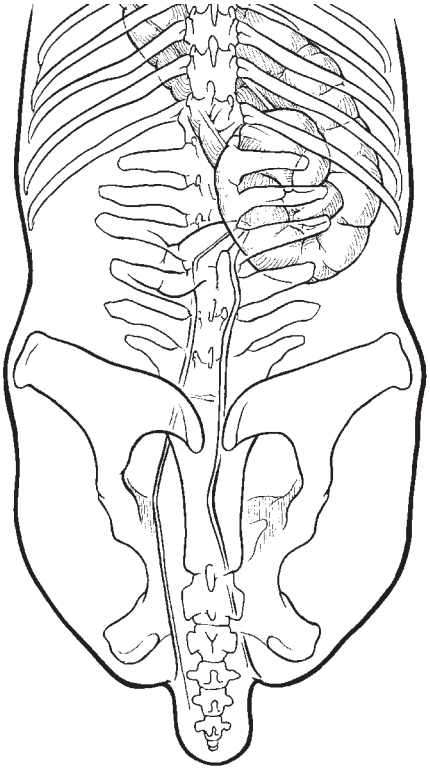


Figure 15-24B

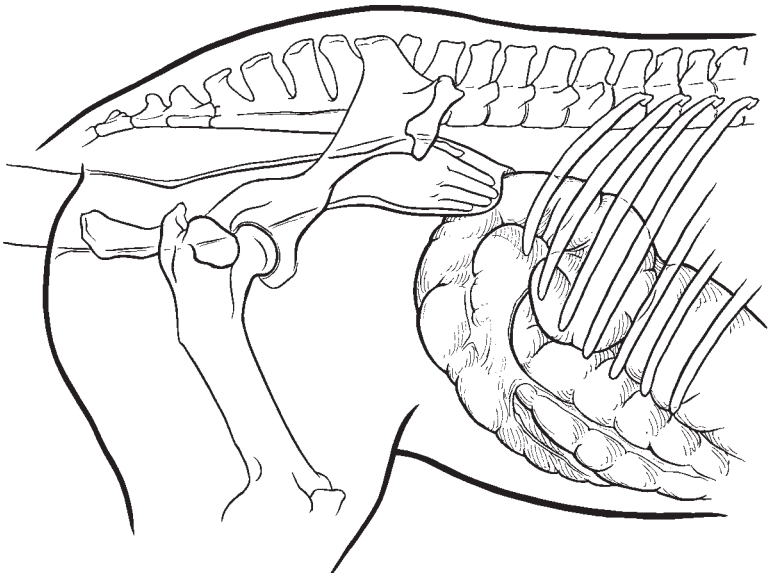
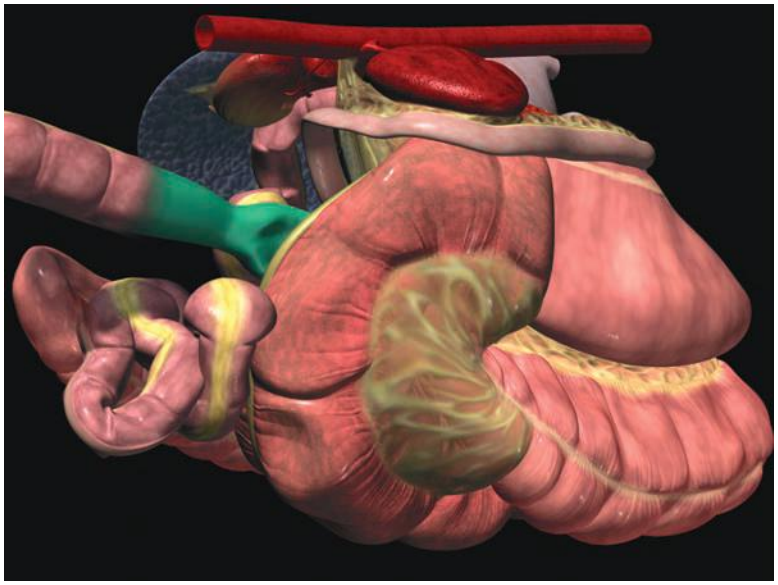


Figure 15-24C



The cecum is located in the right dorsal quadrant of the abdomen. **(A and B)** The cecum is usually not distended but is felt as a soft, fluid-filled structure (From Current Techniques in Equine Surgery and Lameness, ed by White NA, Moore JN (eds). Philadelphia: WB Saunders, 1998, pp 262-270). **C.)** The medial and ventral taenia often can be palpated by moving the hand from cranial to caudal on the medial surface of the cecum to stretch these structures (Courtesy of The Glass Horse, University of Georgia, Athens, 2008).

Figure 15-25A

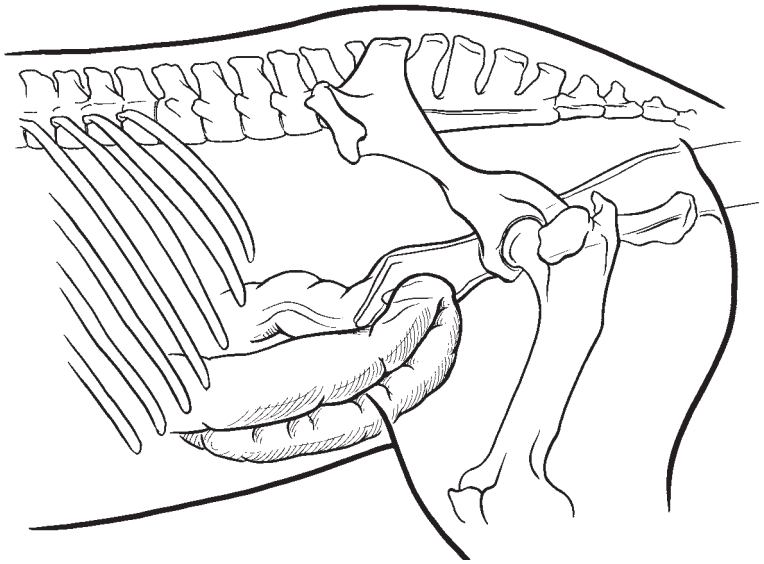
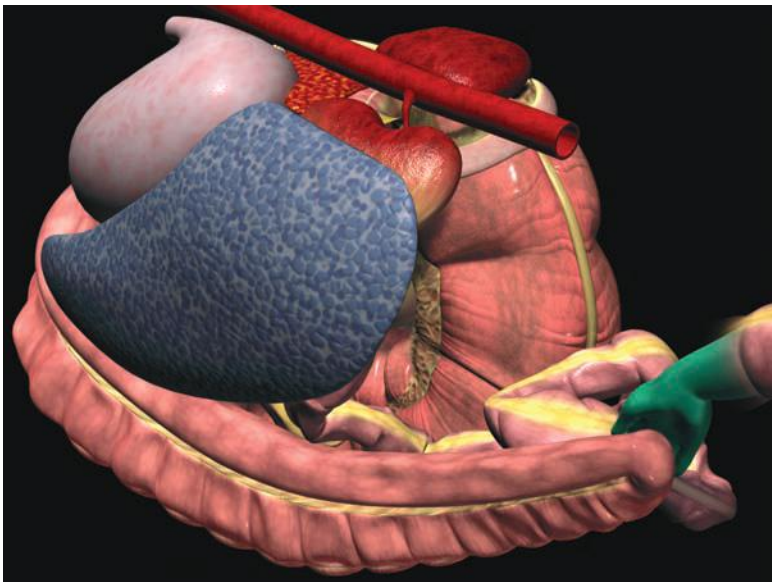
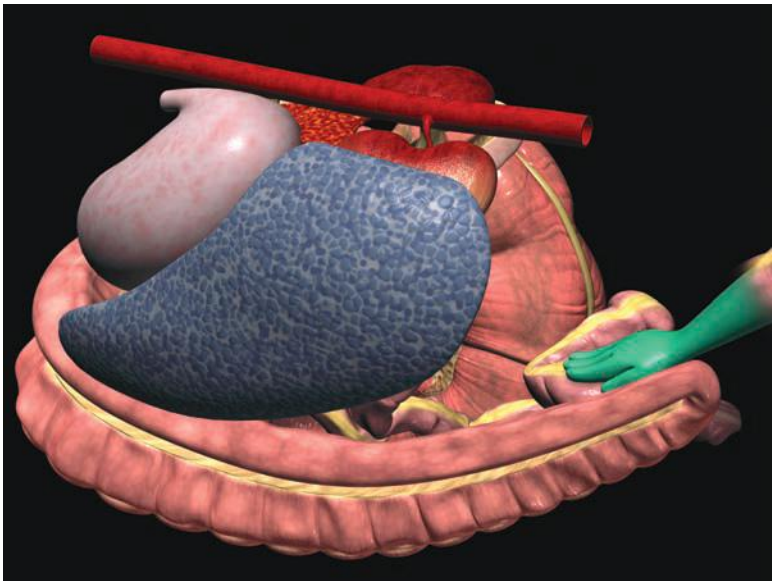


Figure 15-25B



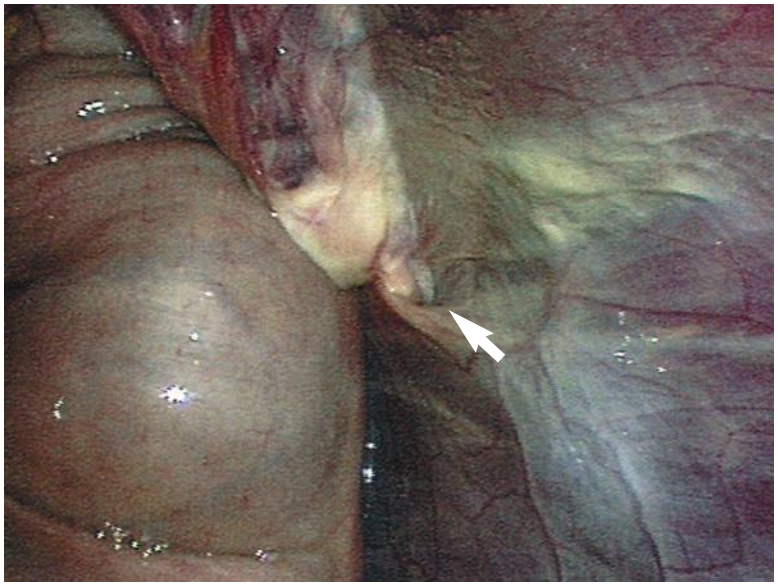
Pelvic flexure of the large colon is normally palpated in the left ventral quadrant and is a soft structure filled with ingesta **A.)** From Current Techniques in Equine Surgery and Lameness, White NA, Moore JN (eds). Philadelphia:WB Saunders, 1998, pp 262-270; **B.)** Courtesy of The Glass Horse, University of Georgia, Athens, 2008). Because of the relative lack of palpable structures on the colon, it is often not distinguished from other intestine except by its contents.

Figure 15-26



The small colon is normally found in the left abdomen and identified by the formed fecal balls and the single antimesenteric taenia. (Courtesy of The Glass Horse, University of Georgia, Athens, 2008).

Figure 15-27



The inquinal rings are palpated to the left and right of the pelvis at the level of the floor of the pelvis. The ring, which is a small slit in the peritoneum (arrow), is felt by moving the fingers over the abdominal wall as seen in this laparoscopic photo.

Stomach and Small Intestine

Abnormalities of the stomach cannot often be palpated on rectal examination because of the cranial position of the stomach. The spleen may be displaced caudally and moved away from the left abdominal wall during gastric distention as occurs with gastric impaction, but this splenic position can also be caused by primary splenic enlargement. The duodenum along the right body wall usually cannot be palpated, and so a proximal duodenal obstruction can be missed. In cases of small-intestinal obstruction or of duodenitis-proximal jejunitis, a distended duodenum may sometimes be palpated as a tubular structure on midline just ventral to the aorta over the base of the cecum.[5,53,54] If no abnormalities indicate an obstruction of the stomach or small intestine but large volumes of reflux are retrieved, a proximal small-intestinal, duodenal, or primary gastric lesion should be suspected. Obstruction in the small intestine or ileus results in a distended small intestine, which feels like several soft to turgid tubes (Figure 15-28). The gas and fluid within the small intestine may move as a result of peristaltic waves, which may be appreciated by the examiner, giving the impression of a change in distention.[5] As the small intestine distends, the loops fold on themselves, creating alignment of the intestine, which can be found in any quadrant but often in the center of the abdomen.[5] Although one or two small intestinal loops are palpable, more may be present that cannot be palpated. When the small intestine is significantly distended, it can take up the space of almost the entire abdomen and can extend into the pelvic canal, so that distended small intestine is the first structure felt on rectal palpation. The examiner should appreciate the amount of distention as this may affect the decision for surgery. If the distention is very tight, even in the case of duodenitis-proximal jejunitis, surgery may be required to decompress the small intestine.

An estimate of the intraluminal pressure may be made by estimating the tension and intestinal diameter. It is possible for distended small intestine to reach a diameter of 5 to 10 cm. The ileum achieves a diameter of 12 to 15 cm when very distended, and could possibly be mistaken for large colon, except that it has a thin mesentery.[5] These measurements can often be confirmed by an abdominal ultrasound examination. Tension within the ileum or its mesentery may cause a painful response to palpation of the ventral and medial cecal bands; this response has been reported to occur with conditions such as epiploic foramen entrapment.[55] It is possible that this may occur with other small-intestinal lesions and is, therefore, not a definitive test for ileal disease.[5] When small intestine is trapped in the inguinal canal, a strand of mesentery, which is not normally attached to the inguinal ring, may be palpated and may be very painful when traction is applied to it.[47] All stallions and geldings must have the region of the inguinal rings examined as part of the examination (Figure 15-29). Jejunojejunal intussusceptions may be distinguished by the thickened, edematous tubular structure that is created along with generalized small-intestinal distention.[51]

When a diagnosis is not made, rectal examinations are best repeated to monitor whether the distention is increasing and is, therefore, indicative of a strangulating lesion rather than ileus or enteritis. The small-intestinal distention often decreases after gastric reflux is removed via nasogastric tube in the case of duodenitis-proximal jejunitis.

Figure 15-28A

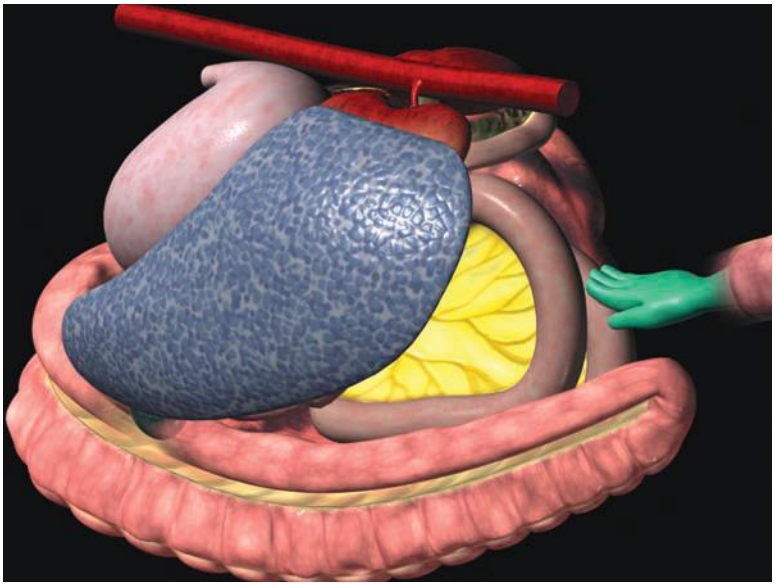
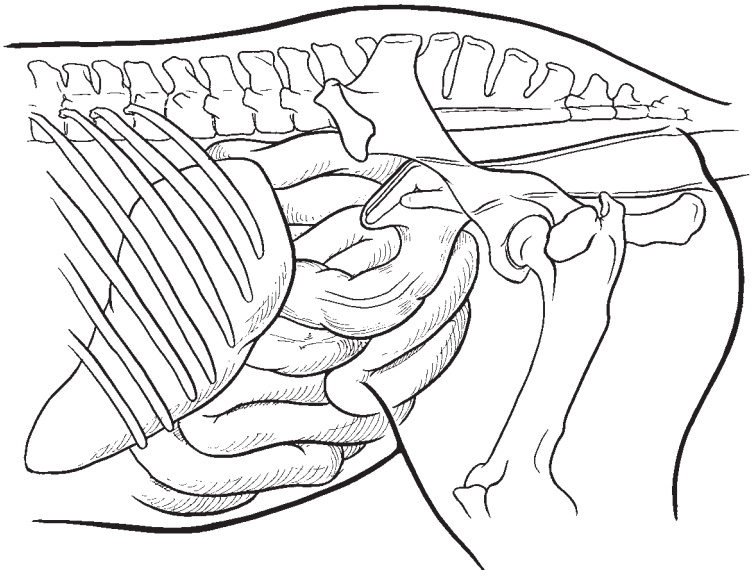
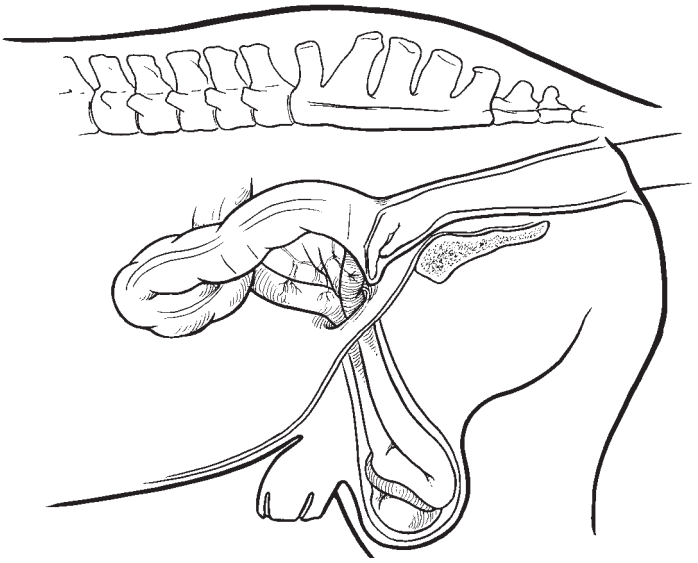


Figure 15-28B



A.) Distended small intestine is tubular and filled with gas or fluid. The distention may be felt as one or more loops early in an obstructive disease (Courtesy of The Glass Horse, University of Georgia, Athens, 2008) or **B.)** may fill the abdomen so the intestine is found just cranial to the pelvis. (From Current Techniques in Equine Surgery and Lameness, White NA, Moore JN (eds). Philadelphia: WB Sanders, 1998, p262).

Figure 15-29



Small intestine entrapped in an inguinal ring may not be distended but it may fill the ring so that the ring cannot be palpated. The intestine or its mesentery becomes taut and is felt to be attached at the inguinal ring. (From Current Techniques in Equine Surgery and Lameness, White NA, Moore JN (eds). Philadelphia: WB Sanders, 1998, p262).

Cecum

The cecum will become large and distended when a primary condition is affecting it or when the large or small colon are obstructed. When the cecum becomes distended, the taeniae become taut, and the organ displaces toward midline. The ventral taenial band, which is normally vertical in orientation, can be traced from the right dorsal to the left cranioventral quadrant across the caudal abdomen (Figure 15-30).[56] With mainly gas distention, the cecum (primary cecal disease or large-colon obstruction) is pushed back to the pelvic inlet, like a tightly distended balloon in the right dorsal quadrant, and may be hard to differentiate from right dorsal displacement of the large colon.[51] However, when the cecum is full of fluid and ingesta, the weight of the apex pulls the organ cranially and ventrally, and it fills most of the right ventral quadrant. When the impaction extends above the cecocolic orifice causing a complete obstruction, the cecal base fills with fluid and the cecum distends to fill both the right dorsal and ventral abdominal quadrants.[51] A significantly thickened cecum may indicate that the cecum is devitalized. A mass or edematous bowel in the right dorsal quadrant may be indicative of cecocecal or cecocolic intussusception.[57]

Figure 15-30A

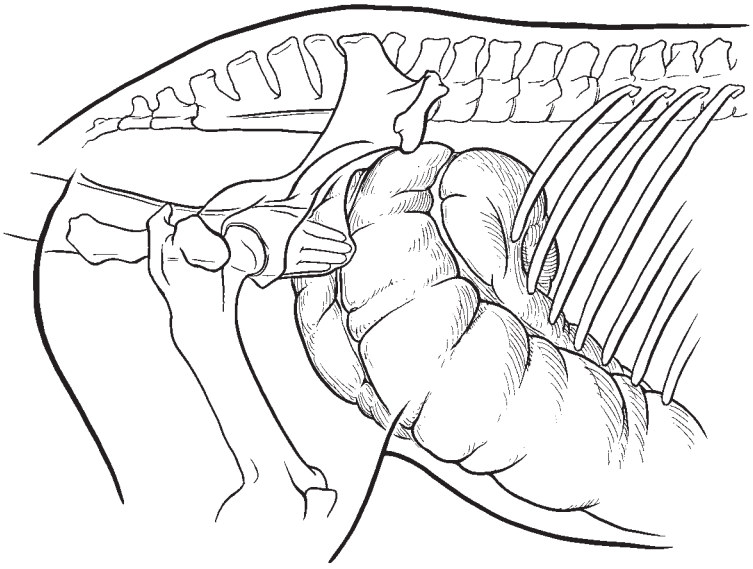
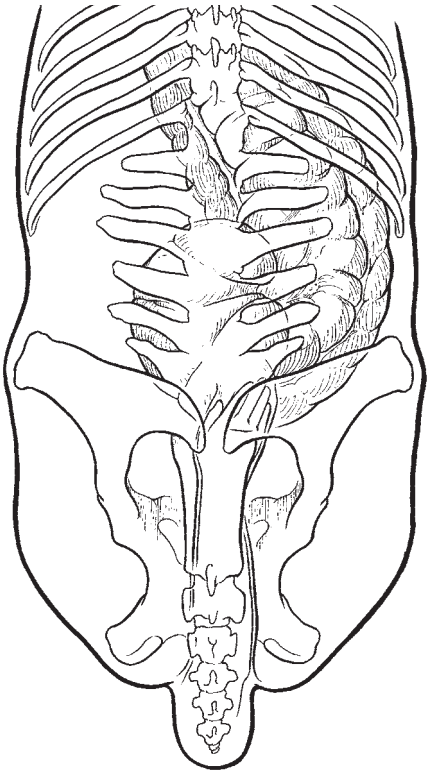


Figure 15-30B



Distention of the cecum can be detected immediately. Characteristically, the cecum is distended back toward the pelvis **(A and B)** and the ventral band courses from the right dorsal to the left ventral quadrants when the cecum is gas filled and ventrally toward midline when the cecum is impacted or fluid filled. (From Current Techniques in Equine Surgery and Lameness, White NA, Moore JN (eds). Philadelphia: WB Saunders, 1998, pp 262-270).

Large Colon

The large colon can move to many different positions when it is displaced or obstructed. The pelvic flexure is usually palpated in the left ventral quadrant, but when it becomes impacted and enlarges, it moves and extends to the right ventral quadrant, or it may be palpable immediately cranial to the pelvic brim (Figure 15-31). In cases of severe impaction, the large colon may fill the entire caudal abdomen, with the pelvic flexure entering the pelvic inlet from the right. When impactions are present, it is important to be able to decide whether the large colon is simply impacted or displaced. A left dorsal displacement in the renosplenic (nephrosplenic) space can be palpated before the large colon is severely distended. The displacement can be diagnosed if the large colon is positioned over the renosplenic ligament, and suspected if it is between the spleen and body wall or if the spleen is displaced medially (Figure 15-32).[58] The medial displacement of the spleen alone is not diagnostic and ultrasonography may be required to confirm the diagnosis. In one retrospective study, the rectal examination was diagnostic of this displacement in 72% of cases,[59] however, it is not always possible to feel the position of the colon if the large colon is distented. Significant distention of the entrapped colon may prevent palpation of the renosplenic space. In this case, the examiner will not be able to differentiate a gas distended large colon from one that is dorsally displaced.

Figure 15-31A

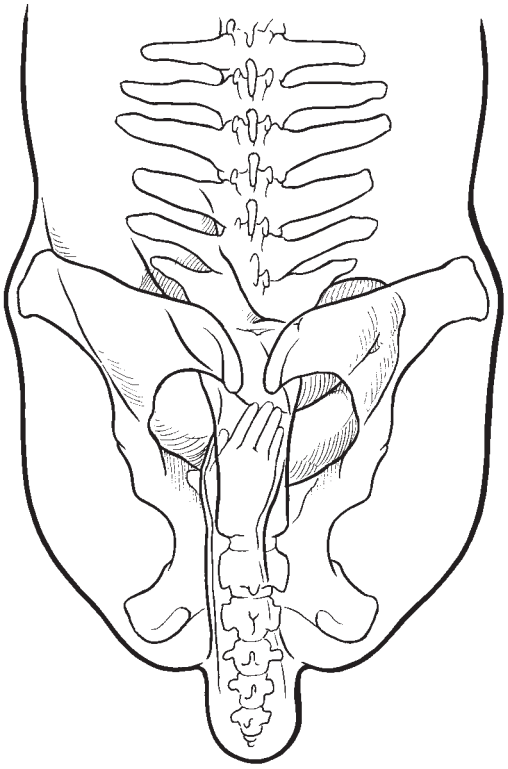
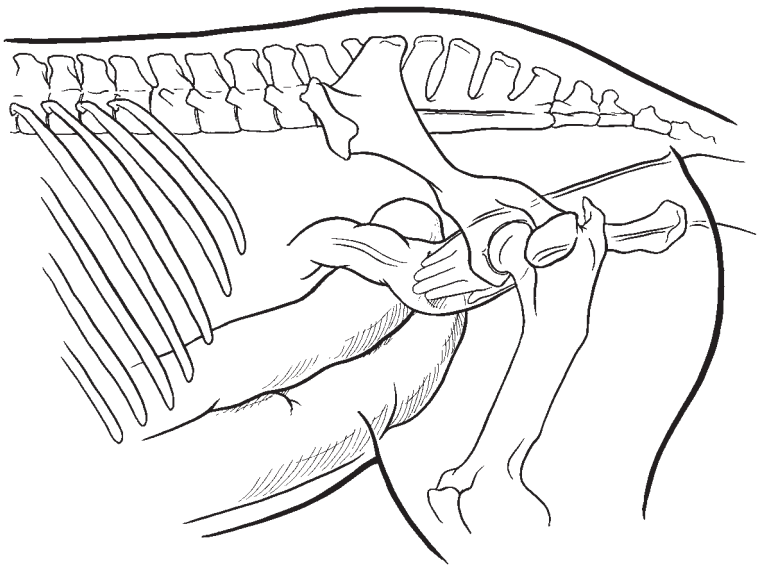


Figure 15-31B



During impaction of the large colon, the pelvic flexure is enlarged and the ingesta is dough-like and can be indented with the fingers. When filled, the colon can be found in the ventral abdomen with the pelvic flexure on the right side **A.)**, and sometimes moved into the pelvic inlet from the right side **B.)**.

The position of the colon varies during right dorsal displacement. In the most common presentation, the colon retroflexes and is found between the cecum and the right body wall.[51] The large colon and the taeniae will be felt cranial to the pelvic rim coursing from the right caudal abdomen transversely toward the left cranial abdomen.[51] The pelvic flexure is usually out of reach in the left cranial abdomen and the colon displaces the cecum medially and cranially, making it difficult to palpate.[51] The cecum may also become distended over time.

Other displacements may result in the large colon being very distended and pushed back into the pelvic canal with the pelvic flexure not being palpable.[5] For example, with a severe cranial displacement, the pelvic flexure will be positioned against the diaphragm, and thus out of the examiner's reach, and the colon may not be very distended.

Large colon volvulus generally creates greater distention compared with a simple displacement, but in the early stages, the distention may not be severe. Often the pelvic flexure is palpable on the right side, but is displaced cranially. Additionally, the haustra of the ventral colon may be located dorsal to the dorsal colon, indicative of at least a 180-degree volvulus. A large amount of the cecum and large colon may be displaced cranially and not be palpable. The presence of severe pain and progressive distention indicates that surgery is necessary. As the large colon fills with gas and fluid, the venous occlusion initiates edema formation in the intestinal wall and mesentery. If the large colon volvulus progresses from 180 degrees to 360 degrees, the large colon will enlarge immediately and push back towards the pelvic inlet, often in a horizontal position. A 360-degree or greater volvulus will cause severe distention, and often the colon is pushed back into the pelvic inlet, which does not allow passage of the examiner's hand beyond the pelvic brim (Figure 15-33). As the colon wall fills with blood and fluid, the haustra become prominent features during palpation of the colon. Affected horses may have decreased venous return and respiratory compromise.

Figure 15-32A

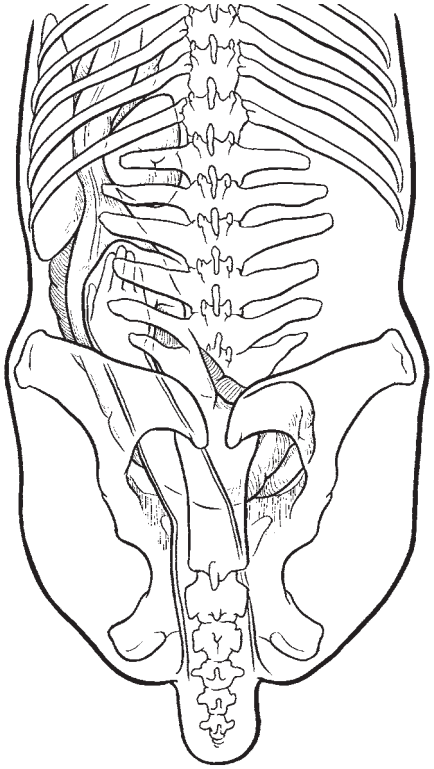


Figure 15-32B

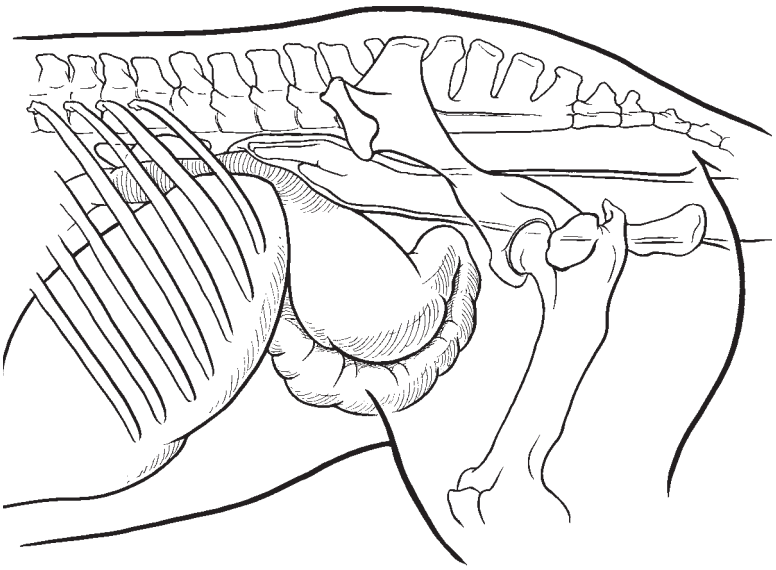
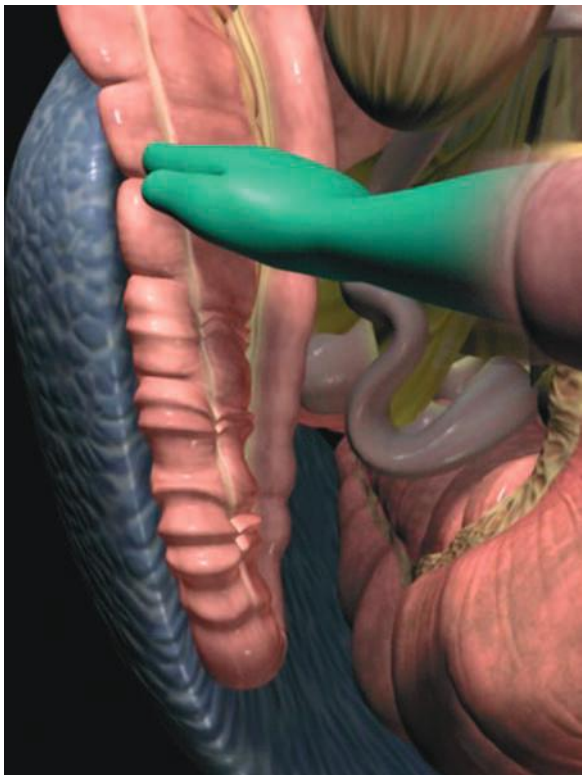


Figure 15-32C



(A and B) During entrapment of the large colon in the renosplenic space, the colon can be felt between the left kidney and the spleen in the left dorsal quadrant (From Current Techniques in Equine Surgery and Lameness, White NA, Moore JN (eds). Philadelphia: WB Saunders, 1998, pp 262-270). The spleen is often displaced and enlarged. **C.)** If the colon is distended, it may prevent palpation of the spleen and can be followed to the region of the renosplenic space (Courtesy of The Glass Horse, University of Georgia, Athens, 2008).

Figure 15-33A

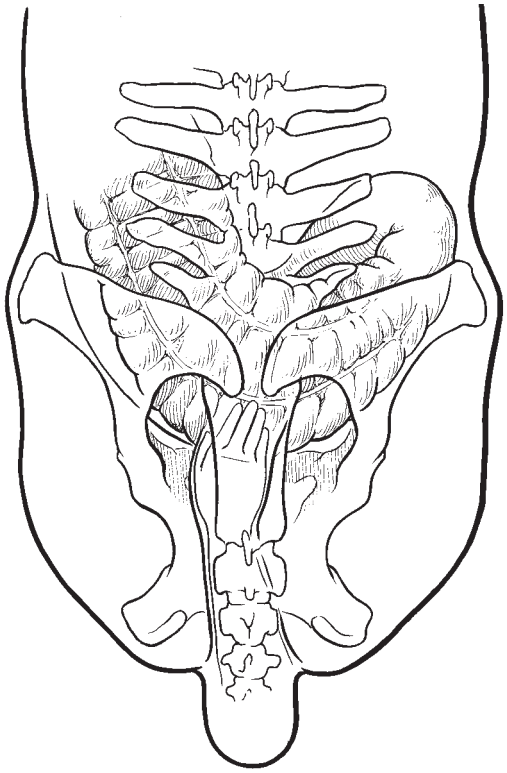
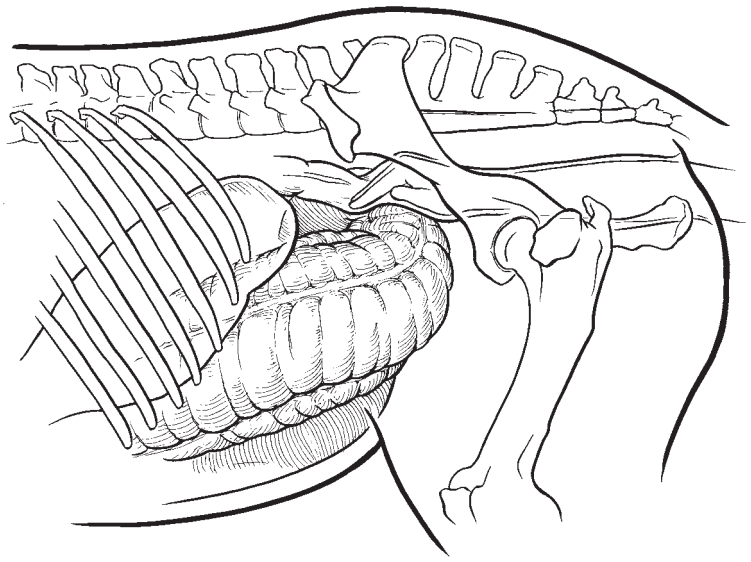


Figure 15-33B



Large colon volvulus rapidly fills the abdomen and is felt as a gas- and fluid-distended viscus, **A.)** which is frequently positioned horizontally in the abdomen and is pushed back toward the pelvic inlet **B.)** As the colon distends, the wall becomes thickened and creates rounded ridges on the surface. (From Current Techniques in Equine Surgery and Lameness, White NA, Moore JN (eds). Philadelphia: WB Saunders, 1998, pp 262-270).

Small Colon

Fecaliths or enteroliths in the small colon may be palpable in the ventral quadrants, but if they are in the proximal portion of the small colon or in the transverse colon they will be out of reach. Enteroliths are not commonly palpable on rectal examination; however, because they can cause complete obstruction, distention of both the large colon and cecum is common. In some cases, distention of the right dorsal colon or transverse colon may be palpable on the dorsal midline or in the dorsal quadrant.[5]

Impaction of the small colon with ingesta results in a long, thick tubular structure with no obvious fecal balls felt on palpation. The small colon is identified by its antimesenteric band, and the impaction often extends beyond the examiner's reach. In severe small colon impactions, the entire small colon may be filled with ingesta and the rectal ampulla may be pulled ventrally and to the left of midline by the weight of ingesta and the tension on the mesentery.[51]

Miscellaneous Abnormalities

Other structures that may be palpated include masses (neoplastic or benign), abscesses, or adhesions. Abscesses usually occur in the small intestinal mesentery and may be associated with adhered loops of small intestine.[5] Other abdominal abscesses may be palpable in various locations and then definitively diagnosed using transrectal ultrasonography. Abnormalities of the spleen may be palpated, primarily as splenomegaly. The enlarged spleen extends medially and more caudally than normal. If a neoplastic process is involved, the splenic border often is rounded and the surface of the spleen may feel irregular or nodular. Intestinal or omental adhesions can be difficult to palpate, but may be felt if they adhere to the inguinal rings, small colon, abdominal wall, or the pelvic canal. Contracted small intestinal adhesions are sometimes palpable at the root of the mesentery and are thick, nodular and hard.[5] Usually in these cases, the small intestine is chronically distended and thickened. Adhesions of the large colon to the abdominal wall or associated with omentum are not usually palpable. In some cases, adhesions between an enterotomy site and the pelvic rim will be palpable.[5]

Late Gestational Mares

Rectal palpation in late gestational mares is a challenge because the gravid uterus prevents a thorough examination of the abdomen. Distended large colon and cecum can be felt around the uterus in some cases, but small-intestinal distention may not be palpable and requires identification by abdominal ultrasonography. Uterine torsion should be considered in the last trimester of pregnancy. Rectal palpation is essential to make the diagnosis because vaginal palpation of affected mares is

rarely of value. The broad ligaments will be taut as they cross the caudal abdomen below and above the cervix in mares with uterine torsion.[51] In most cases, the direction of the uterine torsion can be determined by relative displacement and asymmetry of the left and right broad ligaments,[60,61] however, the broad ligaments may not be palpable and the rectal findings may be inconclusive in mares with chronic uterine torsions.[62]

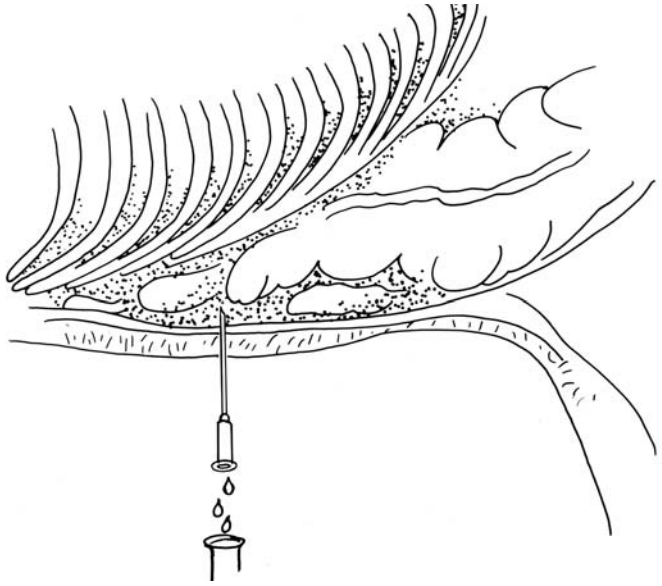
Other Findings

During the examination, the examiner should pay attention to the feel of the peritoneal surfaces. If peritoneal fluid is excessive, the intestines may feel as if they are moving through fluid rather than slipping past each other.[5] Fibrin deposition on the surface of the intestine feels roughened, whereas ruptured intestine and fecal contamination of the abdomen produces crepitus and a rough granular surface. Emphysema may also be palpable after rupture of intestine. For example, crepitus may be detected in the cecal wall or in the roughened fibrin covering of an area of rupture in the bowel wall.[5] When gas escapes into the abdomen, the viscera fill the ventral abdomen, creating an open space filled with gas in the dorsal quadrants. In certain circumstances, such as with a diaphragmatic hernia, the abdomen may feel quite empty and therefore a negative rectal examination does not always rule out a condition requiring surgical intervention.

Abdominocentesis

Abdominocentesis should be performed after the rectal and ultrasound examinations, if possible. If the large colon is massively distended because of an impaction lying against the ventral abdominal wall, the site for the abdominocentesis can be selected to avoid inadvertently puncturing the bowel. Bowel containing a large amount of sand is also at risk of being penetrated. An ultrasound examination can be used to locate a pocket of abdominal fluid. If ultrasound is not available, the abdominocentesis should be performed on the ventral midline or to the right of midline to avoid the spleen and at the lowest, most dependent part of the ventral abdomen. Usually, this site is at the cranial aspect of the ventral midline just caudal to the xiphoid cartilage. The peritoneal fluid can be collected using an 18G 1.5-inch needle or a teat cannula. Using a needle is the simplest method, with the needle being inserted through an aseptically prepared site on the ventral midline and directly into the abdomen through the linea alba (Figure 15-34). If the large colon or cecum is penetrated, the needle can be pulled out enough and then redirected to another point within the abdomen. Once peritoneal fluid flows from the needle, removing the contaminated fluid, the sample can be collected. Placing a second needle may be helpful to eliminate the negative pressure in the peritoneal cavity and allow fluid to flow more freely from the needle. Pushing gently on the side of the horse to shift the weight may also encourage the flow of fluid. Puncture of the intestine with a needle is usually not a serious complication, except in foals in which the intestine may not seal adequately.[5,63] In foals or adult horses with heavy intestine pressed against the ventral abdominal floor, a blunt-ended teat cannula is preferred for abdominocentesis. It may be necessary to avoid the heavy intestine by entering the abdomen at a paramedian location or at a location identified by ultrasonography. The paramedian location may increase the chance of a vessel being encountered in the rectus abdominis muscle, but when placed to the right of ventral midline, an enlarged or displaced spleen can be avoided.[5] Although a blunt teat cannula is normally safer than a needle, inadvertent puncture of the large colon or cecum can occur. Although these punctures normally seal by contraction and fibrin, contamination of the sample with ingesta may make cytologic evaluation impossible.

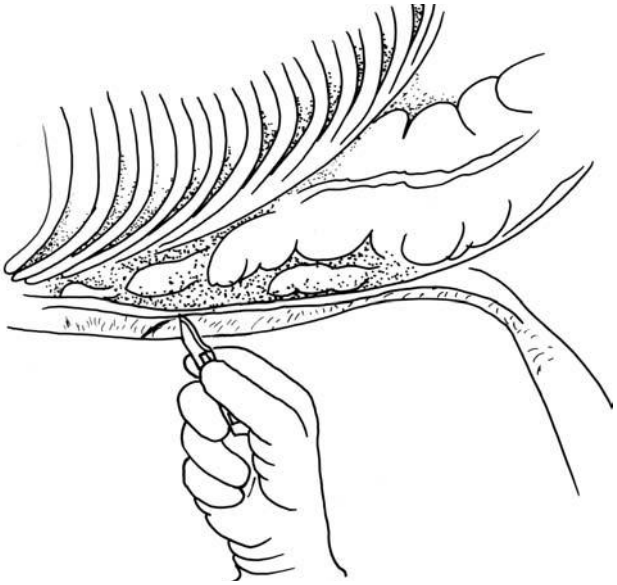
Figure 15-34



Placing an 18-gauge 1-1/2 inch needle through the linea alba often provides the peritoneal fluid needed for analysis.

Before using a teat cannula for abdominocentesis, a small shaved site is aseptically prepared. A small bleb of local anesthetic is injected into the skin at the intended site and up into the abdominal wall with a 23 to 25-gauge needle and a 3-mL syringe. The area is then given a final scrub. Wearing sterile surgical gloves, the veterinarian makes a stab incision with a #15 blade through the skin and part way through the abdominal wall (Figure 15-35) to facilitate passage of the teat cannula. The teat cannula is pushed through the middle of a sterile gauze swab and gently inserted into the stab incision and into the abdomen (Figure 15-36). The swab protects the sample collection tube from blood contamination from the skin incision. The cannula is manipulated until it is felt to "pop" through the peritoneum. Some horses have a large amount of retroperitoneal fat; in these cases, a canine urinary catheter is required to penetrate the peritoneum. Some manipulation of the teat cannula within the abdomen may be required to locate a pocket of fluid. The fluid should be collected in a potassium EDTA tube and serum tube. If only a few drops of peritoneal fluid flow through the cannula, they can be collected into an EDTA tube that has been shaken empty. This will help avoid obtaining a spuriously high protein reading on a refractomer.

Figure 15-35



Making a small incision in the skin and part way through the linea alba allows a teat cannula to be pushed through the peritoneum.

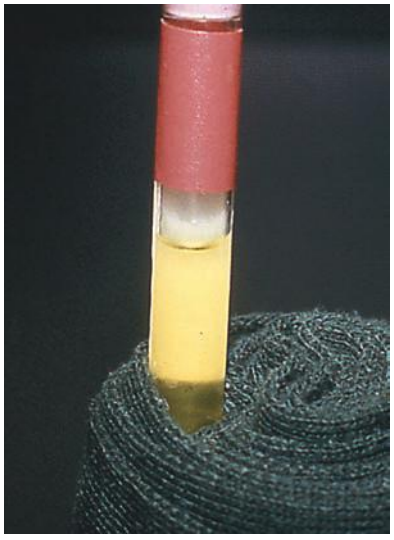
Figure 15-36



A teat cannula is pushed through a small incision using a sterile 4x4 gauze to prevent blood from the stab incision from contaminating the sample.

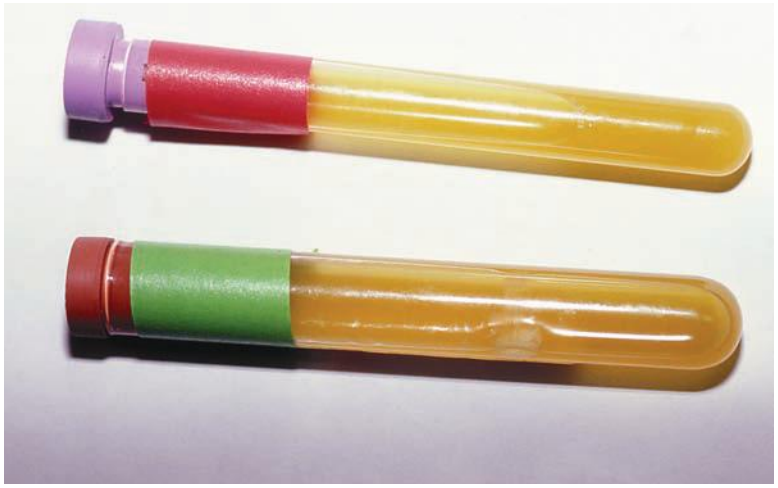
Once the fluid is collected, gross visual examination is performed. Laboratory analysis is completed to evaluate protein concentration, nucleated cell count, cytology, differential count, and a Gram stain for presence of bacteria. Normal peritoneal fluid is clear, pale yellow (Figure 15-37).[45,64,65] The fluid is cloudy if the protein content is increased, or if the number of leukocytes or erythrocytes is increased (Figure 15-38). The presence of red blood cells may increase the turbidity of the fluid, but the fluid may not appear red until a sufficient number of these cells is present in the fluid. The fluid changes in color from golden to orange and then to red as the number of red blood cells in the fluid increases (Figure 15-39). If the fluid is serosanguinous, it is indicative of ischemic or infarcted bowel, and leakage of a large number of red blood cells through the capillaries.[30, 31, 66-68] Reddish brown fluid with or without visible plant material is consistent with bowel rupture. Whitish-yellow opaque fluid indicates large numbers of white blood cells within the fluid.[5]

Figure 15-37



Normal peritoneal fluid is clear and yellow.

Figure 15-38

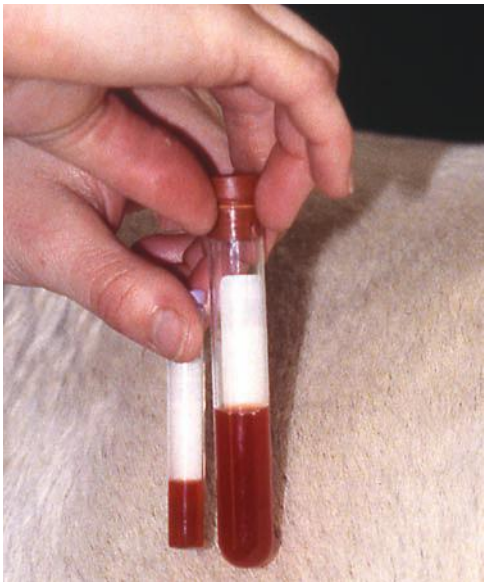


Cloudy or turbid peritoneal fluid indicates an exudate with white blood cells or, rarely, fat or chyle.

Retrieving whole blood from the abdomen is uncommon, but it can occur if the spleen has been punctured, if an intestinal vessel has been lacerated, if there is intra-abdominal hemorrhage from traumatized mesentery, or if there is a hemorrhaging vessel (broodmare after foaling) or hemorrhaging mass such as a neoplastic mass on the spleen. Dark blood may represent venous blood leaking into the abdomen from a traumatized mesenteric vessel, which may be incarcerated through the epiploic foramen or a mesenteric rent. Retroperitoneal fat may sometimes be collected and seen in the sample or mineral oil may be identified if the stomach has ruptured after administration of mineral oil.[5]

Laboratory analysis involves measuring the total white cell count and red blood cell count. If a sample appears to be whole blood, a packed cell volume should be determined. If the number of cells is low, the sample can be centrifuged and the pelleted cells can be smeared onto a slide before staining.[5] The most common stains used are Wright's stain and Gram stain.[64,69] New methylene blue can also be used as a quick technique, but the cellular differentiation is not as good with this stain as it is with Wright's stain.[64] Staining allows a differential count to be calculated and the cells to be evaluated for degenerative changes, and the identification of bacteria or plant material.

Figure 15-39



Serosanguinous fluid indicates intestinal strangulation or hemorrhage.

Although normal peritoneal fluid has been reported to contain 5,000 to 10,000 white blood cells/μL (5-10 x 10^9 /L) for adults and 1,500 cells/ μL (1.5 x 10^9 /L) for foals,[70] most healthy horses rarely have WBC concentrations higher than 3,000/ μL (3 x 10^9 /L). The normal cell distribution reflects a 2:1 ratio of neutrophils to mononuclear cells,[2] with the occasional mesothelial cell.[5] Normal peritoneal fluid should contain no red blood cells. The red discoloration seen grossly is the result of lysed and intact red blood cells. However, small numbers of cells do not alter the color of peritoneal fluid and cannot be seen with the naked eye. To detect the presence of small numbers of red blood cells, which may indicate questionable intestinal viability, spectrophotometric assessment of peritoneal fluid for hemoglobin concentration is required. This determination has been found to have a high sensitivity (80%) and specificity (82%) in selecting horses with colic requiring medical versus surgical treatment.[71] Increased concentration of hemoglobin in the peritoneal fluid is indicative of a much higher necessity for surgery.[71] Visual assessment has a much lower sensitivity of only 51%.[71]

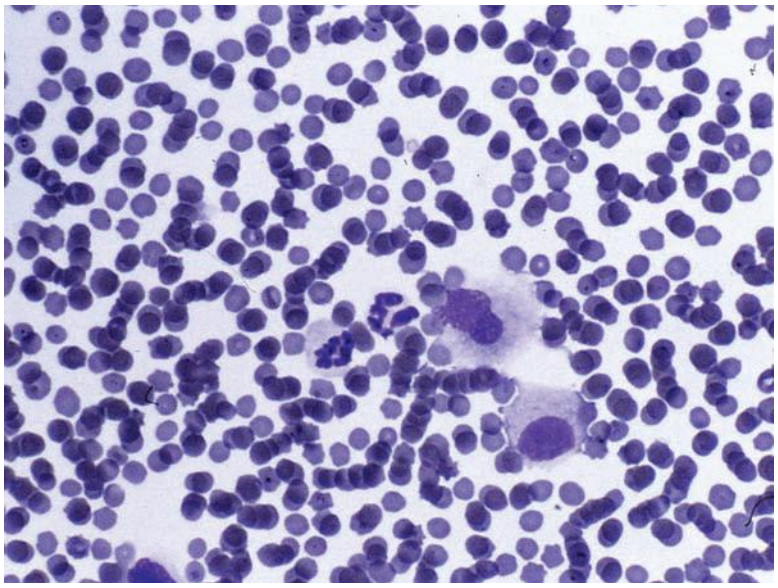
In the early stages of acute obstruction or strangulation, peritoneal fluid changes may not occur because the intestine is not devitalized enough to allow leakage of cells and protein. However, in peritonitis, nonstrangulating infarction, and small-intestinal enteritis, peritoneal changes frequently are present at the time that the clinical signs become apparent.[5] In horses with persistent simple obstruction, the protein concentration in the peritoneal fluid increases but the cell counts and differential remain normal. If obstruction creates enough distention to cause bowel wall ischemia, cell concentrations in abdominal fluid will increase. Peritoneal fluid changes associated with strangulating obstruction occur after approximately 1 to 2 hours, depending on the type and severity of the lesion. Red blood counts exceeding 20,000 cells/μL (20 x 10^9 /L) indicate a severe intestinal injury (Figure 15-40).[67] When the bowel is devitalized, neutrophil numbers increase in the range of 5,000 to 30,000 cells/μL (5-30 x 10^9 /L), and neutrophils may comprise 90% to 95% of the total white cells (Figure 15-41). As the intestine deteriorates further, the number of neutrophils may rise to 100,000 to 150,000 cells/μL (100-150 x 10^9 /L) and the cells appear to degenerate.[64, 65] Degenerative and toxic changes in the neutrophils occur in response to the bacteria and toxins contaminating the abdomen. These degenerative changes include swollen nuclei, karyolysis, homogenous pink-staining chromatin, vacuolation, and karyorrhexis (Figure 15-42).[72]

Peritoneal fluid in horses with nonstrangulating infarction can appear similar to other conditions with an increase in protein and white cell count, however, the white cell count may be extremely high (e.g., 300,000 to 400,000 cells/μL or 300-400 x 10^9 /L). These changes often are present at the time of onset of clinical signs of colic.[73] If the peritoneal fluid contains few red blood cells but has a very high white cell count, nonstrangulating infarction or primary peritonitis should be suspected.[5]

If the peritoneal fluid has the appearance of whole blood, a PCV should be determined. If the PCV exceeds that of peripheral blood, the blood in the peritoneal fluid sample is likely a result of puncture of the spleen during abdominocentesis.[5] If the blood originated from a blood vessel within the abdomen, the PCV will be the same as that of peripheral blood and platelets will be evident. If the blood has been present for some time, erythrophagocytosis by the mononuclear cells will be seen on cytology and platelets will be absent.[5]

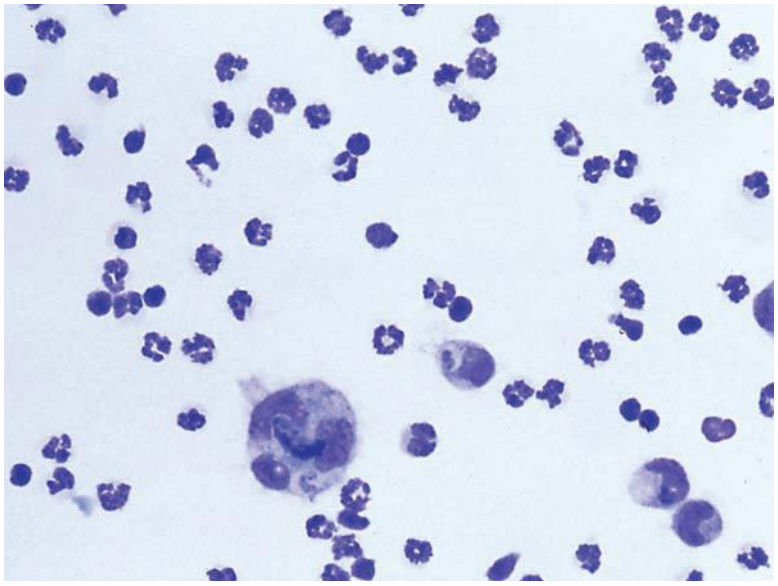
Ratios of either white blood cells or red blood cells to protein concentration have been used to classify the type of disease. When the ratio of the number of neutrophils in the peritoneal fluid to the total protein concentration is less than 3, enteritis and simple obstruction are more likely to be present. In contrast, higher ratios of neutrophils to protein concentration tend to occur when strangulated intestine is present. Also, a ratio of red blood cells to total protein concentration of 15 or less has been shown to be more indicative of duodenitis-proximal jejunitis, whereas higher ratios have been associated with strangulating lesions.[74]

Figure 15-40



Excess red blood cells are an indicator of abdominal hemorrhage.

Figure 15-41

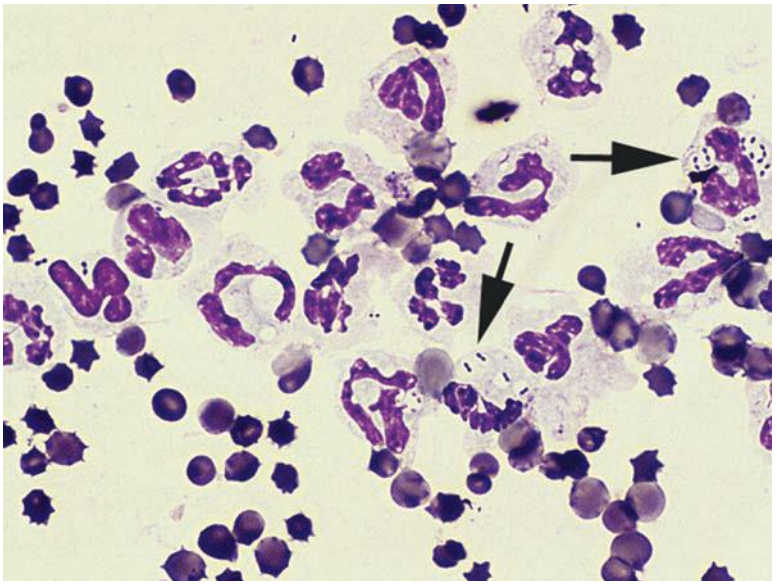


Increased numbers of neutrophils are an indicator of infection, intestinal injury such as strangulation, or bowel leakage.

Bacteria may be present in peritoneal fluid because of leakage through deteriorating bowel or ruptured bowel. The Gram stain allows identification of the type of bacteria present, and helps to identify the presence of a mixed population of bacteria, which is diagnostic for bowel rupture (Figure 15-43). The presence of bacteria does not always indicate a poor prognosis as horses with devitalized bowel and translocated bacteria can survive with appropriate surgical and medical treatment. Ruptured bowel (presence of feed material free floating in the abdomen) is associated with no chance for survival. Because bacteria may be present only in small numbers and may be phagocytized by neutrophils,[5] several slides should be thoroughly examined (Figure 15-42).

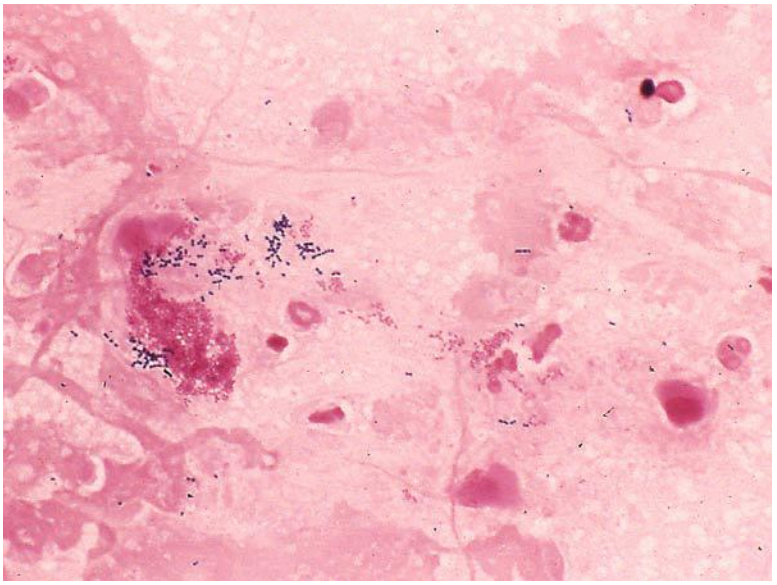
Peritoneal fluid pH and glucose concentration can be used to assist in the diagnosis of septic peritonitis.[75] A serum to peritoneal fluid difference in glucose concentration of greater than 50 mg/dL, peritoneal fluid pH less than 7.3, glucose concentration less than 30 mg/dL, and fibrinogen concentration greater than 200 mg/dL are highly suggestive of septic peritonitis.[75]

Figure 15-42



Neutrophils in peritoneal fluid that have phagocytized bacteria (arrows) and are undergoing karyolysis and karyorrhexis.

Figure 15-43



Gram stain of peritoneal fluid with gram-positive and gram-negative bacteria.

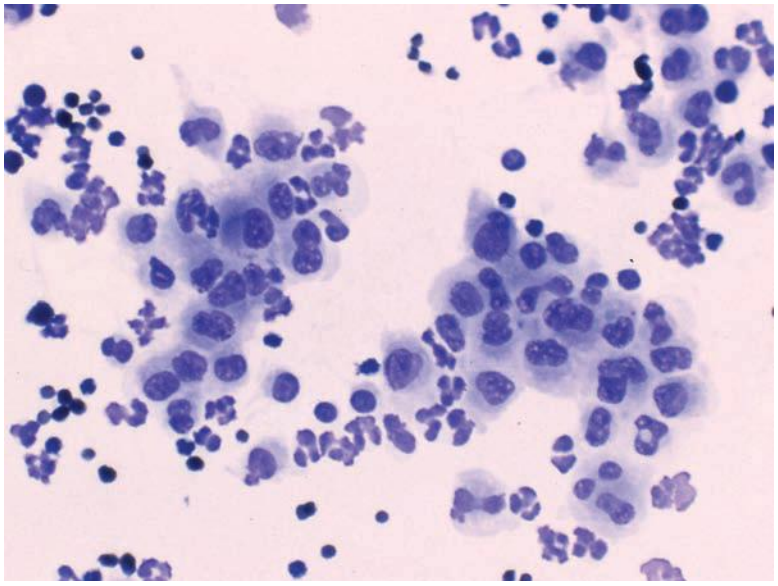
It is possible to obtain normal peritoneal fluid from horses with severe bowel disease because fluid is compartmentalized within the abdominal cavity.[5] For example, horses with intussusception, incarcerated intestine within the epiploic foramen contained in the lesser omental bursa, or diaphragmatic hernia may have normal peritoneal fluid but will have other clinical signs of severe disease.[5]

Care should be taken when interpreting the white cell counts and protein values after abdominal surgery. After a ventral celiotomy, white cell counts can be as high as 100,000 to 150,000 cells/μL (100-150 x 10^9 /L) with protein concentrations ranging from 3.3 to 6.2 g/dL. White blood cells counts as high as 400,000 cells/μL (400 x 10^9 /L) have been observed after abdominal manipulation and intestinal handling in normal ponies.[76,77] Cecal trocharization also increases the white cell concentrations to 30,000 to 60,000 (30-60 x 10^9 /L), and the cells can have signs of degeneration. Although some horses may develop a fever after cecal trocharization, most horses are not clinically ill after this procedure.[5]

After parturition, the volume of peritoneal fluid may increase but laboratory values should be normal unless there is an abnormality of the uterus or intestines. Neoplastic cells are rarely identified in peritoneal fluid; however, when they are present, they are helpful in the definitive diagnosis of the most common abdominal tumors: gastric squamous cell carcinoma or lymphosarcoma. The absence of these cells does not rule out neoplasia. Mesothelial cells may be seen in peritoneal fluid and may occur as sheets of cells (Figure 15-44). These are not specific for a particular problem nor do they represent a neoplastic process.

Peritoneal fluid enzymes, such as creatinine phosphokinase and alkaline phosphatase, exceed serum values with injured intestine and can be of use in identifying horses with chronic disease; however, these tests are not more sensitive than cytology.[65,78] Measuring the intestinal isoenzyme of alkaline phophatase may be useful in diagnosing small-intestinal disease as it is released specifically from this region of intestine.[29,78] Lactate dehydrogenase and lactate increase during ischemia, but values have not been shown to be associated with survival, specific conditions, or sepsis.[65,75] Ratios of serum creatinine and serum to peritoneal fluid creatinine (*peritoneal fluid creatinine ≥2 times serum creatinine*) are invaluable aids in the diagnosis of uroperitoneum secondary to bladder rupture in the foal[79] or adult horse.

Figure 15-44



Mesothelial cells, which normally appear in clumps, have large basophilic nuclei.

Hematology, Blood Gases, and Serum Biochemistry

A total white blood cell count and differential are helpful in classifying the type of acute abdominal disease. A leukocytosis may be present with a mesenteric abscess,[68] in some cases of peritonitis,[80] or duodenitis-proximal jejunitis.[54] A leukopenia indicates gram-negative sepsis or endotoxemia (enteritis, colitis,), salmonellosis, Potomac horse fever or ruptured bowel.[22,23,29,45,81] A depressed horse with a fever, distended small intestine, and leukocytosis is more likely to have enteritis. The white blood cell count rarely changes in the acute stages of intestinal strangulation until endotoxic shock causes margination of neutrophils with subsequent neutropenia. The differential cell count may be useful in cases of Potomac horse fever in which there is often a true monocytosis,[23] and in horses with lymphosarcoma which may have an absolute lymphocytosis.[72]

Measuring blood gases provides information about the acid-base status and lactate concentrations in the patient. The venous blood gas is usually adequate to assess metabolic contributions to acid-base balance, but to assess the respiratory component, arterial blood should be used. Arterial blood is taken from the transverse facial or facial artery. Most horses with simple colic or simple obstruction have normal acid-base status or are slight alkalotic. In the early stages of proximal small-intestinal obstructions or large-colon obstructions, horses are usually alkalotic as a result of fluid retention and chloride loss.[5] Respiratory alkalosis from hyperventilation may precede dehydration and shock in strangulating conditions.[5] Strangulating lesions with sequestered fluid within the intestinal tract eventually cause dehydration and endotoxemia, resulting in reduced tissue perfusion. Reduced perfusion leads to lactic acidosis and can be diagnosed by measuring serum lactate concentration and venous blood gases. Restoration of blood volume is critical and fluid resuscitation with polyionic fluids is recommended.[82] Increased blood lactate concentrations also correlate with decreasing percentage of survival in horses with colic.[83]

Anion gap is a measure of circulating anions, such as lactate, and has been used to predict survival in horses with colic.[84] The anion gap is calculated by subtracting the sum of the choride and bicarbonate concentrations from the sodium concentration. In one study, the survival was 81% when the anion gap was less than 20mEq/L, whereas the survival was 0% when the anion gap was 25mEq/L.[84] The anion gap does not appear to be accurate in conditions with altered serum chloride concentrations such as duodenitis-proximal jejunitis. In these types of cases, increased anion gap does not accurately reflect survival. Blood lactate and anion gap are, therefore, used as indicators of the prognosis rather than as diagnostic aids.[83]

Determination of serum electrolyte concentrations is important to guide adequate treatment and fluid resuscitation. Rarely do electrolyte values help make a diagnosis. Hypomagnesemia and hypocalcemia are often associated with gastrointestinal

disorders and may contribute to ileus. Hypomagnesemia and hypocalcemia are common in the perioperative period, particularly in horses with strangulating lesions or ileus.[28] Serum concentrations of total magnesium and calcium are less sensitive than ionized magnesium and calcium values in detecting horses with hypomagnesemia and hypocalcemia.[28] These electrolyte abnormalities should be corrected once treatment is initiated and, if the hypocalcemia is severe, calcium can be administered intravenously during the examination. Serum calcium and magnesium concentrations are not predictors of survival, but early recognition and correction of deficiencies in these electrolytes may help reduce morbidity and mortality in horses with colic and may help restore intestinal motility.[28]

Hypochloremia may be associated with a proximal small-intestinal obstruction or gastric obstruction,[86, 86] and most commonly causes a metabolic alkalosis. Hypochloremia can also be seen with exhausted horse syndrome when large volumes of sweat have been lost. Marked changes in serum concentrations of sodium and potassium usually occur only in acute colitis, salmonellosis, or ruptured bladder. Many foals with a ruptured bladder have hyponatremia, hypochloremia, hyperkalemia, and a metabolic acidosis at the time of diagnosis.[79]

Serum enzymes can change in diseases involving liver, muscle, and kidney. Sorbitol dehydrogenase, gamma glutamyl transferase (GGT), lactate dehydrogenase, aspartate amino transferase, lactate dehydrogenase, and arginase can all increase with liver cell degeneration or necrosis. Obstructive liver diseases, such as cholelithiasis, cause increases in bilirubin, alkaline phosphatase, and GGT.[66, 87] A highly sensitive test for obstructive disease of the liver is measurement of serum bile acids, which increase dramatically from normal values of 5 μmol/L to reach values of 80 to 100 μmol/L.

Coagulation tests and clotting times are not commonly evaluated in horses with colic, but are indicated when signs of abnormal hemostasis, such as bleeding excessively from the catheter site, nasogastric tubing, or abdominocentesis, are noted. To ensure the validity of the results, these tests are all run with controls. Disseminated intravascular coagulation may occur with endotoxemia during the late stages of strangulating obstruction or severe peritonitis or enteritis. Findings that are indicative of disseminated intravascular coagulation include thrombocytopenia, prolongation of the prothrombin and the partial thromboplastin times, increased fibrin degradation products, and reduced antithrombin III levels.[88, 89]

Ultrasonography

Transabdominal ultrasonography is a safe, direct, noninvasive diagnostic technique that is used routinely in many referral facilities to evaluate colic patients.[90] A sector or linear transducer can be used, to provide a high quality image with standard ultrasound equipment. A 5 MHz transducer provides maximal penetration of 10 cm, whereas 3.5 MHz and 2.0 MHz transducers can locate structures as deep as 22 cm and 30 cm, respectively.[90] A 6 to 7 MHz rectal probe can also be used to evaluate the abdomen per rectum and is especially useful for evaluating masses or bowel in the dorsal regions of the abdomen. The horse can be clipped and ultrasound coupling gel applied. Alternatively, applying large amounts of isopropyl alcohol with a spray bottle or sponge is often sufficient to eliminate the air interface between the skin and transducer to establish a suitable image.[90] The entire ventral abdomen should be examined in the adult horse while it is standing. Foals can be examined standing or in lateral recumbency.

Ultrasound of the stomach can be performed between the left 11th, 12th, and 13th intercostal spaces. When the stomach is distended, it displaces the spleen caudally and ventrally and appears as a large, fluid-filled structure ventral to the lung margin (Figure 15-45).[91] Gastric impactions can be suspected if the visible surface of the stomach extends over five or more intercostal spaces and hyperechoic material is present within the lumen.[92] Tumors of the stomach such as squamous cell carcinoma can also be recognized as a mural mass with heterogenous echogenicity (Figure 15-46).[92]

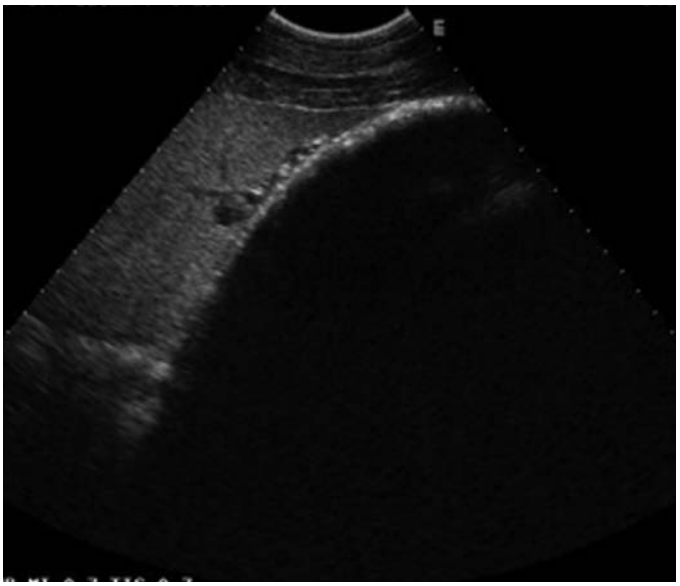
Ultrasound is useful for evaluating the small intestine, which may not be palpable on rectal examination. Distended small intestine can be identified with ultrasound before it can be appreciated by rectal examination. The duodenum can be seen between the 10th and 12th intercostal spaces medial to the right lobe of the liver to the 15th and 16th intercostal spaces underneath the body wall below the ventral aspect of the right kidney (Figure 15-47). Loops of small intestine can be seen in the lower left quadrant medial to the spleen in adult horses and normally appear rounded or tubular with hyperechoic material within the lumen and with active wall movement. If the loops cannot be located, the scanner probe should be moved to the very caudal abdomen near to the penis or mammary gland. The small intestine should be no thicker than 3 mm.[93] Ileus should be suspected when motility is not evident. When ileus is caused by duodenitis-proximal jejunitis, the degrees of distention and increase in wall thickness vary. This syndrome can be difficult to differentiate from other causes of ileus.[90] If the obstruction is simple or strangulating, the small intestine proximal to the obstruction will become distended, appearing as round loops that do not change diameter, have no signs of motility, and often contain fluid (Figure 15-48). The number and

size of loops depends on the severity of the lesion, but the loops can measure 5 to 7 cm or more in diameter, particularly when the ileum is distended. In foals or young horses with ascarid impactions, the parasites may be detected within the intestinal lumen (Figure 15-49).[90] Intestinal wall thickness frequently increases because of mural edema or hemorrhage in cases of strangulating obstruction both in the affected bowel and the intestine orad to the lesion (Figure 15-48). Necrosis can produce a gas echo in the intestinal wall, and sloughing of the mucosa may be accompanied by adjacent anechoic fluid (Figure 15-50).[90] With epiploic foramen entrapment, the edematous loops may be visible on the right side of the abdomen.[90] Intussusceptions can be seen with the ultrasound and appear as a target-like structure with the intussusceptum evident within the lumen of the intussuscipiens and varying amounts of intestinal wall edema and changes in wall thickness (Figure 15-51). Diaphragmatic hernias can also be diagnosed on ultrasound by the presence of loops of small intestine or other intestinal segments in the thoracic cavity, with some degree of peritoneal and pleural fluid (Figure 15-52).[90]

Figure 15-45A

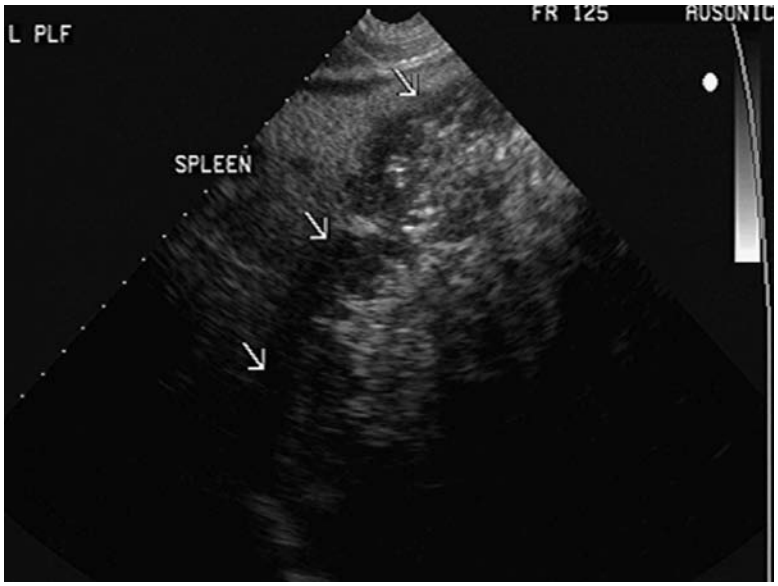


Figure 15-45B



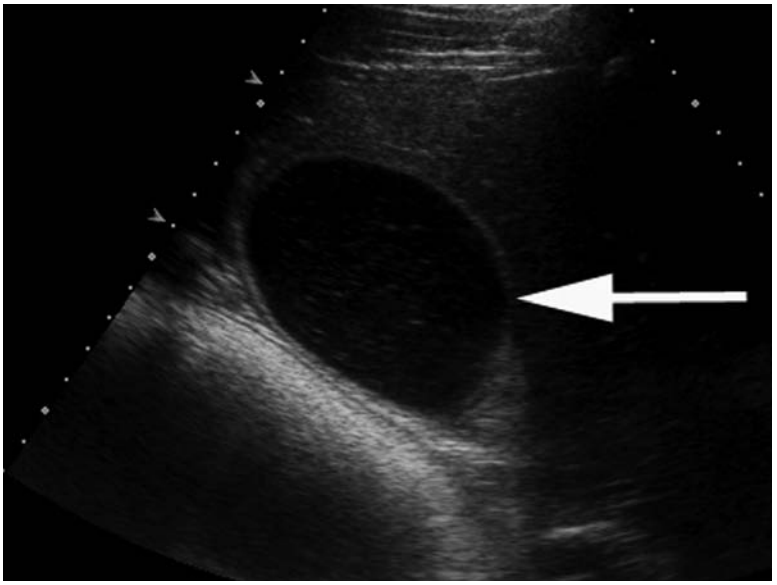
Ultrasonogram of the normal stomach wall (bright white line) and adjacent spleen **(A)** and a distended stomach **(B)**. (Courtesy of Dr. Anne Desrochers, Marion duPont Scott Equine Medical Center, 2008.)

Figure 15-46



Ultrasonogram of a squamous cell carcinoma of the stomach with a thickened and irregular stomach wall (arrows). (Courtesy of Dr. Anne Desrochers, Marion duPont Scott Equine Medical Center, 2008.)

Figure 15-47



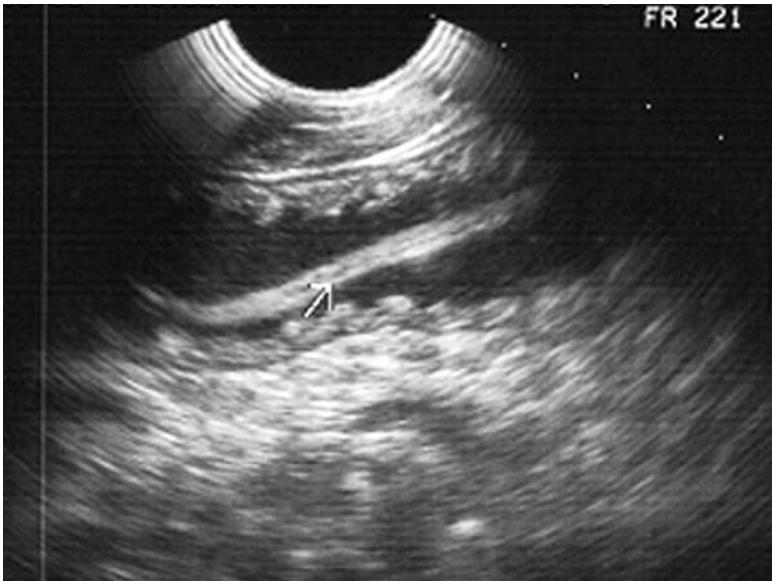
Distention of the duodenum (arrow) over the cecum. (Courtesy of Dr. Anne Desrochers, Marion duPont Scott Equine Medical Center, 2008.)

Figure 15-48



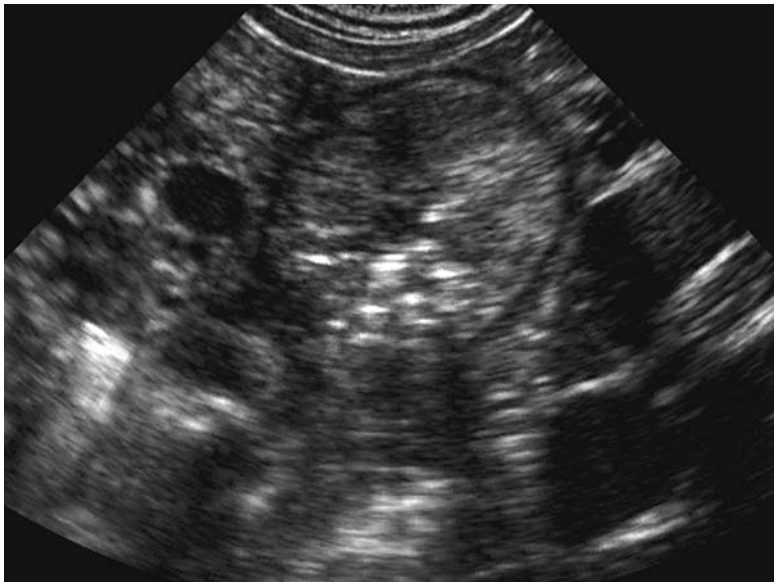
Distended loops of small intestine with increased wall thickness. The normal thickness is 2 to 3 mm. (Courtesy of Dr. Anne Desrochers, Marion duPont Scott Equine Medical Center, 2008.)

Figure 15-49



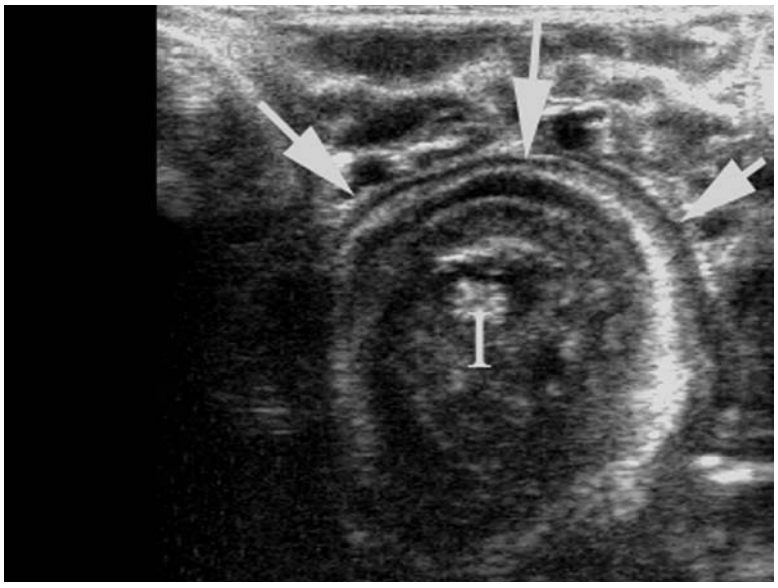
Ultrasonogram of an ascarid in the small intestine of a foal (arrow). (Courtesy of Dr. Anne Desrochers, Marion duPont Scott Equine Medical Center, 2008.)

Figure 15-50



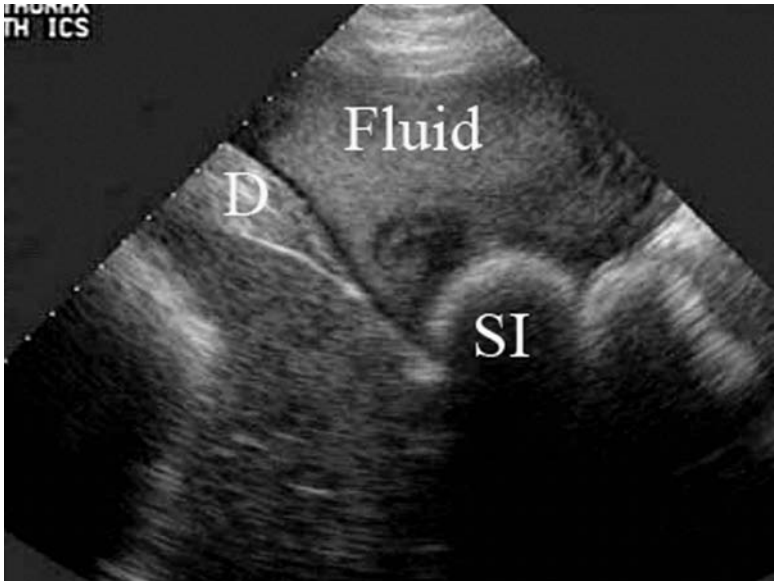
Ultrasonogram of the small intestine with a thickened wall and hyperechoic reflections indicating gas in the intestinal wall. (Courtesy of Dr. Anne Desrochers, Marion duPont Scott Equine Medical Center, 2008.)

Figure 15-51



Ultrasonogram of an intussusception in the small intestine. The concentric circles represent the intussuceptum (I) with the intussuceptiens (arrows). (Courtesy of Dr. Anne Desrochers, Marion duPont Scott Equine Medical Center, 2008.)

Figure 15-52



Ultrasonogram of small intestine within the chest cavity. (D=Diaphragm; SI=Small intestine). (Courtesy of Dr. Anne Desrochers, Marion duPont Scott Equine Medical Center, 2008.)

The large colon is located in the ventral cranial abdomen; the wall usually appears thicker than the small intestine (Figure 15-53). The haustra of the ventral colon can appear as a series of rounded, hyperechoic lines.[90] Large-colon thickening can be detected with ultrasound and may indicate an obstruction (Figure 15-54). Ultrasound can be used in conjunction with rectal examination to diagnose left dorsal displacement of the large colon over the renosplenic ligament. The colon in the left paralumbar fossa appears as a gas echo dorsal to the spleen, thereby preventing imaging of the left kidney (see Chapters 21 and 38). This appearance is not diagnostic for renosplenic entrapment and can occur with other displacements.[59] Pneumoperitoneum may also result in gas pockets being identified dorsally in the abdomen.[90]

Figure 15-53A

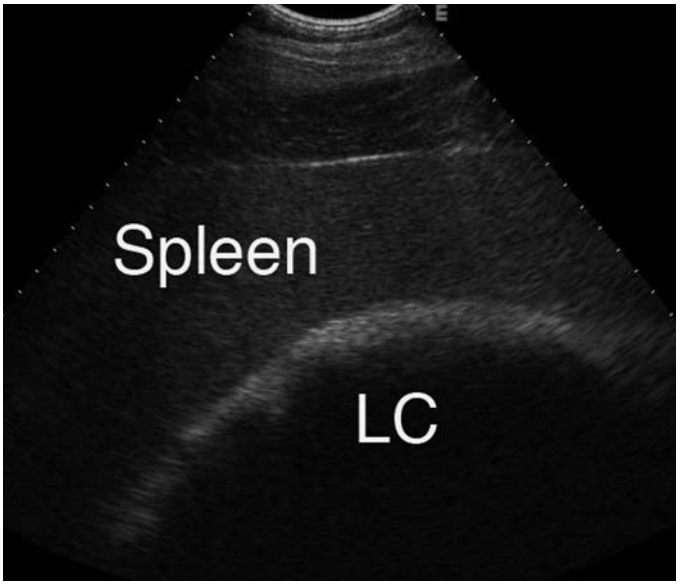
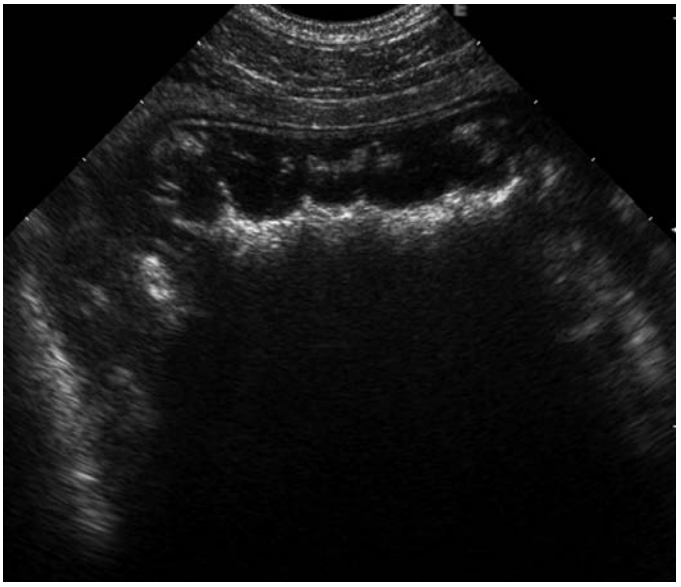
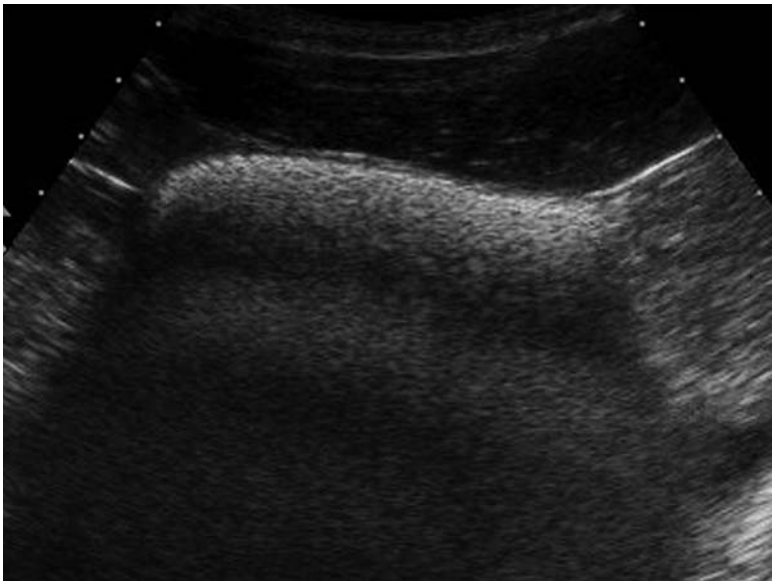


Figure 15-53B



A.) Ultrasonogram of the normal large colon. **B.)** Although thicker than the small intestine, the wall thickness can be increased by fluid in the submucosa and serosa because of obstruction (Courtesy of Dr. Anne Desrochers, Marion duPont Scott Equine Medical Center, 2008.)

Figure 15-54



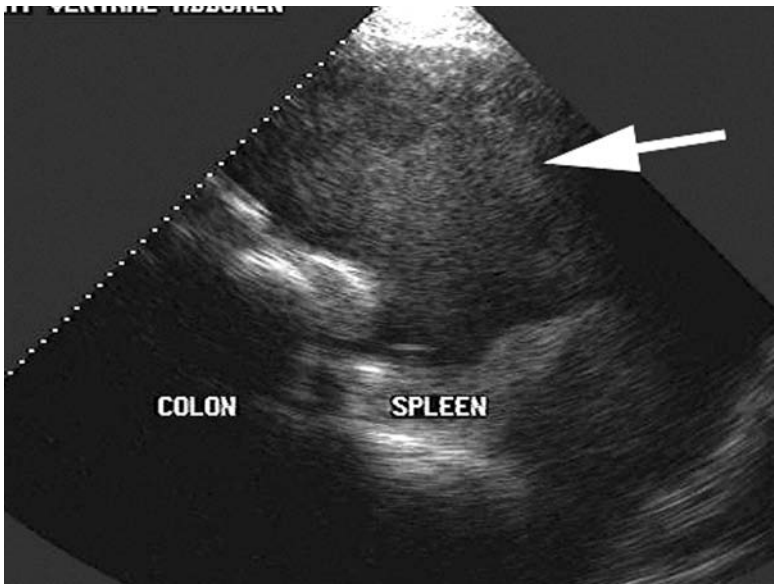
Ultrasonogram of sand in the ventral colon. Sand creates a granular hyperechoic reflection. (Courtesy of Dr. Anne Desrochers, Marion duPont Scott Equine Medical Center, 2008.)

Ultrasound is a practical and reliable method for detecting sand accumulations in the large colon, but it does not replace radiography.[94] The ventral aspects of the sand accumulations appear to be hyperechoic with varying acoustic shadowing in the intestine with decreased or absent motility (Figure 15-54).[94] Although an ultrasound examination will reveal the length of the sand accumulations, information on their height or depth is limited. Rectal and transabdominal ultrasonography may indicate bowel within bowel, which is consistent with cecal intussusception.[57] Ultrasonographic measurement of right dorsal colon mural thickness may be useful in the diagnosis of right dorsal colitis. The thickness of the right dorsal colon increases in affected horses (see Chapter 20).[95] Large-colon wall thickness is also effective in identifying large-colon volvulus.[96]

Ultrasonography allows evaluation of the peritoneal fluid for quantity, echogenicity, motion, and the presence of solid particles or gas echoes. Care must be taken not to confuse hypoechoic fat, which contains bright sparks, with the peritoneal fluid. The echogenicity of the peritoneal fluid increases with increasing cell count. Uroperitoneum will appear anechoic, and in more than 50% of foals with a ruptured bladder, the defect in the bladder wall may be visible.[79] Transrectal ultrasound is required in adult horses to identify the defect in the bladder.[90]

Intraabdominal hemorrhage has a characteristic appearance of swirling masses of echogenic material (Figure 15-55). Free-flowing hyperechoic particles may include plant material or fibrin clots. When the bowel has been ruptured, a large amount of anechoic fluid with hyperechoic flecks can be seen. Ultrasound is also useful for evaluating the gravid uterus and intestinal tract in the pregnant mare, especially in late-term mares. Adhesions, neoplastic masses, intraabdominal abscesses, hematomas, and other abnormalities may all be recognized with ultrasound in certain cases.

Figure 15-55

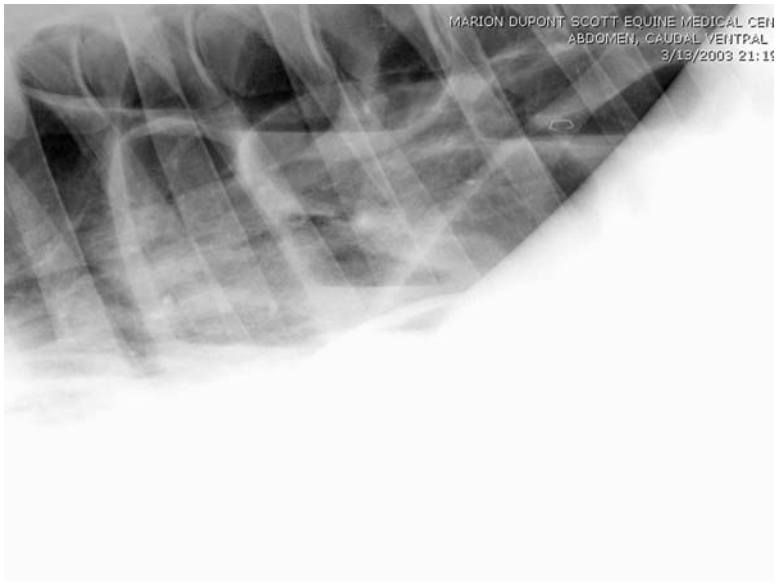


Ultrasonogram of blood in the abdomen. The blood will be swirling with moderate echogenicity. (Courtesy of Dr. Anne Desrochers, Marion duPont Scott Equine Medical Center, 2008.)

Radiographs

Plain and contrast radiographs are not used commonly in the assessment of the adult horse's abdomen because of the large body size and the limited availability of equipment. Even if the equipment is available, the scatter from the radiation makes a high-quality image impossible. Thoracic radiographs can be useful in the diagnosis of diaphragmatic hernia (Figure 15-56). Small intestine, large colon, and stomach can be detected in the chest during diaphragmatic hernia.

Figure 15-56



Radiograph of diaphragmatic hernia in a horse. Small intestine has filled the chest cavity.

Radiography is useful for diagnosing enteroliths and may be used as a screening test in regions where enteroliths are common (see Chapter 38).[97] The technique requires x-ray machines capable of 600 to 800 mAs and 120 kVp. Four views are recommended (Table 15-5).

Radiography of the cranioventral abdomen is a useful means of monitoring the resolution of sand accumulation and confirming the effect of medical treatment in the removal of sand (see Chapter 38).[98]

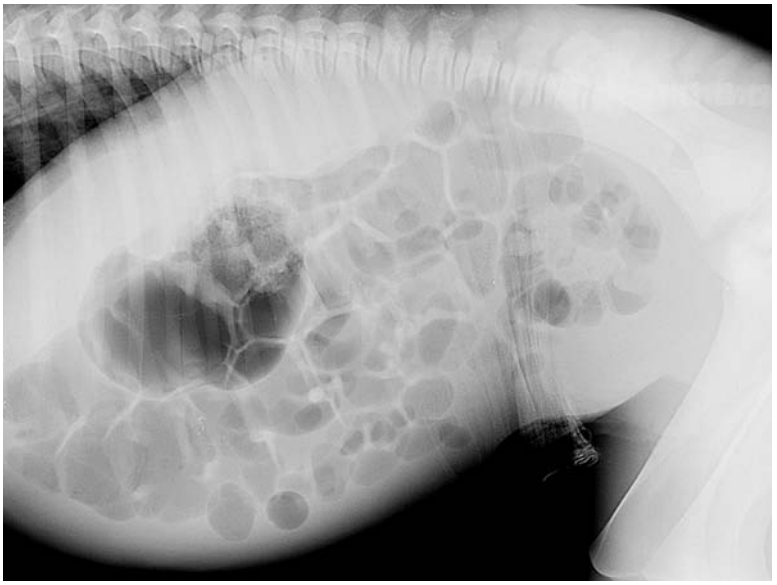
Table 15-5
Radiographic Techniques for Examination of the Abdomen in Adult Horses

Cassette Position	Exposure
Zone 1: Cranial Ventral	60-8 mAs; 110 kVp
Zone 2: Caudal Ventral	180-240 mAs; 110 kVp
Zone 3: Cranial Dorsal	600-900 mAs; 120 kVp
Zone 4: Caudal Dorsal	240-400 mAs; 110 kVp

1. Focal spot to film distance equals 48 inches
2. 14 x 17 inch cassettes
3. 8:1 80 line per inch grid
4. 1 mm sheet lead placed behind the cassette to reduce radiation scatter

Radiographs are useful for evaluating the foal's abdomen, and can help provide information about the small intestine, large colon, and bladder. The technique for the standing lateral view of the foal is 20 mAs and 88 kVp for a 20-cm wide abdomen, using 10:1 focused grid at 72-inch focal distance,[99] or 15 mAs at 80 to 100 kVp with an 8:1 focused grid at 40 inches, both with rare-earth screens.[100] Similar techniques appear satisfactory for newer digital or computed radiographs. Enteritis often appears as slight small-intestinal distention with only small amounts of gas (Figure 15-57). In contrast, obstructed small intestine has distinct multiple loops of intestine with fluid lines, and frequently indicates a strangulating lesion (Figure 15-58). Large-intestinal obstruction in neonates may be a result of meconium impaction or of large- or small-colon atresia. Atresia of the large colon can be diagnosed by the abnormal configuration of the distended colon.

Figure 15-57



Radiograph of foal with enteritis. The small intestine has generalized filling but is not severely distended.

Contrast radiography helps to define gastric outflow obstructions in foals and can help visualize obstructions in the rectum and small colon. Barium solution (2.5 to 5 mg/kg as a 30% to 40% solution) is administered via stomach tube; gastric emptying of the barium normally occurs in 30 to 120 minutes. Barium retention indicates an outflow obstruction at the pylorus or duodenum or gastric stasis, which can be due to gastric ulceration. In adult horses, at least a liter of barium solution must be used to observe gastric emptying. Infusion of barium in the rectum can help outline a meconium impaction but care must be taken not to use an excessive volume, which could cause rupture of the rectum or small colon.

Figure 15-58



Radiograph of foal with strangulated small intestine. The small intestine is severely is distended. Loops of the small intestine arch within the abdomen, and fluid lines are seen at different levels within the abdomen.

Gastric emptying can be determined by scintigraphy using a technetium-99m-sulfur colloid cooked in egg white and administered by stomach tube or in sweet feed. Images from the left and right side are taken at 0, 15, 30, 60, 90, 120, and 150 minutes. Using a time-versus-activity curve, the gastric emptying half time (t1/2) can be calculated. Normal t1/2 is 49 ± 30 minutes.[101]

Endoscopy

Gastroscopy can be performed in the standing adult horse with moderate sedation (xylazine or detomidine), and in neonates with no sedation or with a small amount of xylazine.[102] In adult horses, feed should be withheld for 6 to 10 hours, and foals should be allowed to nurse up to 4 hours prior to gastroscopy.[102] The diameter of the endoscopes range from 10 to 14.5 mm. Endoscopes having a diameter of 10 mm can be passed through the foal turbinate region, whereas the larger diameter endoscopes will only pass through the turbinate regions of yearlings and adults. The endoscopes come in varying lengths. Endoscopes of 110 cm in length will reach the stomach of foals up to 30 to 40 days of age.[103] In weanling foals, a human slim colonscope with a diameter of 12.5 mm can be used. For most equine gastroscopy, a minimum length of 200 cm is required, but at this length the antrum and pylorus cannot be adequately examined.[103] The 200-cm endoscope will allow examination of the duodenum in foals up to 6 months of age, but a 280- to 300-cm long endoscope is required to perform complete gastroscopy and duodenoscopy in adult horses.[103]

The endoscope should be inserted carefully into the ventral meatus. The endoscope is passed down the esophagus and into the stomach. The esophagus can be examined thoroughly at the end of the examination as the endoscope is withdrawn. The esophageal sphincter and entrance to the stomach is usually 170 to 180 cm from the nares. Some resistance may occur at this point, but it should be fairly simple to pass the endoscope into the stomach.[103] The stomach must be distended by insufflation in order to evaluate the glandular and non-glandular areas. If a large volume of feed material and fluid are in the stomach after an adequate period of starvation, a gastric outflow obstruction should be suspected.[103]

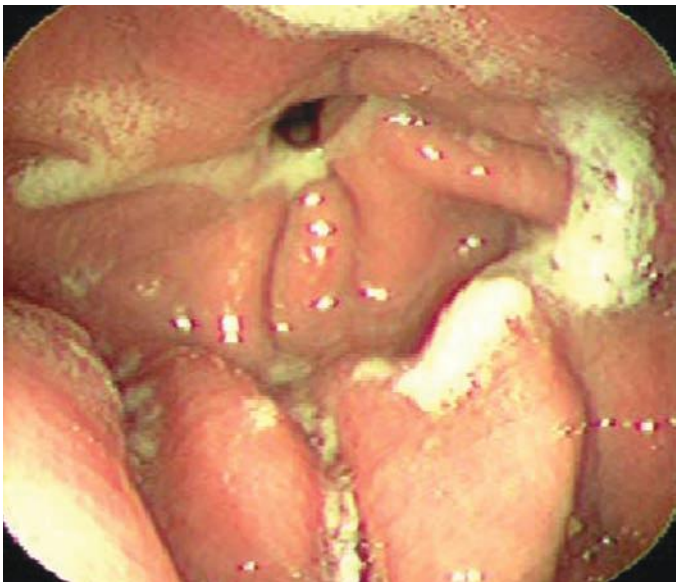
After the endoscope enters the stomach, it travels against the right side and then dorsally and is advanced to the caudal portion where the lesser curvature and cardia can be seen (Figure 15-59).[103] The endoscope is then advanced across the ventral ridge of the lesser curvature so that the antrum and pylorus can be seen (Figure 15-60).[103] The endoscope cannot be advanced to the pylorus and into the duodenum unless gastric contractions are adequate (Figure 15-61).[103] The stomach and duodenum can be assessed; biopsies can be taken for further information, if required, but are not of much value from the gastric mucosa. A larger specimen can be obtained from the glandular mucosa and duodenum as the tissue can be torn with the small biopsy forceps.[103] Gastric ulceration, gastric impaction, gastric squamous cell carcinoma, gastric outflow obstructions, or abnormalities within the duodenum or duodenal papilla can be diagnosed with endoscopy (see Chapter 34).

Figure 15-59



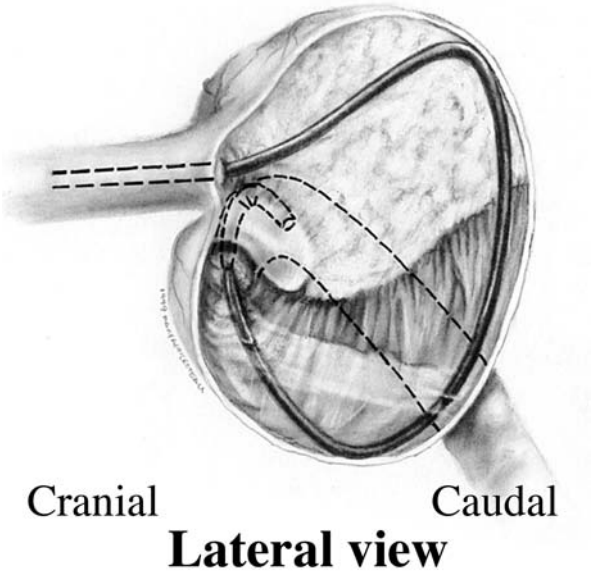
Endoscopy of the stomach. The endoscope moves along the greater curvature and allows visualization of the cardia, margo plicatus on the lesser curvature of the stomach.

Figure 15-60



Endoscopy of the stomach antrum and entry into the pylorus.

Figure 15-61



Drawing of the 3-meter endoscope being passed along the greater curvature of the stomach and entering the duodeum.

Laparoscopy

Diagnostic laparoscopy may be indicated in certain cases of recurrent, chronic, or acute colic,[104,105] especially if rectal examination, hematology, abdominocentesis, and ultrasonography have not provided a diagnosis, and the options for exploratory laparotomy are limited.[106] In cases of chronic colic, visualization of adhesions, serosal irritation, and abdominal masses may be helpful in making a diagnosis in the standing horse. Limitations to the examination are present in either the standing or anesthetized recumbent horse, as much of the viscera remain hidden with the horse in either position.

The laparoscope used for evaluating the equine abdomen is usually a 10-mm diameter laparoscopic telescope with a lens angle of 30 degrees. Horses must be held off feed a minimum of 24 hours; visualization of the abdomen is improved after 36 to 48 hours. Water should always be freely available during the period when feed is withheld. The 30-cm long 30-degree viewing telescope is adequate for exploration, although longer scopes may help visualization of the stomach, pelvic inlet, and duodenum. Laparoscopic portals include the paralumbar fossa on the left and right sides, and the umbilicus or linea alba when the horse is in dorsal recumbency. Prior to proceeding with abdominal laparoscopy in a standing horse, a rectal examination should be completed to locate organs on the left (spleen and colon) and right (cecum) sides of the abdomen. Scope insertion is via incision and placement of cannulas through the appropriate portal. Insufflation of the abdomen with CO_2 after a cannula has been passed into the abdomen is helpful to facilitate visualization.

Two main laparoscopic surgical approaches are used. One is a standing flank approach, for which the feed should be withheld for 24 to 48 hours prior to surgery whenever possible.[106] The horse is restrained in stocks and given a continuous infusion of detomidine and butorphanol to provide analgesia and sedation. The abdomen is insufflated with CO_2 gas. The laparoscope is usually first inserted into the left flank. The procedure can then be repeated on the right side; residual gas in the abdomen will reduce the chance of penetrating the cecum.[106] The other approach is via the ventral abdomen with the horse under general anesthesia. Withholding food is even more important in these situations to allow acceptable evaluation of the abdomen. The abdomen is insufflated just caudal to the umbilicus, and the laparoscope placed in that position. To evaluate the caudal abdomen, the horse is tilted head down 30°, described for humans as the Trendelenburg position, and the reverse position is used for evaluating the cranial aspect of the abdomen. The success of this technique depends on the accessibility to the organs of interest. It is sometimes impossible to move around a distended viscus and visibility is limited, which is why withholding feed before surgery is important. Normally, the following structures can be seen with laparoscopy: small colon, greater curvature of the stomach, right dorsal colon, pelvic flexure of ascending colon, cecum, jejunum, duodenum, and occasionally, the ileum.[106] Caudal aspects of the right and left lateral caudate lobes of the liver and the pancreas can be seen by looking through the epiploic foramen.[106] The lateral surface of the spleen and the renosplenic ligament lie beneath the left laparoscopic portal in the standard paralumbar fossa location and both kidneys can be seen through their peritoneal coverings.[106] In the caudal abdomen, the bladder, ovaries, uterus, and inguinal rings can be seen. Certain structures can be biopsied, if necessary, such as abdominal masses, liver, spleen, mesenteric lymph nodes, kidney, or ovary.[106] Intestine cannot normally be biopsied unless a portal incision is enlarged and the intestine is brought out of the incision.[106]

An overall sensitivity of 75% has been recorded for diagnostic laparoscopy.[106] The larger abdominal organs cannot be manipulated with either laparoscopic approach and thus lesions can be missed. Laparoscopy is not a good test for confirming the absence of disease.[107] Certain conditions, for example duodenal adhesions, may only be definitively diagnosed with laparoscopy in a standing horse.[108] It is a useful technique to examine horses when the owners cannot afford an exploratory laparotomy, but the technique provides limited information. Laparoscopy can be useful for splenic conditions, diagnosing adhesions post-operatively, evaluating penetrating wounds to the abdomen, and neoplastic conditions.

Fecal Examination

Gross, cytologic, biochemical, bacteriologic, immunologic, and electron microscopic evaluations can be performed on fecal samples. The fecal contents should be examined for the presence of sand, gravel, undigested feed material, watery consistency (increased transit time), mineral oil (if administered previously), and parasites. The feces can be placed in a rectal sleeve filled with water to allow the sand to settle out. This can be a useful monitoring method to determine whether sand is being passed during treatment.

Assessing fecal occult blood, although possible, can be difficult to interpret as the sample may be contaminated from previous rectal examinations where some minor bleeding has occurred from the mucosa. Determining fecal occult blood may be useful for diagnosing ulceration in the gastrointestinal tract, such as right dorsal colitis, but the available tests are not highly sensitive or specific for digested blood.[109] It may also be useful in certain cases of chronic weight loss.[5] Cytologic

examination is used mainly to evaluate the parasite burden of the animal.[102] Fecal culture is used primarily to detect *Salmonella sp*. Fecal biopsy has been used to obtain cultures for salmonella, but has a limited use, as biopsies taken for enteritis are not reliable.[5]

Transit Time

Measurement of fecal transit time may be helpful in detecting obstructions or problems with motility. The technique is not commonly used, but can be helpful in cases of chronic or recurrent colic.[110] Plastic beads (4 mm diameter) administered orally are retrieved in the feces at timed intervals. Beads are first observed at 14 hours, with all beads passing at 72 hours. If the horse had an obstruction requiring surgery, the beads were retained at 36 to 48 hours.[110] Mineral oil commonly administered as a laxative will provide a crude estimate of fluid transit, with oil first detected at approximately 12 to 18 hours. Use of mineral oil does not rule out obstruction of an intestinal lumen with blockage of ingesta.

Exploratory Laparotomy

Often a definitive diagnosis is not obtained until an exploratory laparotomy is performed. This is used as both a diagnostic procedure and a treatment. Not all parts of the intestinal tract can be exteriorized for evaluation, therefore careful palpation is an important aspect of the surgery (see Chapter 26). Examples of chronic problems that are diagnosed only by palpation are pancreatitis, duodenal adhesions, duodenal thickening or impaction, gastric tumors, pyloric thickening, cholelith, diaphragmatic hernia, mesenteric and mesenteric artery disease, colonic foreign bodies, muscular hypertrophy of the ileum, and adhesions.[5]

False Colic

Other painful conditions or regions within the abdomen other than the gastrointestinal tract may manifest clinical signs that resemble colic (see Chapter 42). Muscular pain can resemble colic. Exertional rhabdomyolysis, the dissolution of muscle with exercise, is a common muscle disorder in horses. Horses with severe rhabdomyolysis may show signs of colic, become recumbent, and develop myoglobinuria.[111] Diagnosis is usually based on the clinical signs (which can also include excessive sweating, increased respiratory rate, firm, and painful muscle contractions) and also increased serum muscle enzyme concentrations.[111]

Horses with liver disease may also present with signs consistent with colic (see Chapter 11). For example, horses with cholangiohepatitis commonly present with the nonspecific clinical signs of fever, icterus, colic, weight loss, and encephalopathy.[112] The history will often include reports of recurrent bouts of mild to moderate colic with fever in the preceding days to weeks prior to the present episode. In chronic cases, the horse will usually have experienced chronic weight loss and encephalopathy.[112] Serum biochemical abnormalities combined with the clinical signs help in the diagnosis. Marked increases in hepatobiliary enzymes GGT and AP, moderate increases in hepatocellular enzymes aspartate transaminase (AST) and sorbitol dehydrogenase (SDH), elevated serum bile acids, and elevated total serum bilirubin are common findings in horses with liver disease.[112] Hematologic changes may also include chronic, active inflammation with neutrophilia and hyperfibrinogenemia and, if the condition is more than 2 to 3 weeks in duration, hyperglobulinemia.[112] A definitive diagnosis requires a liver biopsy. Before this procedure is done, clotting profiles should be checked.[112]

The pulmonary system can also be extremely painful and may cause clinical signs mimicking colic (see Chapter 42). A horse with pneumonia may appear depressed and anorexic and have reduced fecal output, which may be caused by ileus secondary to dehydration. Pleuropneumonia is a painful condition. Affected horses may present with fever, anorexia, depression, coughing, respiratory distress, stiff gait, weight loss, sternal or limb edema, and/or colic.[113] When in the painful acute stage, affected horses may stand with their elbows abducted and may grunt with pain, have intercostal muscle spasm, or may demonstrate escape maneuvers.[113] This pain may be confused with abdominal pain. The pain subsides when the disease becomes more chronic and fluid is increased within the pleural space. It is very important to do a thorough examination and auscultate the chest as well as the abdomen. In pleuropneumonia, lung sounds are normal dorsally, and are absent or heard only as bronchial tracheal sounds ventrally.[113] A pneumothorax or hemothorax or any space-occupying lesion within the thorax that significantly reduces tidal volume and results in hypoxia will cause the horse to become extremely distressed, and this can be confused with intense pain. This situation can be encountered with a diaphragmatic hernia when the horse is in pain and also in respiratory distress.

Problems within the urogenital tract can also cause abdominal pain and colic (see Chapter 42). In acute renal failure such as aminoglycoside toxicity, the horse usually presents with polyuria, depression, and anorexia.[114] The depression and anorexia

may be confused with an alimentary problem, and if the horse has mild stranguria with oliguria, it may appear to be stretching and straining, which can be a sign of abdominal discomfort. The most common clinical sign of chronic renal failure is weight loss,[114] but rarely, abdominal pain can occur if the horse has bilateral nephroliths or if a calculus obstructs a ureter.[115,116] Cystic calculi may also cause stranguria among the other clinical signs. Similarly, a distended bladder will cause abdominal discomfort, and this may occur with obstruction or a neurologic dysfunction. Mild colic can also be associated with renal carcimonas.[114] Ruptured bladder is a common condition in foals and may manifest as gastrointestinal clinical signs, including tenesmus associated with constipation, diarrhea, and gastric reflux.[79] Straining to urinate may sometimes be confused in foals with tenesmus from meconium impaction.

It is also possible that horses may have abnormal behavioral conditions that manifest as colic. In one report, a gelding that presented with a 5-day history of colic with the typical signs of pawing, looking at the flank, kicking and biting at the flank was not diagnosed during the medical examination.[117] This horse was observed in hospital and would display the signs when it was able to see hay but not allowed to eat it. Based on the history of similar feeding behavior at home and because no other cause for the colic could be identified, it was concluded that the initial colic may have been real abdominal pain with subsequent psychosomatic colic secondary to stress, redirected aggression, or displacement activity.[117]

Decision for Surgery

Determining the need for surgery in a horse with colic is often done in an emergency situation. Although the decision is best based on a diagnosis, a specific diagnosis is not always possible, and use of clinical signs is necessary to make the decision. The specific signs most helpful in indicating the need for surgery are presented in Table 15-6. A thorough examination must be performed prior to deciding to perform surgery as each sign has inherent errors when used alone. There are circumstances when the diagnosis cannot be made and no rectal examination findings are definitive. However, clinical signs such as

Table 15-6
Indications for Surgical Treatment of Colic*

Pain	Uncontrollable and/or severe Does not completely respond to flunixin meglumine or detomidine or requires a second treatment.
Gastric reflux	Alkaline yellow fluid >4 L
Rectal examination	Distended small intestine Distended and displaced large colon Distention that cannot be treated medically Palpable foreign body
Auscultation	Intestinal sounds absent
Peritoneal fluid	Increased protein with RBC and degenerate neutrophils
Contraindications for Surgical Intervention of the Equine Acute Abdomen	
Pain	No pain or depression
Temperature	> 102.5°F
CBC	Neutrophilia or neutropenia (< 3000/µL)
Auscultation	Progressive intestinal sounds

*These signs are generalizations and may not fit individual cases.

unrelenting pain that does not respond to analgesics are an indication to perform surgery as part of the diagnostic process. No strict guidelines or list of parameters exist that determine the need for surgery as there are varying degrees of severity, and a range of clinical signs for the diseases, and every horse can respond in a different way. Therefore, every case should be judged on its own merits based on history and a thorough examination. In certain cases, a rapid decision can be made if a diagnosis is made from the clinical signs. The history and presentation may indicate immediate surgical intervention, such as a broodmare presented 5 days after foaling with an acute history of severe abdominal pain, severe large colon distension, and clinical signs of endotoxemia indicative of a large-colon volvulus. In this case, the need for surgery is immediate based on a presumptive diagnosis.

Pain by itself, if persistent or recurrent, is an indication for surgery. This is particularly true if there is no response to analgesic administration. Horses with moderate or severe pain are more likely to require surgery than horses with mild pain. Horses that have constant pain, particularly after an analgesic has been administered, are significantly more likely to need surgery. Horses that have return of pain or those requiring a second administration or multiple administrations of an analgesic are also more likely to need surgery. The key is monitoring of signs, as horses may show pain after administration of an analgesic but the signs can be markedly decreased. Any recurrence should be considered a return of pain and, therefore, an indicator of the need for surgery. Return of pain in horses that have a problem that can normally be treated medically is still important. Horses with impactions of the large colon or cecum (including sand impactions) can have recurrent pain and can usually be treated medically. However, if the pain persists and there is no evidence of bowel motility with no response to treatment, surgery is indicated. With the advent of potent analgesics, veterinarians have used the response to treatment to effectively determine which horses need surgery. This is logical and if used with other physical signs, monitoring pain after treatment is highly successful in determining which horses will need surgery.

Rectal temperature is usually not increased in horses with acute strangulation or obstruction. Horses with enteritis frequently have an increased rectal temperature, suggesting that surgery is contraindicated.

Indicators of hydration and perfusion, such as heart rate, mucous membrane color, mucous membrane refill, PCV, and plasma protein concentration are not usually specific for diseases requiring surgery.[118] In most cases, signs of shock are linked to complete obstruction, strangulation, or enteritis, so that these values by themselves do not indicate a need for surgery. Heart rate can be misleading, as low or near normal rates can be observed early in very painful diseases. In this instance, pain should be considered the most important sign. High heart rates, although associated with severe diseases and poorer survival rates, do not always indicate the need for surgery. Diseases such as enteritis and tympany may cause high heart rates but do not normally require surgery.

Nasogastric reflux increases the likelihood that the small intestine is obstructed by a disease that requires surgical treatment. Reflux can also be caused by ileus or duodenitis-proximal jejunitis, which can most often be treated medically. Obstructions of the colon can also lead to nasogastric reflux, but these conditions do not always require surgery. Because of the lack of sensitivity, other physical signs should be used in conjunction with gastric reflux to make a final determination about the need for surgery. Conversely, the lack of gastric reflux does not rule out the need for surgery.

Duodenitis-proximal jejunitis, which can cause large volumes of gastric reflux, can create a diagnostic dilemma, as this condition causes pain, gastric reflux, distended small intestine and high peritoneal protein concentration, which together indicate a need for surgery. However, fever and subsequent depression are also observed, suggesting the signs are due to enteritis. If in doubt, this type of case should have surgery to make sure a strangulating or obstructing lesion is not present.

Horses with complete absence of borborygmi are significantly more likely to require surgery compared with horses with normal, decreased, or increased intestinal sounds. If borborygmi do not return after an analgesic or other treatment, the disease should be considered more serious, possibly requiring surgery.

Finding an intestinal abnormality on rectal examination is not always indicative of a need for surgery; however, any abnormal distention or abnormal positioning of the intestine, which has no accompanying diagnosis, is most likely due to a lesion requiring surgical intervention. If no abdominal abnormalities are found during the first examination, repeat rectal examinations are indicated, particularly if other signs suggest a disease requiring surgery. Distention not felt at the first examination may become evident in the near future.

If abnormal peritoneal fluid is present, bowel injury requiring surgery is usually present. If the fluid is normal but other physical

signs indicate that surgery is necessary, the bowel injury is probably early with no changes in abdominal fluid. Peritoneal fluid should not be used as the only determinant for surgery, as waiting for a change could delay surgery and decrease the chance for survival. Acute increases in peritoneal fluid protein concentration alone are sufficient to warrant surgery if other physical signs are also suggestive. If colic persists for days, peritoneal fluid should be monitored for increases in protein concentration and cell counts, as both are indicators of bowel injury and may suggest exploration is needed earlier rather than later. When veterinarians are undecided because signs are confusing and not sufficient to make a decision about the need for surgery, surgery will most likely be required. Under these conditions, the horse should be referred to a surgical facility for a second opinion where surgery can be performed immediately, if needed.

Frequently, heart rate and mucous membrane color and laboratory values are normal at the onset of colic. The parts of the examination that are most helpful in the early period are observation of pain, rectal examination, abdominal auscultation, and the response to analgesic administration. If pain is constant or returns within several hours after administration of an analgesic such as flunixin meglumine or detomidine, the horse most likely needs surgery. Normal values for heart rate, mucous membrane color and refill, and peritoneal fluid should be disregarded if pain persists, rectal findings are abnormal, and a lack of response to an analgesic indicate surgery.

Deciding to perform surgery on foals with colic is more difficult because of the inability to complete a rectal examination. However, foals rarely need surgery and radiographs can help distinguish between enteritis, obstructions, and strangulation requiring surgery. Chronic distention of the stomach may indicate pyloric stenosis and warrants surgical exploration.

The decision for surgery is accompanied with a responsibility to provide support for the period of transport, if needed. Specific recommendations for referral of horses with colic are listed in Table 15-7. It is important to initiate treatment such as antimicrobial agents, flunixin meglumine, and intravenous fluid therapy prior to transport if shock or a strangulating lesion are present; however, these should be completed rapidly so as not to delay delivery of the horse to a surgical facility as soon as possible.

Table 15-7
Referral Procedures and Recommedations

1. Know the directions to and procedures of the referral hospital.
2. Provide detailed history and treatment to date.
3. Provide adequate analgesia for the duration of the trip.
3. Place a stomach tube to allow any spontaneous gastric reflux.
4. Administer treatments for shock and antibiotics if necessary prior to transport.
5. Prepare owner for costs and need for prepayment of a portion of estimate.

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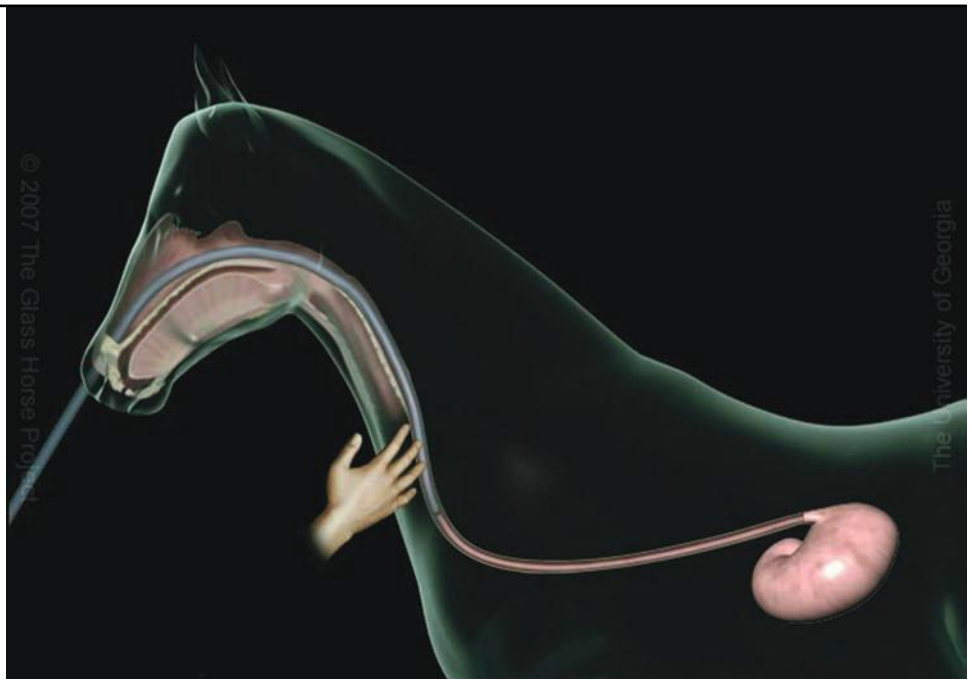
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Medical Management

Part 6



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Medical Management of Gastrointestinal Diseases

Chapter 16

Tim S. Mair

Analgesia

Relief of visceral pain in horses with colic is essential on humane grounds. It is also essential to try to minimize injury to the horse and attending personnel during evaluation and therapy. Even in mild cases, owner distress over animal pain is an important consideration.

The most satisfactory method of pain relief is the correction of the underlying disease process. This may take time, however, and it is frequently necessary to achieve temporary relief of severe pain by administration of analgesics to allow a thorough clinical examination. It is important to select an analgesic drug that will yield the desired effect without creating complications such as inhibiting intestinal motility, predisposing to hypovolemia and shock, or masking the signs of developing endotoxemia. The commonly used analgesic drugs, their dosages and relative efficacy for the control of abdominal pain are summarized in Table 16-1.

Table 16-1

Analgesic Drugs and their Relative Efficacy for the Control of Abdominal Pain.

Drug	Dosage	Efficacy
Dipyrone	10 mg/kg	poor to moderate
Phenylbutazone	2.2-4.4 mg/kg	poor to moderate
Flunixin meglumine	0.25-1.1 mg/kg	good to excellent
Ketoprofen	1.1-2.2 mg/kg	good
Xylazine hydrochloride	0.2-1.1 mg/kg	excellent
Detomidine hydrochloride	10-40 μg/kg	excellent
Romifidine hydrochloride	40-80 μg/kg	excellent
Acepromazine	0.03-0.1 mg/kg	poor
Morphine sulphate	0.3-0.66 mg/kg*	good
Meperidine (Pethidine)	2.0 mg/kg	poor
Butorphanol tartrate	0.05-0.075 mg/kg**	good
Pentazocine	0.3-0.6 mg/kg	poor

* Use only with xylazine or another α2-adrenoceptor agonist to avoid CNS excitement

** Doses in the upper range may cause ataxia

Walking

Walking the horse with mild colic frequently appears to be beneficial, and in some cases may be the only treatment necessary. Walking appears to have an analgesic effect, in addition to stimulating intestinal motility. It also helps to prevent injury to the horse caused by its falling to the ground and rolling.

Gastric Decompression

Gastric distention occurs most frequently secondary to small intestinal obstruction or small intestinal ileus. Because horses do not vomit, nasogastric intubation is necessary to determine whether gastric distention is present and to provide relief. Decompression of the stomach is necessary to relieve pain, and to prevent gastric rupture and death. Large volumes of reflux (10 to 20 liters) may be obtained in some cases, and if necessary, an indwelling nasogastric tube may be left in place to allow frequent (approximately every 2 hours) decompression.

Non-Steroidal Anti-Inflammatory Drugs (NSAIDs)

The eicosanoids, including prostaglandins, leukotrienes and thromboxanes, play a central role in the inflammatory response. These substances are derived from arachidonic acid, which is produced via the action of phospholipase A_2 on phospholipids in cell membranes (see Chapter 6). Once released, arachidonic acid becomes the substrate for several different enzyme systems. The cyclooxygenase (COX) enzymes metabolize arachidonic acid to form prostaglandins (PGs) and thromboxanes (TXs), whereas the lipoxygenases produce leukotrienes (LTs). In many tissues, PGs and TXs are produced constitutively, and these have many homeostatic roles. In the gastrointestinal tract for example, PGs of the E series (particularly PGE2) have a protective role in the gastric mucosa, protecting it from acids and hypertonic solutions.[1]

The COX enzymes exist in at least two isoforms, known as COX1 and COX2.[2] The COX1 enzyme is produced constitutively in many tissues, and this isoform is responsible for the production of PGs involved in homeostatic functions.[3] COX2 products can be induced in many cells, especially those involved with the inflammatory response. In addition to their roles in inflammation, PGs have important roles in the regulation of body temperature and in mediating pain. Many of the side effects of NSAIDs (such as gastric ulceration, renal impairment, and platelet dysfunction) are believed to be caused by the inhibition of the constitutively-expressed COX1 isoform. For this reason, NSAIDs that selectively block the COX2 isoform may offer therapeutic advantages by virtue of decreased side effects. Although a number of selective COX2 inhibitors are available for use in humans, few of them have been studied in veterinary species. In addition, enzyme selectivity appears to vary between species. Currently, no NSAID has been shown to be totally selective for COX2 inhibition in the horse.

The NSAIDs are among the most frequently used drugs in horses.[4] They are commonly used to treat musculoskeletal inflammation and pain, colic, fever and soft-tissue inflammation. In the treatment of pain not associated with inflammation, it has been suggested that opiates, rather than NSAIDs, may be more effective. However, evidence suggests that NSAIDs are effective at providing analgesia independently of their anti-inflammatory actions. In addition, evidence exists that NSAIDs and opiates may work synergistically to induce analgesia. Although most of the NSAIDs have relatively short half-lives, their duration of action can be very long. This may be due, in part, to their binding with high avidity to the COX enzyme. They also tend to accumulate and persist at sites of inflammation. The most frequently recognized side effect of NSAIDs in horses is gastrointestinal ulceration, which results from the inhibition of production of cytoprotective PGs.[5] Ponies appear to be more susceptible to the ulcerogenic effects of NSAIDs, with signs of toxicity occurring at doses that are usually well tolerated by horses.[6] The gastric mucosa and the right dorsal colon appear to be particularly susceptible to these ulcerogenic effects of the NSAIDs.[7] Prolonged treatment with NSAIDs and concurrent hypovolemia appear to predispose horses to ulceration of the right dorsal colon. The inhibition of protective PGs can also result in renal damage (including renal papillary necrosis and acute renal failure), especially in horses that are geriatric, volume-depleted, hypotensive, or have pre-existing renal, cardiac, or liver disease.[8]

Aspirin

Aspirin (acetylsalicylic acid) is the oldest known NSAID. In addition to inhibiting COX, aspirin inhibits the formation and release of kinins, stabilizes lysozomes, and uncouples oxidative phosphorylation.[5] Aspirin has a short half life (approximately 7 minutes after intravenous administration), which limits its use as an analgesic or anti-inflammatory agent. However, aspirin can be useful as an anti-thrombotic agent, and at relatively small doses it can significantly prolong bleeding times. For this purpose, aspirin is usually administered orally daily or every other day at a dose rate of 17 to 20 mg/kg.

Phenylbutazone

Phenylbutazone is the most commonly prescribed NSAID in horses. The plasma half life of phenylbutazone depends on the dose administered and the metabolic capacity of the animal, but is usually in the range of 3 to 8 hours. Both the parent phenylbutazone and its active metabolite oxyphenbutazone are highly bound to plasma proteins, and may displace other protein-bound compounds.[9] Therefore, phenylbutazone should be used judiciously with other highly protein-bound drugs, such as warfarin, gentamicin, and sulphonamides. Phenylbutazone can be administered intravenously or orally. In the treatment of gastrointestinal disease, it is most commonly administered intravenously. Feedstuffs, especially hay, can delay the absorption of orally administered phenylbutazone, but the bioavailability is unaffected. The use of phenylbutazone has been banned in many European countries because of concerns about its effect on human health if it enters the human food chain.

Phenylbutazone has a relatively narrow therapeutic index in horses. Although dose rates of 4.4 to 8.8 mg/kg (2 to 4g for a 450-kg horse) are commonly used, the higher end of this dose rate should only be used for short periods (2 to 3 days). The clinical signs of NSAID toxicity include depression, colic, anorexia, fever, and diarrhea.[10] Physical and clinical pathologic findings include oral and gastrointestinal ulcers, low serum protein concentrations, renal necrosis, and neutropenia. Despite its narrow safety margin, phenylbutazone is a highly effective and commonly used NSAID in horses. The dosage should not exceed 4.4 mg/kg every 12 hours. Phenylbutazone has been shown to be superior to flunixin meglumine in maintaining gastric motility during endotoxemia, but this is likely to be of only minor importance in horses being treated for abdominal pain.

Flunixin Meglumine

Flunixin meglumine is considered to be the most effective of the NSAIDs used to control visceral pain in horses. It has been shown to block the production of prostaglandins, specifically thromboxane and prostacyclin, for 8 to 12 hours after a single dose. Its analgesic effects are comparable to opioid analgesics, but it does not induce the side effects of the opioids such as CNS excitation and ileus.[5] The duration of analgesia produced by flunixin meglumine varies from 1 hour to more than 24

hours, depending on the cause and severity of the pain. In addition to its analgesic and anti-inflammatory effects, flunixin meglumine prevents some of the early hemodynamic effects of endotoxemia at doses lower than those used for anti-inflammatory effects.[11-13]

At the recommended dose of 1.1 mg/kg, flunixin meglumine has a plasma half life of 1.5 to 3 hours; however, it persists in inflammatory exudates for much longer. In foals less than 1 month of age, the plasma half life is longer than it is in adults. The pharmacokinetics of flunixin meglumine may also be different in older horses compared with young adults, with a longer plasma half life and decreased clearance.[14]

Flunixin meglumine is available in both parenteral and oral preparations. The bioavailability of the oral preparations is good. Although the parenteral preparation can be administered intramuscularly, necrotizing soft-tissue infections have been reported,[15] so flunixin meglumine should be administered intravenously or orally. Although flunixin meglumine has a better therapeutic index than phenylbutazone, the basic side effects are similar. Gastrointestinal ulceration was produced when the drug was administered at 1.1 mg/kg 3 times a day for 12 days.[16]

One risk associated with the use of flunixin meglumine in treating colic of unknown cause devolves from its ability to mask clinical signs of intestinal strangulation or obstruction by reducing heart rate, relieving pain, and improving mucous membrane color. If administered to horses in which the precise cause of colic has not been ascertained, it is essential to monitor closely rectal examination findings, nasogastric reflux, peritoneal fluid, heart rate, and respiratory rate over the next few hours. The clinical evaluation of horses with colic that have already received flunixin meglumine must be adjusted as a result. Thus, flunixin meglumine should be administered to control severe pain and diminish the effects of endotoxins in horses needing transport to a referral center for intensive care, closer monitoring, or surgery (i.e., in horses in which the need for surgery has already been established).

Ketoprofen

Ketoprofen, like most other NSAIDs in horses, has a short plasma half life (1 to 1.5 hours).[17] Its bioavailabilty is poor when administered orally or rectally, and it is most commonly administered intravenously. Although high doses may cause gastrointestinal and oral ulceration, the therapeutic index for ketoprofen is high, and it is considered to be less toxic than either phenylbutazone or flunixine meglumine.[16] Ketoprofen is an effective anti-inflammatory and analgesic agent in horses, and in one study was shown to be as effective as flunixin meglumine in alleviating abdominal pain.[18] It also has the ability to reduce many of the early effects of endotoxins in horses.[11]

Eltenac

Eltenac is a potent nonsteroidal anti-inflammatory drug with antipyretic and antiedema properties. It has a short plasma half life (1.7 to 3 hours).[19] Limited information is available concerning the efficacy of eltenac in treatment of gastrointestinal pain, but the antiedema properties may make it useful in the post-operative colic patient. It also reduces many of the early responses to endotoxins. The effects of eltenac appear to be long-lasting, and a dosing interval of once every 24 hours is recommended for most conditions.

Suxibuzone

Suxibuzone is a derivative of phenylbutazone. Its efficacy is similar to phenylbutazone, but it may be less toxic in terms of gastrointestinal ulceration.[20]

Meclofenamic Acid

Meclofenamic acid is typically administered orally to horses. It has a slow onset of action, requiring 36 to 96 hours of therapy before clinical effects are evident,[5] and it is, therefore, rarely used in the treatment of gastrointestinal pain.

Carprofen

Carprofen is considered an effective analgesic agent and a weak anti-inflammatory agent.[4] Unlike many other NSAIDs in the horse, the half life of carprofen is long (14 to 31 hours).[9] Carprofen also appears to have a good therapeutic index in horses, possibly because of the selective inhibition of the COX2 enzyme; however, this selectivity has not yet been proven in horses. The efficacy of carprofen in the treatment of gastrointestinal pain in horses has not been studied. Although it appears to be more efficacious as an analgesic than an anti-inflammatory agent, studies in laboratory animals have suggested that it is an effective analgesic only when the pain is associated with inflammation.[21]

Naproxen
Naproxen can be administered intravenously or orally to horses. Little information is available about its therapeutic index. Although it appears to be an effective NSAID in horses, its speed of action is very slow, often requiring several days of therapy.[22] This limits its use in animals with gastrointestinal pain.

Dipyrone
Dipyrone is a weak analgesic drug that can provide only short-term relief for mild abdominal pain. Combined with hyoscine N-butylbromide, it is effective in relieving intestinal spasm. Its failure to help reduce or stop pain in individual cases should signal that a condition exists that is more serious than a simple intestinal spasm or tympanitic colic.

Sedative-Tranquilizers
α2 Adrenoceptor Agonists
The α2 agonists create a clinical effect by binding to α2 adrenoceptors.[23] The pharmacologic effects of the α2 agonists used commonly in horses are similar, and differences between drugs are primarily a function of duration of effect.[24] The pharmacologic effects of these drugs include both central effects and effects on peripheral receptors in target tissues. The α2 agonists cause sedation, with lowered head carriage, decreased locomotor activity, and decreased response to touch, sound, or visual stimulation.[23,24] The degree of sedation is dose-dependent; at higher doses, ataxia is produced. Medetomidine is reported to produce the greatest degree of ataxia, and romifidine causes the least degree of ataxia at similar levels of sedation when compared with xylazine or detomidine.[25]

These agents are effective analgesics in horses with abdominal pain,[26,27] but they have the disadvantage of decreasing gastrointestinal motility for the duration of the period of sedation. These drugs also relax smooth muscle in the distal airways. The α2 agonists can produce hyperglycemia, sweating, mydriasis, and decreased hematocrit. The onset of action after intravenous injection is rapid for all the agents. Their major uses in horses are for sedation, as premedication prior to general anesthesia, and for analgesia.[23] The effects of α2 agonists can be reversed with yohimbine, tolazoline, atipamezole, or idazoxan.

Xylazine
The recommended dose rate of xylazine is 0.2 to 1.1 mg/kg intravenously or up to 2.2 mg/kg intramuscularly. At a dose rate of 1.1 mg/kg IV, the visceral analgesia provided by xylazine appears to be similar to that of flunixin meglumine and the opioid agonists. The duration of effect of xylazine is much shorter (usually 10 to 30 minutes) than that of flunixin meglumine, making xylazine more useful for controlling pain during evaluation of the cause of colic and of the need for specific therapy.

Potentially detrimental side effects of xylazine include bradycardia, decreased cardiac output, transient hypertension followed by hypotension, ileus, and decreased intestinal blood flow. These effects may restrict its use in horses in shock. In contrast to the bradycardia, hypertension, and intestinal hypotension, which last only a few minutes, the ileus and hypotension can be prolonged. A reduced dosage of 0.2 to 0.4 mg/kg IV can be administered in an attempt to reduce the severity and duration of the side effects. Alternatively, xylazine can be used at the lower dosage in combination with a narcotic agonist such as butorphanol.

Detomidine
The recommended dose rate of detomidine is 4 to 20 μg/kg intravenously or up to 40 μg/kg intramuscularly. The same complicating effects are likely to be present for detomidine as for xylazine, however detomidine's duration of action is longer (60 to 120 minutes, depending on the dose). Detomidine reduces intestinal motility similarly to xylazine and can mask many of the clinical signs that the clinician uses to diagnose the cause of the colic. Because detomidine is such a potent drug, any signs of colic observed within an hour after administration are an indication that a severe disease is present, which may require surgery. Therefore, detomidine is a useful drug when used with caution and preferably at the low dose rate of 10 μg/kg IV.

Romifidine
Romifidine has a similar action to xylazine and detomodine, but appears to produce less ataxia. The duration of action is longer than either xylazine or detomidine. At a dose rate of 40 to 80 μg/kg IV, romifidine provides potent analgesia lasting 1 to 3 hours. It can also be administered intramuscularly at a dose rate of 120 μg/kg.[28]

Medetomidine

Medetomidine is recommended for intravenous administration at 5 μg/kg; however, it can cause significant ataxia and is, therefore, more commonly used as a constant infusion to produce sedation.

Phenothiazines

The phenothiazines are classified as neuroleptics, tranquilizers, or antipsychotic agents.[23] They produce a calming effect, while retaining sensitivity to noise. Ataxia is not generally seen after their use. Their mode of action involves antagonism of the neurotransmitter dopamine in the basal ganglia and limbic forebrain.

Phenothiazines do not produce analgesia, but they can potentiate the efficacy of other analgesic drugs, such as the opioids. Other effects of phenothiazines include lowering of the systolic, mean, and diastolic blood pressures. The risk of severe hypotension and collapse renders these drugs contraindicated for use in horses that are volume-depleted as a result of colic or blood loss. Phenothiazines also reduce the hematocrit and can cause penile prolapse in males. The magnitude and duration of the latter effect appears to be dose-related; at doses of 0.4 mg/kg, the penile protrusion can persist for 10 hours.[29] Priapism has been reported as a long-term complication of acepromazine, and for this reason the drug is not recommended for use in breeding stallions.

Acepromazine

Acepromazine is the phenothiazine used most commonly in horses for tranquilization, premedication prior to general anesthesia, and as an analgesic when combined with an opioid. In view of its effects on blood pressure, acepromazine is not recommended as a routine medication agent in colic.

Opioid Analgesics

The analgesic and sedative effects of the opioids result from interaction with central and/or peripheral opioid receptors. When used in combination with acepromazine and α2 agonists, opioids can provide good standing restraint in the horse. Their use alone in horses has been limited by undesirable physiologic and behavioral side effects.[30]

The analgesic effects of the opioids are mediated at both the supraspinal and spinal levels via the effects on the three different opioid receptor families. These drugs also induce behavioral changes, which vary between different species. In horses, opioids produce CNS excitation and dysphoria. The excitement and increased locomotion seen in horses can be diminished by the concomitant administration of acepromazine or α2 adrenoceptor agonists.[31] The opioids are potent respiratory depressants, but do not alter cardiovascular performance. They tend to decrease the propulsive activity of the gastrointestinal tract by inhibiting peristalsis, while increasing tone in intestinal smooth muscle. The gastrointestinal effects are variable depending on the segment of bowel and the opioid agent used.

Morphine

Morphine is a μ-opioid receptor agonist. It is a potent analgesic, but can cause severe excitement in horses unless used in combination with sedative drugs such as acepromazine or xylazine. Morphine is known to inhibit jejunal and cecocolic motility and to increase the overall muscle tone in the colon.[32]

The recommended dose rate of morphine for standing restraint is 0.3 to 0.6 mg/kg intravenously in combination with acepromazine (0.05 mg/kg) or xylazine (0.5 to 1.0 mg/kg), detomidine (0.01 to 0.02 mg/kg) or romifidine (0.05 to 0.08 mg/kg).[23] It can also be given as an epidural injection.

Meperidine (Pethidine)

Meperidine is a μ-receptor agonist with relatively few side effects. It provides slight to moderate analgesia of relatively short duration in horses with abdominal pain. It has only about 10% of the potency of morphine. The recommended dose rate of meperidine is 0.6 to 1.0 mg/kg intravenously in combination with either acepromazine (0.05 mg/kg) or xylazine (0.5 to 1.0 mg/kg). It can also be administered intramuscularly at a dose of 1 to 2 mg/kg. Used repeatedly, meperidine can potentiate obstructions from impactions by reducing colon activity. It has been shown to reduce intestinal motility in the jejunum.[33]

Methadone

Methadone is a synthetic μ-opioid receptor agonist that is 3 times as potent as morphine. It can be administered intravenously to horses at 0.1 mg/kg in combination with either acepromazine (0.05 mg/kg) or xylazine (0.5 to 1.0 mg/kg), detomidine (0.01 to 0.02 mg/kg) or romifidine (0.05 to 0.08 mg/kg) to produce sedation that lasts for several hours.

Butorphanol

Butorphanol is an opioid agonist and antagonist that produces the best pain relief of the drugs in this group, with the fewest side effects. However, when assessed in a multicenter trial examining the efficacy of different analgesic drugs in horses with colic, butorphanol was not considered clinically effective.[27] It can be used in combination with xylazine or the other $\alpha 2$ adrenoceptor agonists in horses with moderate to severe abdominal pain to increase the level of analgesia. The dose is 0.01 to 0.05 mg/kg intravenously in combination with either acepromazine (0.05 mg/kg) or xylazine (0.5 to 1.0 mg/kg), detomidine (0.01 to 0.02 mg/kg) or romifidine (0.05 to 0.08 mg/kg). Doses exceeding 0.2 mg/kg can cause excitement.

Butorphanol reduces gastrointestinal motility and decreases defecation.[34] When combined with detomidine, butorphanol prolongs gastric emptying time.[35] When combined with xylazine, it reduces duodenal motility for 1 hour after treatment[36] and cecal motility for 150 minutes.[37] Butorphanol is potent enough to stop colic for short periods when the colic is caused by severe intestinal disease, but the pain caused by large-colon volvulus or small-intestinal strangulation may not be altered. When administered without xylazine or another $\alpha 2$ adrenoceptor agonist, even small doses of butorphanol may occasionally cause head jerking and ataxia.

Pentazocine

Pentazocine is an agonist-antagonist opioid with a potency one third of morphine. Pentazocine (0.33 to 1.1 mg/kg IV) has been recommended to provide analgesia in horses with colic, but in cecal balloon models of equine colic, it provided analgesia for less that 30 minutes.[38]

Choice of Analgesics in Colic

The choice of which analgesic drug or which combination of drugs to use as the first-line treatment for an individual horse suffering from colic is usually governed by the clinician's previous experience with different drugs, the potential complications associated with different drugs, and the severity of colic pain exhibited by the horse. The response (or lack of response) of the horse to different analgesic drugs is an important factor to consider when reaching a diagnosis of the cause of colic and in determining the need for surgical intervention. The choice of which drugs are administered, their dosages, and knowledge of their potency as analgesics and their side effects, are, therefore, extremely important. In some cases, the horse will already have been given an analgesic drug by the owner, which may complicate the process of making a diagnosis or assessing the need for surgical intervention.

The initial choice of analgesic drugs should be based on the clinician's provisional diagnosis of the underlying cause of the colic and the need for chemical restraint. For example, horses demonstrating signs of mild pain associated with spasmodic colic usually respond well to a spasmolytic agent or nonsteroidal anti-inflammatory drug. On the other hand, a horse demonstrating violent colic behavior may require sedation and chemical restraint to prevent injury and to permit a thorough clinical examination. In addition, the ability of the clinician to monitor and reexamine the horse following treatment should be considered. Potent analgesic drugs and agents that may effectively mask the signs of endotoxemia, which are so important in determining the necessity for surgery, should be avoided in horses in which the cause of colic has not been diagnosed and in which close monitoring and frequent reexaminations are not possible.

The selection of analgesics based on the severity of colic and the underlying disease classification is shown in Table 16-2.

Table 16-2
Selection of Initial Analgesic Drugs

Disease category/severity	Drugs
Mild nonspecific colic and spasmodic colic	NSAID (e.g., phenylbutazone, dipyrone)
	Spasmolytic (e.g., hyoscine) Opioid (eg pentazocine, butorphanol)
Severe undiagnosed colic	α2 agonist–opioid combination
	NSAID (e.g., phenylbutazone) Flunixin meglumine (only if close monitoring possible)
Simple obstruction	Flunixin meglumine
	α2 agonist–opioid combination
Strangulating obstruction	Flunixin meglumine
	α2 agonist α2 agonist–opioid combination
Enteritis	Flunixin meglumine
Peritonitis	Flunixin meglumine

Treatment of Intestinal Spasm and Spamodic Colic

Increased frequency of intestinal contractions, as in spasmodic colic, or spasms occurring oral to intraluminal obstructions (such as impactions) causes pain that can be relieved by spasmolytic drugs. Another indication for the use of spasmolytic drugs is to relax the rectum, thereby facilitating palpation of the abdomen per rectum.[39] The most commonly used spasmolytic drugs include the cholinergic blockers atropine, hyoscine N-butylbromide (scopolamine), and propantheline bromide. These drugs compete with acetylcholine for muscarinic receptors on smooth muscle cells. They cause smooth muscle relaxation and decreased intestinal motility, and therefore, are contraindicated in horses that have ileus. Prolonged use of these drugs can predispose to large-intestinal impactions.

Atropine

Atropine is not recommended for use in horses with colic because it is a potent inhibitor of intestinal motility that can persist for several hours or even days, creating tympany and complicating the initial problem with ileus.[40-42] Even when used as a topical ocular treatment to produce mydriasis, individual horses may develop ileus and colic. However, a single subcutaneous dose of 0.02 mg/kg is considered safe in most horses. This dose may also be used in horses with a rectal tear to facilitate evacuation of the rectum.[39]

Hyoscine (Scopolamine)

Hyoscine N-butylbromide (scopolamine) has a shorter muscarinic cholinergic blocking effect compared with atropine and is effective in relaxing the bowel wall. It is safe to use in conjunction with other analgesic drugs, including nonsteroidal anti-inflammatory drugs, and is available in Europe as a compound antispasmodic combined with dipyrone. Hyoscine is administered at a dose of 0.2 to 0.3 mg/kg intravenously. The spasmolytic effect lasts only 20 to 30 minutes,[43] and it is, therefore, unlikely to mask any signs associated with more serious forms of colic.

Propantheline Bromide

Propantheline bromide is available as a parenteral solution for injection in some countries. Spasmolytic effects are obtained at a dose rate of 0.1 to 0.2 mg/kg.

Treatment of Obstruction

Luminal obstruction by impacted, dehydrated intestinal contents is a common cause of colic in the horse. Such obstructions impede the aboral movement of ingesta, fluid, and gas. The most common site of impaction is the large colon, specifically in

the left ventral colon orad to the pelvic flexure. Impactions can also arise in the stomach, small intestine (especially the ileum), cecum, right dorsal colon (orad to the transverse colon), and small colon. These sites represent areas of transition of intestinal movement, a sphincter between different segments of intestine, or regions of intestinal narrowing.[44,45] The etiology of impactions is poorly understood. Dehydration, lack of exercise, poor dentition, overfeeding, and feeding bulky, indigestible fibrous food are commonly blamed, but some form of abnormality of intestinal motility may be involved (see Chapter 2; section C).

The pathophysiologic effects of luminal obstruction by an impaction are often slow to develop and progress (compared with strangulating obstructions). In the stomach, cecum, large colon, and small colon, the obstruction is frequently incomplete, allowing fluid and gas to pass around the impaction. Pain arises from intestinal distention and intestinal spasms at the site of the impaction. Complete obstruction is more common in small-intestinal impactions, but it can occur in other sites as well. Complete obstruction leads to more rapid distention of the bowel proximal to the obstruction, and more rapidly developing signs of colic, hypovolemia, etc. Persistent distention of the bowel may lead to circulatory failure and ischemic damage to the bowel wall.

In most cases, the objectives of treatment of horses with impactions are to hydrate and lubricate the impacted ingesta, thereby allowing the normal intestinal motility to move the ingesta aborally into the next intestinal segment. This can usually be achieved by enterally administered therapies, sometimes in combination with analgesic drugs, intravenous fluid therapy and/or prokinetic drugs. In certain cases, however, especially those involving a complete intestinal obstruction, surgical treatment to prevent intestinal rupture may be necessary.

Restricted Feeding

Restricted feeding is advisable in horses with impactions until such time as the impaction resolves. Continued feeding may allow the impaction to enlarge, thereby making it more difficult to resolve. Horses with large impactions can make a full recovery with medical therapy, even when held off feed for as long as 6 days.[45] However, there may be benefits in stimulating gastrointestinal motility by allowing horses to eat limited amounts. Very small quantities of grass or bran mashes fed frequently may be helpful in this respect, and are unlikely to be detrimental.

Walking

Walking exercise may also be helpful in managing horses with impaction colic. Walking appears to stimulate gastrointestinal motility and defecation.

Analgesic Drugs

The administration of analgesics is helpful to preserve gastrointestinal motility as well as being required on humane grounds. Analgesic drugs commonly used in the treatment of impaction colic include the nonsteroidal anti-inflammatory agents, such as phenylbutazone and flunixin meglumine. These drugs are effective analgesics while having minimal deleterious effects on intestinal motility. Flunixin meglumine at a dose rate of 0.25 to 0.5 mg/kg 4 times a day has proved to be effective in many cases.[44,45] The lowest effective dose should be used. If 0.5 mg/kg is not sufficient to relieve pain, then increasing the dose up to 1.0 mg/kg may be successful, although this dose may suppress the pain and other signs that indicate the need for surgery.[45] If pain is observed within 1 hour after flunixin meglumine administration, surgery should be considered to either empty the colon or to determine whether another intestinal problem exists.

Although other analgesic drugs, such as α2-adrenergic agonists, opioid analgesics and spasmolytic drugs, can also be effective at controlling pain associated with impactions, their routine use is not recommended because of the side effects of reducing gastrointestinal motility. In some instances, the administration of such drugs will be required to achieve effective analgesia. Titrated in small amounts, these drugs appear efficacious with few detrimental effects.

Laxatives

Laxatives are commonly used in horses with impaction colic to increase the water content and softness of ingesta, thereby facilitating its transit through the intestine. In severe impactions, the effectiveness of laxatives is increased by concurrent administration of oral and intravenous fluids. Laxatives should never be administered orally in horses with nasogastric reflux.

Mineral Oil (Liquid Paraffin)

Mineral oil (liquid paraffin) is the most frequently used laxative in equine practice. It is a surface lubricant and is administered

at a dose rate of 5 to 10 mL/kg once or twice a day by nasogastric tube. Its effects are considered mild, and it is safe for prolonged use. It is commonly administered with water or saline, and is considered by many clinicians as the lubricant of choice for mild colonic impactions.

Passage of the oil (as evidenced by the presence of oil on the perineum and tail) indicates a patent intestinal tract. In the normal, unobstructed intestine, oil takes approximately 12 hours to reach the anus after delivery into the stomach. Identification of the oil on the perineum should not always be taken as evidence of lack of obstruction, because the oil may pass around an impaction without resolving it. This is frequently the case for sand impactions.

In most cases of impaction colic, mineral oil can be safely administered every 12 hours until signs indicating resolution of the impaction are seen. These include the presence of oil on the perineum, passage of oil-coated feces, cessation of pain, and clearing of the impaction as revealed by repeated rectal examinations. Most colonic impactions resolve within 3 to 5 days.

Other Oils

Raw linseed oil has been used as a laxative to treat impaction colic,[46] but it is not as safe as mineral oil. When administered at a dose rate of 2.5 mL/kg every 12 hours, linseed oil causes anorexia, depression, mild colic, and biochemical abnormalities consistent with intestinal inflammation.[47] Diarrhea persisting for several days can follow its administration.

Castor oil is not recommended for use in horses. It can cause acute, severe colitis and diarrhea, and has been used experimentally at a dose rate of 2.5 mL/kg to induce colitis in ponies.[48]

Psyllium Hydrophilic Mucilloid

Psyllium hydrophilic mucilloid is a bulk-forming laxative that increases the fluid and ion content of feces by absorbing water. This softens the impaction and stimulates bowel activity. It has been considered particularly useful for treating impactions caused by ingested sand. A dose of 1 g/kg can be administered per os up to 4 times a day. As a long-term treatment, psyllium hydrophilic mucilloid may be administered daily for several weeks to help eliminate sand from the large colon. In one study, psyllium hydrophilic mucilloid was not efficacious in treating experimental sand impactions.[49]

Psyllium powder mixed with water can be administered by nasogastric tube. The mixture tends to form a thick gel that may not pass easily down the tube, so administration as soon as the powder is mixed with water is recommended. Psyllium is also available in pelleted form, which horses generally find more palatable than a mixture of psyllium powder and other feeds.

Osmotic Laxatives

Magnesium sulphate (Epsom salt) can be used as an osmotic laxative (or "ionic cathartic") in horses. Classically, magnesium sulphate was believed to be poorly absorbed from the intestinal tract; remaining in the lumen of the bowel and drawing water into the gut by virtue of its osmotic pressure. Therefore, it helps to hydrate the ingesta, and facilitates passage of impactions. However, it has been shown that much of the magnesium is actually absorbed in the small intestine. In addition, magnesium sulphate stimulates water secretion in the small colon by a gastrocolonic reflex action immediately upon administration.[50] The precise mechanism of this action is unclear. Undiluted magnesium sulphate causes enteritis by osmotic damage to the mucosal cells, so each dose of 0.5 to 1.0 g/kg should be diluted in 4 liters of warm water and administered by nasogastric tube once or twice a day. Epsom salt should not be administered for longer than 3 days (once a day) because it can result in severe enteritis and possible magnesium intoxication. This treatment has been used for impactions of the cecum, large colon, and small colon.

Other osmotic laxatives can be used similarly. These include Glauber's salts (sodium sulphate) and table salt (sodium chloride). Recent studies suggest that sodium sulphate (1 g/kg) may be more efficient than magnesium sulphate in increasing the water content of colonic contents and feces. However, the use of sodium sulphate at this dose rate can result in hypernatremia, hypochloremia, and hypocalcemia. For this reason, a lower dose rate (0.5 g/kg) with monitoring of serum electrolytes has been recommended.[51]

Dioctyl Sodium Succinate (DSS)

DSS is an anionic, surface-active agent with wetting and emulsifying properties. It reduces surface tension and allows water and fat to penetrate the ingesta. A dose of 10 to 20 mg/kg can be administered as a 5% solution by nasogastric tube every 48 hours. DSS can cause damage to the mucosa, and it increases fluid permeability of colon cells; this can result in mild abdominal pain and diarrhea, especially if doses higher than 20 mg/kg are used.[50,52] Administration of higher doses can case severe mucosal damage and death.

DSS is commonly mixed and administered with mineral oil.[44] It has been suggested that this mixture should not be used since the surfactant effects of the DSS may reduce the droplet size of the mineral oil sufficiently to allow the oil to be absorbed. The concurrent administration of magnesium sulphate and DSS has been associated with hypermagnesemia, flaccid paralysis, and systemic collapse in horses.[53] Administration of both drugs at the same time should, therefore, be undertaken with extreme caution. Administration of magnesium sulphate at a low dose-rate (0.5 g/kg) with sodium sulphate (0.5 g/kg) and DSS (25 mg/kg) given every 24 hours has been used in the treatment of impactions.[46] This combination of drugs allows for a "full" dose of sulphate salts to be administered, but with only half of it in the form of magnesium sulphate; the risk of hypermagnesemia is, therefore, reduced.

Enteral Fluid Therapy

Horses with gastric and intestinal impactions often benefit from orally administered fluids.[54] If there is no abnormal gastric reflux and the horse tolerates the initial dose of oral fluids, up to 8 L/450-kg horse of water, isotonic, or hypertonic fluids may be given every 30 minutes to 1 hour to an adult horse. Enteral water therapy is often effective in resolving colonic impactions resistant to initial administration of analgesics and laxatives, although this takes on average 2.5 days, with a total water volume ranging from 85 to 208 liters. Serum electrolytes should be monitored when the horse is receiving enteral water therapy, as this can result in severe hyponatremia. Granular sodium chloride may be added to the water if electrolytes are desirable; however, constant administration of saline may result in hypernatremia and hyperchloremia. Frequent monitoring of serum electrolyte concentrations should be used to determine when changes in electrolyte composition are necessary. A balanced electrolyte solution composed of sodium chloride, potassium chloride, and sodium bicarbonate is effective in increasing colonic water and providing for systemic hydration without causing electrolyte imbalance (Table 16-3). This formula has been effective in treating large-colon impactions that were resistant to initial treatments with mineral oil and analgesics.[45]

Oral fluids are ideally administered via gravity flow rather than by pump. An indwelling enteral feeding tube is easier to manage than a nasogastric tube. Clinical monitoring of horses receiving enteral fluid therapy should also be undertaken. Although rare, ileus and gastric distention may occasionally develop in horses with impaction colic, in which case continued enteral fluid therapy would be contraindicated; any increase in pain, respiratory rate, or heart rate during oral fluid therapy should be considered a possible indication to stop the therapy. Rarely, gravity administration of isotonic fluids may be given per rectum. This would only be indicated for horses with colonic impactions when oral fluids cannot be administered and economic considerations prevent administration of IV fluids.

Table 16-3

Electrolyte Concentrations Mixed with Tap Water to Make a Balanced Enteral Fluid.

a) Measurements in grams to create a balanced electrolyte solution.

Salt	g/liter	g/5 liters
NaCl	5.37	26.85
KCl	0.37	1.85
NaHCO3	3.78	18.9

b) Estimated amounts for rapid measurement of electrolyte components.

Ingredient	amount/5liters	Total dose per 5 liters
Salt	3 teaspoons	equals 21 g NaCl
Litesalt	1 teaspoon	equals 3.5 g NaCl and 2 gKCl
Baking Soda	4 teaspoons	equals 20 g NaCO3

Intravenous Fluid Therapy

Intravenous fluid therapy can also be used for treating horses with impactions of the large intestine. In these cases, crystalloids should be administered rapidly (8 mL/kg/hour) without colloids such that plasma protein decreases to less than 4.5 g/dL (<45 g/L). The increase in hydrostatic pressure and decrease in plasma oncotic pressure induced by such overhydration should cause movement of the fluids into transcellular fluid sites (i.e., intestinal lumen), causing the impaction to soften. This can generally be done without harm to other body organs assuming there is no generalized capillary disorder, and cardiac, renal, and respiratory functions are normal. When large amounts of fluids are given to horses, they should ideally be warmed to near body temperature prior to administration. The average time for resolution of impactions treated with intravenous fluids is approximately 2 days, with total fluid volumes ranging from 54 to 350 liters. During this treatment, total plasma protein concentration should be monitored (to ensure that a low concentration is maintained), and electrolyte concentrations should be monitored to ensure that hypocalcemia and hypokalemia do not occur. The most common complication of this treatment is thrombophlebitis. Careful monitoring of the catheter site is necessary, and the catheter should be changed at the first indication of vein inflammation or thrombus formation.

Diarrhea may occur after either enteral or intravenous fluid therapy, as well as after the administration of magnesium sulphate or sodium sulphate. Diarrhea usually indicates successful hydration and movement of the impaction, but in some cases it may arise as a result of colitis. Such cases may require intensive treatment for the colitis (see Chapter 20).

Nutritional Support after Evacuation of Colon Impactions

Once the impaction has resolved, feed should be reintroduced and slowly increased over 48 hours. Hay or grass should be provided in small quantities (0.25 to 0.5 kg every 3 hours).[45] This time interval allows the stomach to empty and does not overload the cecum or colon. After 12 to 24 hours, hay or grass may be fed ad libitum. If colic occurs during the period of increasing food intake, feed should be withheld, and the horse examined to check that an impaction has not reformed. Grain and concentrates should not be introduced into the diet until such time as the horse has reestablished normal fecal production on a hay or grass diet. Introduction should be gradual during a 4- to 7-day period.

Treatment of Flatulence and Tympany

Gastric Tympany

Primary gastric tympany may occur if a horse eats highly fermentable material, thereby generating a large volume of gas. Gas also may accumulate secondary to generalized impaired gastrointestinal motility from a variety of disorders. Normally, excessive gas in the stomach exits either via the small intestine or the esophagus (eructation). If gastric distention is excessive, these normal release mechanisms may be impeded and the gas will continue to accumulate. In severe gastric distention, rupture of the stomach may ensue. Treatment involves removal of excessive gas via a nasogastric tube, or at surgery via needle aspiration. An underlying reason for the gastric dilation should be determined and appropriately treated. The cause of gastric dilation in horses is not similar to frothy bloat in ruminants; therefore, treatments designed for this condition are not indicated for gastric dilation in horses.

Cecal Tympany

Cecal tympany may be primary or secondary in origin. Primary cecal tympany occurs because of rapid gas production or reduced cecal motility, whereas secondary cecal tympany occurs because of an outflow obstruction. Rapid gas production is most commonly seen in horses that are on lush, rapidly growing pasture, high grain diets, or horses eating wilted grass. Cecal tympany results in abdominal distention localized primarily to the region of the right flank.

Many horses with primary cecal tympany will respond to analgesia and removal of the source of gas production. If, however, cecal distention does not readily resolve or if distention continues to worsen, cecal trocarization can be performed. A region (about 5 cm^2 in area) centered between the last rib and the tuber coxa in the right flank is clipped and aseptically prepared. Lidocaine (lignocaine) or mepivicaine is injected subcutaneously, then directed deep through the muscle. A 14-gauge, 13- to 15-cm catheter and stylet are directed through the body wall until gas escapes. The needle is generally directed across the body wall, perpendicular to the skin surface (Figure 16-1A). Decompression is best accomplished with suction. Completion of a rectal examination during cecal decompression may help keep the gas in the dorsal region of the cecum and prevent the cecum from slipping away from the needle as the cecum decreases in size (Figure 16-1B). When decompression is complete, a broad-spectrum antibiotic should be injected through the lumen prior to removal to reduce the likelihood of development of cellulitis along the needle track in the body wall.

Figure 16-1A

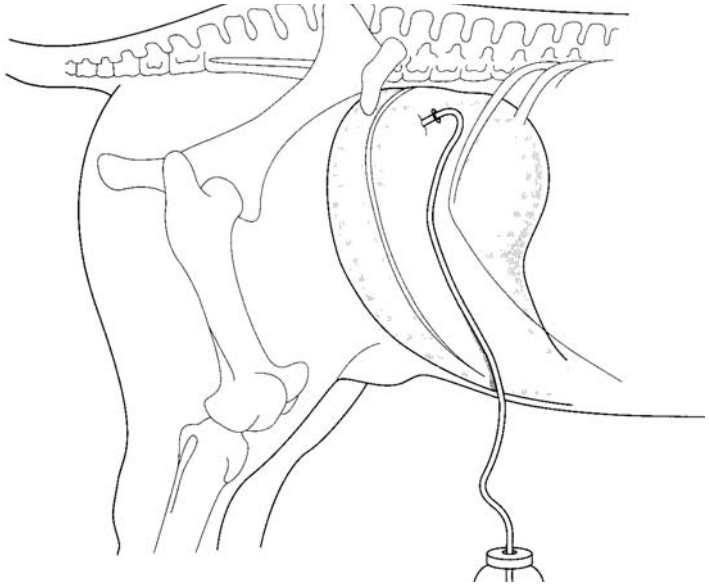
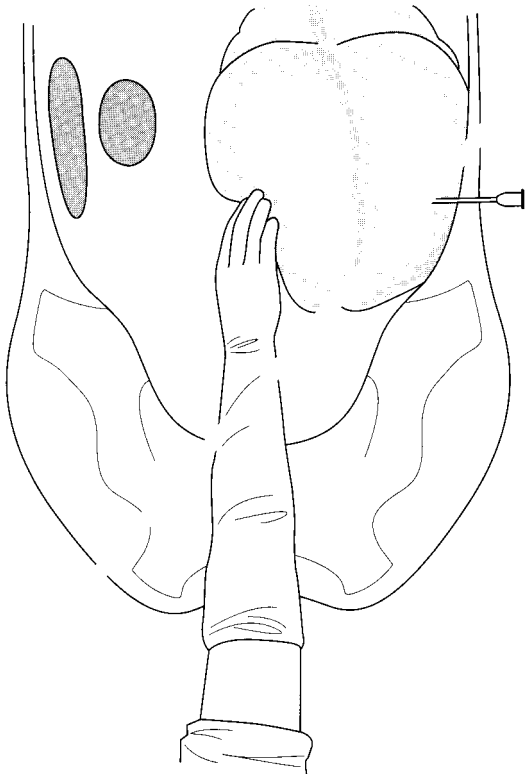


Figure 16-1B



Cecal decompression via right paralumbar needle aspiration. **A.)** Placed at the level of the ventral aspect of the right tuber coxae, and one half the distance between the last rib and the tuber coxae, a 12-15 cm needle is inserted into the distended cecum. Suction is recommended to remove the gas rapidly. **B.)** Rectal palpation during the decompression can assist in gas removal and maintaining needle placement in the cecum. (With permission Butterworth-Heinemann; from Handbook of Equine Colic; NA White and B Edwards, 1999).

Large Colon Tympany

Tympany is often idiopathic but may arise from overproduction of gas or, more commonly, from delayed evacuation of normal gas, or from obstruction. Gas overproduction has been associated with a rapid dietary change to highly fermentable concentrates or forages. Delayed evacuation of gas may be associated with a number of factors leading to diminution of colonic motility, including parasitism, lack of exercise, colitis, peritonitis, stressors such as transport or surgery, and parasympatholytic agents including drugs, toxins, or plants. Displacements or impactions can also result in tympany.

Horses with mild to moderate colonic distention exhibit signs of mild to moderate abdominal pain and corresponding increases in heart rate. Such cases may spontaneously resolve or be successfully managed medically by treatment with analgesics and with mineral oil to promote colonic evacuation and reduce gas production.

In severe cases of colonic tympany, signs include marked colic pain, abdominal distention, tachycardia, tachypnea, and cardiovascular deterioration. Horses can appear cyanotic as a result of excessive pressure on the diaphragm causing thoracic compression. Marked distention of the colon is evident on rectal and ultrasonographic examination, but colonic mural thickness is normal and there is no evidence of displacement or lumenal obstruction. Such horses may not be readily distinguished from those affected with colonic tympany secondary to volvulus or colonic displacement. Surgical exploration may be necessary to eliminate the presence of such surgical lesions. Percutaneous trocarization of the large colon and/or cecum may lead to dramatic relief of clinical signs in some horses. In other cases, spontaneous resolution of tympany can occur after administration of analgesics. Exercising the horse may help to speed resolution of the tympany, if this is deemed possible.

Treatment of Ileus

Ileus (adynamic ileus) is the impairment of aboral transit of intestinal contents. Post-operative ileus is the most common indication for pharmacologic manipulation of intestinal contractile activity in the horse. Traumatic handling of the intestines, intestinal distention, resection and anastomosis, and intestinal ischemia and inflammation all may contribute to the development of ileus in the post-operative period. Ileus may also occur in association with proximal duodenitis-jejunitis (anterior enteritis), colitis, and peritonitis.

An imbalance between the factors controlling excitation and inhibition of gastrointestinal smooth muscle predisposes horses to ileus. Consequently, an attempt has been made to identify prokinetic agents that potentially would restore the balance between excitatory and inhibitory control of contractility. Pharmacologic modulation aimed at increasing excitatory activity has principally involved the administration of parasympathomimetic agents that increase cholinergic transmission, such as bethanecol or neostigmine. Attempts to block inhibitory components of contractility have focused on the sympathetic system. Metoclopramide, which among other activities has antidopaminergic properties, and nonsteroidal anti-inflammatory drugs have also been used in attempted treatment of ileus. The pharmacologic management of ileus is discussed in greater detail in Chapter 4, Intestinal Motility and Transit.

In addition to the use of anti-inflammatory and prokinetic drugs, general supportive therapy (including fluid therapy and analgesic drug therapy) is required (see Chapter 17, Treatment of Shock and Chapter 32, Monitoring Treatment for Abdominal Disease). Continuous or repeated gastric decompression must be provided in addition to drug therapy.

Prokinetic drugs (see Chapter 4, Intestinal Motility and Transit; and Table 16-4)

Neostigmine Methyl Sulphate

Neostigmine is an acetyl-cholinesterase inhibitor that directly stimulates intestinal contractions. Doses of 0.0044 mg/kg (2 mg for an average-sized adult horse) can be administered subcutaneously or intravenously. The duration of effect is short (15 to 30 minutes) and up to 5 doses may be given at 20- to 60-minute intervals. If no response occurs to this dose rate, and assuming that the horse is not showing any evidence of side effects, the dose of neostigmine can be increased by 2-mg increments up to a total of 10 mg per treatment. Neostigmine induces disorganized segmental contractions, and can actually decrease propulsive motility of the jejunum and delay gastric emptying.[40,55] It can also cause abdominal pain by stimulating spasmodic regional contractions. For these reasons, many clinicians do not favor its use in clinical cases; however, studies have shown that neostigmine can improve cecal and colonic motility.

Table 16-4

Dose Rates of Commonly Used Prokinetic Drugs

Neostigmine	0.0044 mg/kg	IM or SC	q 20-60 mins (total dose<10 mg)
Metoclopramide	0.25 mg/kg	IV	Infuse over 30-60 mins (in 500 mL saline)
	0.04 mg/kg	IV	Continuous infusion (0.04 mg/kg/hr)
Cisapride	0.3-0.4 mg/kg	PO	
Lidocaine	1.3 mg/kg	IV	IV bolus over 5 mins **Followed by:**
	0.05 mg/kg/min	IV	Continuous infusion (in saline or LRS)
Erythromycin	0.50-1.0 mg/kg	IV	Infuse over 1 hr (in 1L saline) q 6 hrs
Acepromazine	0.01 mg/kg	IM	q 4hrs
Yohimbine	0.15 mg/kg	IV	1,4,7 and 10 hrs post-operatively
Bethanecol	0.024 mg/kg	IV or SC	q 4-6 hrs

Metoclopramide

Metoclopramide is a nonspecific dopaminergic antagonist that also augments the release of acetylcholine from intrinsic cholinergic neurons and has adrenergic blocking activity.[56] It is a potent gastrointestinal stimulant when given at a dosage of 0.25 mg/kg IV (diluted in 500 mL of saline and administered over a period of 30 to 60 minutes), but in some cases has proved unsuitable because it can produce severe CNS side effects (excitement, sweating, and restlessness). However, it may be safely administered to most horses as a continuous infusion at 0.04 mg/kg/hour.[57]

Domperidone

Domperidone, a dopaminergic antagonist, does not cross the blood-brain barrier, and at a dose rate of 0.2 mg/kg IV, has been shown to block dopaminergic receptors and prevent experimentally induced post-operative ileus. It has potential for use in clinical cases.

Cisapride

Cisapride is a substituted benzamide with gastrointestinal prokinetic properties. The mode of action is believed to be enhancement of release of acetylcholine from postganglionic intramural interneurons leading to increased calcium flux.[58]

Cisapride does not have any dopamine blocking activity. In normal horses, cisapride augments the amplitude of gastric contractions, stimulates jejunal activity coordinated with gastric contractions, enhances contractile activity of the large and small colons, and stimulates coordinated activity at the ileocecocolonic junction.[59,60] An injectable preparation of cisapride is no longer available, but 10-mg tablets available for the treatment of motility disorders in people can be administered orally in horses. Although anectdotal evidence exists that cisapride is also effective when administered rectally (0.2 mg/kg), which offers advantages in horses with gastric reflux, studies have demonstrated that the drug cannot be detected in the blood of horses after administration by this route.

Lidocaine (Lignocaine)

Lidocaine has been used in horses with colic primarily to treat ileus, but it is an effective analgesic as well. Lidocaine exerts its analgesic properties by decreasing afferent traffic through small C fibers. In addition, it has anti-inflammatory properties and decreases the influx of inflammatory cells.[61] The plasma concentrations necessary for analgesia are much lower than those required to block normal peripheral nerve conduction. Lidocaine has also been shown to decrease reperfusion injury by inhibiting the release of free radicals and decreasing the migration of neutrophils at the site of injury. Preliminary studies suggest that the prokinetic effect of lidocaine may be useful in post-operative ileus.[62] An initial intravenous bolus at a dose rate of 1.3 mg/kg (administered slowly over 5 minutes) can be followed by a continuous intravenous infusion at a rate of 0.05 mg/kg/minute (diluted in saline or lactated Ringer's solution). Signs of toxicity include muscle fasciculations, ataxia, and possible seizures; these signs are more likely to happen if the initial bolus is administered too rapidly.

Erythromycin Lactobionate

Erythromycin is a macrolide antibiotic that appears to have a prokinetic action on the intestine that is independent of its antimicrobial action. It acts on enteric cholinergic neurons through motilin and/or 5-HT3 receptors to stimulate the release of acetylcholine.[63,64] A dose of 2.2 mg/kg diluted in 1 liter of saline and infused over 60 minutes may be administered every 6 hours. Alternatively, it may be administered as a continuous intravenous infusion at a rate of 0.1 mg/kg/hour. A recent study in normal horses determined that a lower dose of 1.0 mg/kg is effective in stimulating both cecal and small-intestinal propulsive activity.[65] Doses higher than 10 mg/kg can potentially disrupt propulsive activity. There has been some concern that the prokinetic response may diminish with repeated treatments because of down-regulation of motilin receptors. An association between erythromycin therapy and the occurrence of *Clostridium difficile* induced colitis in a small number of horses has led some clinicians to question the safety of this therapy.

Acetylpromazine (Acepromazine) and Yohimbine

These drugs are α-adrenergic antagonists. Their use is based on the assumption that sympathetic hyperactivity contributes to post-operative ileus. Norepinephrine inhibits the release of the excitatory neurotransmitter acetylcholine by stimulating α-2 receptors located presynaptically on cholinergic neurons. Acepromazine facilitates small-intestinal transit in normal ponies.[66] The drug can also produce hypotension via antagonism of α-1 adrenergic receptors, so it is essential that the horse be well hydrated prior to administration.

Yohimbine hydrochloride is a competitive antagonist that is selective for α-2 adrenergic receptors, and therefore is not associated with the hypotensive effects seen with acepromazine. When administered at a dose rate of 0.15 mg/kg intravenously, yohimbine can reduce the severity of post-operative ileus, especially when used in combination with bethanechol.[67]

Bethanechol

Bethanechol is a muscarinic cholinergic agonist, which stimulates gastrointestinal smooth muscle cells causing them to contract.[56] At a dose rate of 0.02 mg/kg (subcutaneously) bethanechol was shown to improve gastrointestinal motility in an experimental model of post-operative ileus when administered in combination with yohimbine.[68] Bethanechol has also been shown to increase the rate of gastric and cecal emptying in normal horses. A common use of bethanechol in horses is in the treatment of gastric atony following correction of an outflow obstruction in foals with duodenal ulcers. Side effects, including abdominal cramps, diarrhea, salivation, and gastric secretion, arise from enhanced parasympathetic tone.

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Treatment of Shock

Chapter 17

Kevin T. T. Corley

Support of the Cardiovascular System

The cardiovascular system is key to survival of horses with acute abdominal disease. Abdominal disease can lead to profound cardiovascular changes, principally through loss of water and electrolytes from the circulation to the gastrointestinal tract and by absorption of toxins. The principal toxin involved is endotoxin, a component of the cell wall of gram-negative bacteria. This toxin interacts with immune-series cells to cause the synthesis and release of a cascade of soluble mediators, including the cytokines IL-1 and TNF-alpha. These mediators, in turn, cause profound changes in both the contractility of the heart and the resistance of the blood vessels to blood flow. Both the effects of the toxins and loss of water from the circulation can severely reduce progressive blood flow through the capillary beds in the organs. The principal job of the blood flow through the organs is to deliver oxygen to the individual cells. As capillary blood flow is reduced, the metabolic processes of these cells are severely curtailed, and they may die. This, in turn, leads to organ failure and, ultimately, death.

There are two main prongs of therapy to support of the cardiovascular system, designed to prevent the sequence of events outlined above. The first, and often the only one employed, is to replace and maintain the lost constituents from the blood (water, electrolytes, proteins) with fluid therapy. The second is to directly alter either the contractility of the heart or the resistance of blood vessels to blood flow, using vasoactive drugs, principally inotropes, vasopressors and vasodilators.

Fluid Therapy

Fluid therapy is an essential part of managing horses with acute abdominal disease. Fluid therapy can serve one or several of the following purposes: Restore circulating volume; rehydrate the tissues; correct electrolyte disturbances; correct acid-base disorders; increase plasma colloidal oncotic pressure; rehydrate or over-hydrate the gastrointestinal contents.

Hypovolemia and Dehydration

Hypovolemia is defined as a decrease in circulating blood volume. The classic example of hypovolemia is acute arterial hemorrhage, in which the circulating volume is decreased rapidly without a change in the remainder of the extracellular fluid volume. Dehydration is defined as a loss of interstitial fluid without a change in the circulating volume. Powerful physiologic mechanisms protect the circulating volume during dehydration at the expense of extravascular fluid, and it is only with severe dehydration that animals also become hypovolemic.

In horses with severe gastrointestinal disease, hypovolemia and dehydration are often present together. Horses with less severe disease are frequently dehydrated but not necessarily hypovolemic. Even though they may coexist in the same horse, hypovolemia and dehydration are important to distinguish, because their therapy is different. Hypovolemia requires emergency treatment to rapidly restore circulating volume. Cconsiderable evidence links markers of hypovolemia on hospital admission with morbidity and decreased survival in equine colic.[1,2] Hypovolemia is treated with rapid volume expanders, such as colloids, hypertonic saline, or large volumes of crystalloids administered intravenously. Little objective evidence is available regarding the treatment of hypovolemia in horses. However, studies in pediatric and adult human sepsis have shown dramatic improvements in outcome with early restoration of volume.[3,4] Dehydration is treated over 12 to 24 hours with oral or intravenous crystalloid fluids. Suggested fluids and volumes for hypovolemia are presented in the section of this chapter on treatment strategies.

Ongoing Losses

Excessive fluid losses from horses with acute abdominal disease frequently do not stop when treatment is initiated, and these must be taken into account in the fluid therapy plan. The most dramatic ongoing fluid losses are with severe diarrhea or nasogastric reflux, and, in either, they may reach 200 mL/kg/day (100 L/day for a 500-kg horse).[5] Even without such obvious losses, horses with primary abdominal disease may lose significant amounts of fluid through sweating, inadequate intake or, rarely, through polyuric renal failure.

Treatment for ongoing losses is aimed at replacing the amount lost to maintain hydration. This is relatively simple when the amount of fluid lost can be measured, as in the case of nasogastric reflux. Reflux is collected in a graduated bucket (Figure 17-1), and the amount collected over a 4- to 12-hour period is compared with the amount of fluid administered. If the fluid lost exceeds the amount given, the fluid administration rates are adjusted both to replace this amount over the next 12 to 24 hours, and to account for the higher level of ongoing losses than originally estimated. If the excessive losses have resulted in hypovolemia (on the basis of clinical and laboratory evidence), this must be treated acutely. It is much harder to estimate losses from diarrhea, sweating, and urination than from nasogastric reflux. In the case of diarrhea and urination, it is possible to attempt either to collect the feces or urine, or to use absorbent bedding and measure the increase in weight. These are

almost never done in clinical practice, except in the case of recumbent neonatal foals, for which feces or urine may be readily collected and weighed on incontinence pads, or urine may be collected with an indwelling Foley catheter and closed collection system (Figure 17-2). When ongoing fluid losses cannot be measured, they must be estimated. These estimates may be inaccurate, and the amount of ongoing loss can dramatically change. Therefore, it is important to frequently reassess the adequacy of fluid therapy through clinical examination and relevant laboratory investigations. These are discussed later in this chapter.

Figure 17-1



Gastric reflux measured in a graduated bucket to estimate fluid loss.

Figure 17-2



Collection of urine with an indwelling catheter in a foal.

Maintenance

All horses have a daily fluid requirement to replace losses from metabolic processes, sweat, urination, defecation, evaporation from the respiratory tract, and any lost salivation or lacrimation. Normally this requirement is met by a combination of drinking and the water content of feed. If a horse is deprived of feed, it will normally drink more to match these losses. For horses with reduced water intake (a frequent occurrence with abdominal disease), this maintenance requirement must be met by fluids administered via a nasogastric tube or intravenously.

The exact maintenance requirement for horses is unknown, and probably varies among individuals. The mean daily water intake (including the water content of feed) of normal resting adult horses is 57 to 64 mL/kg/day at ambient temperatures of 41 to 77°F (5 to 25°C).[6,7] Although this may not strictly represent the minimal fluid requirements, it is a useful guideline for the 'maintenance rate' (2.5 mL/kg/hour) in adult horses. Thus, a 500-kg horse requires approximately 30 L/day for maintenance, in addition to any fluids to replace ongoing losses. The maintenance requirement of neonatal foals is significantly higher and is usually estimated to be 4 to 5 mL/kg/hour.[8,9] Although the fluid intake of nursing foals considerably exceeds this figure,[10,11] clinical experience suggests that these rates are appropriate for fluid maintenance in foals receiving no enteral fluids. It is important to take into account the fluid component of all infusions when calculating fluid rates to avoid inadvertent volume overload in neonatal foals receiving a number of intravenous infusions.

Oncotic Pressure and Physiologic Roles of Albumin

The net amount of fluid that leaves the circulation in the capillaries is determined by the difference in hydrostatic pressure and oncotic pressure between the fluid in the capillary and the interstitial space. Colloidal oncotic pressure refers to the osmotic pressure exerted by the molecules that do not freely pass from the vascular lumen into the interstitial space. The oncotic pressure holds water in the circulation and draws fluid back into the circulation at the end of the capillary beds.[12] The fluid remaining outside the capillaries may be returned to the circulation via the lymphatic system, but, if excessive, will result in tissue edema.

The number of particles in a solution determines its osmotic pressure. Thus, solutions containing smaller molecules can exert a higher osmotic pressure since saturated solutions will contain more molecules per unit volume. However, small molecules diffuse more easily out of the vascular space. Therefore, the net oncotic pressure exerted by a solution is a balance between the osmotic pressure exerted by that solution and the rate of diffusion of that solution out of the vascular bed. In normal plasma, most of the oncotic pressure gradient (approximately 80%) is produced by albumin. Globulins contribute the remainder of the oncotic pressure, with fibrinogen exerting little effect (<0.01% of total).[13] The normal colloid oncotic pressure of plasma is less in neonatal foals (17-21 mm Hg) than in mature Thoroughbred horses (20-22 mm Hg).[14,15]

Albumin has other important physiologic functions, including binding ions, drugs, and hormones and serving as a carrier for fatty acids and other water-insoluble compounds in the plasma.[16] When the plasma concentration of albumin is decreased, the free (or non-bound) fraction of an albumin-binding drug will increase. However, for most drugs, plasma clearance will also increase, resulting in an unchanged free concentration of the drug and, therefore, no change in drug activity.[17,18] Albumin also acts as a buffer in acid-base disturbances, and decreased albumin concentration contributes to a metabolic alkalosis.[19]

Acid Base Balance

Principles, Causes and Recognition

The most common acid-base disturbance in horses with gastrointestinal disease is metabolic acidosis, due to lactic acidosis (hypovolemia, endotoxemia), hyponatremia (colitis, peritonitis, intestinal volvulus) or hyperchloremia (occasionally seen in horses with colitis). Metabolic alkalosis, due to hypochloremia (high volume gastric reflux or colitis) or hypoalbuminemia (severe enterocolitis, excessive fluid therapy), respiratory alkalosis (hyperventilation due to pain), and respiratory acidosis (hypoventilation due to extreme abdominal distension, central depression) can also occur.[19]

Acid-base balance is determined by the examination of arterial pH, arterial carbon dioxide tension (P_aCO_2), and the base excess. The pH gives the overall acid-base balance. It is calculated as the negative log of the hydrogen ion concentration. A decreased pH represents an overall acidosis and an increased pH represents an overall alkalosis. The normal range is approximately 7.35 to 7.48.[19] The arterial carbon dioxide tension represents the respiratory component of the acid-base balance. Carbon dioxide combines with water to form carbonic acid, which, in turn, forms bicarbonate and hydrogen ions, in the following equation:

$$CO_2 + H_2O \leftrightarrow H_2CO_3 \leftrightarrow H^+ + HCO_3^-$$

If the amount of carbon dioxide increases in the blood (for example, because of compromised respiration in a horse with a diaphragmatic hernia), the equilibrium in this equation moves to the right, resulting in a higher hydrogen ion concentration and a lower pH. This is a respiratory acidosis. If the amount of carbon dioxide decreases in the blood (for example, becuase of hyperventilation associated with pain), this equilibrium moves to the left, resulting in a lower hydrogen ion concentration and a higher pH. This is a respiratory alkalosis.

Base excess represents the metabolic component of the acid-base balance. Base excess is a measure of the strong acid needed to restore pH of whole blood to 7.4 at a P_aCO_2 of 40 mm Hg. The base excess effectively represents a corrected value for bicarbonate. As can be seen in the equation above, as the carbon dioxide tension changes, the bicarbonate concentration changes. The base excess, therefore, corrects the bicarbonate to remove this effect, by calculating what the bicarbonate would be if the carbon dioxide tension was 40 mm Hg. This removes the respiratory influence on bicarbonate and leaves only the metabolic influence. One further calculation is performed to convert bicarbonate to base excess. The difference between the corrected bicarbonate and its normal value (usually taken to be either 24.4 or 25 mmol/L) is calculated. Therefore, a base excess of –5 mEq/L represents a corrected bicarbonate of 19.4 or 20 mmol/L. A negative base excess represents a metabolic acidosis and a positive base excess, a metabolic alkalosis.

Physiologic compensatory mechanisms exist that attempt to return the pH toward normal. Respiratory compensation of metabolic disturbances is fairly straightforward. In metabolic acidosis, the increase in H^+ stimulates the respiratory center to increase ventilation, increasing excretion of CO_2 by the lungs, and decreasing the P_aCO_2 in the blood. This response is initially mediated by peripheral chemoreceptors, but the full response does not occur until there is a change in pH in the cerebrospinal fluid (CSF), which takes 14 to 17 hours in dogs.[20] The decrease in ventilation in response to a metabolic alkalosis appears to be entirely centrally mediated, and thus only occurs after a change in CSF pH. The expected change in P_aCO_2 in metabolic acidosis is a decrease of 1 mm Hg for each 1 mEq/L decrease in base excess. In metabolic alkalosis, the expected increase in P_aCO_2 is 0.6 mm Hg, for each 1 mEq/L increase in base excess.[21]

Respiratory acid base disorders result in metabolic compensation. In acute respiratory alkalosis, sodium is exchanged for chloride by red blood cells, resulting in a mild hyperchloremia and hyponatremia. With chronicity, there is increased reabsorption of chloride and decreased reabsorption of sodium in the renal tubules. In an acute respiratory alkalosis, lactate is increased for the first 6 to 8 hours in dogs.[20] This is because of an increase in lactic acid production, particularly by red blood cells.[22] With acute respiratory alkalosis, no change in base excess is expected. In chronic respiratory alkalosis, a decrease of 0.4 mEq/L in base excess is expected for each 1 mm Hg decrease in P_aCO_2.[21] In acute respiratory acidosis, the reverse happens; the red blood cells take up chloride, and release sodium. Again, it is the kidneys that mediate the compensation in chronic respiratory acidosis; ammonium chloride is excreted, resulting in a decrease in plasma chloride but not sodium. With acute respiratory acidosis, no change in base excess is expected. In chronic respiratory acidosis, an increase of 0.4 mEq/L in base excess is expected for each 1 mm Hg increase in P_aCO_2.[21] Occasionally, respiratory and metabolic dysfunction can both contribute to the development of an acid base disturbance, particularly an acidosis. For example, a horse with a large-colon volvulus may have a metabolic acidosis because of accumulation of lactate from hypovolemia and a failing circulation. If the colon is significantly distended, this may interfere with the movement of the diaphragm, and reduce respiration, resulting in an additional respiratory acidosis. This is termed a mixed disturbance.

Classification of acid-base disturbances is important to effectively direct treatment. They are classified as acidosis or alkalosis, metabolic or respiratory, and compensated or uncompensated. The majority of acid-base disturbances can be classified by the following three steps (Table 17-1). The first step is to look at the measured pH. If the pH is below 7.40, the primary problem is likely to be an acidosis. If the pH is above 7.40, the primary problem is likely to be an alkalosis. The second step is to determine whether the P_aCO_2 or base excess matches the pH. An increased P_aCO_2 or negative base excess matches an acidotic pH. A decreased P_aCO_2 or positive base excess matches an alkalotic pH. If P_aCO_2 matches the pH, the primary problem is respiratory. If the base excess matches the pH, the primary problem is metabolic. If both match the pH, then it is a mixed respiratory and metabolic problem. The third step is to decide whether compensation is present. This depends on the increase or decrease of the P_aCO_2 or base excess that does not agree with the current pH. If the P_aCO_2 or base excess is within its normal range, almost certainly no compensation exists. If P_aCO_2 decreases during a primary metabolic acidosis, it most likely represents compensation. A few cases do not fit this scheme. For example, metabolic acidosis may be primary, due to hypovolemia, and not compensatory in a horse with colitis and pain that induces tachypnea.

Table 17-1
Scheme for Classifying the Majority of Acid-base Disturbances

Disturbance	pH	P_aCO_2	Base Excess
Uncompensated Metabolic Acidosis	Decreased	Unchanged	Negative
Compensated Metabolic Acidosis	Decreased	Decreased	Negative
Uncompensated Respiratory Acidosis	Decreased	Increased	Unchanged
Compensated Respiratory Acidosis	Decreased	Increased	Positive
Mixed Metabolic and Respiratory Acidosis	Decreased	Increased	Negative
Uncompensated Metabolic Alkalosis	Increased	Unchanged	Positive
Compensated Metabolic Alkalosis	Increased	Increased	Positive
Uncompensated Respiratory Alkalosis	Increased	Decreased	Unchanged
Compensated Respiratory Alkalosis	Increased	Decreased	Negative
Mixed Metabolic and Respiratory Alkalosis	Increased	Decreased	Positive

P_aCO_2 = arterial tension of carbon dioxide

Physiologic Role and Abnormalities of the Major Electrolytes in Plasma

Horses with acute abdominal disease can have profound changes in the plasma concentrations of the major electrolytes. Understanding the roles of these electrolytes, and the prevalence and causes of changes in their concentrations can help prioritize therapy. Electrolyte and acid-base abnormalities are usually corrected during rehydration therapy after treatment for hypovolemia. The choice of fluid composition for this phase of therapy is, therefore, dependent on the plasma electrolyte concentrations.

Sodium

Sodium is the major cation in plasma, and sodium and glucose concentrations are the main determinants of plasma osmolality.[23] Changes in plasma osmolality can lead to central nervous system edema or dehydration,[24,25] because the cerebrospinal fluid equilibrates slowly with the plasma but will change rapidly if osmotic gradients are high. Plasma sodium concentration is mainly controlled by the hormone vasopressin (formerly called antidiuretic hormone). Excessive secretion of vasopressin can occur post-operatively or from pain,[26] resulting in free-water retention and hyponatremia. In this case, the plasma volume may be normal. Hyperglycemia is common in post-operative colic patients, presumably as part of the physiologic response to cortisol release.[27] Glucose acts as an osmotic agent, expanding the extracellular space, and, therefore, effectively diluting sodium. This effect is moderate (a decrease of 1.7 mmol/L in sodium for each increase of 100 mg/dL (5.6 mmol/L) glucose in humans[24]), but may exacerbate other causes of decreased sodium concentration. Hyponatremia may also occur in horses with peritonitis or bowel obstructions, which can lose sodium and water into this "third space," resulting in hypovolemic hyponatremia.[24] It is also possible to cause iatrogenic hyponatremia by repeated instillation of water without electrolytes into the stomach, as might be done to relieve a large-colon impaction.[28]

Hypernatremia is reported to occur in 12% of post-operative colic patients.[29] It results in hypertonicity, hyperosmolality, and cellular dehydration.[25] Hypernatremia usually occurs because of water loss, but may result from a net gain of sodium. Diarrhea, drainage of gastric reflux, renal failure, and diuresis can all cause hypernatremia. Prolonged water restriction or excess administration of salt or sodium bicarbonate may also result in iatrogenic hypernatremia.[25,26]

Potassium

Potassium is primarily an intracellular ion, and thus, decreases in whole body potassium may not be detected by plasma measurements.[30] Although erythrocyte potassium content has been used to estimate whole body potassium,[30] its accuracy has not been validated. Moreover, the extracellular potassium concentration (reflected in the plasma) is critical for neuromuscular transmission and is more relevant to clinical signs than whole body potassium stores.[31]

Hypokalemia is common in horses after colic surgery,[29] because of enhanced mineralocorticoid and glucocorticoid release and the infusion of large amounts of sodium-containing fluids, which increase distal tubular flow and renal potassium loss.[31] Hypokalemia can also occur in colitis, after heavy sweating, and in metabolic alkalosis. In colic patients, the most relevant clinical sign of hypokalemia is reduced intestinal motility.[26,32] However, the association between hypokalemia and ileus in the horse remains undetermined. Other clinical signs include muscle weakness, lethargy, and inability to concentrate urine.[26]

Cardiac conduction abnormalities are rare except in severe hypokalemia and in pre-existing cardiac dysfunction.[32] The effect of potassium on acid-base status is small and need not be considered clinically.[19]

Hyperkalemia has been reported to occur in association with metabolic acidosis, as a result of potassium exchange for hydrogen ions across cell membranes; however, this is chiefly a phenomenon of mineral (inorganic) acidosis rather than lactic acidosis.[33,34] In horses with colic, the predominant cause of acidosis is lactic acid accumulation associated with poor tissue perfusion and hypovolemia.[35] One study found a moderate inverse correlation between plasma potassium concentration and pH, but no correlation between potassium and lactate concentration, in jugular venous blood from horses undergoing surgery for treatment of abdominal diseases (Adams C and Corley KTT, unpublished observations, 2004).

Chloride

Chloride is the major anion in the extracellular fluid. Chloride ions are important in maintaining acid-base balance, renal tubular function, and the production of gastric acid.[36] In humans, chloride is the major determinant of metabolic acid-base status[37] High concentrations of chloride are present in gastric acid and small intestinal secretions, and chloride is normally absorbed from the upper small intestine.[38] In the kidney, chloride reabsorption is heavily influenced by both plasma sodium concentration and acid-base balance. Both active and passive chloride transport mechanisms contribute to its reabsorption. Renal reabsorption of chloride is affected by several hormones, including parathyroid hormone, calcitonin, vasopressin, and angiotensin II.[38]

Chloride ion concentration is dependent on whole body water balance. Therefore, plasma chloride concentrations must be interpreted relative to plasma sodium ion concentrations.[19,38] Large amounts of chloride can be lost from high-volume gastric reflux or in secretory diarrhea, resulting in hypochloremia and metabolic alkalosis. Post-operative colic patients have a high prevalence (54%) of hyperchloremia.[29] Hyperchloremia can occur as a result of loss of water in excess of electrolytes, in which case it occurs in concert with hypernatremia. Hyperchloremia may also result from metabolic compensation for respiratory alkalosis and renal tubular acidosis, and loss of water and sodium in diarrhea.[19,38]

Calcium

Calcium is involved in excitation and contraction of cardiac muscle and the maintenance of vascular tone. It is a positive inotrope, causing an increase in smooth muscle contractility.[39-41] Other functions of calcium include neuromuscular transmission, enzyme and hormone production, and coagulation.[41] It is also involved in cell messaging and receptor coupling.[42] Calcium is primarily extracellular, with 99% located in bones and teeth. Only 1% exists in the extracellular fluid, of which roughly half is protein bound, and approximately 47% ionized in the plasma.[43] Many commonly used analyzers measure total plasma calcium, which is partly dependent on the plasma albumin concentration. The formula for correcting total calcium for the measured albumin concentration is:

$$\text{Corrected calcium (mg/dl)} = \text{Measured Calcium (mg/dl)} + 0.8\,(4 - \text{albumin (g/dL)})$$[44]

Acid-base alterations affect the protein binding of calcium, with acidosis increasing ionized calcium as it is displaced from protein-bound sites by hydrogen ions.[45]

Low plasma ionized calcium concentrations are common in horses with gastrointestinal diseases requiring surgical intervention[43] and in horses with colitis. Possible causes of hypocalcemia include lactic acidosis,[45] endotoxin-induced changes in calcium homeostasis,[44,46] loss of calcium in sweat,[47] and functional disturbances of the small intestine (the main site of calcium absorption in the horse[48]). Clinical signs of hypocalcemia reported in the horse include synchronous diaphragmatic flutter, tetany, muscle spasm, and seizures.[49] In horses after colic surgery, decreasing ionized calcium concentrations were correlated with the following changes on the electrocardiogram: increased heart rate, increased QT interval corrected for heart rate, decreased PR interval, and decreased QRS interval.[39] Experimentally induced hypocalcemia (<3.52 mg/dL; 0.83mmol/L) induced cardiac arrhythmias in 4 of 7 ponies, which were fatal in 2.[50] Hypocalcemia may be associated with post-operative ileus in the horse,[43] but this has not been investigated.

Hypercalcemia occurs rarely in horses with acute abdominal disease unless there is concurrent chronic renal failure or neoplasia. Hypercalcemia can cause muscle weakness, depression and seizures due to increased CSF calcium concentrations.[41] Experimentally induced hypercalcemia in ponies resulted in ventricular fibrillation or cardiac arrest at ionized calcium concentrations of 4.55 to 10.0 mmol/L.[50]

Magnesium

Magnesium plays a crucial role in many metabolic and cellular functions in the body, especially those involving adenosine triphosphate (ATP) and the production of energy.[51] It is an important coenzyme for the sodium-potassium ATPase pump.[52] Abnormalities of the normal resting membrane potential can result from interference with the normal function of this pump, causing membrane destabilization and hyperexcitability. Magnesium is an essential cofactor in many enzymatic reactions in the body.[52] Magnesium also directly competes with calcium for some of its binding sites, allowing greater binding of calcium to enzymes in hypomagnesemia. One such enzyme is phospholipase A_2. Increased calcium binding results in greater activity of this enzyme, which leads to the increased formation of eicosanoids, particularly thromboxane A_2,[53] which may play a role in thrombophlebitis.[54]

In one study, 54% of horses with gastrointestinal disease had low plasma ionized magnesium concentrations.[39] Causes of hypomagnesemia include decreased intake, gastrointestinal losses (e.g., prolonged nasogastric reflux, malabsorption), alterations in distribution (e.g., endotoxemia, parenteral nutrition administration), renal losses (e.g., prolonged administration of lactated Ringer's solution or other magnesium-free fluids, hypophosphatemia, acidemia, renal tubular acidosis),[55,56] and excessive sweating.[47] In the horse, severe hypomagnesemia can result in ventricular arrhythmias and also muscle tremors, ataxia, seizures, and calcification of elastic tissue.[57] Other clinical manifestations of hypomagnesemia reported in humans include supraventricular tachycardia, atrial fibrillation, thrombosis, anemia, decreased muscle strength, increased nephrotoxicity of aminoglycoside drugs, increased pulmonary vascular resistance, and sudden death.[52,53,56,58] Hypomagnesemia can also result in hypokalemia that is refractory to potassium supplementation.[59]

Hypermagnesemia is less common than magnesium deficiency in intensive care patients. The prevalence reported in post-operative colic patients is 11 to 14%.[29,60] Magnesium antagonizes the effects of calcium at the neuromuscular junction; signs of hypermagnesemia include sweating, flaccid paralysis, coma, and recumbency as a result of a blockade of peripheral neuromuscular transmission.[61] Iatrogenic hypermagnesemia can occur in horses after administration of magnesium sulfate (Epsom salts) by nasogastric tube, for the treatment of large-colon impactions. The recommended dosage of magnesium sulfate is 0.5 to 1.0 g/kg, and toxicity has been reported when twice the normal dosage has been administered. Any conditions that reduce renal excretion of magnesium, such as hypovolemia, or allow increased intestinal absorption of magnesium, such as delayed intestinal transit due to colic, drug therapy, or increased permeability of the intestinal wall, may allow toxicity to develop.[62]

Phosphate

Only 1% of total body phosphorus is present in the blood, with the majority of the remainder in the bone.[63] Phosphate (inorganic phosphorus) is the most abundant intracellular anion.[36] Phosphate homeostasis is controlled by parathyroid hormone, calcitonin, and vitamin D, and involves the intestine, kidneys, and bone. Absorption of phosphate from the intestine is affected by calcium, which binds to intraluminal phosphate to form insoluble complexes, thus reducing bioavailability of both ions.[63] Phosphate in the body is important as an enzyme cofactor, a buffer, and in the production of adenosine triphosphate (ATP) for energy. It is an important part of proteins and lipids, and is also essential for normal functioning of the coagulation cascade and the immune system.[36]

The prevalence of hypophosphatemia in post-operative colic patients is 44%.[29] Possible causes include withholding feed during the acute colic episode and post-operative period. Increases in circulating catecholamine and glucose concentrations, which occur after colic surgery, induce intracellular shifts of phosphate.[63] Extensive bowel resection can also result in hypophosphatemia, because the distal small intestine is a major site of phosphate absorption in the horse.[64] In experimental studies in rats, endotoxin administration resulted in increased renal excretion of phosphate.[65] If this response to endotoxemia also occurs in horses, this may also contribute to hypophosphatemia. The prevalence of hyperphosphatemia in horses after colic surgery is 12%.[29] Large quantities of phosphate are present in intestinal tissue. Ischemic damage to the intestinal wall leads to leakage of phosphate into both the intestinal lumen and peritoneal fluid, which occurs at an early point after onset of intestinal ischemia. The phosphate in the peritoneal space may reach the systemic circulation via the portal system and lymphatics. Supporting this, the correlation between serum and peritoneal fluid phosphate concentrations was high in horses with colic.[66]

Types of Fluid

Crystalloids

Crystalloid solutions consist of electrolytes in water. Crystalloid solutions may be isotonic, hypertonic, or hypotonic. Isotonic

solutions have approximately the same osmolality as plasma and thus may be given rapidly, in large volumes, into peripheral veins. Hypertonic solutions act to draw water into the extracellular fluid (ECF) from the intracellular fluid and represent a method of rapidly restoring circulating volume at the expense of tissue hydration. Hypotonic solutions are usually only used to correct plasma hypertonicity. Because true hypotonic solutions (e.g., sterile water) cause erythrolysis,[67] they can only be given slowly via a central vein.[68] For this reason, isotonic solutions containing a metabolizable substrate, such as dextrose; no electrolytes are usually used.

Crystalloid fluids rapidly pass from the circulation to the interstitial fluid. This means that their resuscitation effect may be short-lived and that they can cause edema. Only 30% of isotonic fluids and 10% of hypotonic fluids remain in the circulation after 30 minutes.[69] The increase in interstitial fluid may actually decrease tissue oxygen uptake in normal animals by increasing the diffusion distance between capillaries and cells.[70] However, crystalloids remain the least expensive and, in many circumstances, the best fluids for administration to the horse. All fluid therapy plans involve crystalloid fluids, and these are frequently the only fluids administered.

Homemade or "carboy" fluids, while considerably less expensive than fluids available commercially, have been associated with producing clinical signs of endotoxemia in normal horses[71] and a 7-fold increase in the risk of thrombophlebitis,[72] and thus cannot be recommended.

Balanced Electrolyte Solutions

For most situations, commercial isotonic polyionic crystalloid solutions are the safest fluids with which to resuscitate hypovolemic horses. They increase plasma volume without directly causing profound electrolyte disturbances, because they contain approximately the same electrolyte concentrations as plasma. Therefore, balanced polyionic fluids are always a good choice when laboratory information is not available immediately. It also follows that polyionic crystalloid solutions are often not sufficient to correct electrolyte imbalances.

Two classes of polyionic fluids are available, those for resuscitation and those for maintenance. Maintenance fluids (Normosol-M*, Plasma-lyte M**, Plasmalyte-56** etc.) contain higher potassium (15-30 mEq/L) and lower sodium (40-60 mEq/L) and chloride (40-60 mEq/L) concentrations than resuscitation fluids (Normosol-R,* Plasma-lyte 148,** Isolec,*** lactated Ringer's solution,** etc.). Currently, maintenance fluids are not available commercially in volumes exceeding 1 L, which has led to the practice of adding potassium chloride (at 10-20 mEq/L) to resuscitation formulas so that they can be used as maintenance fluids in equine medicine. Commercially available maintenance fluids should be considered as a treatment option in equine neonates.

The different alkalinizing agents (or "bicarbonate substitutes") used in resuscitation fluids are clinically relevant. The alkalinizing agent in plasma is bicarbonate. Bicarbonate-containing fluids are unstable when stored and may produce profound metabolic alkalosis. Therefore, Hartmann, an American pediatrician, replaced bicarbonate with lactate to make lactated Ringer's solution (also called Hartmann's solution). Lactate is metabolized in the liver, but this process is slow enough to avoid the rapid changes in plasma pH that occur with bicarbonate. Sodium bicarbonate and sodium lactate both increase the strong ion difference resulting in a metabolic alkalosis. The cation (sodium) remains in the ECF while the anion (bicarbonate or lactate) is metabolized.[73] It is the speed of metabolism of the anion and the renal excretion of sodium that determine the ultimate alkalization. It may seem counter-intuitive to administer lactate-containing fluids to a horse with lactic acidosis resulting from poor tissue perfusion; however, clinical trials in human patients in hemorrhagic shock have shown that lactate-containing fluids do not exacerbate the lactic acidosis of hypoperfusion.[74,75] It appears that, in shock, the liver's capacity for metabolizing lactate is not overwhelmed, but instead the delivery of lactate to the liver by the circulation is impaired. Restoring the circulating volume, even with fluids containing moderate amounts of lactate, is sufficient to allow the liver to clear the circulating lactate.[76] Whereas this is true for hemorrhagic shock, uptake of lactate by the liver may be impaired in severe septicemia.[77] In endotoxic and septic horses, and those with liver disease, lactated Ringer's solution should be used with caution. Alternative alkalinizing agents to lactate are present in some commercially available polyionic fluids (e.g., acetate and gluconate in Normosol-R). The muscles primarily metabolize acetate, and a variety of tissues throughout the body metabolize gluconate. Lactated Ringer's solution contains calcium whereas Normosol-R contains magnesium. Calcium solutions should not be mixed with whole blood; blood and its products should be stored with a compound that chelates calcium ions. Similarly, calcium solutions should not be mixed with sodium bicarbonate as they react to produce calcium carbonate. Clearly, calcium solutions are contraindicated in hypercalcemia. Fluids containing magnesium can, therefore, be used in more clinical situations than those containing calcium.

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Normal Saline

Isotonic (0.9%) sodium chloride is used commonly as an intravenous replacement fluid in species other than the horse. Isotonic sodium chloride has a higher ratio of chloride to sodium than does plasma and, therefore, reduces the strong ion difference and causes a mild hyperchloremic acidosis in normal ponies.[78] This limits its utility as a resuscitation fluid in the horse, as most horses requiring fluid resuscitation already have acidosis. Isotonic sodium chloride should not be used for resuscitation of horses with acute abdominal disease unless this is indicated by measured electrolyte abnormalities. Sodium chloride solution has been advocated in the treatment of hyperkalemia, to avoid the potassium-containing polyionic fluids. This does not apply to the horse, however; in the absence of clinical signs of hyperkalemia and with the exception of horses with hyperkalemic periodic paralysis or with a ruptured bladder, the hyperkalemia is likely to reflect acidosis, and polyionic fluids are probably appropriate.

Hypertonic Saline

Hypertonic saline (2-4 mL/kg of 7-7.5% sodium chloride) has been advocated as a method of quickly restoring circulating volume in horses with severe endotoxemia.[79] Administration of 7% sodium chloride results in an increase in the ECF of 4 to 5 times the infused volume for at least 60 minutes after it is infused.[80] The hypertonic saline draws fluid into the ECF from the intracellular fluid, principally from muscle and liver cells[80] without providing significant fluid replacement. The administration of hypertonic saline should always be followed within 2 1/2 hours of administration (the point in experimental studies when cardiac output begins to fall below baseline values[79]) by the administration of large volumes of isotonic polyionic crystalloids. The volume of crystalloid fluids given should be based on the severity of clinical signs of hypovolemia and dehydration, but should be in excess of 5 times the volume of hypertonic saline infused. As well as increasing ECF volume, hypertonic saline reduces the capillary endothelial swelling that may occur as part of the systemic inflammatory response syndrome and, therefore, improves tissue microcirculation and oxygen delivery.[81] Furthermore, in experimental hemorrhagic shock, hypertonic saline reduces neutrophil activation, resulting in reduced lung injury.[82]

Administration of hypertonic saline solution, at a dose rate of 5 mL/kg immediately after administration of endotoxin to horses, attenuated the cardiovascular derangements associated with endotoxemia more effectively than an equivalent volume of isotonic saline.[79] Despite the positive experimental evidence for the use of hypertonic saline in endotoxemia, it should be used with caution during resuscitation in dehydrated horses. Cardiovascular improvements after the administration of hypertonic saline in 3% to 8% of dehydrated rats were significantly reduced,[83] and resuscitation of 8% to 10% of dehydrated rats with hypertonic saline resulted in greater renal dysfunction and decreased survival compared with the administration of lactated Ringer's solution.[84] Given the beneficial effects of hypertonic saline in experimental endotoxemia and sepsis, it may have a role after initial fluid resuscitation; however, this has not been evaluated clinically in horses with endotoxemia. Because of the risks associated with rapid changes in plasma osmolality,[25] 7% saline should probably not be administered to neonatal foals.

Combination of dextran 70 (a colloid) with hypertonic saline resulted in acceptable resuscitation in experimental dehydration in calf and swine models.[85,86] In the horse, however, the administration of a highly concentrated formula of hypertonic saline-dextran 70 resulted in clinically apparent intravascular hemolysis and hemoglobinuria.[87] Whether less concentrated formulas are suitable for the horse remains to be investigated. The combination of an alternative colloid, hetastarch or pentastarch (6-10 mL/kg), and hypertonic saline (4 mL/kg) may be an appropriate solution for resuscitation of horses that are both hypovolemic and dehydrated. Clinical experience suggests that hypertonic-saline-hetastarch and hypertonic-saline-pentastarch are particularly useful in horses with marked hypovolemia and hypoproteinemia, such as those with severe colitis, but this has been not been formally evaluated in experimental studies or in a series of clinical cases.

Sodium Bicarbonate

Sodium bicarbonate has been advocated for the correction of metabolic acidosis in horses;[88,89] however, the cause of the acidosis must be considered carefully prior to starting treatment. Sodium bicarbonate may be beneficial in acidosis caused by hyponatremia or hyperchloremia;[19] however, in lactic acidosis, which is far more common in the horse, treatment with sodium bicarbonate is highly controversial.

It is the author's opinion that there are no grounds for administering sodium bicarbonate to horses with lactic acidosis, irrespective of the arterial (or venous) pH. This contradicts previous recommendations that it should be used when the pH decreases below 7.1[88] or 7.22.[89] Treatment of lactic acidosis with sodium bicarbonate is based on four suppositions: low blood pH is directly harmful; sodium bicarbonate is able to increase blood pH when infused intravenously; increasing the blood pH with sodium bicarbonate improves patient status; any adverse effects of sodium bicarbonate are outweighed by its benefits.[90] These suppositions are not supported by data available currently in horses, humans, and laboratory animals. For a

full discussion of the issues surrounding sodium bicarbonate treatment for lactic acidosis, the reader is referred to reviews by this and other authors.[8,90]

Dextrose-Containing Solutions

Dextrose (5%, D5W) and 5% glucose solutions are used to replace a deficit of pure water (without accompanying electrolyte deficits), and are effectively hypotonic because the dextrose is rapidly metabolized to carbon dioxide and water. Use of these solutions is indicated in cases where fluid loss exceeds electrolyte loss, which can occur in horses with strangulating intestinal lesions.[23] Hypernatremia and hyperchloremia are also relatively common in neonatal foals in which resuscitation formulas are used as maintenance fluids.[91] The volume of distribution of D5W is likely to be larger than that of a balanced electrolyte solution, which could result in a diminished ability to maintain the circulating volume. Horses receiving D5W should be monitored carefully because rapid administration can lead to hyperglycemia. If the plasma glucose concentration exceeds the renal threshold (approximately 180 mg/dL or 10 mmol/L), osmotic diuresis will result, which can reduce the benefit of the fluid administration. In species other than the horse (humans and dogs), high concentrations of glucose have been shown to be detrimental in both acute renal and acute cerebral injury.[92,93] It is importat that 5% dextrose and glucose solutions not be considered a form of parenteral nutrition. One liter of 5% dextrose provides approximately 170 kcal (712 kJ) of energy and 1 L of 5% glucose provides approximately 190 kcal (796 kJ). To provide 11.5 Mcal/day, the caloric requirement of a 500-kg horse standing in a stall,[94] it would be necessary to administer 60 to 70 L per day, which would produce serious electrolyte abnormalities. Consequently, 50% dextrose and 50% glucose solutions may be preferable to the 5% solution. Each milliliter of 50% dextrose is equivalent to 1.7 kcal (7.1 kJ), and each mL of 50% glucose is equivalent to 1.9 kcal (8 kJ).

An alternative is a solution of 2.5% dextrose and 0.45% sodium chloride, which, once the dextrose has been metabolized, has an effective osmolality one-half that of plasma. It is retained better in the circulation (20% after 30 minutes compared with 10% for D5W)[69] and can be used in the treatment of moderate plasma hypertonicity or when plasma glucose concentration is a concern. It should be noted that a rapid reduction in plasma tonicity has been associated with the development of cerebral edema, resulting in coma, seizures, and death in other species.[25] This has not been documented in the horse.

Colloids

Colloids are solutions containing large sugar or protein molecules, in addition to the water and electrolytes that are in crystalloid solutions. All colloids, except albumin, contain a mixture of large and small protein or sugar molecules. The larger molecules allow colloid solutions to persist longer in the circulation than do crystalloid solutions. The smaller molecules exert osmotic pressure to draw fluid into the circulation in a similar way to hypertonic saline. Solutions with a large number of smaller molecules allow a rapid increase in the circulating volume, greater than the actual volume infused.

The use of colloids has been advocated for the resuscitation of hypovolemic horses and for the treatment of severe hypoproteinemia.[95] Colloids have two advantages over crystalloids, which makes them attractive for fluid therapy. Firstly, because of their persistence in the circulation, a colloid solution three to six times lower in volume is required to produce the same resuscitative effect as a crystalloid solution.[96] This is particularly useful in acute resuscitation of severely dehydrated horses or in the field where large amounts of crystalloids may be difficult to transport. Secondly, the administration of colloids can increase colloidal oncotic pressure, in contrast to the administration of large volumes of crystalloids.[14,97]

The molecular weight of a colloid solution is the most important factor in determining its pharmacology. All currently available synthetic colloids are polydisperse (made up of a mixture of molecules of differing molecular weights). Albumin is a monodisperse solution, as all molecules have a molecular weight of 69 kD. The average molecular weight refers to the average size of molecules in the solution. As a rule, the higher the average molecular weight, the longer the colloid will persist in the circulation. The chemical nature of the colloid also influences its persistence in the circulation, but generally to a lesser degree than the molecular weight. The number of molecules in the solution determines the osmotic pressure, which can be considerably greater than plasma (e.g., 342 mm Hg for urea-linked gelatin). Colloids with a smaller average molecular weight exert a higher osmotic pressure and expand the plasma volume more rapidly, by drawing fluid from the interstitial space into the vasculature and thus increasing the circulating volume in excess of the amount of fluid infused. However, smaller molecular weight colloids are cleared faster from the circulation and may leak more readily into the interstitium.

Leakage of proteins into the interstitium is important in edema formation, a common feature in critically-ill horses, particularly those with colitis. Edema impairs delivery of oxygen to the tissues, as it both compresses capillary beds and increases the diffusion distance between the capillaries and the cells. Therefore, edema may contribute significantly to morbidity and mortality. Endotoxemia[98] and ischemia–reperfusion injury[99,100] induce capillary damage, which allows plasma albumin to leak

into the interstitium. This not only reduces the oncotic pressure within the vasculature, but also allows the extravasated albumin to exert an osmotic pressure that holds fluid in the interstitial space. Large colloid molecules do not leak as readily, allowing their oncotic pressure to draw fluid back into the vasculature. Larger colloid molecules may also plug the gaps in the capillary endothelium.[101,102] Even in conditions of severe capillary leak, very large molecules are not able to escape the vasculature unless the integrity of the capillary endothelium is totally destroyed.[103]

All of the artificial colloid solutions available currently are removed from the circulation by the reticuloendothelial system, resulting in colloid-containing vacuoles, which may persist for years.[104,105] The presence of these vacuoles does not appear to interfere with the function of the reticuloendothelial system.[106]

It remains to be seen whether colloids offer any advantage in terms of clinical outcome when compared with crystalloids in horses. Some of the theoretical benefits of colloids over crystalloids have not been observed in some experimental models and clinical trials. For example, increased extravascular lung water was documented in an endotoxic pig model[107] but not in a septic rat model[108] when crystalloid and hetastarch resuscitation were compared. In preterm hypotensive human infants, treatment with 5% albumin resulted in significantly greater fluid retention than treatment with isotonic saline, and the two treatments were equivalent in other respects.[109] A very large, randomized clinical trial of critically ill human patients demonstrated no difference between albumin and saline for fluid resuscitation. Subgroup analysis suggested a moderate benefit of saline in trauma patients; in septic patients, which may be the most relevant to the horse with colic and endotoxemia, the analysis suggested a slight benefit of albumin.[110] To date, no large randomized trials have compared hydroxyethyl starches or gelatins against crystalloids in either humans or horses. For these reasons, the clinician should keep an open mind about the relative merits of crystalloid and colloid resuscitation in horses. One precaution when using colloids is that the plasma total solids or total protein concentration is no longer a useful guide to plasma oncotic pressure.[111]

Hydroxyethyl Starches

Hydroxyethyl starches are modified polymers of amylopectin. Several different hydroxyethyl starch preparations are marketed around the world. They all consist of a polydisperse solution of starch molecules in which hydroxyethyl groups have been substituted for a number of the glucose subunits. The solutions differ in the number of glucose units substituted and the average molecular weight. The greater the number of glucose molecules substituted, the longer the half-life of the solution in vivo. The degree of substitution is usually given as a proportion of substituted residues, which results in a number between 0 and 1, with higher numbers representing greater substitution and hence a longer half-life. The average molecular weight is also important, with lower molecular weight solutions having a greater oncotic pressure but a shorter persistence in the circulation.

Hydroxyethyl starches are eliminated by renal excretion, extravasation, and uptake by the reticuloendothelial system, and for a very small percentage (<1%) of molecules, by biliary excretion.[105,112] Larger molecules are cleaved by serum α-amylase prior to elimination. This cleavage generates smaller molecules, with a higher oncotic pressure, and contributes to a long persistence of increased colloid oncotic pressure in normal animals.[14] Uptake by the reticuloendothelial system can result in the presence of phagocytic cells containing starch granules in the liver, spleen, skin, small intestine, striated muscle, and lymph nodes[104,106] These deposits are dose-dependent and decrease with time, but may persist for up to 4 1/2 years after infusion of hydroxyethyl starch in humans.[104]

Hetastarch

Hetastarch is the only hydroxyethyl starch marketed for resuscitation in the United States. It is available as a 6% solution in isotonic saline or in an isotonic lactated electrolyte solution. Hetastarch is a polydisperse solution with a wide range of molecular sizes (10 to 3000 kD) and a high average molecular weight (450 kD) and degree of substitution (0.75). Hetastarch exerts an osmotic pressure of approximately 31 mm Hg in solution[113] and, at a dose of 10 mL/kg, increases the plasma colloidal oncotic pressure of normal ponies from 24 to 27 mm Hg.[14] In normal dogs, hetastarch expands the plasma by 140% of the volume infused.[105] The effects on plasma volume in the normal horse are likely to be similar but have not been investigated. Hetastarch is slowly degraded in the circulation and, thus, has a long half-life. In normal ponies, the increase in colloidal oncotic pressure after a dose of 10 mL/kg lasts longer than 120 hours.[14] In hypoproteinemic horses and foals, the clinical effects appear to be shorter, typically lasting 24 to 36 hours.[97]

In normal ponies, hetastarch is safe, but high doses (20 mL/kg) decrease circulating von Willebrand factor, factor VIII coagulant activity, and activated partial thromboplastin time and prolong bleeding times.[14] Although a dose of 10 mL/kg of hetastarch did not affect hemostasis in normal ponies,[14] endotoxemia may produce coagulation derangements[114] that might render endotoxemic horses susceptible to development of clinically important coagulation changes at this or lower doses. A

recent study from human medicine suggests that administration of hydroxyethyl starches is associated with a higher incidence of renal failure than administration of gelatins.[115] However, the hydroxyethyl starch and gelatin groups were not equivalent at study entry, the amount of fluid administered differed between the groups, and the definition of acute renal failure was questionable in this study. Therefore, further work is required to establish any link between hydroxyethyl starch administration and renal failure.

Hetastarch may decrease vascular permeability after ischemia-reperfusion injury,[101,102] which makes it a theoretically attractive solution for administration to horses prior to surgical correction of strangulating intestinal lesions. This effect on reperfusion injury is not simply a function of high molecular weight; a similar affect could not be demonstrated for a dextran solution with an average molecular weight of 250 kD.[116] Evidence exists that hetastarch reduces neutrophil chemotaxis through the endothelium in vitro.[117] Therefore, a potential exists for hetastarch to reduce neutrophil-mediated damage in ischemia-reperfusion, endotoxemia, and other inflammatory tissue insults; however, this effect has not yet been demonstrated in vivo.

The rapid increase in circulating volume that occurs after administration of hypertonic saline and the increase in oncotic pressure and more prolonged effects of hetastarch may make this combination appropriate for the resuscitation of severely dehydrated horses, especially those with severe colitis. Although hetastarch (up to 10 mL/kg) and hypertonic saline (2-4 mL/kg) have been combined with apparent success in a number of clinical cases, this combination has not been evaluated critically. If used, this combination should be followed up with crystalloid fluids.

Pentastarch and Pentafraction

In Europe, several hydroxyethyl starch preparations are available commercially. Pentastarch, one of the more commonly used preparations, has been tested in horses[118,119] and is approved for use in horses in Switzerland. It is available as a 6% or 10% solution in isotonic sodium chloride. Pentastarch has a smaller average molecular weight (200 kD) than hetastarch and is thus expected to produce a greater initial increase in the plasma volume. The initial increase in plasma volume in human patients is reported to be 145% of the volume infused for the 10% solution and 100% of the volume infused for the 6% solution.[120] The degree of substitution (0.5) is less than hetastarch, which is expected to lead to faster degradation by serum amylases.

In human medicine, smaller average molecular weight starches have less profound effects on hemostasis.[121] This may also be the case in horses, although only one dose has been tested. In healthy horses, a 8 mL/kg dose of a 10% pentastarch solution resulted in a slight decrease in the thrombin time 12 hours after administration, which returned to normal after 24 hours. No effect on prothrombin time or partial thromboplastin time was documented.[119] In healthy horses, the initial phase half-life of pentastarch is 5.6 hours and the terminal phase half-life is 122 hours. However, the effects on PCV, plasma total solids, and plasma viscosity appear to last only 12 to 24 hours[119] In equine clinical cases, the half-life may be as short as 2 hours.[118] Pentastarch, although available in the United States, is only approved for leukapheresis in human medicine.

A new hydroxyethyl starch has been developed to avoid the large molecular weight molecules that are thought to be mainly responsible for the effects on coagulation factors and the low molecular weight molecules, which are rapidly eliminated. This preparation, pentafraction, has an average molecular weight of 280 kD with a range of 100 to 500 kD. Initial results with this starch in laboratory animals are promising.[122]

Dextrans

Dextrans are polysaccharides composed of linear glucose residues. They are produced from a polysaccharide synthesized by the bacteria *Leuconostoc mesenteroides* grown on sucrose media. Different molecular weight dextrans are produced by acid hydrolysis of the parent molecule. Two dextran solutions are available commercially in the United States, dextran 40 (10% solution in isotonic saline) and dextran 70 (6% solution in isotonic saline); the number refers to the average molecular weight, 40 kD and 70 kD, respectively. Both of these solutions are polydisperse. Dextran molecules less than 50 to 55 kD are excreted in the urine.[105] Larger molecules are extravasated and taken up by the reticuloendothelial system or excreted through the gastrointestinal tract.[113]

In human patients, the peak plasma volume expansion after infusion of dextran 40 is 210% of the volume infused. One hour after infusion, the plasma expansion is approximately 140% of the volume infused.[123] In dogs, the peak effect of dextran 70 is a 140% plasma expansion. After 1 hour, the expansion effect of dextran 70 is approximately 100% of the volume infused.[105] Within 12 hours, 60% of the dextran 40 and 35% of the dextran 70 have been cleared from the vascular space.[113] In dogs, the increase in plasma volume 24 hours after dextran 70 injection is only 1.1% of the volume infused.[105]
In humans, dextran administration is associated with a decrease in factor VIII activity, decreased fibrin clot formation, and

dilutional coagulopathy[13] Dextran 70 inhibits equine platelet aggregation in vitro,[124] but other effects on hemostasis have not been investigated. Dextran 70 has been used for its presumed antithrombotic properties in horses with a clinical diagnosis of verminous aneurysm.[125] Dextran 70, when combined with hypertonic saline in a highly concentrated solution, resulted in a transient, severe intravascular hemolysis and hemoglobinuria in horses.[87] Whether this would occur with a less concentrated solution is unlikely, but this has not been studied formally. Dextran 40 was reported to cause acute renal failure in 4.7% of human patients.[126] It is not known whether this is a risk in the horse.

Gelatins

Gelatins are produced by chemical modification of bovine collagen. Despite their bovine origin, the risk of transmission of bovine spongiform encephalopathy by these products is apparently negligible.[127] Two types of gelatin are marketed in Europe, although neither is currently available in the United States. Urea-linked gelatin† is marketed as a polydisperse solution with an average molecular weight of 35 kD, and succinylated gelatin†† is marketed as a polydisperse solution with an average molecular weight of 30 kD. Because of their relatively small molecular size, gelatins have high osmotic pressure (342 mm Hg) but are eliminated rapidly by the kidneys. The small size of the molecules in gelatin solutions also means that more of this colloid is extravasated than other colloids, leading to greater edema formation.[128,129] The high osmotic pressure means that it is possible to cause fluid overload in normal horses with gelatin. In one study, normal ponies undergoing anesthesia were given an extremely large dose of urea-linked gelatin (average dose 48 mL/kg). This caused significant fluid overload and pulmonary edema.[130] In human patients, allergic reactions are reported for both gelatin preparations, with urea-linked gelatins having the higher incidence at 0.146%.[131] There is no evidence that urea-linked gelatin causes allergic reactions in horses.[130]

Plasma

Plasma has been used extensively in horses with colitis and in neonatal foals for the passive transfer of immunity. Plasma may either be purchased commercially or collected from donors. The ideal plasma donor is a young, healthy gelding with a known, entire history that has never been administered a blood product. For blood collection from the donor, a catheter is placed in the jugular vein with the tip pointing towards the head of the animal. Using a 10- or 12-gauge catheter speeds up collection. A collection bag containing anticoagulant (100 mL acid citrate dextrose for each 900 mL whole blood collected[132]) is connected to the catheter, and the jugular vein is occluded beneath the catheter until the bag is full. Centrifugation or plasmapheresis are the most effective methods of separating the plasma from the cells. It is possible to get reasonable separation of the plasma and cells by sedimentation. The bag should be placed with the administration set uppermost in an ice bucket. Separation is reasonable after 2 hours, but ideally the bag should be left for 12 hours, if the circumstances allow.[133] However, if the plasma is being collected for replacement of clotting factors, no more than 6 hours should elapse between collection and administration or freezing, as factors V and VIII are not stable beyond 6 hours.[134] These clotting factors are also depleted if frozen plasma is stored for longer than 1 year. Albumin, globulin, and factors II, VII, IX, and X are stable for at least 1 year.[134] Horses with colitis are at high risk of coagulopathy,[114] and therefore, fresh plasma, collected and administered within 6 hours, is preferred to frozen plasma, if available.

Although classically prescribed for hypoalbuminemia, the utility of plasma for replacing protein is unclear. Approximately 80% of the colloidal oncotic pressure of plasma is provided by albumin, and thus, many of the reservations expressed about albumin apply to plasma. At least 6 to 8 L are required to treat clinically significant hypoproteinemia in adult horses, and even so, the effects may be short-lived. Plasma administration does not have the advantage of the larger molecular weight colloids of potentially drawing fluid back into the circulation in damaged capillaries, but it may prevent a low plasma oncotic pressure[132] leading to generalized edema. Plasma may have a role in replacing antithrombin III, protein C, and other cofactors that are depleted during the systemic inflammatory response syndrome. When used for this purpose, fresh plasma is preferable, because plasma that has been frozen for longer than 1 year may no longer contain high concentrations of these proteins.

Whole Blood

Used judiciously, blood transfusion is a potentially life-saving treatment. It should be considered in all horses with a PCV of less than 18% (hemoglobin concentration less than 6 g/dL) and is imperative in horses with a PCV of less than 12%. Blood transfusion is not necessary in mild anemia (PCV >24%); human patients with mild anemia who received blood transfusion therapy have a worse outcome.[135] Hemorrhage is uncommon in horses with acute abdominal disease; however, horses with hemoperitoneum may present in acute pain, and may, occasionally, require transfusion. In septic shock, blood transfusion has been suggested as a method of increasing oxygen delivery to the tissues by increasing the oxygen carrying capacity of the blood. In septic human patients, however, blood transfusion was associated with an increase in oxygen delivery but not in oxygen uptake,[136] suggesting that the increased supply of oxygen is not available to the tissues. This is supported by work in

† Haemaccel, Intervet, Cambridge, UK †† Gelofusine, B. Braun Medical Ltd, Sheffield, UK

laboratory animals that suggests that tissue oxygen uptake is superior at a PCV of 20% or 30% to that at a PCV of 40%, despite the higher oxygen delivery at the higher PCV.[137] The most likely explanation for this is that the increasing PCV increases blood viscosity,[138] causing blood sludging and reduced flow through the capillaries. This may be especially important in shock, where blood viscosity may be increased independently from the PCV.[139]

Blood transfusion recipients are usually cross-matched with potential donors prior to blood collection; however, the reliability of these tests in the horse is questionable.[133,140] It may be appropriate to select donors negative for the major antigens (Aa and Qa) so that cross-matching is not necessary.[133] Several laboratories offer blood-typing for horses. For neonatal isoerythrolysis, washed red cells from the dam are the transfusion of choice. Washing removes the plasma, which contains anti-erythrocyte antibodies. The red cells are washed by repeatedly separating the cells from the plasma and suspending them in isotonic saline. Ideally, the separation of the cells from the plasma or saline should be done with a centrifuge or plasmaphoresis machine, but it is acceptable to allow the cells to settle, remove the plasma, and then suspend them in saline. Three washes are usually adequate.

In all cases, the recipient should be monitored closely for signs of a transfusion reaction during the infusion of the initial 50 mL of blood. Signs of transfusion reactions include pyrexia, tachycardia, tachypnea, sweating, icterus, lying down, frequent defecation, proteinuria, and hemoglobinuria.[141] None of these signs is invariably present, but pyrexia and sweating are frequently the most prominent signs. In one study of normal horses given repeated incompatible transfusions, icterus and proteinuria were the only clinical signs that lasted for longer than 24 hours, and transfusion reactions did not occur before the sixth incompatible transfusion.[141] In another study, one horse died, apparently of an anaphylactoid reaction, during the second transfusion.[140] Disease transmission is possible with blood transfusion and is a particular concern in areas where equine infectious anemia is endemic.[142] All donor animals should be tested regularly for this disease.

Whole blood should be collected into bags containing acid-citrate dextrose, as described earlier for plasma. If possible, the blood should be used immediately, but erythrocytes may remain viable in a refrigerator for as long as 3 to 4 weeks.[133] The amount of blood needed for transfusion can be calculated using the following equation:

$$\text{Amount of blood (mL)} = \frac{\text{Bodyweight (kg)} \times (\text{Desired PCV} - \text{Current PCV}) \times Z}{\text{PCV of Donor}}$$

Where Z is blood volume of the recipient per kg bodyweight
(80 mL/kg for adult horses[133]; 150 mL/kg for a 2-day old foal[143,144])

Studies of the length of survival of transfused erythrocytes in recipient horses have produced variable results. In adult horses, the half-life of ^{59}Fe-labeled donor erythrocytes was 4 days in 3 of 6 horses and less than 24 hours in the other 3 recipients.[140] This methodology does not permit autologous transfusions as a control. In 2- to 5-day old foals, the mean half-life of ^{50}Cr-labeled donor erythrocytes was 5.5 days compared with 11.7 days for autologous erythrocytes.[145]

Blood Subsititutes

Stroma-free hemoglobin preparations have been developed in response to the need for safe, infection-free, sustainable sources of blood in human medicine and to eliminate the need for cross-matching. Unfortunately, unmodified free hemoglobin has too high an affinity for oxygen, is rapidly eliminated by the kidneys, causes a substantial increase in oncotic pressure, and may cause renal injury. For this reason, research has focused on modified polymers of hemoglobin. Polymerized bovine hemoglobin has already been registered in the United States and Europe for use in dogs, where the recommended dose is 10 to 30 mL/kg. Successful use of this product has been reported in a foal with neonatal isoerythrolysis[146] and an early version of the product was used with apparent success in an anemic miniature horse[147]; in both cases, a compatible blood donor could not be found. Although not clinically significant in this case, the anemic mare had increased pulmonary and systemic pressures, reported side effects in humans,[148] after infusion of the hemoglobin product.[147] More concerning is that, in an experimental trial in ponies with normovolemic anemia, 1 of 6 ponies experienced an anaphylactic reaction.[149]

These products are an exciting development, which may have a particular application in equine medicine because of the difficulty of reliable cross-matching for blood transfusion; however, currently available products may not be optimal for use in the horse.

Oral Fluids

It is possible to treat moderately dehydrated horses effectively with oral replacement solutions.[150,151] Oral fluids do not need to be sterile, can be made up on the farm, and are considerably less expensive and easier to transport than intravenous fluids. It is apparently not necessary to add glucose to oral fluids for horses, but electrolytes should be added, if feasible. Isotonic or hypotonic fluids should be administered.[152]

Oral fluids can be a successful alternative or adjunct to intravenous fluids in many mildly dehydrated horses with large-colon impactions.[28,153] Unfortunately, oral fluids are insufficient for moderately to severely dehydrated horses. Rapid administration of a glucose- and glycine-containing electrolyte solution (8 L/30 min) resulted in incomplete fluid absorption in horses with castor oil-induced diarrhea.[154] The oral rehydration solutions available commercially may not be ideal for fluid replacement in horses.[154]

The administration of plain water is of minimal benefit to restore plasma volume in horses exercised in hot and humid conditions.[155] However, the administration of an oral rehydration solution or an electrolyte paste together with provision of fresh drinking water may be sufficient to supplement water and electrolytes after vigorous or prolonged exercise in dehydrated horses with only mild hypovolemia.[155,156]

Composition and Recipes

A possible isotonic solution consists of 4.9 g/L table salt and 4.9 g/L Lite salt‡ to produce final concentrations of 123 mmol/L sodium, 34 mmol/L potassium, and 157 mmol/L chloride.[152] This is approximately equal to 15 mL of table salt and 15 mL of Lite salt per 4 L of water. If using sodium chloride alone, no more than 9 g (approximately half a tablespoon or 7.5 mL) should be added per liter. A measured quantity of these fluids should be given via a nasogastric tube. The amount administered at any one time should not exceed 8 to 10 L for a 500-kg horse, with at least 30 minutes allowed to elapse between each administration. Before each dose, the stomach should be refluxed and the administration delayed if more than 2 L of fluid are recovered. Some horses will show signs of abdominal pain when large doses of oral fluids, especially if the fluids are cold, are administered.

Electrolyte Replacement Strategies

Sodium

The fluid choice for hyponatremia depends on whether concurrent hypochloremia is present. Sodium chloride is the best choice, if the plasma chloride concentration is also low. If the chloride concentration is normal or increased, then sodium bicarbonate should be administered. If the horse is not markedly dehydrated[84] and the hyponatremia is severe, then hypertonic solutions may be indicated (7 to 7.5% sodium chloride and 5 to 8.4% sodium bicarbonate). In other species, rapid correction of sodium deficits has been shown to cause demyelination of the pontine and extrapontine neurons, resulting in severe neurologic dysfunction.[24] It has not been established whether this is a risk or not in the horse and, therefore, it is necessary to follow the guidelines for sodium restoration in other species. These guidelines state that sodium should be corrected at a rate of 1 mEq/L/hour in acute hyponatremia, and at less than 0.5 mEq/l/hour in chronic hyponatremia, in neither case to exceed 8 mEq/L during the first 24 hours.[26] Sodium can be replaced in oral fluids. Some horses with hyponatremia will preferentially drink electrolyte-supplemented water. The water should be isotonic or slightly hypotonic. Fresh water should always be provided in addition to the electrolyte-supplemented water. These sodium-supplemented solutions may also be delivered by nasogastric tube. In foals, sodium chloride and sodium bicarbonate (1 teaspoon, up to 4 times a day) may be administered by oral syringe. Mixing the sodium salt with yoghurt makes a paste, which foals tend to retain better when given by oral syringe.

Hypernatremia is corrected with low sodium fluids such as 5% dextrose or 2.5% dextrose and 0.45% sodium chloride. Again, in other species, the recommendation is that hypernatremia not be corrected too rapidly: Sodium should be lowered by 0.5 mEq/L/hour, not to exceed 12 mEq/L in the first 24 hours.[26]

Potassium

Treatment of hypokalemia involves potassium replacement, either intravenously or orally. Rapid administration of potassium intravenously can lead to very high circulating potassium concentrations and cardiac arrhythmias. Therefore, potassium should be infused at a maximum rate of 0.5 to 1 mEq/kg/hour. Potassium chloride is the ideal replacement salt, especially in horses that are refluxing and are hypochloremic.[32] High crystalloid flow rates result in increased urine production and kalliuresis, and can make it harder to replace potassium by the intravenous route. Oral supplementation with potassium can, therefore, be

‡ Morton Salt, Chicago, Illinois, USA

more effective in horses and foals in which this route is available. The dose is 0.1 to 0.2 g/kg, by mouth or nasogastric tube. For foals, this is usually divided into 3 or 4 doses given at intervals of at least 4 hours. Horses that are also hypomagnesemic may be refractory to potassium replacement therapy, unless the magnesium deficit is simultaneously corrected.[59]

Several treatment options exist for hyperkalemia. In the absence of clinical signs, polyionic fluids should be administered. Possible treatments for symptomatic or severe (>7 mEq/L) hyperkalemia include calcium gluconate (1 mL/kg intravenously over 10 minutes), sodium bicarbonate (1-2 mEq/L intravenously over 15 minutes), and 50% dextrose solution (2 mL/kg intravenously over 5 minutes).[26]

Chloride

Treatment of hypochloremia can usually be achieved with intravenous 0.9% sodium chloride, which contains more chloride relative to sodium than plasma. In horses with high-volume gastric reflux, intravenous administration of histamine 2 receptor antagonists (e.g., cimetidine at 6.6 mg/kg intravenously, 4 times daily) reduces gastric hydrochloric acid secretion and may, therefore, reduce chloride loss. In humans, hydrochloric acid has been administered intravenously to treat severe hypochloremia[157] but carries substantial risks for the patient.[158]

Hyperchloremia should be treated with 5% dextrose if accompanied by hypernatremia and with sodium bicarbonate if severe and accompanied by a low or normal plasma sodium concentration.[150]

Calcium

Hypocalcemia is usually treated with 20%, 23%, or 40% calcium gluconate or calcium borogluconate solution administered intravenously. Approximately 0.2 to 1.0 mL/kg of the 20% or 23% solution or 0.1 to 0.5 of the 40% solution will be required,[43] but the amount will depend on the ongoing losses, and the ionized calcium concentration should be checked frequently during therapy. Calcium solutions are irritating to the veins and should be diluted in crystalloid fluids prior to administration. Calcium solutions should not be mixed with sodium bicarbonate or whole blood. The plasma calcium concentration should be checked 4 to 8 hours after calcium supplementation because ongoing losses and redistribution into cells may result in further hypocalcemia. Hypocalcemia can be a sequel to magnesium deficiency and, therefore, magnesium should be supplemented in horses with refractory hypocalcemia.

Treatment for severe hypercalcemia (ionized calcium concentration exceeding 9 mg/dL (2.25 mmol/L)) should include intravenous fluids lacking calcium (sodium chloride or Normosol-R) and intravenous administration of magnesium sulfate (see treatment of hypomagnesemia below).

Magnesium

Hypomagnesemia can be treated by intravenous or oral supplementation. Intravenous administration of magnesium sulfate (at 2 mg/kg/min, not to exceed 50 mg/kg) is recommended for the treatment of ventricular arrhythmias associated with hypomagnesemia.[159] Higher doses should be avoided because they cause significant muscle weakness; 140 mg/kg of magnesium sulfate administered intravenously can induce recumbency in normal horses.[61] For the treatment of hypomagnesemia in the absence of cardiac signs, 8 to 32 mg magnesium sulfate/kg can be used as an initial dose in horses with normal renal function. Oral supplementation with magnesium-lactate-citrate or magnesium oxide is possible, but oral administration of magnesium sulfate should be avoided because of its laxative effects.

Treatment of iatrogenic hypermagnesemia has been reported in horses.[62] The horses were treated with 250 mL of 23% calcium gluconate solution, repeated after 1 hour, and polyionic intravenous fluids to promote diuresis.

Phosphate

Treatment of hypophosphatemia has not been reported in the horse, and in humans no good evidence exists for beginning treatment in the absence of clinical signs.[63] Treatment options reported in small animals include intravenous (0.01-0.03 mmol phosphate/kg/hour) and oral (0.5-2 mmol phosphate/kg/day) administration of either potassium phosphate or sodium-potassium-phosphate.[160] This phosphate dose has been used with apparent clinical success by the author in mature horses. The potential effects of potassium phosphate on the plasma potassium concentration must be considered before beginning treatment. Intravenous administration of glucose-1-phosphate[161] and sodium phosphate have also been reported in humans. The safety of these treatments has not been evaluated in the horse.

Hyperphosphatemia may not require treatment. It appears that increased plasma phosphate concentrations are not directly toxic.[162] The treatment recommended in small animals includes intravenous fluids to correct any acidosis and promote renal phosphorus excretion and dextrose-containing fluids to promote translocation of phosphorus into cells.[160]

Delivery Systems

During the early period of resuscitation of moderately to severely hypovolemic horses, it is important to use both a large-gauge catheter and a wide-bore sterile delivery system to allow rapid delivery of fluids. A 10- or 12-gauge catheter is recommended by the author for severely hypovolemic adult horses and a 12- or 14- gauge catheter for moderately hypovolemic horses. Sixteen-gauge catheters are sufficient for neonatal foals and moderately hypovolemic weanlings and miniature horses. During total parenteral nutrition (TPN), double-lumen catheters can provide a dedicated line for the TPN and avoid the need to interrupt the TPN when administering incompatible drugs.

To place a catheter, the hair should be clipped over the vein and the area should be prepared aseptically, ideally with a chlorhexidine scrub solution.[163] The catheter should be handled and placed wearing sterile gloves. In young and fractious horses, a bleb of local anesthetic placed subcutaneously at the catheter site makes catheterization easier. The aseptic scrub should be repeated after the local anesthetic is deposited. A small stab incision through the skin can be helpful when using a local anesthetic or if 10-gauge or Seldinger ("over the wire") catheters are used. For fluid therapy, the catheter should be directed toward the heart. After placement, the catheter should be flushed with heparinized saline (5 units/mL) and fixed in place either with instant bonding glue (for short-term use), staples, or sutures.

In the horse, the easiest vein to catheterize is the external jugular vein. The cephalic and the lateral thoracic veins may also be catheterized. These veins carry less serious consequences if they become occluded by thrombophlebitis; however, the maximum fluid rate attainable through these smaller veins (approximately 5 L/hour in adult horses) is less than that attainable using the jugular vein. Furthermore, infectious thrombophlebitis may be serious at any site. If one jugular vein is thrombosed or occluded, it is inadvisable to catheterize the contralateral jugular vein and risk bilateral jugular thrombosis, which can result in life-threatening swelling of the head. Both the cephalic and the lateral thoracic veins can be technically difficult to catheterize. Good sedation or restraint is required to catheterize the cephalic vein because horses have a tendency to move during catheter placement. The cephalic and saphenous veins are relatively easily catheterized in neonatal foals. The lateral thoracic vein can be hard to identify and has a flat profile, which can make it difficult to pass a catheter into the lumen. The vein can be identified by ultrasonography and is probably best catheterized using the Seldinger ("over the wire") technique.[164] In the cephalic, saphenous, and lateral thoracic veins, valves can impede the passing of a catheter stylet or wire.

A variety of fluid administration sets are available commercially. Sets that include large-bore tubing and a coil are suitable for most situations in adult horses and are recommended. Coils can also be helpful in neonatal foals, but wide-bore tubing is unnecessary. The flow rate can be estimated by counting the number of drops per 10 seconds in the drip chamber or can be set by using an electronic infusion pump. In all situations, a record should be kept of the time the infusion was started and of the infusion rate to ensure that the desired volume is being delivered in the appropriate time.

The frequency of replacement of catheters and administration sets depends on the local environmental conditions and the catheter material. Catheters made from polytetrafluoroethylene (Teflon) are associated with an increased incidence of thrombophlebitis and have a tendency to crack and kink.[165] These catheters should not be left in place for longer than 72 hours. In contrast, soft catheters made from polyurethane or silicone rubber can often be left in place safely for at least 14 days[165] or as long as 6 weeks when monitored properly. These catheters should only be replaced when there is a suspected problem. It is unclear how frequently administration sets should be replaced when used in a horse stall. The current recommendations of the Centers for Disease Control (CDC) for human hospitals is not to replace administration sets more frequently than every 72 hours, except when used to administer blood- or lipid-containing parenteral nutrition, in which case they should be changed every 24 hours.[166]

Indwelling cecal catheters have been proposed for fluid therapy in horses to avoid the expense of sterile fluids. Although it is possible to deliver fluid by this technique, the high rate of serious complications precludes the use of cecal catheters.[167] Repeated administration of oral fluids can be delivered through an indwelling nasogastric tube. The tube should be plugged with a syringe barrel between administrations to prevent excessive influx of air. Continuous enteral fluid therapy can be provided with a enteral feeding tube[§] connected to a coiled administration set designed for intravenous fluid therapy.[168]

§ 18 French, 100-inch nasogastric feeding tube, MILA International Inc., Florence, KY, USA

Thrombophlebitis

Thrombophlebitis is a common complication of intravenous fluid therapy.[72] A thrombus may cause mechanical blockage of venous drainage, resulting in local edema, and may be a nidus for infection. Edematous occlusion of the nasal passages can result from bilateral jugular vein thrombosis and can be fatal. It is, therefore, inadvisable to catheterize the contralateral jugular vein if one jugular vein shows signs of thrombosis. Bacterial endocarditis, particularly of the tricuspid valve, can occur as a sequel to septic thrombosis.

Thrombophlebitis can be identified by heat, swelling, or the presence of any exudate around the catheter insertion site or a palpable thrombus ("corded" feel) in the catheterized vein. Catheterized veins should be examined at least daily. Ultrasonography of the catheterized vein can help identify thrombus formation. It is prudent to continue to check the vein for 2 to 3 days after catheter removal because thrombophlebitis may develop or become apparent in this period.

Topical nitroglycerin ointment has been shown to be an effective treatment for thrombophlebitis in humans.[169] Local application of hot packs and topical application of dimethyl sulfoxide ointment on the affected vein are also used for treatment in the horse. Catheters should be removed aseptically from thrombosed veins, and bacterial culture (preferably by the roll-plate technique[170]) and in vitro susceptibility testing, carried out. A fine-needle aspirate of the thrombus can also be submitted for bacterial culture. Fluid-filled pockets within the thrombus can often be identified by ultrasound[171] and should be aspirated after surgical preparation of the overlying skin. Empirical antimicrobial treatment should include an agent with a broad spectrum of activity, including for streptococci and staphylococci,[171] and good tissue penetration, such as doxycycline.

The risk factors for thrombophlebitis include administration of "carboy" fluids,[72] the presence of diarrhea[72] or endotoxemia,[54] polytetrafluoroethylene (Teflon) catheter material, and a long duration of catheterization.[165] Several other risk factors for thrombophlebitis have been identified in people but not studied in horses. These include inexperienced personnel placing the catheter,[172] administration of total parenteral nutrition,[173] and large-bore catheters.[174]

Recognition of Hypovolemia and Dehydration

Clinical Signs

The clinical signs of hypovolemia and dehydration in the adult horse are listed in Table 17-2. Hypovolemia is defined as insufficient circulating blood volume, whereas dehydration is defined as loss of water from the tissues. It is important to distinguish between these conditions because hypovolemia requires immediate treatment but dehydration is optimally addressed over a period of 12 to 24 hours. In most clinical scenarios, however, hypovolemia and dehydration occur concurrently.

Traditionally, clinical signs have been used to estimate percent of dehydration and formulate a fluid plan for replacement of the fluid deficit. Recent evidence from small animal medicine suggests that this method is unreliable.[175] In the horse, clinical signs, at best, may be an approximate guide to the severity of dehydration (Table 17-3). It should be noted that some clinical signs associated with marked and severe dehydration are actually signs of hypovolemia. Horses that are considered to be moderately dehydrated probably require at least 50 mL/kg bodyweight of crystalloid fluids to replace fluid deficits. In a 500-kg horse, this would represent 25 L. The degree of dehydration is at best an approximation, and should not be relied on to accurately predict fluid requirements. For this reason, the response to fluid therapy should always be monitored.

Table 17-2
Clinical Signs of Hypovolemia and Dehydration in the Horse

Hypovolaemia	Dehydration
Tachycardia	Prolonged skin tent
Cold extremities	Tacky mucous membranes
Tachypnea	Sunken eyes
Decreased pulse pressure	
Reduced jugular fill	

It is important to make a judgement on the fluid status based on the whole animal and not just the signs listed in Table 17-3. For example, in horses with colic, tachycardia may be caused by hypovolemia or pain. To determine the source of the tachycardia, the accompanying clinical signs, and the response to analgesics or fluid loading should be assessed.

In mature horses, tachycardia due to hypovolemia is a physiologic response to maintain cardiac output in the face of reduced stroke volume. Unfortunately, this physiologic response does not occur in many critically ill neonatal foals.[176] This means that hypovolemia can be more difficult to recognize in foals, and because of poor compensation, it is associated with far higher morbidity and mortality. Other clinical signs of hypovolemia are also inconsistently present in neonatal foals. The clinical signs of dehydration are similar in the foal to those in the mature horse; however, the skin tent may be shorter, because of the increased elasticity of the skin.

Table 17-3

Clinical Signs Associated with Different Degrees of Dehydration in the Horse

Degree of dehydration	Skin tent (seconds)	Mucous membranes	Capillary refill time	Heart rate (pain may also increase heart rate)	Other signs
Moderate	1-3	Moist or slightly tacky	Normal (<2 seconds)	Normal	Decreased urine output
Marked	3-5	Tacky	Variable Often 2-3 seconds	40-60bpm	Decreased arterial blood pressure
Severe	5 or more	Dry	Variable Often >4 seconds	60bpm or greater	Reduced jugular fill Barely detectable peripheral pulse Sunken eyes

Note that not all signs are consistently present in all horses

Laboratory Tests

Packed Cell Volume and Total Solids Concentration

The laboratory tests used most commonly to assess hypovolemia are the packed cell volume (PCV) and the plasma total solids. Unfortunately, these tests are neither sensitive nor specific.[175] The PCV may be increased substantially by splenic contraction, making small increases very hard to interpret. A PCV of over 50% usually represents hypovolemia. The plasma total solids (protein measured by refractometer) or total protein concentration (measured by a chemistry analyzer) also increases with hypovolemia. However, significant protein loss can occur in disease (particularly with colitis), resulting in a low or normal protein concentration despite hypovolemia. Further, hypergammaglobulinemia (e.g., in cyathostomosis) can increase the plasma total protein concentration in the absence of hypovolemia. The PCV and plasma total solids are most useful when greatly increased or when used serially to monitor the response to fluid therapy.

Creatinine

Plasma or serum creatinine concentrations are useful in the assessment of renal perfusion in the absence of renal dysfunction. High normal creatinine concentrations (1.5-1.8 mg/dL or 130-160 μmol/L) can be associated with subclinical hypovolemia and should be evaluated in light of the history and clinical signs. Creatinine concentrations up to 3.5 mg/dL (310 μmol/L) are common in moderate to severe hypovolemia and concentrations as high as 5.0 mg/dL (450 μmol/L) are possible with prolonged hypovolemia. Even in severe hypovolemia, the creatinine concentration will not increase by much more than 2.3 mg/dL (200 μmol/L) per day.[177] If the creatinine concentration is higher than would be suggested by the clinical signs and other laboratory parameters, and if it does not decrease appropriately with fluid therapy, renal dysfunction should be suspected.

Lactate

In the non-exercising horse, increased blood lactate concentrations are sufficient evidence of a metabolic disturbance to initiate fluid therapy. They are an indication of poor tissue perfusion or increased circulating epinephrine (adrenaline) concentrations.[178] Hypovolemia and endotoxemia are common causes of increased lactate concentrations in the horse. Endotoxemia

increases tissue lactate production both through circulatory changes, which reduce blood flow to the tissues, and by inappropriate anaerobic metabolism.[179] Whereas lactate is a good indicator of the need to start fluid therapy, continued high lactate concentrations should be assessed in the context of cardiovascular parameters such as pulse rate, urine output, and blood pressure, because decreases in plasma lactate concentration can lag behind improved cardiovascular status.[178] High blood lactate concentrations have been associated with decreased survival in equine colic[2] and in neonatal foals.[180] Lactate can be measured in the field using hand-held blood gas analyzers.[¶] An increased circulating lactate concentration should be suspected when there is a metabolic acidosis (decreased pH, negative base excess) in the absence of hyperchloremia or hyponatremia.[19]

Urine Specific Gravity

Urine specific gravity is useful for monitoring the response to fluid therapy. Urine specific gravity can be measured easily in the field using a refractometer. High urine specific gravity (>1.040) indicates possible hypovolemia and normal renal concentration of urine. Isothenuria (1.010) indicates possible renal damage or a recent high fluid load. Rising or continually high specific gravity in the face of fluid therapy may indicate that insufficient fluid is being delivered to the horse. In the neonatal foal with normal renal function, urine specific gravity may increase early in fluid deprivation, before changes in other indicators such as heart rate, PCV, central venous pressure (CVP), and arterial blood pressure. The normal urine specific gravity in the neonatal foal is 1.000 to 1.008.

Other Methods

Central Venous Pressure

Cardiac filling pressures, and the changes in these pressures in response to fluid therapy, are the most accurate method of determining fluid requirements in the hospitalized animal. It is relatively easy to measure central venous pressure (CVP) in the horse. In adult horses, sterile polyethylene tubing (PE190, outside diameter 1.70 mm, at least 1.5 m long) can be passed through a 12-gauge jugular catheter into the thoracic vena cava or right atrium. In neonatal foals, the tip of a 20-cm long catheter placed halfway down the jugular vein is usually intrathoracic and CVP can be measured directly from the catheter. The tubing or catheter is connected to a pressure transducer or manometer at the level of the sternal manubrium.[181] The normal CVP of the adult horse is between 5 and 14 mm Hg.[181] In foals less than 14 days old, the normal CVP is 2 to 9 mm Hg.[182] In horses with normal cardiac function, a high CVP indicates fluid overloading, whereas a low CVP indicates insufficient circulating volume.

Fluid Challenge

The change in CVP in response to "fluid challenge" (bolus of fluids)[183] is perhaps more accurate than CVP values alone, but this awaits formal evaluation in the horse. The "fluid challenge" method of monitoring fluid therapy may prove particularly useful in animals with acute renal failure or pulmonary edema. In horses without pulmonary edema, a "fluid challenge" without measuring CVP can also be useful in the assessment of the fluid status of the horse. In horses with tachycardia, hypotension, or oliguria, the purpose of the "fluid challenge" is to determine whether additional fluids alone may reverse the abnormality or whether another intervention is required. If no improvement occurs 10 minutes after a 10-mL/kg bolus of crystalloids or a 2- to 3-mL/kg bolus of colloids, it is unlikely that fluids alone will be successful. The author uses this form of "fluid challenge" routinely in hypotensive individuals before starting a dobutamine infusion,[184] as the latter drug may cause significant tachycardia in cases resuscitated with insufficient fluid.[185]

Treatment Strategies

A fluid therapy plan should be divided into three stages: initial resuscitation, rehydration, and maintenance. The focus of resuscitation is the rapid reversal of hypovolemia. Rehydration aims to replace fluid losses. The maintenance phase aims to prevent the occurrence of further fluid deficits. In severely hypovolemic horses, a transition phase, in which fluid rates are higher than those calculated for the rehydration phase, may be necessary after initial resuscitation. The need for this should be assessed based on the clinical and laboratory responses to the initial resuscitation. Although plasma electrolyte imbalances may influence the choice of fluid during initial resuscitation, their correction usually takes place during the rehydration phase.

The Horse or Foal Presenting with Acute Hypovolemia

The resuscitation phase is critical in horses with acute hypovolemia, as it aims to rapidly restore circulating volume. However, it is important to note that aggressive resuscitation should not be used in horses with uncontrolled hemorrhage. Although

[¶] i-STAT, Heska, Fort Collins, Colorado, USA

uncommon in horses with acute abdominal disease, some horses may have uncontrolled intraabdominal bleeding. These horses frequently, but not always, will have pale mucous membranes.

Aggressive therapy should be used when uncontrolled hemorrhage can be reasonably ruled out. The treatment of hypovolemia can be thought about in two ways, both of which result in similar treatment patterns. Hypovolemic horses typically require 20 to 80 mL/kg of crystalloid fluids acutely.

The "shock dose" concept is borrowed from small animal medicine. The shock dose for adults and neonatal foals is 50 to 80 mL/kg bodyweight (bwt) of crystalloid fluids. Depending on the perceived degree of hypovolemia, a quarter to one half of the shock dose is given as rapidly as possible (over less than 20 minutes) and the horse is reassessed. If the horse requires additional fluids, another quarter of the shock dose is given, and again the horse is reassessed. The final quarter of the shock dose is only given to severely hypovolemic horses.

The incremental "fluid bolus" concept is borrowed from human medicine. It is actually a much more practical method for resuscitation of neonatal foals. The caveat is that it assumes a similar bodyweight between all patients, and for this reason, it has not been adopted in small animal medicine. The fluid bolus method is simply to give a bolus of 10 L of crystalloids to an adult horse or 1 L to a neonatal foal (i.e., approximately 20 mL/kg bwt), and then reassess. The bolus should be given over 15 to 20 minutes. Up to 3 further boluses may be given, reassessing the animal after each. Most obviously hypovolemic animals require at least 2 boluses. In adult horses where their bodyweight (500 kg) is obviously different from neonatal foals (50 kg), the method needs to be adjusted so that the bolus is approximately 20 mL/kg bwt. In pony foals and very premature Thoroughbred foals, boluses of 500 mL are usually appropriate. In large draft foals, the first bolus should be 2 L.

In adult horses, the high end of the intravenous resuscitation rate (10 L over 15 minutes for a 500-kg horse) may be difficult to achieve. In adult horses with severe hypovolemia, both jugular veins may be catheterized with large-bore catheters (10 to 12 gauge), allowing approximately 35 L to be administered by gravity per hour, if a wide-bore administration set (e.g., arthroscopy tubing) is used. One of the jugular catheters should be removed immediately after the initial resuscitation phase, to reduce the risk of bilateral jugular vein thrombosis. An infusion pump may also be used to achieve high rates of fluid delivery, but the high pressures may cause damage to the intima of the vein and increase the risk of thrombosis. In neonatal foals, a 16-gauge catheter will allow flow rates of up to 58 mL/kg/hour for a 50-kg foal and 48 mL/kg/hour for a 60-kg foal. In larger foals, a larger-bore catheter should be used to achieve higher flow rates.

Aggressive fluid therapy should be avoided in uncontrolled hemorrhage, because it may increase bleeding. In humans and laboratory animals, aggressive fluid therapy in uncontrolled hemorrhage has been demonstrated to increase mortality.[186-188] This and other evidence suggest that, if blood pressure can be measured, fluid therapy should be titrated to maintain the mean arterial pressure as close to 60 mm Hg as possible, without increasing the systolic pressure over 90 mm Hg. If blood pressure cannot be measured, then a fluid rate of 2 to 3 mL/kg/hour should be used, until the hemorrhage can be stopped.

After acute resuscitation, rehydration is almost always required. The rehydration phase aims to replace extravascular fluid losses. Crystalloid fluids are a logical choice for rehydration, as they readily diffuse into the interstitial fluid from the vasculature.[69,189] Rehydration should take place over the first 12 to 24 hours of therapy. The amount given should be based on the clinical estimate of the degree of dehydration and the response to fluid therapy.

Typically, horses with obvious clinical signs of dehydration will require 50 to 100 mL/kg bwt (25-50 L for a 500-kg horse) of fluid to replace their deficits. After treatment of hypovolemia, a fluid plan should be made for the first 24 hours that includes fluids for rehydration, maintenance, and ongoing losses. Clinical signs are not an accurate way of estimating fluid requirements,[175] and so frequent monitoring is required to ensure that adequate volumes of fluids are being delivered. When fluid losses have been adequately replaced, the urine specific gravity should be less than 1.020, except in horses with renal failure. Ensuring adequate fluid therapy in horses with renal failure is difficult, and is probably best achieved by measurement of the response of CVP to fluid therapy as described previously, but this is probably only practical in hospitals.

The Horse with Acute Diarrhea

Horses with acute diarrhea frequently present with marked to moderate hypovolemia. This should be treated as described above. Protein loss is common in horses with diarrhea, and, therefore, colloids are often used early in the course of treatment for colitis. In horses with profound hypovolemia, manifested by tachycardia, very high packed cell volumes (>65%), and purple mucous membranes, the author has found the combination of a hydroxyethyl starch (hetastarch or pentastarch; 8-10mL/kg)

and hypertonic saline (2-4mL/kg) particularly effective for acute reversal of hypovolemia. After reversal of hypovolemia, many horses with acute colitis still have significant dehydration, which must also be addressed as described above.

It is extremely important to provide enough fluids to cover ongoing losses in horses with diarrhea. As mentioned above, fluid loss may be as high as 200 mL/kg/day in horses with diarrhea (100 L/day for a 500-kg horse).[5] Thus, a horse with severe diarrhea might require approximately 260 mL/kg/day (approximately 5.5 L/hour) of crystalloid fluids to provide basal requirements and replace ongoing losses. Horses with less frequent or less watery diarrhea require less fluid. The rate should be estimated based on the volume and consistency of the diarrhea. The adequacy of the rate should then be reassessed frequently based on both clinical signs and laboratory data. Some horses with less severe diarrhea (infrequent defecation or semi-solid consistency) can be effectively treated with free access to water, and supplementation via nasogastric tube, as required. Electrolytes, particularly sodium, chloride, and potassium, are frequently deranged in horses with acute diarrhea.

The Horse with Ongoing Reflux

Horses with marked nasogastric reflux are also frequently hypovolemic during the first examination and should be treated as previously described. Horses with nasogastric reflux are less likely to be hypoproteinemic than horses with severe colitis. Ongoing losses are also a significant issue in horses with significant nasogastric reflux. In these horses, the amount of reflux should be measured and replaced with intravenous fluids, in addition to the maintenance requirements. As with all fluid administration, responses to fluid therapy should be monitored frequently.

The Horse with a Large-colon Impaction

Horses with large colon impactions can frequently be treated with nasogastric fluids, without the need for intravenous fluids. The exception is the horse with moderate to marked hypovolemia. Part of the physiologic response to protect the circulating volume is to divert blood flow away from the gastrointestinal tract, thus reducing the capacity of the gastrointestinal tract to absorb water. In experimental models of hypovolemia in the horse, oral fluids were not sufficient to reverse hypovolemia.[154] Nasogastric fluids should also be avoided if there is palpable distended small intestine, any reflux on passage of the tube, or greater than 2 L of reflux just prior to any scheduled nasogastric administration of fluids.

The author uses the following protocol for nasogastric fluids in the horse with a large-colon impaction: After first attempting to obtain reflux, approximately 1 L/100 kg bwt of water with approximately 1 g/kg of magnesium sulfate is delivered by nasogastric tube. Additional fluids are given at 30-minute intervals, after first refluxing the horse, for a further 4 administrations. For the second to fifth administration, 1/100 kg bwt of water plus sodium chloride granules (7.5 mL/L) and Lite Salt granules (7.5 mL/L) is administered. The schedule of 5 administrations, every 30 minutes, can be repeated every 8 hours; however, the author only gives magnesium sulfate every 24 hours. If there is more than 2 L of reflux, the water is not given, and the horse is again refluxed in 30 minutes. If there is no reflux at this second check, the schedule of fluid administration is repeated at the point where it was interrupted. If the reflux continues, the horse should be thoroughly re-examined, including repeat examination per rectum, and intravenous fluids should be given in place of further oral therapy. A few horses show mild to moderate signs of abdominal discomfort on administration of these oral fluids. The options for these horses depend on the degree of confidence in the diagnosis. If there is total confidence that the diagnosis is a primary large-colon impaction, analgesics may be administered. Alternatively, an indwelling stomach tube can be placed, and oral fluids given at approximately the same rate (2 L/kg/hour) by constant infusion.[150]

The choice of water, magnesium sulfate, and electrolytes, rather than mineral oil (liquid paraffin), dioctyl sodium succinate, or intravenous fluids, is based on recent research suggesting these are the most effective treatments to hydrate colonic contents.[28,168,190]

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Treatment of Endotoxemia

Chapter 18

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Endotoxemia is a major cause of morbidity and mortality in horses with acute abdominal disease.[1,2] In a number of surveys of horses with colic, endotoxin has been detected in the blood in 27%,[3] 74%,[4] and 84%,[5] of cases. The highest blood concentrations of endotoxin are detected in horses with lesions of the colon or cecum.[4] Horses with detectable endotoxin in the blood[3,6] or those with clinical signs attributable to endotoxemia[2] have been shown to have poor hospital survival rates when compared with horses without endotoxemia.

Endotoxin is the lipopolysaccharide (LPS) component of the outer cell membrane of gram-negative bacteria and is released during rapid bacterial proliferation or death.[7] Endotoxin consists of inner hydrophobic lipid A and core oligosaccharide components, which are well conserved among bacterial species,[8] and an outer O-specific polysaccharide, which varies among bacterial species.[9] Lipid A is the toxic portion of the LPS molecule.[9] When endotoxin enters the systemic circulation, it binds to an acute phase-reactant protein, LPS-binding protein (LPS-BP). LPS-BP increases endotoxin binding to, and activation of, mononuclear cells, endothelial cells, neutrophils, and platelets.[7] Activation of these cells results in the release of numerous pro-inflammatory mediators, including tumor necrosis factor (TNF), interleukins (IL), and arachidonic acid metabolites. Tissue factor, and other procoagulant mediators, are also released, resulting in activation of the extrinsic coagulation cascade.[7] Some direct activation may also occur of factor XII and the intrinsic coagulation cascade. These pro-inflammatory and procoagulant mediators result in the clinical and laboratory changes associated with endotoxemia (see Chapter 12).

Initial clinical and clinicopathologic signs of experimental administration of endotoxin to horses are tachycardia, tachypnea, pyrexia, hyperemic mucous membranes and accelerated capillary refill time, dullness, inappetence, ileus, colic, leukopenia, and hemoconcentration. These signs may progress to severe tachycardia and tachypnea, hypothermia, dry and dark mucous membranes, prolonged capillary refill time, cold extremities with poor peripheral pulses, coagulopathy, multisystem organ failure, and death.[7,9,10] The cardiovascular and coagulation changes caused by endotoxemia can predispose to postoperative complications such as ileus, adhesions, colitis, thrombophlebitis, and laminitis. These complications are leading causes of colic-related euthanasia.[9,10]

In normal horses, a large amount of endotoxin exists in the lumen of the gastrointestinal tract. Little of this endotoxin is absorbed in the normal horse, because of the intestinal mucosal epithelial cells and their secretions, and normal intestinal motility[3,9] The small amount that is absorbed is efficiently cleared by the hepatic reticuloendothelial cells and circulating antibodies.[4] The intestinal barrier can be compromised in horses with acute abdominal disease, as a result of intestinal obstruction, ileus, and inflammation, and loss of mucosal integrity because of ischemia, resulting in absorption of significant amounts of endotoxin. If enough endotoxin is absorbed, the liver is unable to clear it.[12] Although endotoxin does not appear to have direct effects on the ability of the liver to detoxify substances (such as endotoxin itself), endotoxin-mediated circulatory changes limiting the blood supply to the liver can compromise liver function.[13]

Several treatment strategies are possible for endotoxemia. The first strategy is to bind or block endotoxin, to prevent its interaction with host cells, so that the inflammatory and procoagulant cascades are not initiated. The next strategy is to interfere with the inflammatory cascade, to prevent the downstream activation of other cells or systems. It is also possible to intervene in the coagulation cascade. Lastly, maintaining intracellular homeostasis and metabolism are other possible ways that drugs can modulate endotoxemia.

Drugs that Bind or Block Endotoxin

Drugs that prevent endotoxin interacting with its target cells are potentially highly effective, as they can prevent cell activation and the subsequent release of inflammatory and procoagulant mediators. Many of these agents have been shown to be extremely effective in experimental models, when the drug can be given prior to, or at the same time as, the endotoxin. In clinical cases, however, endotoxin release into the circulation may occur many hours before veterinary intervention is possible.[3] In these circumstances, cell activation and mediator release may have already occurred, and blocking further interaction of endotoxin and cells may have little or no effect on the clinical course. Large amounts of endotoxin are likely to be absorbed when the blood supply is returned to the compromised intestine during surgery for colic. Therefore, these drugs may be most effective if the initial dose is given prior to correction of the lesion. Endotoxin may also be released at the time of antimicrobial administration;[114] it may be argued that these drugs should, therefore, be administered at the same time as pre-operative antibiotic treatment. Significant endotoxin tolerance in the horse develops after 24 hours[15] and, therefore, 24 hours may be sufficient as a therapy period for this class of drug.

Polymyxin B

Polymyxin B is a cyclic cationic mixture of 2 N-mono-acetylated decapeptides, which has antimicrobial activity against many gram-negative organisms. Polymyxin B also binds the conserved lipid A region of the lipopolysaccharide (LPS) endotoxin.[8] The binding of polymyxin B with endotoxin forms a stable complex, altering the conformation of endotoxin and preventing its binding to cell receptors and cell activation. Experimental treatment with polymyxin B prior to endotoxin administration prevented the behavioral changes and increase in heart rate and rectal temperature that occurred when polymyxin was not given. Furthermore, the initial decrease in neutrophil count and the increases in plasma tumor necrosis factor alpha and thromboxane B_2 that occur with endotoxin administration were greatly reduced with polymyxin B pretreatment.[16] Experimental and clinical studies have also shown that polymyxin B can reduce clinical and laboratory signs of endotoxemia when given after endotoxin exposure.[16-20]

Polymyxin B is potentially neurotoxic and nephrotoxic,[21] raising concerns about its use in critically ill patients.[22] Nephrotoxicity has not been demonstrated in experimental studies in horses, even when large doses (up to 36,000 IU/kg) have been administered.[20,23] Reversible neurologic signs, including coughing and ataxia have been noted at doses of 18,000 and 36,000 IU/kg[20] but not at doses of 10,000 IU/kg or less.[16,19] Fortunately, the endotoxin-binding and neutralizing properties of polymyxin B occur at much lower doses than those at which neurotoxicity has been demonstrated. Polymyxin B conjugated to dextran 70 was developed, as it was thought to reduce toxicity of polymyxin B without interfering with its neutralizing properties.[24] This combination has been shown not to interfere with the in vitro activities of other antimicrobial agents.[25] The conjugate was shown to be effective in horses, but caused sweating, tachypnea, and increased plasma concentrations of thromboxane B_2,[23] and has, therefore, been largely abandoned.

The recommended dose for polymyxin B is 5,000 to 6,000 IU/kg IV every 8 to 12 hours.[16,19,26] This dose has been given to a large number of horses during or after colic surgery, with no apparent adverse effects (Corley KTT and Hallowell GD, unpublished. McKay RM, personal communication, 2002). It is preferable to dilute polymyxin B in a salt-free solution, such as 5% dextrose in water. Polymyxin B is most efficacious when given just prior to, or within 30 minutes of, the release of endotoxin.[16] As with all endotoxin blocking agents, when given after 30 minutes, substantial cell activation and cytokine release may already have occurred.[7]

Lyophylized Immunoglobulin Products

An alternative way to bind and neutralize endotoxin is with specific antibodies. These antibodies are usually raised against the lipid A part of endotoxin, in horses vaccinated with the core region of either *Salmonella typhimurium* or the J5 mutant of *Escherichia coli*. As stated earlier, these core regions are well conserved between the LPS of different species of bacteria.[27] In humans, polyclonal antisera raised to these two organisms were originally shown to improve the survival rate with gram-negative septicemia and septic shock;[28] however, subsequent studies with the same and similar anti-endotoxin antibodies have not demonstrated improved survival.[29-31] Small studies investigating the efficacy of these products in equine clinical cases and experimentally induced models have also yielded conflicting results. Some studies have demonstrated decreased mortality and shorter length of hospital stay, while others have demonstrated no benefit or even possible harm.[19,32-34] These conflicting results ultimately reflect the small scale of the trials. Differences in the dose of endotoxin, and timing of treatment relative to onset of endotoxemia (both of which are undeterminable in clinical cases), and the relative dose and affinity of the immunoglobulin product administered, may have also played a role. At present, lyophylized immunoglobulin products should be considered as an expensive, unproven treatment.

A new approach is to vaccinate horses, so that they generate their own anti-endotoxin antibodies.[35] There is some evidence that this technique works in laboratory animals,[36,37] and efforts are continuing to produce a suitable vaccine for use in humans.[38] Antibodies to endotoxin have been produced in ponies, using an anti-idiotype antibody to vaccinate them.[39] Anti-endotoxin vaccines will require considerable development before they become available and effective for equine patients.

Competitive Inhibition of Endotoxin Binding

Novel lipid A portions from plant bacteria, for example *Rhodobacter spheroides* and *Rhizobium* species, can act as endotoxin antagonists. These molecules competitively inhibit interaction of LPS with its binding protein or other receptors.[40,41] The lipid A-like portion of these products binds to human monocytes, but does not activate them, thus competitively blocking binding of endotoxin.[42] A related synthetic compound (E5531), based on the structure of *R. spheroides*, has also shown promise in humans;[43,44] however, the action of these drugs may be host species-dependent. Investigations in vitro have shown activation of equine monocytes, leading to cytokine release, which could potentially exacerbate clinical signs.[45] It is thought that this difference is related to species differences in Toll-like Receptor 4,[46] which is involved in monocyte activation in response to

endotoxin. Work continues to produce synthetic lipid A derivatives that block endotoxin without activating monocytes,[47] and it is possible that one of these molecules will be suitable for use in the horse.

Anti-Inflammatory Agents

Endotoxin exerts its effect through inflammatory and pro-coagulant mediators. Anti-inflammatory agents aim to reduce expression of either one key mediator or a class or group of mediators, thus reducing the effects of the endotoxin. Drugs aimed at key mediators target early parts of the inflammation cascade and aim to prevent the cascade from starting or to prevent positive feedback loops from escalating the response. Drugs used to prevent production of mediators usually target later members of the inflammation cascade, which are directly responsible for the myriad clinical and clinicopathologic signs of endotoxemia. The advantage of targeting the inflammatory response is that it can be effective even after immune-series cells have been activated, in contrast to the endotoxin blocking or binding agents. The disadvantage is that the immune response is highly complex, and the disrupted parts may play important roles in either homeostasis or repair of certain organs. Furthermore, the immune response may be very different in animals with seemingly similar clinical signs and scenarios. The way forward with these agents appears to be targeted administration to well defined subsets of horses with endotoxemia. The ability to define these subsets, however, is still some years away.

Nonsteroidal Anti-Inflammatory Drugs

Nonsteroidal anti-inflammatory drugs (NSAIDs) are commonly used as part of a treatment regimen for horses with endotoxemia.[48] The action of NSAIDs is to inhibit cyclooxygenase (COX) enzymes. These enzymes catalyze the production of prostaglandin G_2 from arachidonic acid.[49] Prostaglandin G_2 is an unstable intermediate, and is the precursor of many prostaglandins (PG) and thromboxanes (TX). The functions of these mediators are varied and include gastrointestinal tract protection (PGE_2), changes in vascular tone (PGE_2, PGI_2), control of platelet aggregation (PGI_2, TXA_2), and control of inflammation (TXA_2, PGE_2, PGI_2).[50] Two COX enzymes have been identified: COX-1 is preformed and constituitively expressed and is responsible for producing PGs required for homeostatic ("house-keeping") functions. COX-2 is newly synthesized in response to inflammatory stimuli, such as endotoxin. The PGs produced by COX-2 are mainly pro-inflammatory.[50]

The popularity of NSAIDs for treating endotoxemia is linked to their dual function as analgesic and anti-inflammatory drugs.[1] The drugs most commonly used include flunixin meglumine, phenylbutazone, and ketoprofen.[48] Carprofen, eltenac, vedaprofen, ketorolac, meclofenamic acid, suxibuzone, ibuprofen, and meloxicam are alternative NSAIDs for which pharmacokinetic studies have been performed in horses or foals.[50-53] Flunixin and phenylbutazone have been most extensively studied with regard to endotoxemia.

Flunixin was shown 25 years ago, in an experimental model, to reduce the cardiovascular effects of endotoxin, including hypotension, decreased peripheral perfusion, and vasodilation, when administered shortly after endotoxin.[54] Other studies have found that the administration of flunixin meglumine or phenylbutazone, prior to endotoxin, reduced endotoxin-associated respiratory signs, colic, diarrhea, hypoxemia, hyperglycemia, prolonged coagulation times, hemoconcentration, and lactic acidosis.[55-58] The profound neutropenia and leukopenia associated with endotoxin administration were not altered by a single dose of flunixin,[56] but were lessened by repeated doses.[59] Pretreatment with flunixin or phenylbutazone ameliorated endotoxin-induced changes in gastric and left dorsal colon contraction. Phenylbutazone was more effective than flunixin.[60] Flunixin, phenylbutazone, ketoprofen, carporfen, meloxicam, and eltenac have all been demonstrated to reduce the endotoxin-induced synthesis of several prostaglandins and thromboxane, demonstrating COX inhibition as their mode of action against endotoxemia.[61-65]

Although NSAIDs clearly ameliorate the clinical signs associated with endotoxemia, important side effects and potential toxicities may result in changes in their use in horses over the next several years. Classically described toxicities include gastrointestinal ulceration (gastric ulceration and right dorsal colitis), nephropathy, and hepatopathy.[50,66,67] Toxic effects are more likely to occur when NSAIDs are given to hypovolemic animals, a risk in horses with acute abdominal disease, and when inappropriately large doses are given.[66] The potential to cause toxic effects differs between individual NSAIDs, and some evidence exists that ketoprofen is less toxic than flunixin, which, in turn, is less toxic than phenylbutazone.[68] Suxibuzone has also caused gastric ulcers of less severity and in fewer horses than phenylbutazone.[69] In addition to these classic toxicities, NSAIDs have recently been shown to retard full recovery of equine jejunal mucosa after ischemic injury.[70] The delayed recovery results in a prolonged period of impaired intestinal epithelial layer barrier function, but importantly does not promote LPS absorption.[79] The effect appears to be COX-1 mediated, as replacement of flunixin with deracoxib does not result in this increased permeability.[72] This work suggests a possible role for COX-2 inhibitors in equine medicine; however, a strong note

of caution should be taken from the experience with COX-2 inhibitors in human medicine, where many serious and unexpected side effects were noted.[73]

The analgesic and cardiovascular effects of flunixin have caused concern that this drug may mask the signs of surgical colic. For this reason, and to reduce the risk of the toxicities just listed, experiments were performed to find a dose of flunixin that significantly decreased endotoxin-mediated prostaglandin release, without significant effect on clinical signs.[59,74] This dose is 0.25 mg/kg of flunixin every 8 hours, and has been termed "the anti-endotoxic" dose. This term is perhaps misleading, as higher doses of flunixin ameliorate clinical signs as well as decrease prostaglandin production. It should be noted that 0.25 mg/kg dose provides less analgesia than a standard 1.1 mg/kg dose. There is some evidence that providing good analgesia after surgery for colic can improve outcome, at least in terms of duration of hospitalization.[75] For these reasons, the authors use the standard dose of flunixin (1.1 mg/kg every 12 hours), delaying the first dose until hypovolemia has been reversed, if possible.

Despite the apparent positive effects of NSAIDs in endotoxemia, there is no evidence that they improve survival in horses. In humans, a large clinical trial of ibuprofen in septicemia (which has many features in common with endotoxemia) showed no difference in mortality between the treatment and placebo groups.[76] Interestingly, survival was improved in a subset of people with hypothermic sepsis.[77] Although an equivalent subgroup is not immediately apparent for equine endotoxemia, it is increasingly becoming apparent that targeted use of drugs for subgroups with a particular disease spectrum yields better results than blanket administration.[78,79] The use of NSAIDs for endotoxemia, which has become dogma in equine medicine, may change over the next few years.

Corticosteroids

Corticosteroids inhibit the release of arachidonic acid from membrane phospholipids and, therefore, also reduce the production of inflammatory mediators produced in response to endotoxin.[80] However, experimental studies have shown little effect of corticosteroids on the clinical and clinicopathologic disturbances associated with endotoxin administration. In a comparison of flunixin, dexamethasone, and prednisolone succinate, flunixin was superior to the corticosteroids for almost all measured parameters. Importantly, flunixin reduced endotoxin-mediated hemoconcentration and lactate production to a much greater extent than the corticosteroids. Prednisolone succinate delayed, but did not prevent, the reduction in circulating neutrophils.[56] In a separate study, the only improvement seen with prednisolone succinate pretreatment for endotoxemia was a lessened secondary decrease in stroke volume.[81] Human clinical trials in sepsis have failed to show any benefit of high-dose steroid administration;[82] however, there is renewed interest in low-dose repeated corticosteroid administration in human septic shock. These lower dose regimens have been shown to reduce the requirements for vasoactive drugs, and to improve outcome in patients with relative adrenal insufficiency.[78,83] Little information exists about adrenal function in equine colic. The limited evidence available shows no evidence of adrenal insufficiency.[84]

Pentoxifylline

Pentoxifylline is a methylxanthine derivative that has been shown in vitro to increase erythrocyte membrane flexibility.[85] Erythrocytes need to change shape or "deform" to pass through the smallest capillaries.[86] Increasing the membrane flexibility allows better flow of red blood cells through these narrow capillaries and should result in reduced blood viscosity and improved oxygen supply to the tissues.[86] Pentoxifylline has been shown to improve survival in experimental endotoxemia in laboratory animals[87,88] and in human neonatal sepsis.[89] These studies showed that improved tissue oxygen delivery was due to several mechanisms, including increased erythrocyte and leukocyte deformability and motility, inhibition of the action of inflammatory cytokines, lower blood viscosity, and decreased platelet aggregation.[87,88,90] In horses in both in vitro and ex vivo models, pentoxifylline suppressed endotoxin-induced TNF-α and IL-6 production, even when administered after the endotoxin.[91,92] However, in horses administered endotoxin in vivo, pentoxifylline reduced the increase in respiratory rate and fall in rectal temperature induced by endotoxin, but had little other potentially beneficial effects.[93,94] A study investigating the combination of flunixin and pentoxifylline, administered 15 minutes before endotoxin infusion, concluded that the combination may help offset deleterious hemodynamic effects of endotoxin more effectively than either drug alone.[94] This conclusion is not supported by the data presented in the paper, as the only hemodynamic parameter presented was pulse rate, which was lower in the flunixin group than in the combination group. Further work is needed to define what benefits, if any, pentoxifylline administration provides in clinical cases of equine endotoxemia.

A potential problem with administration of pentoxifylline to the horse is that oral bioavailability of the drug is highly variable among individuals, and the half-life of the drug when given intravenously is relatively short.[95] The currently recommended dose

for pentoxifylline in the horse is 8.4 mg/kg, by mouth, every 12 hours.[96] At the time of writing, an intravenous preparation of pentoxifylline is only available commercially in a few countries (including Ireland and New Zealand).

Anti-Tumor Necrosis Factor Antibodies

Tumor necrosis factor has been shown to play a key role in endotoxin-mediated cellular damage in vivo.[97] In a variety of experimental trials, in both laboratory animals and horses, monoclonal and polyclonal anti-tumor necrosis factor antibodies provide protection when given prior to challenge with LPS, but not when administered afterward.[98-101] Initial trials in human septic patients did not demonstrate any benefit of administration of anti-TNF antibodies.[102,103] However, in one study, administration of an anti-tumor necrosis factor F(ab')2 monoclonal antibody fragment reduced 28-day mortality, and attenuated the severity of organ dysfunction in patients with increased circulating concentrations of interleukin-6; there was no benefit to patients with normal circulating concentrations of IL-6.[79] This study suggests that anti-TNF antibodies could, possibly, have a beneficial effect in a subgroup of our equine endotoxemia patients, and should be reexamined.

Lidocaine

In rabbits, lidocaine inhibits cytokine production, the inflammatory response, hypotension, and metabolic acidosis when administered after endotoxin exposure.[104,105] The anti-inflammatory actions of lidocaine are due, in part, to reduction in leukocyte-endothelial cell interaction and down-regulation of MHC Class II on the surface of monocytes.[106,107] Lidocaine is commonly used in horses with post-operative ileus[108] and to reduce inhalational agent requirements during anesthesia.[109,110] It may have additional benefits in horses undergoing surgery for acute abdominal disease as an anti-endotoxic agent, and these should be investigated.

Dimethyl Sulfoxide

Dimethyl sulfoxide (DMSO) is an inexpensive solvent that is a by-product of the chemical industry.[111] It has been shown to be an anti-inflammatory agent with antithrombotic, endothelial-sparing, and free-radical scavenging properties.[111,112] These properties should make this a potentially useful agent in the treatment of endotoxemia; however, DMSO did not suppress PGE_2 production by endotoxin-treated synovial explants.[64] When investigated in endotoxemic calves, DMSO was not protective against LPS-induced eicosanoid production or clinical signs. In fact, clinical compromise, hypotension, and hypoglycemia were prolonged in the calves receiving DMSO, compared with those given LPS alone.[113] Current evidence suggests that DMSO has no role as an anti-endotoxic agent, but this should not preclude its use for other applications such as prevention of adhesions.[114]

Omega-3 Fatty Acids

Arachidonic acid, the precursor of the prostaglandins, thromboxane, and leukotrienes, is an omega-6 fatty acid. Feeding diets rich in omega-3 fatty acids leads to decreased concentrations of arachidonic acid and its metabolites in plasma, and a shift of these fatty acids from the phospholipid portion in a tissue to the triacylglycerol and/or cholesterol ester pools.[115,116] Feeding omega-3 fatty acid-rich substances has been shown to have a beneficial effect on experimental murine endotoxemia and clinical human sepsis.[117,118] Results in horses have been mixed. Horses fed an omega-3-rich diet for 8 weeks prior to endotoxin challenge showed no beneficial effect in their response to endotoxin, compared with horses fed a regular diet.[119] In an equine ex vivo model, horses were administered omega-3 fatty acids as an infusion. Peripheral blood monocytes taken from these horses were demonstrated to have reduced endotoxin-induced production of the inflammatory mediators thromboxane B_2 and TNF-α.[120] Infusion of omega-3 fatty acids at the time of endotoxin challenge, therefore, may be a future anti-endotoxic treatment in the horse.

Modulation of the Coagulation System

The cytokine release associated with endotoxemia results in activation of the extrinsic coagulation pathway, leading to microthrombi formation.[121] This microthrombi formation may prevent blood flow through the microcirculation in the affected tissue, resulting in decreased local oxygen supply and ultimately tissue or organ failure. Disseminated intravascular coagulation is well reported in horses with colic and colitis.[122-125] The procoagulant state can exhaust supplies of preformed coagulation factors, and exceed the capacity of the liver to synthesize new coagulation factors, resulting in impaired coagulation.[121] The response of the coagulation system to endotoxemia can be complex and can be dissimilar in different organ beds. The coagulation response in any particular tissue depends on the local concentration of tissue factor, local and global concentrations of clotting factors, and anticoagulation factors such as antithrombin III and protein C. Therapy for endotoxin-induced coagulopathies is not always straightforward, therefore, and it can be rational to inhibit coagulation at the same time as providing clotting factors.

Despite these caveats, therapy aimed at the coagulation system may be extremely important in endotoxemia. In human severe sepsis, a parallel condition, many trials have tried to try to improve outcome. After many failures, the first single agent shown to improve survival was the anticoagulant agent, activated Protein C.[126]

Plasma

Equine plasma has many potential benefits as a treatment for endotoxemia. In addition to clotting factors, plasma contains acute-phase proteins, fibronectin, elastase and proteinase inhibitors, complement and complement inhibitors, and antithrombin III,[127] all of which may be depleted in endotoxemia.[121,124,128,129] However, in the hypercoagulable state, providing plasma, and therefore clotting factors, may exacerbate intravascular coagulation. Some clinicians, therefore, elect to give an anticoagulant such as heparin at the same time as plasma to horses with suspected coagulopathies. Disadvantages of plasma include the small risk of anaphylactic reaction, the large volumes required, and the requirement to either defrost or collect from suitable donors, which requires time and personnel. Albumin, the main colloid in plasma, may not be the ideal colloid for restoring plasma oncotic pressure. When protein loss occurs through the gastrointestinal system, the added albumin from plasma will be lost at an equal rate to the endogenous albumin it is being used to replace. Furthermore, in endotoxin- or ischemia-reperfusion-induced capillary damage, albumin may leak out of the vascular space into the tissues.[130,131] Further information on collection and administration of plasma is given in the section on fluid therapy (see Chapter 17).

Unfractionated Heparin

Heparin is a family of straight-chain, highly sulfated anionic polysaccharides, with molecular weights varying from 4,000 to 40,000, obtained from porcine intestinal mucosa or bovine lung. Unfractionated heparin (UFH) refers to the originally described and most commonly used heparin, which contains molecules of a wide range of molecular weights. Heparin binds to antithrombin III, promoting a conformational change that greatly increases the affinity of the complex for serine proteases, which the antithrombin III complex inhibits by binding to their active site irreversibly.[132] The main serine proteases that are inhibited by antithrombin III are the activated clotting factors IIa (thrombin), Xa, Ixa, and XIa. Unfractionated heparins inhibit Xa and IIa approximately equally. Some additional antithrombotic activity is mediated through alternate mechanisms, including enhanced release of tissue factor pathway inhibitor (TFPI) and enhancement of factor Va inactivation by activated Protein C.[133]

UFH has been widely used to treat endotoxin and systemic inflammatory response syndrome (SIRS)-induced hypercoagulable state in both animals and people. Heparin has not been formally investigated as an anti-endotoxic agent in the horse. In a sustained endotoxemia model in sheep, a continuous heparin infusion was shown to dramatically improve survival.[134] Although heparin has not been formally evaluated in human sepsis, circumstantial evidence exists that it may improve survival.[135] Other possible indications for heparin therapy are prevention of adhesions and laminitis, both associated with conditions causing clinical endotoxemia. UFH has been shown to prevent the development of intraabdominal adhesions in some equine models, but not others.[114,136] The evidence for benefit in preventing laminitis is similarly conflicting. In an experimental model, heparin reduced the incidence of carbohydrate overload-induced laminitis.[137] One retrospective study of heparin administration in horses with duodenitis and proximal jejunitis suggested that heparin prevented laminitis,[138] whereas another retrospective study in horses with surgical small intestinal lesions showed no effect.[139] The incidence of laminitis was fairly low in both studies, and all that can be concluded is that heparin does not prevent all laminitis when given prior to onset of clinical signs. Enough tantalizing evidence exists of a possible benefit for heparin, that further prospective, studies are indicated.

It should be noted that UFH has undesirable side effects including increased risk of hemorrhage, rapid and severe decrease in PCV, thrombocytopenia, reduction in RBC mass, reaction at the injection site, and RBC agglutination with possible impairment to tissue blood flow.[132] In addition, individual variation to UFH therapy is marked.[140]

The low cost of this drug makes it affordable for most patients. The recommended loading dose is 150 U/kg, subcutaneously (SQ). This is followed 12 hours later by 125 U/kg, SQ, given for a total of 6 doses at 12 hourly intervals. The dose should then be maintained at 100 U/kg, SQ, every 12 hours.[132] Clinical experience suggests that a dose of 40 U/kg, SQ or IV, every 8 hours may be sufficient for some horses.

Low Molecular Weight Heparins

Because of the undesirable side effects of UFH, there has been much interest in the development of a safer alternative. This has led to the production of low molecular weight heparins. Low molecular weight heparins (LMWH) consist of a mix of molecules with average molecular weight between 4,000 to 5,000.[132] LMWH, like UFH, bind to antithrombin III to exert their

effect; however, the complex of antithrombin III and these small molecules is unable to bind to IIa (thrombin). The main inhibitory effect of LMWH is, therefore, on Xa, for which molecule size is not important.[133] The LMWH have been widely used in humans; they appear to have similar antithrombotic properties to UFH, but have fewer adverse effects, longer half-life, and dose-dependent coagulation effects.[141,142] Fewer side effects have also been observed in horses for LMWH compared with UFH.[143,144] Studies in the horse of two LMWH preparations (dalteparin and enoxaparin), reported similar pharmacokinetics to humans.[144] This led to the recommendation of once daily subcutaneous administration; however, absorption of enoxaparin after subcutaneous injection was significantly reduced in critically ill human patients.[145] Assuming the pharmacokinetics in critically ill horses may mirror that in critically ill humans, the chapter authors give their initial dose of dalteparin to horses, intravenously. The regime used is 100 anti-Xa U/kg intravenous loading dose, followed by 50 anti-Xa U/kg SQ 12 hours later. This is followed by 50 anti-Xa U/kg SQ every 24 hours. The rationale for the higher initial dose, despite the linear dose-response, is that the first 24 hours of therapy of an endotoxic horse are a time of high intravenous fluid therapy and, therefore, a higher volume of distribution. The LMWH are significantly more expensive than UFH, to the extent that cost also limits their use in human medicine.

Platelet Activating Factor Antagonists

Platelet activating factor (PAF) is involved in many of initial clinical signs of endotoxemia, including hypotension, platelet aggregation, increased vascular permeability, and ileus.[97,146] In rat endotoxemia models, survival was improved when high doses of various PAF antagonists were administered. Lower doses improved hypotension, but not survival.[147-149] However, as with many drugs tested in human sepsis, PAF antagonists failed to improve outcome in two separate clinical trials. There was no improvement in survival with administration of either a PAF receptor antagonist[150] or a PAF acetylhydrolase, which rapidly degrades PAF.[151] Although PAF-antagonists have been shown to reduce the endotoxin mediated increase in heart rate, packed cell volume and reduction of abnormal gastrointestinal motor activity in ponies,[152] and to delay onset of fever, tachycardia, leukopenia, and lactic acidemia in horses given endotoxin,[153] the results of human trials suggest that these drugs may not be effective in clinical patients.

Other Drugs Modulating the Coagulation System

Other human drugs currently licensed include antithrombin concentrate, direct thrombin inhibitors, and activated protein C. Activated protein C has antithrombotic, anti-inflammatory and pro-fibrinolytic properties, and has been shown to significantly reduce mortality in septic human patients.[126] Currently, these drugs are cost prohibitive for use in horses, and it should be noted that recombinant human proteins, such as activated protein C, may be immunogenic in the horse.

Drugs Affecting Intracellular Metabolism

Calcium and Calcium Antagonists

Endotoxemia can cause marked hypocalcemia;[154,155] however, although endotoxemic animals may be hypocalcemic, a proportionate increase may occur in intracellular calcium, leading to cellular dysfunction and death.[154,156] Intravenous administration of calcium has long been used in equine colic patients post-surgery to prevent or treat hypocalcemia and try to combat ileus.[155,157] Experimental models of endotoxic shock in rats and pigs have shown that calcium administration may increase mortality and worsen cardiovascular parameters.[154,158,159] Furthermore, calcium antagonists have been shown to improve cardiovascular function and survival in rat, murine, and canine models of endotoxic shock,[160-162] but only limited trials of calcium antagonists in human clinical sepsis have been performed.[163] The effects of calcium and calcium antagonists on equine endotoxemia are yet to be elucidated.

Conclusion

Although this chapter has discussed drugs specifically aimed at endotoxin or its direct effects, supportive therapy with fluids and, sometimes, inotropes or pressors remain the mainstay of treatment for clinical endotoxemia. The perfect drug or drug combination to treat endotoxemia in the horse has not yet been found. Horses continue to suffer from endotoxemia, and the clinician must make choices between imperfect drug strategies to treat them. The authors currently use a combination strategy, aimed at blocking endotoxin, reducing inflammatory mediators, and modulating coagulation. In a horse with suspected endotoxemia, or at high risk of endotoxemia, we administer flunixin, polymyxin B, and dalteparin early, after initial fluid resuscitation. We frequently give fresh plasma from donors in the first 6 to 12 hours of therapy. The length of therapy with these drugs depends on the clinical course of the disorder in the horse, but is often in the region of 24 hours for polymyxin B, 3 to 4 days for dalteparin, and 5 to 7 days for flunixin. This treatment strategy will no doubt evolve, or may change completely, as more research into treatment of equine endotoxemia is published.

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Treatment of Peritonitis

Chapter 19

John F. Peroni

Medical Treatment

Treatment of septic peritonitis should have two immediate goals: stabilizing the horse and addressing the underlying cause. Dehydration is corrected by administering balanced polyionic fluids intravenously at twice maintenance rate (2-4 L/hour) to correct the deficit, and then slowed to maintenance rate (1-2 L/hour) until the horse is able to drink adequately. Oral fluid administration can also be performed, although this should be done with caution in horses in which the septic process has caused ileus. Hypertonic (7.2%) saline solution (5mL/kg) to correct severe dehydration and restore cardiovascular function is most efficiently used in conjunction with twice maintenance rate intravenous isotonic fluid administration.[1] When necessary, concurrent electrolyte imbalances should be addressed by supplementing the intravenous fluids with potassium (20-40 mEq/L) and calcium gluconate (500 mL of a 23% solution added to 5-10 L of isotonic fluids).

When microbial culture results are available from peritoneal fluid analysis, antimicrobial therapy should be initiated based on reported sensitivity patterns. Peritonitis in the horse is often characterized by infection with multiple organisms belonging to Enterobacteriaceae, *Streptococcus* and *Staphylococcus* species.[2,3] Other common bacterial species are *Rhodococcus equi* in foals and, among the anaerobes, *Bacteroides, Clostridium,* and *Bacillus*. In most cases, a broad-spectrum antimicrobial is selected empirically prior to obtaining culture results and includes the intravenous adminstration of an aminoglycoside and a β-lactam antibiotic, which act synergistically against a wide variety of bacterial isolates. The concurrent oral or per rectum administration of metronidazole should be considered to widen the spectrum of activity and include anaerobic microorganisms. Because the antimicrobial agent must achieve good penetration within a closed cavity (the peritoneal cavity), lipophilic agents, such as fluorquinolones (e.g., enrofloxacin), may be a good choice. Furthermore, localized peritonitis originating from an intra-abdominal abscess may not respond well to hydrophilic antimicrobials (e.g., gentamicin) because of poor pentration.[4,5] The ease of administration of oral antimicrobials is an advantage because horses with peritonitis often require prolonged treatment. These include chloramphenicol, trimethoprim-sulpha, enrofloxacin, and rifampin. Chloramphenicol has a broad spectrum of activity and good tissue penetration. It is, however, bacteriostatic and can be dangerous in immunocompromised horses. The half-life of chloramphenicol is 1.5 to 4 hours in horses with normal renal and hepatic function, thus requiring frequent oral administration. Moreover, chloramphenicol may cause inappetence in horses after oral treatment, and has been associated with aplastic anemia in people involved in its administration. Trimethoprim-sulpha is commonly used for long-term treatment after intravenous antimicrobials are discontinued, but has been criticized because of the propensity for development of bacterial resistance and lack of efficacy for *Streptococcus sp.* Rifampin, with erythromycin, is the antimicrobial agent of choice for treating *Rhodococcus equi* infections in foals.

The decision to discontinue antimicrobial therapy is based on the results of serial peritoneal fluid analysis aimed at assessing total nucleated cell counts, which should decrease progressively in response to treatment. Antimicrobials should, however, be continued for several weeks following the attainment of a normal peritoneal fluid analysis.

Together with antimicrobial therapy, administration of appropriate anti-inflammatory therapy using flunixin meglumine is essential to address the effects of peritoneal inflammation and endotoxemia. Additional anti-inflammatory treatment can be achieved with the intravenous administration of dimethyl sulfoxide (DMSO), an oxygen free-radical scavenger commonly used in treatment of acute gastrointestinal conditions. In horses with signs of endotoxemia, hyperimmune plasma containing antibodies against endotoxin should be considered. In addition, large volumes of plasma may be useful to restore plasma protein concentrations in hypoproteinemic animals. Polymyxin B administration was shown to be an effective inhibitor of endotoxin-induced inflammation in healthy horses and, other than in the presence of azotemia, should be considered as a valuable ancillary treatment option for endotoxemia (see Chapter 18).[6]

Interventional Treatment

Medical management alone can be successful in the treatment of primary peritonitis and when horses are not severely compromised by the septic process. In other situations, it may be necessary to implement more aggressive measures such as abdominal lavage with or without surgical exploration of the abdomen. Abdominal lavage is performed in conjunction with abdominal drainage in an attempt to clear the peritoneal cavity of excess fluid, bacterial contamination, cellular and organic debris, and blood by-products such as fibrin.[7] Controversy exists regarding the necessity of abdominal drainage in primary peritonitis. The argument made against the procedure is that drains may serve as an entry point for further abdominal contamination, leading to ascending infections. Drain placement, in the standing horse, may also cause inadvertent iatrogenic perforation of the abdominal viscera. Moreover, a study reviewing its application in clinical cases documented a high incidence of minor complications such as obstruction of the drains (26%), leakage of fluid (16%), and subcutaneous fluid accumulation around the drain (12%).[8] Despite these complications, the veterinary literature reports that abdominal drainage

and lavage in horses is successful in treating and preventing peritonitis and abdominal adhesions.[7-9] Open peritoneal drainage has been experimentally evaluated in horses and has been successfully used in small animals and human patients.[10-13] The procedure is not routinely performed in horses because it is associated with incisional infections and requires a second surgery to repair and close the abdominal wall.[13]

Abdominal drains are placed with the horse standing or at the end of an exploratory celiotomy. In either case, 36 Fr to 40 Fr thoracic trocar catheters (Tyco Healthcare Group, Mansfield, MA) are placed percutaneously in the most ventral aspect of the abdomen. At surgery, it is important to place the catheter away from the celiotomy incision, to the right of midline, and as close as possible to the diaphragm in order to minimize possible occlusion of the drain by the omentum.[14] In the standing horse, pharmacologic and physical restraints are necessary to safely place abdominal drains. After local infiltration of the rectus abdominal muscle and fascia with local anesthetic, a stab incision is made through the skin, subcutaneous tissue, and external rectus sheath. The trocar and catheter can be bluntly inserted through the internal rectus sheath and peritoneum, avoiding forceful sudden penetration of the abdomen. Alternatively, the trocar can be removed and the catheter tip, held with sterile mixture thoracic forceps, gently guided into the abdomen. The best location of the drain can be selected or verified with transabdominal ultrasound. Once the drain is in place, the free end is occluded with a one-way valve system (Heimlich valve) and secured to the abdomen with sutures and an abdominal bandage.

The amount of fluid and the lavage solutions used to infuse into the equine abdomen are chosen empirically. It is important that the abdomen be lavaged with large amounts of sterile balanced polyionic solutions with neutral pH. Lactated Ringer's or 0.9% saline solutions are not irritating and do not create an osmotic gradient that may cause significant fluid shifts into the peritoneal cavity.[7] A volume of 20 L can be safely infused through the catheter and allowed to settle in the abdomen in order to cover as much of the serosal surfaces as possible before it is drained out. As the lavage solution distends the peritoneum, horses may experience abdominal discomfort. This can be controlled by infusing fluids gradually and by walking the horse regularly throughout the process. The addition of antiseptics in the lavage solutions is contraindicated because fluids containing povidone iodine solutions cause significant peritoneal inflammation.[15] Solutions containing antibiotics such as potassium penicillin (5 million IU/10 L) cause only minimal irritation, although the effectiveness of this approach in treating peritonitis has not been critically studied. It is presumed that the addition of antimicrobials to lavage solutions may influence the systemic administration of antimicrobials because of peritoneal absorption. Therefore, care should be taken when medications with similar toxicities are given parenterally and intraabdominally. In contrast, a study evaluating the effects of peritoneal lavage, without added antimicrobials, on systemically administered gentamicin in healthy horses, found no effect of lavage on the pharmacokinetics of gentamicin, indicating that no dose adjustments are needed during concurrent systemic antimicrobial therapy and abdominal lavage.[16] Abdominal lavage can be carried out once or twice a day for 3 to 5 days and discontinued when the solution retrieved from the abdomen appears clear. Samples obtained from the lavage solution can be submitted for cytology and compared with the initial peritoneal fluid sample to evaluate the progress of the disease. Results, however, should be interpreted with caution, as an inflammatory response is likely to occur as a result of the presence of the drain and the lavage procedure.

Surgical treatment of peritonitis is always indicated when secondary peritonitis occurs after loss of integrity of the bowel wall, the abdominal wall, or both. An exploratory celiotomy may also be elected if the source of a primary peritonitis cannot be determined from the diagnostic workup. Surgery is also indicated for the management of abdominal abscesses. The veterinary literature includes reports of three cases managed with marsupialization of the abscess to allow drainage to the exterior.[17,18]

During an exploratory celiotomy, several goals can be accomplished. The intestinal tract can be examined for puncture wounds, which can be over-sewn to interrupt continued contamination. Often, however, the exact source of contamination cannot be determined because small perforations may heal on their own after contamination has occurred. When peritonitis occurs after intestinal surgery, the celiotomy serves the purpose of revisiting the surgical site, which may necessitate reconstruction to prevent further leakage of intestinal contents. Traumatic disruptions of the abdominal wall can be dealt with via celiotomy by debriding and reconstructing the defect.

In horses, abdominal lavage can be carried out effectively via celiotomy. The most appropriate approach to a contaminated abdomen is via a ventral midline celiotomy, which allows good exposure and exteriorization of 75% of the intestinal tract.[19] Lavage is performed by instilling large volumes (30 L - 40 L) of fluid into the abdominal cavity with the large colon and cecum exteriorized in order to optimize fluid distribution and retrieval. Warm balanced isotonic solutions are poured into the abdomen by an assistant and then removed using active surgical suction devices. The procedure should be continued until the fluid retrieved from the abdomen appears clear.

Laparoscopy can also be helpful in the surgical management of equine peritonitis. Laparoscopy allows clinicians to inspect the abdomen with the horse either standing or under general anesthesia, while avoiding the invasiveness of a celiotomy.[20,21] Laparoscopy may be used to confirm the presence of an abdominal abscess or adhesions and to inspect the site of entry of an abdominal wound. A more detailed description of the approach to abdominal wall trauma is presented in Chapter 43.

Complications and Prognosis

Complications are often associated with septic peritonitis, and the prognosis depends on the development of secondary problems associated with the infection. Horses with septic peritonitis are prone to developing laminitis. This condition is best addressed by instituting aggressive preventive measures such as the administration of nonsteroidal anti-inflammatories, controlling endotoxemia, avoiding dehydration, and providing support to the hooves (see Chapter 44).

Inappetence and generalized ileus occur frequently during septic peritonitis and may require careful dietary management along with gastric decompression via an indwelling tube in horses with gastric reflux. Horses may require parenteral nutrition to sustain energy and body weight (see Chapter 23). Medications such as lidocaine (1.3 mg/kg bolus, followed by 0.05 mg/kg/min continuous-rate infusion) and erythromycin (1-2 mg/kg bolus every 12 hours) may assist the restoration of gastrointestinal motility (see Chapter 4).

The prognosis for horses with peritonitis depends on the initiating cause and on the timing of the therapeutic intervention. Treatments should be administered as early and aggressively as possible to avoid long-term complications such as formation of adhesions and abscesses. Horses with primary peritonitis may respond favorably to antimicrobial treatment alone, particularly if results of culture and sensitivity tests demonstrate good sensitivity to the selected antimicrobial. Peritonitis secondary to intestinal leakage or infarction is often fatal unless spillage of fecal material is limited or immediately addressed. Tertiary peritonitis can be difficult to treat because the duration of the infection usually limits the effectiveness of the therapeutic regimen.

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Diagnosis and Treatment of Enteritis and Colitis in the Horse

Chapter 20

Harold McKenzie

Diagnosis

The definitive determination of the etiology underlying enteritis and colitis can be challenging. For some syndromes, such as duodenitis-proximal jejunitis, no definitive etiologic agent has been identified, requiring that diagnosis be based on clinical signs and non-specific clinicopathologic abnormalities. Additional diagnostic uncertainty in regard to enteritis and colitis is caused by the low sensitivity of some of the diagnostic tests available, such as fecal culture for *Salmonella* spp. organisms. In cases where a definitive diagnosis can be made, the results may not be available for several days to weeks, requiring that decisions regarding treatment be made on an empiric basis. Despite these shortcomings, definitive diagnostic information can be of great utility in some cases in allowing more appropriate therapeutic intervention and accurate prognostication. Ultimately, obtaining a definitive diagnosis is of most importance when dealing with potentially infectious agents, in order to minimize the risk of dissemination of the disease throughout a farm or hospital population.

Specific Syndromes

Duodenitis-Proximal Jejunitis – Anterior Enteritis

While bacterial organisms, such as *Salmonella* spp. and *Clostridium* spp., have been identified in both the enterogastric reflux and intestinal contents obtained from some horses with duodenitis-proximal jejunitis, no causal relationship has been established.[1] The potential involvement of infectious organisms is plausible in this syndrome, given the profound acute inflammatory response observed in the small intestine in the absence of other identifiable insults and the presence of profound hypersecretion.[1] The lack of a definitive cause, combined with the similarities in clinical presentation between duodenitis-proximal jejunitis and small intestinal obstruction, makes definitive diagnosis of this condition difficult and can present difficulties in determining whether horses require abdominal exploratory surgery.

The most consistent clinical findings with duodenitis-proximal jejunitis include: a history of mild colic followed by profound depression, large-volume enterogastric reflux (as much as 15 to 20 liters every 2 hours), mild to moderate small intestinal distention on abdominal ultrasonography and/or rectal examination, low grade fever (101.5° - 102.5°F), clinical dehydration, tachycardia (60-80 bpm), decreased borborygmi, and injected mucous membranes.[1,2] The clinical findings with small intestinal obstruction may include: moderate to severe colic typically persistent, minimal to moderate volume enterogastric reflux, moderate to severe small intestinal distention on abdominal ultrasonography and/or rectal examination, normal rectal temperature, moderate to severe clinical dehydration, tachycardia (may exceed 100 bpm), decreased borborygmi, and injected mucous membranes.[2] Differentiation of duodenitis-proximal jejunitis and small intestinal obstruction is important because of the risks associated with delaying surgery in horses with obstruction. Whereas distended small intestine is commonly detected in both syndromes, the degree of distention is typically more severe with obstructive disease; with rectal palpation revealing multiple tightly distended, poorly compressible (hose pipe) loops of small intestine, as compared with more compressible loops of small intestine in horses with duodenitis-proximal jejunitis.[2,3] The results of rectal examination cannot, however, be used to definitively differentiate the two disease processes. Similarly, abdominal ultrasonography often reveals greater distention with obstructive disease (small intestinal diameters typically of 6 cm or greater), as compared with duodenitis-proximal jejunitis (typically, 4 to 6 cm small intestinal diameter), but these differences are not definitive. Thickening of the small intestinal wall is not consistently observed in horses with duodenitis-proximal jejunitis, and some observable motility may still be present. The presence, however, of small intestinal distention in combination with thickening of the small intestinal wall and a lack of small intestinal motility on abdominal ultrasonography is strongly correlated with the presence of small intestinal strangulation obstruction.[4]

Fever has been reported in many horses with duodenitis-proximal jejunitis, but is not always present.[2] The tachycardia seen in duodenitis-proximal jejunitis is typically less pronounced that than associated with strangulating obstruction.[2] Peritoneal fluid analysis is not useful in differentiating obstruction from proximal enteritis, as both syndromes can be associated with serosanguineous discoloration of the abdominal fluid, as well as elevations in the protein concentration and white blood cell count. It has been reported that horses with duodenitis-proximal jejunitis typically have lower total nucleated cell counts and total protein concentrations in peritoneal fluid than do horses with strangulating obstruction, although the total protein concentration usually exceeds the normal range.[2,3] Peripheral leukocytosis has also been reported in horses with duodenitis-proximal jejunitis.[3]

Ultimately, the most useful clinical parameter is the persistence of substantial abdominal discomfort after gastric decompression via nasogastric intubation. Most horses with duodenitis-proximal jejunitis cease to have pain after gastric decompression and exhibit profound depression.[3] The persistence of substantial discomfort is strongly suggestive of obstruction, and constitutes grounds for exploratory abdominal surgery, especially if other clinical parameters are also suggestive of obstructive disease. Although early reports suggested that the outcome for horses with duodenitis-proximal jejunitis that underwent

surgery was worse than for horses treated medically,[2] more recent experience has demonstrated no substantial difference in outcome.[5,6] In some cases, it appears that surgical decompression of the small intestine may actually be beneficial in shortening the time to resolution of enterogastric reflux.

Salmonellosis

Salmonella is reported to be the most frequently diagnosed etiologic agent in equine infectious diarrhea.[7] Thousands of serotypes of *Salmonella* have been identified; however, the majority of equine cases of salmonellosis are typically associated with one of a few serotypes, including: *Salmonella enterica* subspecies *enterica* serovar *typhimurium*, serovar *enteritidis*, serovar *krefeld*, serovar *saint-paul*, serovar *anatum*, serovar *newport*, and serovar *infantis*.[8-21] The most commonly implicated of these is *Salmonella enterica* subspecies *enterica* serovar *typhimurium*. Diagnostic testing for *Salmonella* organisms relies primarily on fecal culture, using selective enrichment media (selenite broth, tetrathionate broth, or Rappaport-Vassiliadis enrichment broth) to enhance the detection of *Salmonella* spp. by increasing the number of organisms, and selective isolation media (brilliant green agar, MacConkey agar, or xylose lysine desoxycholate (XLD) agar) to decrease the interference of other enteric organisms in the isolation process. Suspected isolates should be cultured on lysine iron agar and triple sugar iron agar to aid in the differentiation of *Salmonella* colonies from other enteric bacteria. Once isolated in culture, *Salmonella* organisms should be further identified by means of standard biochemical techniques or using a biochemical identification kit (API 20E, bioMerieux, Inc., Hazelwood, MO). All confirmed isolates should then be further characterized by means of antimicrobial sensitivity testing, serotyping, and phage typing.[9,11]

When performing fecal culture, a minimum of 10 grams of fecal material should be submitted.[22] *Salmonella* organisms are more consistently shed in formed stool than in diarrheic stool,[22] increasing the likelihood of isolating the organism as the animal recovers from clinical disease. The time required to isolate and identify *Salmonella* organisms from fecal samples using culture represents one of the primary limitations of this approach, as it may require 3 to 4 days to obtain a definitive result on any single fecal culture. In addition, fecal culture exhibits a low sensitivity for the detection of *Salmonella* shedders in the equine population, although the use of multiple cultures (5), combined with utilization of selective media, allows for adequate sensitivity levels to be achieved.[23] Culture of rectal mucosa with fecal material substantially increases the sensitivity of culture techniques.[24] Fecal culture remains the gold standard for clinical monitoring of equine patients, despite its limitations and the recent development of more sensitive techniques, such as PCR.

PCR tests are available for the detection of *Salmonella* spp. DNA in feces. These offer a more rapid turnaround time and higher sensitivity than culture techniques, but do not allow for further identification of the organisms or for antibacterial susceptibility testing.[25] The PCR techniques that have been developed for the detection of *Salmonella* DNA in equine feces have been demonstrated to be both highly sensitive and specific.[26-29] The high sensitivity of these PCR techniques results from the qualitative, rather than quantitative, characteristics of these assays and the ability of these assays to detect even a single DNA fragment containing the targeted DNA sequence. As a result, PCR testing can result in much higher numbers of positive results than can culture techniques, as seen in one study where 40% of clinical fecal samples were positive on PCR testing, as compared with 2% positive results with culture.[29] An even more dramatic example of this phenomenon was observed in a study that revealed that 17% of horses presented to the outpatient service of a veterinary teaching hospital were positive for *Salmonella* DNA on fecal PCR testing, yet none of these animals were culture-positive; 65% of hospitalized horses were PCR positive, while only 10% were culture-positive.[25] A recent study found an even greater disparity between PCR and culture techniques when analyzing environmental samples, with 0.001% (1/783) of the samples positive on culture and 14% (110/783) of the samples positive on PCR testing.[28] The wide disparity between the results of culture and PCR techniques likely reflects the ability of the PCR techniques to detect DNA from nonviable (dead or inactivated) organisms in the feces or the environment. This possibility was supported by the report that the use of enrichment culture techniques did not increase the detection of *Salmonella* from clinical fecal samples.[29] On the basis of these results, it is apparent that PCR techniques may be overly sensitive for routine clinical application.

Further characterization of *Salmonella* organisms cultured from clinical cases is important epidemiologically, both for the equine population and the human population potentially exposed to these organisms. This characterization can be achieved by means of serotyping and phage typing, although these tests are not routinely performed in all clinical laboratories. Phage typing has recently revealed the emergence of *Salmonella enterica* subspecies *enterica* serovar *typhimurium* definitive type (DT) 104 as an increasingly common animal pathogen.[10,11] Equine salmonellosis due to DT104 represents a serious concern, as the organism exhibits antimicrobial multiresistance and presents an increased risk of zoonosis.[10,30] It has been recommended that the phage type distribution of Salmonella isolates should be monitored to ascertain if DT104 remains a common equine pathogen.[10,11]

Clostridial Enterocolitis

The two primary agents of clostridial enteritis in the horse are *Clostridium difficile* and *Clostridium perfringens*. Although the detection of these organisms by means of fecal culture and their characterization with cytotoxicity assays has historically represented the gold standard for the diagnosis of clostridial enterocolitis, culture has been supplanted to some extent in the clinical setting by analysis of fecal toxin. The first reason for this transition is that culture of these clostridial organisms is challenging because of their anaerobic nature and the presence of competing species, and it can only be performed in properly equipped diagnostic laboratories.[31,32] More importantly, the presence of these organisms in the feces of animals with diarrhea is not definitively diagnostic, as these organisms can be present in low numbers in the gastrointestinal flora of healthy horses and foals. For this reason, quantitative culture is required to determine whether the number of organisms present exceeds that observed in normal animals.[33]

The presence of certain clostridial toxins in the feces is more diagnostic than the presence of the organisms on fecal culture, because of the association between these toxins and the pathogenicity of the clostridial organisms.[31] For this reason fecal toxinalysis is considered to be of greater clinical utility than fecal culture in the detection of clostridial enterocolitis. The specific toxins of interest include C. *difficile* toxins A and B, and *C. perfringens* enterotoxin (CPE), α-toxin, β-toxin, and θ toxin.[34] ELISA tests for several of these toxins (*C. difficile* toxins A and B, and CPE) are commercially available (TechLab®, Blacksburg, VA), and, while less sensitive than traditional tissue culture techniques, the ELISA toxin assays have proven to be useful in the detection of equine clostridial enterocolitis.[33,35] The ELISA toxin assays provide rapid results, as they only require 1.5 to 2 hours to run and are easily performed in most clinical laboratories. These assays are based on the presence or absence of a visual color change, providing a yes/no result regarding the presence of toxins in the feces, and do not require spectrophotometric analysis.[36,37]

Additional diagnostic techniques that have been utilized in clostridial enterocolitis include fecal cytology, latex agglutination for *C. perfringens* enterotoxin, and PCR for *C. perfringens* toxin genotyping. Fecal cytology may be useful if large numbers of organisms are present, but lacks sensitivity and is not specific for the type of clostridial organism present.[38] Latex agglutination testing has been demonstrated to be poorly specific for *C. perfringens* enterotoxin in foals with diarrhea.[39] Molecular techniques have been developed for the detection of clostridial DNA encoding for the clostridial toxins, and these techniques have variable sensitivity and specificity.[39-41] PCR analysis is useful for epidemiologic studies of clostridial enterocolitis, but is likely overly sensitive and inadequately specific for clinical application, as it may detect the presence of even very small numbers of organisms that may be present as part of the normal flora. PRC analysis can only be performed in specialized laboratories.[31]

Equine Monocytic Ehrlichiosis (Potomac Horse Fever)

Diagnosis of equine monocytic ehrlichiosis has primarily depended on the presence of typical clinical signs (fever, diarrhea) in combination with seasonal (summer) and geographic information (occurrence in an endemic area). Definitive diagnosis of equine monocytic ehrlichiosis requires detection of *Neorickettsia risticii* in the blood or feces of affected individuals by means of culture, but this is not a readily available or practical diagnostic tool.[42,43] A diagnosis of equine monocytic ehrlichiosis is typically made after detection of antibodies to *N. risticii*, using a serum indirect fluorescent antibody (IFA) test or ELISA test.[44-47] Although the ELISA tests are more sensitive than the IFA test, they are not readily available, and the IFA test is more widely used. Because the latent period after infection can be as long as 14 days, seroconversion may occur prior to the development of clinical disease, limiting the diagnostic usefulness of serologic testing.[48] Additionally, prior vaccination and the presence of high serum titers in clinically healthy animals substantially decrease the usefulness of a single serum titer. For these reasons, it has been recommended that acute and convalescent titers be determined, with either rising or falling serum titers being suggestive of infection. A further confounding factor arises from the fact that the IFA test can suffer from a high false-positive rate, further limiting its diagnostic usefulness.[49]

PCR techniques have been developed for the identification of *N. risticii* DNA in peripheral blood or feces, and these have been shown to be highly sensitive and specific.[43,50] The nested PCR and real-time TaqMan PCR techniques do not appear to suffer from the excessive sensitivity that is a concern with some of the PCR tests used for other diseases such as salmonellosis. The results with the nested PCR were well correlated with the results of standard culture techniques, and the nested PCR and TaqMan techniques are highly correlated with one another.[43,50] Unfortunately, these PCR tests are not readily available for clinical use.

Viral Enterocolitis

The only well described viral enterocolitis in horses is rotaviral diarrhea in foals. The diagnosis of this disease is most readily made by detecting the organism in the feces of the affected foal. This test is not definitive for causation, as healthy foals can shed the organism, especially if they have been exposed to diarrheic foals shedding large numbers of viral particles.[51] The presence of the virus in association with clinical diarrhea in foals is, however, considered to be strong evidence of causation.[51,52] Serology is of limited use in the diagnosis of rotaviral diarrhea, as foals commonly have detectable levels of rotaviral-specific antibodies derived from colostrum,[53] and this test is not utilized clinically. Electron microscopy has represented the "gold standard" for detection of rotaviral particles in fecal material, but it is not readily available and is of somewhat low sensitivity. Large numbers of viral particles must be present to be identified on electron microscopy. This technique may lack specificity as other viral particles may appear similar to rotavirus on electron microscopy. The presence of rotaviral particles is readily ascertained, however, with enzymatic immunoassays (EIA) that detect the presence of rotaviral specific antigens (the group A VP6 antigen) in fecal samples (Rotazyme, Rotaclone). The Rotazyme test (Abbott Diagnostics, Inc., Abbott Park, IL) has been demonstrated to be of equal or greater sensitivity and specificity than electron microscopy in the detection of rotaviral particles.[54,55] Other tests exist for the detection and characterization of rotaviral particles in feces, such as electrophoretic genomic analysis and PCR-amplified RNA genogrouping, but these are more relevant for epidemiologic purposes than for clinical diagnosis.[56,57]

Intestinal Parasitism

While the incidence of clinical disease resulting from endoparasitism has decreased with the increasingly widespread use of effective anthelmintic administration, gastrointestinal parasitic infestation still represents an important clinical entity. Small strongyle infestation (cyathostomiasis) has been increasingly appreciated as a cause of diarrhea in horses, often in association with hypoproteinemia and weight loss, and *Strongyloides westeri* infestation remains an important clinical entity in foal diarrhea.[51,58-60] Although several techniques exist for the detection of parasite larvae or eggs in fecal material, the detection of helminthic parasitic infestation can be challenging, as clinical disease resulting from endoparasitism may occur during the prepatent period, before the parasitic organisms begin to shed eggs or pass larval stages in the feces. This is especially true in the case of cyathostomiasis, where the reported sensitivity and specificity of fecal flotation is less than 40% for the detection of strongyle eggs, larval stages, and adult parasites, and this requires that additional diagnostic tools be employed. Diagnosis of cyathostomiasis from the examination of fecal material is enhanced by the use of techniques such as the Baermann technique for detection of larval stages and the modified McMaster technique for the detection of strongyle ova and larval stages.[61] Definitive diagnosis of cyathostomiasis, however, requires postmortem examination of the intestine or the collection of large intestinal biopsies, as small biopsy samples may not contain a representative population of organisms. Intestinal biopsies should be examined for the presence of third and fourth stage larval cyathostomes, using both transillumination and peptic digestion techniques.[62]

Protozoal Enterocolitis

Cryptosporidium parvum has been associated with diarrhea in foals, but like rotavirus, this organism may also be shed by healthy foals, especially after exposure to diarrheic foals shedding large numbers of this organism.[51,63] The detection of large numbers of the organism in the feces of a diarrheic foal is, however, considered to be significant and suggests a causative role for this organism. Tests that may be used to identify cryptosporidial organisms in fecal material include acid-fast staining, immunofluorescence assays, and flow cytometry.[64] The most readily performed of these is acid-fast staining, which has been reported to be more sensitive but less specific than the immunofluorescence assay.[64] The Kinyoun acid fast stain can be performed on a fecal-smear slide preparation in most clinical laboratories, and consists of a three-step process of staining, decolorizing, and counterstaining, followed by examination at 400X and 1000X magnification.[65] Readily identifiable pale to bright pink oocysts should be detected in multiple high-power fields in order to support the clinical involvement of cryptosporidial organisms.[65] Although the direct immunofluorescence assays are readily available, they require a fluorescent microscope for reading the stained slide, and cannot be easily performed in most clinical diagnostic laboratories, rendering them less useful in the clinical setting.

Proliferative Enteropathy

The antemortem detection of the causative organism, *Lawsonia intracellularis*, in horses with proliferative enteropathy is difficult because isolation of the organism in feces requires challenging cell culture techniques,[66] and histologic evaluation of biopsy specimens from the intestine may be unrewarding as the sample may be obtained from an unaffected region of the intestine.[67] Serologic testing may be used to document that exposure to this organism has occurred.[68] Fortunately, newer techniques, such as immunochemical staining and PCR testing, provide specific diagnostic tests that can be performed on

fecal material.[67,68] Unfortunately, the sensitivity of fecal PCR testing may be relatively low. Immunochemical staining has been reported to have a higher sensitivity than fecal PCR in pigs with porcine proliferative enteropathy.[69] Postmortem diagnosis relies on histologic examination of infected tissues and the use of silver stains, immunofluorescence, and PCR techniques.[67,68,70]

NSAID-Associated Right Dorsal Colitis

The clinical presentation of horses with this condition can vary from seemingly healthy horses with soft stools to those suffering from profuse watery diarrhea with signs of endotoxemia and shock. Intermittent colic may be present. Peripheral edema is a common, but not universal, finding in this condition, because of the loss of albumin through the damaged gastrointestinal mucosa, resulting in hypoalbuminemia and hypoproteinemia. Diffuse gastrointestinal ulceration may be present, with the affected areas including the oral cavity, stomach, and right dorsal colon. Many affected horses present with ulceration of only the right dorsal colon, however. The diagnosis of this condition is basically presumptive in nature, and is based on a history of NSAID administration in combination with clinical signs suggestive of toxicity. Although a history of excessive dosages of NSAIDs is strongly suggestive, toxicity can occur even with dosages within the normal range.[71] Concurrent renal toxicity may be present, and this may result in azotemia, hyposthenuria, and proteinuria.

Definitive diagnosis of right dorsal colitis requires surgical exploration of the abdomen and demonstration of focal thickening and inflammation of the right dorsal colon.[72] Noninvasive diagnostic techniques include transabdominal ultrasonography and labeled white blood cell scintigraphy.[73,74] Ultrasonographic evaluation of the right dorsal colon is most readily performed at the level of the 11th, 12th, and 13th rib spaces on the right hand side just below the caudoventral lung border, where the colon will be imaged deep to the liver.[73] At these sites, the mural thickness of the right dorsal colon wall should be 0.36 cm (range 0.24 to 0.6 mm) and the ratio of the mural thickness of the right dorsal colon to the right ventral colon should be 1 (range 0.7 to 1.6).[73] Labeled white blood cell scintigraphic examination of horses with right dorsal colitis has revealed increased radiopharmaceutical uptake in the right dorsal colon region at 20 hours after injection of the labeled white blood cells, with no uptake observed in this region in normal horses.[74] As definitive diagnosis is not often possible, it is important that one rule out other causes of enterocolitis before making the presumptive diagnosis of right dorsal colitis.

Treatment

The treatment of enteritis and colitis in most cases is supportive in nature, as many of these conditions have poorly defined etiologies (e.g., duodenitis proximal enteritis-anterior enteritis) or are caused by agents that are not likely to respond to specific therapy (e.g., rotaviral diarrhea, salmonellosis). The inflammatory nature of enteritis and colitis results in similar patterns of clinical and clinicopathologic alterations in horses with these conditions, and as a result, the principles of treatment of these diseases are often similar. Substantial losses of fluid from the circulating volume usually necessitate supportive fluid therapy; accompanying losses of protein may necessitate colloid therapy as well. Electrolyte derangements are often present, requiring that supplementation be provided either enterally or parenterally. Anti-inflammatory therapy is indicated in many of these conditions to address both the local and systemic components of the inflammatory response. Antimicrobial therapy is not indicated in all cases, and the exceptions will be discussed where appropriate. Disruption of normal segmental and/or progressive motility may necessitate decompression by nasogastric intubation or surgical intervention, and prokinetic therapy may be of benefit. Decreased voluntary feed intake or forced withholding of feed often necessitates nutritional support. The management of these cases can be intensive, often requiring hospitalization.

Supportive Therapies

Gastric Decompression

The potential for the accumulation of enterogastric reflux within the stomach exists in any disease process in which normal progressive gastrointestinal motility is disrupted. The inability of the horse to regurgitate makes it imperative that nasogastric decompression be performed in any equine presenting with signs suggestive of gastrointestinal distress. While the passage of a nasogastric tube is associated with some risk of esophageal trauma, the incidence of complications is low,[75] and the risk of gastric rupture far outweighs any risks associated with intubation. As reflux may be ongoing, it is often best to leave the nasogastric tube in place to allow for frequent decompression (every 1 to 2 hours initially). Failure to adequately decompress the stomach can result in gastric rupture. This is not prevented by simply having a nasogastric tube in place; active decompression is required.[76] The risk of complications associated with intubation increases with increasing duration of intubation, so it is best to remove the tube when the production of enterogastric reflux has abated.[75] Determination of the optimum time for removal of the nasogastric tube is complicated by the fact that the presence of the nasogastric tube may result in

the generation of a low volume of enterogastric reflux. Therefore, the tube can be removed once the volume of reflux decreases to 1 to 2 liters every 2 to 4 hours, provided the patient can be closely monitored for recurrence of abdominal pain.[77] If pain recurs, the nasogastric tube must be replaced, and the stomach should be decompressed if fluid is again present. Some horses continue to reflux for up to 7 days, necessitating repeated attempts to remove the nasogastric tube. Some horses with colitis yield moderate volumes (2-4 L) of enterogastric reflux on initial nasogastric intubation, presumably because of the presence of small-intestinal ileus, but this typically resolves within the first 12 hours of treatment and does not usually require prolonged nasogastric intubation.

Fluid Therapy

Horses with enteritis or colitis often present with dehydration, which occurs secondary to fluid losses in the form of diarrhea or enterogastric reflux alone or in combination with decreased voluntary fluid intake. The correction of dehydration typically requires fluid replacement therapy, as these patients are often unable to correct their fluid status by voluntary intake. The goal of fluid therapy is to improve cardiovascular function, thereby resulting in improved tissue oxygen delivery and organ function. The fluid therapy plan should address both the correction of existing deficits, and the provision of fluids to replace ongoing losses and provide for basal metabolic requirements. The estimate of clinical dehydration allows for an approximate determination of an initial resuscitation volume (e.g., 5% dehydration in a 500-kg horse equals a 25 L fluid deficit), which should be corrected rapidly, usually within the first 2 hours after initiating therapy. Additional information regarding an animal's hydration status can be obtained from clinicopathologic data, including: hematocrit, serum total protein concentration, serum lactate concentration, serum creatinine concentration, and urine specific gravity. Unfortunately, these parameters are all susceptible to other influences that decrease their sensitivity as markers of dehydration. The hematocrit can be reduced by blood loss, blunting the expected increases associated with dehydration and hemoconcentration, while the serum total protein concentration can be decreased as a result of protein loss or increased because of chronic inflammatory disease. Serum lactate concentration may be increased because of tissue hypoperfusion associated with hypovolemia and shock, but also may be increased as a result of defects in tissue oxygen extraction (cytopathic hypoxia) despite adequate tissue perfusion.[78] Renal insufficiency can result in increased serum creatinine concentrations without dehydration, while it may prevent appropriate increases in urine specific gravity in the presence of dehydration. Urine specific gravity will normally reflect the hydration status of the patient, but may not be appropriately increased in dehydration if renal insufficiency is present.

Intravenous Route

In most cases of enteritis and colitis, fluid replacement is best accomplished via the parenteral route, as this allows for the rapid administration of large volumes of fluid in acute situations, and also allows for correction of any electrolyte deficits. Although the use of the intravenous route for fluid delivery can be more difficult than the enteral route in the field, the availability of administration sets that allow horses to freely move within a stall greatly facilitates this process (IV 1000 Stat Large Animal IV Set, International WIN, Ltd., Kennett Square, PA.). Intravenous fluids for replacement may be administered at rates of 10 to 20 mL/kg/hour in the moderately dehydrated patient, but more aggressive therapy is required when the patient is in shock, with rates as high as 30 to 40 mL/kg/hour being readily achieved using a 10- or 12-gauge intravenous catheter. Higher rates are difficult to achieve in the horse because of the limitations of the available equipment, but 60 to 80 mL/kg/hour may be achievable by simultaneous catheterization of both jugular veins with 2 large-bore catheters. These aggressive rates of supplementation do increase the risk of pulmonary edema, however, and should be used with caution (see Chapter 17), especially in foals. Maintenance rates of fluid administration are typically 2 to 3 mL/kg/hour adults and 4 to 5 mL/kg/hour foals, but this will need to be increased to account for additional fluid losses resulting from reflux or diarrhea.

Enteral Route

Enteral fluid therapy has been proposed for horses with colitis, as small-intestinal function is usually normal in these animals.[79-81] The enteral route is intrinsically more physiologic, and has the additional advantages of reduced cost and simplicity.[80] Oral rehydration solutions are widely used in the treatment of human patients with diarrhea, and the reported outcomes with oral rehydration are equivalent or superior to those reported with intravenous fluid therapy.[82,83] The enteral route of administration can be used successfully in the treatment of horses with mild cases of colitis, but more severely affected patients are often unable to tolerate the administration of the volumes of fluids required to correct their deficits and replace their ongoing losses, and may exhibit increased discomfort or abdominal distention or may even develop enterogastric reflux.[80,84]

Administration of enteral fluids is easily accomplished using a large-bore stomach tube or a smaller indwelling enteral feeding tube (18 Fr. x 100-inch, MILA International, Inc., Erlanger, KY). Enteral fluid solutions are easily prepared using tap water, and an isotonic solution can be formulated by combining 5 L of water with 1.5 tablespoons (28 g) of table salt, one half teaspoon

(3 g) of Lite salt (NaCl and KCl, Morton Salt, Chicago, IL) and 1.5 tablespoons (17 g) of baking soda ($NaHCO_3$).[80] Enteral fluids should be administered as either repeated bolus doses of up to 6 to 8 L/hour, although more rapid rates of administration are reported in the literature.[80,81] The author's experience suggests that these more aggressive rates of administration result in substantial worsening of diarrhea and abdominal discomfort. Alternatively, the enteral fluids may be administered as a continuous-rate infusion at a rate of 3 to 6 L/hour, which seems to be tolerated better than bolus therapy by some horses.[80]

Types of Intravenous Fluids

Parenterally administered fluid solutions are generally classified into one of three types: hypotonic, isotonic, and hypertonic. The most widely used of these are the polyionic crystalloid solutions, which are classified as either replacement or maintenance solutions. Isotonic replacement fluids are the most widely used type of fluids in equine medicine, and they are most appropriate for use in rehydration, as they provide substantial amounts of sodium to aid in expansion of both the extracellular fluid volume and the intravascular volume. Examples of replacement fluids include normal (0.9%) saline, Ringer's solution, lactated Ringer's solution, Plasmalyte-148 (Baxter Healthcare Corp., Deerfield, IL) and Normosol-R (Abbott Laboratories, North Chicago, IL). Replacement fluid solutions are commonly used to provide maintenance fluid support after initial rehydration in horses, but they contain relatively high concentrations of sodium and low concentrations of potassium. Most adult horses appear to be able to eliminate the excess sodium via renal excretion, while foals are less tolerant of this type of sodium load and may become hypernatremic if replacement fluids are used for maintenance purposes. The low potassium content of the replacement solutions requires that supplemental potassium be added to the fluids in the form of potassium chloride (20 mEq/L) in most cases, especially in horses unable to eat because of anorexia or dietary restriction.

Maintenance fluids are isotonic or hypotonic polyionic crystalloid solutions that contain lower concentrations of sodium and chloride than replacement solutions and deliver relatively more potassium. Examples of maintenance solutions include 0.45% saline with 2.5% dextrose, Plasmalyte 56 (Baxter Healthcare Corp., Deerfield, IL) and Normosol-M (Abbott Laboratories, North Chicago, IL). Maintenance fluid solutions may contain dextrose, which is used to bring the solution to an osmolality close to that of serum (250-300 mOsmol/L) as these solutions are often hypotonic, because of their low concentrations of sodium and chloride. Maintenance fluids provide relatively more free water to replace the fluid volume lost as a result of insensible losses, which typically consist of water loss without concurrent electrolyte losses. Use of maintenance solutions aids in preventing the development of hypernatremia and hyperchloremia, but may be contraindicated in animals with substantial ongoing losses of electrolytes resulting from diarrhea or renal disease.

Hypertonic fluids are rarely administered as the sole fluid solution and are reserved for resuscitation of horses in life-threatening shock to provide rapid restoration of circulating blood volume and hemodynamic stabilization.[85-87] Because of the relatively transient nature of the effects of hypertonic saline, and the fact that the increase in circulating volume is achieved by shifting fluids from the extravascular space, hypertonic saline must be rapidly followed by the administration of isotonic solutions to maintain volume expansion. Other hypertonic solutions include sodium bicarbonate; this solution has been used in the treatment of acidosis associated with severe dehydration and shock. Good evidence exists, however, that this treatment is not effective at normalizing serum pH in horses exposed to sublethal doses of endotoxin, despite increasing the serum bicarbonate concentration, and it actually results in increases in serum lactate concentration.[88] The primary uses for sodium bicarbonate solutions are the treatment of hyponatremia without hypochloremia and hyperchloremic metabolic acidosis.

Colloids

Most horses with enteritis or colitis respond well to the administration of balanced electrolyte solutions as volume-replacement therapy, but some require the concurrent administration of colloid solutions (see Chapter 17). Colloid therapy is most helpful in two clinical situations: severe hypovolemia and hypoproteinemia. Both natural and synthetic colloid solutions are available for administration to equine patients. Equine plasma and whole equine blood are the only natural colloid solutions currently available for use in equine patients. Although purified equine albumin has been developed, this product is not currently available. The synthetic colloids include hydroxyethyl starch solutions (Hetastarch; Hespan 6% hetastarch in normal saline, Baxter Healthcare Corp., Deerfield, IL), dextrans (Dextran 40, 70, and 75), gelatins (Haemaccel Veterinary Infusion Solution; 3.5% polygeline isotonic solution, Intervet UK, Milton Keynes, North Bucks, UK) and polymerized bovine hemoglobin (Oxyglobin; hemoglobin glutamer-200 (bovine), Biopure Corp., Cambridge, MA). Gelatin colloids are not commercially available in the United States at this time.

The most physiologically appropriate and widely used colloid for the treatment of hypoproteinemia is equine plasma. The drawbacks associated with the use of plasma therapy include cost (a single dose of 4 to 8 L of plasma typically costs $500 to $1000) and a relatively short duration of action, because of the loss of the exogenous proteins resulting from capillary

leak within the gastrointestinal mucosa or the systemic circulation.[89] The use of hydroxyethyl starch solutions for the treatment of equine hypoproteinemia has been reported,[90] and this therapy appears to be clinically effective. Additionally, hydroxyethyl starch solutions are somewhat less expensive than equine plasma, as a typical dose of 5 to 10 mL/kg costs approximately $250 to $500. Hydroxyethyl starch has the additional advantages of a longer duration of action than plasma and the reported ability to decrease the severity of capillary leak in shock and sepsis.[91-94] Hydroxyethyl starch infusion has been shown to result in hemorrhagic diathesis in septic human patients, and the author has observed this apparent effect in critically ill equines as well. The primary cause of the coagulation disorders associated with these compounds appears to be primarily a dilutional effect on the endogenous clotting factors in critically ill patients, many of whom are suffering from clotting-factor depletion secondary to consumption.[95] Interestingly, similar alterations in hemostatic function have also been reported in association with administration of gelatin and dextran colloids.[96,97] Avoidance of hemostatic dysfunction can best be achieved by limiting the total dose of hydroxyethyl starch to less than 10 to 20 mL/kg and monitoring the clotting profile of patients administered large doses of these solutions.

The use of dextrans is not well reported in the horse, with only dextran-polymyxin B and dextran-hypertonic saline solutions having been mentioned in the literature.[98,99] The relatively low molecular weight of the dextran solutions means that the duration of their colloidal effects will be shorter than those seen with high molecular weight colloids such as hydroxyethyl starch, but the effects may be greater in magnitude because of the greater number of osmotically active molecules. Polymerized bovine hemoglobin (Oxyglobin) shows great promise, as it represents a potent colloid that also increases oxygen transport to the tissues, and it appears to be safe and effective in the horse at doses as high as 15 mL/kg.[100] Use of this solution will likely be restricted to neonatal foals, however, because of the expense of this product.

Electrolyte Supplementation

Horses with inflammatory gastrointestinal diseases often develop hypokalemia and hypocalcemia; hypomagnesemia also may occur. Hypokalemia, which for clinical purposes can be defined as a serum potassium concentration less than 3.5 mEq/L,[101] is such a common finding in horses withheld from feed that the fluids utilized for maintenance therapy should typically contain additional potassium. This is routinely accomplished by the supplementation of the fluid solution, which is typically a resuscitation fluid, with 20 mEq of potassium chloride per liter. When administering fluids at rates higher than maintenance, care must be taken to ensure that the rate of potassium delivery does not exceed 0.5 mEq/kg/hour.[101,102] Hypocalcemia, defined here as a serum ionized calcium concentration of less than 5.0 mg/dL, is also a common occurrence in horses with gastrointestinal disease. Intravenous supplementation with calcium gluconate solution is commonly provided to these horses. Adult horses typically receive 100 to 300 mL of a 23% calcium gluconate solution,[103] although clinically, some horses require as much as 500 to 1000 mL to fully correct their hypocalcemia. Hypomagnesemia has been described in horses with gastrointestinal disease,[104,105] but routine assessment of this disorder is complicated by the fact that serum total magnesium appears to be less relevant than serum ionized magnesium, and the equipment required to assess serum ionized magnesium is not readily available. Intravenous supplementation with moderate dosages (4-16 mg/kg) of magnesium sulfate is well tolerated by the horse, even in normal magnesium status, provided that renal function is normal.[101] Hypomagnesemia has been associated with the development of hypocalcemia and hypokalemia in both veterinary and human patients.[106] In the author's experience, supplementation with magnesium sulfate has been beneficial in aiding the correction of persistent hypocalcemia and/or hypokalemia in equine critical care patients.

Anti-Inflammatory Therapy

Nonsteroidal Anti-Inflammatory Drugs (NSAID)

The NSAIDs are extremely important drugs in the management of equine gastrointestinal disorders, primarily because of their potent analgesic properties, but also because of the demonstrated ability of some of these drugs to modify the systemic inflammatory response to gastrointestinal disease. Drugs in this class include: phenylbutazone, flunixin meglumine, ketoprofen, carprofen, ibuprofen, meclofenamic acid, and etodolac. Of these, the most commonly used drug for the treatment of gastrointestinal disease is flunixin meglumine, which is a potent visceral analgesic with a well demonstrated ability to suppress abdominal pain in equine gastrointestinal diseases when administered at 1.1 mg/kg orally, intramuscularly, or intravenously.[107] In addition, flunixin has been shown to suppress the systemic response to endotoxin when given as a pretreatment at doses as low as 0.25 mg/kg, thereby minimizing the severity of endotoxemia-associated hypotension, hypovolemia, hemoconcentration, pulmonary hypertension, tachypnea, tachycardia, and lactic acidosis.[108-112] Additionally, flunixin meglumine and phenylbutazone have been shown to attenuate the development of ileus after endotoxin exposure.[113] Although other NSAIDs, such as ketoprofen, have been demonstrated to have some "anti-endotoxemic" effects, flunixin meglumine remains the drug of choice in the treatment of horses with gastrointestinal disease resulting in colic and/or endotoxemia.[99,114] Care should be taken when using the NSAIDs as all of the available compounds are potentially ulcerogenic

and nephrotoxic in nature, due to their interference with the maintenance of mucosal blood flow in the intestine and medullary blood flow within the kidney. Of the commonly used NSAIDs, the toxic potential of phenylbutazone is most widely recognized.[72,115,116]

Steroidal Anti-inflammatory Drugs (SAID)

The SAIDs are potent anti-inflammatory compounds, and they are extremely important in the management of equine gastrointestinal disorders. This is especially true for more chronic conditions, such as inflammatory bowel disease, which are immune mediated. SAIDs have not proven to be as effective as the NSAIDs in suppressing the acute systemic response to endotoxin in the horse, and are not effective analgesics, so they have a limited role in the treatment of acute gastrointestinal diseases.[111,112,117] The literature, however, includes some mention of the use of corticosteroids in the treatment of acute equine typhlocolitis.[118] The primary utility of this class of drugs is in the suppression of gastrointestinal inflammation, such as occurs acutely in larval cyathostomiasis after the destruction of the encysted larvae within the bowel wall following anthelmintic administration, or in chronic infiltrative bowel diseases. Some work has demonstrated that the SAIDs exert many of their effects by mechanisms other than their well described suppression of the pathways of arachidonic acid metabolism leading to the production of the prostanoids and leukotrienes.[119-121] The SAIDs have potent effects on the expression of genes encoding inflammatory and anti-inflammatory mediators, with overall inhibitory effects on the production of pro-inflammatory mediators and facilitating effects on the production of anti-inflammatory mediators.[121] It has become clear that these effects are responsible for the potent, dose-dependent anti-inflammatory and immunosuppressive effects of these drugs.

Prednisone and prednisolone are commonly used corticosteroids in the treatment of acute and chronic gastrointestinal inflammatory conditions, although evidence exists that prednisone is poorly absorbed by the horse after oral administration.[122] Prednisolone is usually administered at dosages of 1 to 2 mg/kg once daily. This drug appears to be clinically effective in some cases, but the dosage may need to be increased to 4 mg/kg per day to achieve adequate immunosuppressive effects in refractory cases. One significant limitation to the use of prednisolone is cost, especially at higher dosages. Dexamethasone is often used for the treatment of inflammatory bowel disease, due to the higher potency and lower cost of this drug on a daily basis. The dosage of dexamethasone is 0.02 to 0.1 mg/kg/day, with the upper end of the dosage range producing potent immunosuppressive effects. The possibility of the potential association of corticosteroids and laminitis must be considered, especially when corticosteroids are used in conditions that represent risk factors for laminitis or when high dosages of the more potent corticosteroids are used.[123]

Anti-endotoxin Therapies

As bacterial endotoxin plays an important role in the development of severe systemic inflammation (endotoxemia) associated with gastrointestinal disease, there has been significant interest in finding ways to inhibit systemic responses to endotoxin. Two basic approaches have been used in an attempt to neutralize endotoxin, with the first being the administration of anti-endotoxin antibodies and the second being the use of chemicals that bind endotoxin.[124] The development of antibodies to bacterial endotoxin has been challenging because of the antigenic variation of endotoxins among species of gram-negative bacteria. For this reason, antibodies have been targeted against the more conserved core and lipid A regions of the endotoxin molecule.[124] Extensive studies of anti-endotoxin antibodies were performed in humans in an effort to develop these therapies for clinical use, but the conflicting results of these studies meant that none of the products were licensed for human use.[125] Studies regarding the efficacy of anti-endotoxin antibodies in experimental equine endotoxemia and in horses presenting with colic have also yielded conflicting data, resulting in uncertainty regarding the clinical application of this type of therapy.[126-129] Of additional concern is the report that describes worsened clinical signs of endotoxemia and increased systemic inflammation associated with the administration of anti-endotoxin antiserum in a foal model of endotoxemia.[129] Serum and plasma products containing anti-endotoxin antibodies are commercially available for use in the horse and are used in some cases, but the uncertainty in the literature regarding this therapy needs to be resolved before specific recommendations can be made.

The use of the anti-endotoxin agent polymyxin B has been extensively examined in a variety of animal species and in humans, and good evidence exists that polymyxin B binds endotoxin and prevents it from initiating or potentiating the systemic inflammatory response. The use of polymyxin B in humans has been limited by concerns regarding the nephrotoxic potential of this compound, and this has led to the development of extracorporeal filters containing polymyxin B-immobilized fibers that are used for hemofiltration in patients with endotoxemia and sepsis.[130,131] Polymyxin B has been examined in several equine endotoxemia models and has been demonstrated to decrease the severity of both the clinical signs of endotoxemia and the severity of the systemic inflammatory response.[129,132,133] Based on these reports, the current recommendations for clinical use of polymyxin B are to initiate therapy as early as possible, using a dosage of 1,000 to 5,000 IU/kg every 8 to 12

hours.[124] Although no evidence of nephrotoxicity has been reported in horses administered low dosages of polymyxin B, it is recommended that horses be adequately hydrated and that serum creatinine concentrations be monitored when administering this drug.[124] Prolonged administration of polymyxin B should be avoided to minimize the risk of nephrotoxicity. Given the relatively low sensitivity of serum creatinine as a marker of nephrotoxicity, one should consider performing urinalysis on a regular basis to monitor urine specific gravity as well as urine sediment for casts and for the development of enzymuria.

Analgesic Therapy

The provision of analgesia in horses with gastrointestinal diseases is most commonly accomplished using NSAIDs, primarily flunixin meglumine, and α-2 adrenergic agents such as xylazine and detomidine. Flunixin meglumine (1.1 mg/kg IV or IM) is widely used as a visceral analgesic in horses, and it is effective, although the degree of analgesia is less than that produced by administration of the α-2 agents.[134,135] Detomidine (0.11 to 0.22 mg/kg IV or IM) and xylazine (0.5 to 1 mg/kg IV or IM) are potent visceral analgesics in horses; however, their use is accompanied by profound sedation and their effects are fairly transient.[136] Opioid analgesics, such as butorphanol and fentanyl, can be used as an alternative to, or adjunctive therapy with, NSAIDs or α-2 agents. Butorphanol can be administered as intermittent boluses (0.02 to 0.13 mg/kg IV) or as a continuous-rate infusion (initial loading dose of 17.8 μg/kg followed by a continuous infusion of 23.7 μg/kg/hour).[137] Fentanyl can be administered by use of a transdermal patch delivery system (Duragesic, Janssen Pharmaceutica Products, L.P., Titusville, NJ), which provides controlled release of the drug and is able to maintain expected therapeutic serum levels of fentanyl for 48 hours after patch placement in horses.[138] The dosage rate reported for transdermal administration of fentanyl in adult horses is two 10-mg patches (20 mg total dose) applied to a shaved area of the medial or lateral antebrachium or gaskin, then covered by a nonadherent dressing secured with an adhesive bandage.[138] Fentanyl is a potent analgesic, and care should be taken that its use does not interfere with the assessment of the patient, especially regarding the need for colic surgery. An additional concern regarding the use of the opioids for analgesia in patients with gastrointestinal disease is the depressant effects of the opioids on gastrointestinal motility.[139-143] While this may potentiate ileus in some patients, it may be of benefit in patients with hypermotility, such as those with profuse diarrhea.

Prokinetics

Because of the frequent development of ileus in patients with enteritis, prokinetic drugs are often used in the treatment of these disorders. In contrast, animals with colitis rarely require prokinetic therapy. The effects of the prokinetic drugs typically derive from their ability to either increase the local activity of the enteric nervous system or to minimize the inhibitory effects of the sympathetic nervous system on the activity of the enteric nervous system. A detailed discussion of the mechanisms of these compounds is included in Chapter 4. The more commonly used drugs in animals with enteritis include the parasympathomimetic bethanechol, the benzamide metoclopramide and the sympatholytic and local anesthetic drug lidocaine. Of these, bethanechol and lidocaine are most commonly used by the author. Lidocaine administration is reported to result in suppression of the visceral afferent neurons, thereby inhibiting the reflex-mediated increased activity of the sympathetic innervation of the intestine.[144] Additional beneficial effects of lidocaine therapy may include anti-inflammatory effects and direct stimulation of intestinal smooth muscle.[145-147] The results of 2 studies of lidocaine therapy in post-operative ileus suggest that lidocaine administration, at a loading dosage of 1.3 mg/kg using 2% lidocaine solution, followed by a continuous-rate infusion of 0.05 mg/kg/minute, is beneficial in decreasing intestinal inflammation and promoting a more rapid return of small intestinal function.[148-149]

Direct stimulation of cholinergic receptors using the cholinomimetic drug bethanechol has also been shown to enhance gastric and cecal emptying in the horse.[150-152] When administered at dosages of 0.018 to 0.024 mg/kg subcutaneously every 8 hours, bethanechol appears to decrease the duration of enterogastric reflux in horses with postoperative ileus and in some horses with duodenitis-proximal jejunitis-anterior enteritis. Metoclopramide promotes the release of acetylcholine from postsynaptic cholinergic neurons and antagonizes dopamine and α-2 adrenoreceptors, and these effects result in increased gastric and small intestinal motility and decrease the severity of postoperative ileus.[153] The recommended dosage regimen for metoclopramide is a continuous-rate infusion of 0.4 mg/kg/hour.[154]

Nutritional Support

The basic goal of nutritional supplementation is to prevent the development of a negative energy balance in patients unable to meet their nutritional needs through voluntary intake. Determining the patient's metabolic requirements is complicated by the fact that critical illness has been considered to result in an increased metabolic rate, but this effect appears to be inconsistent in human patients and has not been well documented in the horse. The presence of systemic inflammation induces protein catabolism, which, in combination with physical inactivity, leads to the loss of muscle mass regardless of the patient's overall energy balance.[155-157] The degree of protein catabolism is certainly heightened, however, in the presence of a negative

energy balance. In addition to protein catabolism, the presence of a negative energy balance can lead to excessive mobilization of the animal's fat stores, leading in some cases to hypertriglyceridemia. This latter response can be associated with additional decreases in voluntary intake of feed and secondary complications such as hepatic lipidosis and azotemia.[158]

Horses should ideally have free-choice access to roughage as well as supplemental feeding with concentrates to meet at least their maintenance metabolic energy requirements (roughly 16 Mcal for a 500-kg horse).[157] Unfortunately, equine patients with proximal enteritis are unable to ingest feed because of the inherent small-intestinal dysfunction associated with this condition. Horses suffering from colitis can often be allowed to ingest feed, as long as substantial ileus is not associated with their condition. Some horses with colitis may be anorectic because of the depression and discomfort associated with their illness, impairing their ability to meet their metabolic needs through voluntary intake. Most adult horses can reasonably be maintained without nutritional support for several days, as they will mobilize their endogenous energy reserves (fat, muscle) to meet their metabolic needs. Some horses and ponies appear predisposed to excessive fat mobilization, however, and they should not be maintained without nutritional support because of the risks of hypertriglyceridemia and hyperlipemia.

Enteral nutritional support can be accomplished by the administration of liquid diets via repeated nasogastric intubation or an indwelling nasogastric feeding tube. Commercial liquid diet formulations are available, with products designed for either horses or humans. The use of commercial liquid-enteral diets may be associated with the development of diarrhea and laminitis in the horse, and they must be introduced slowly over as much as 7 days to minimize the development of gastrointestinal disturbances.[157] This type of therapy is obviously not ideal for use in horses with inflammatory gastrointestinal diseases, because it may exacerbate the existing disease process. The alternative approach to enteral support is the feeding of slurries made according to proprietary formulations[159] or from commercial feedstuffs such as Equine Senior (Purina Mills, St. Louis, MO).[157] These diets must also be introduced slowly, and this represents a significant limitation in acutely ill horses as adequate energy may not be delivered in a timely manner.

More rapid delivery of nutrition can be accomplished using the parenteral route. This route is the only one available in horses with small-intestinal dysfunction (see Chapter 23). Parenteral nutrition can be characterized as partial or complete, based on whether or not it meets the animal's entire nutritional needs. Total parenteral nutrition requires the use of both carbohydrate and lipid sources of energy, in combination with amino acids. Partial parenteral nutrition can be accomplished with carbohydrate or carbohydrate/amino acid solutions. Supplementation of the intravenous fluids with dextrose at a moderate rate of 5 to 10 Kcal/kg/day (1.5 to 3 L of 50% dextrose per day) appears to be beneficial in clinically ill horses with decreased or absent appetite, as the dextrose minimizes the degree of fat mobilization secondary to a negative energy balance, and has been shown to correct hypertriglyceridemia.[157,158]

Specific Therapies

Antimicrobial Therapy

The role of antimicrobial therapy in the treatment of equine enteritis and colitis is controversial, as for many of these conditions the etiologic agent is not definitively known or is not bacterial. Often antimicrobial therapy is used in patients suffering from gastrointestinal disease resulting in fever and leukopenia, which may indicate the presence of bacterial infection or may result from the effects of bacterial toxins such as endotoxin. There are additional concerns that severe gastrointestinal disease may be associated with impairment of the barrier function of the gastrointestinal mucosa, resulting in an increased risk of bacterial translocation and leading to localized infection or septicemia and infections distant to the intestine (pneumonia, endocarditis, meningitis, etc.). The efficacy of systemic antimicrobial therapy in the prevention of bacterial translocation in gastrointestinal disease has not been established.[160]

The administration of antimicrobials carries the risk of antimicrobial-associated enterocolitis in the horse, secondary to alterations in the gastrointestinal microflora. In addition, the indiscriminate use of antimicrobial drugs increases the risk of development of microbial resistance to the drugs, with ramifications both for the individual patient and for the hospital population, as well as for the human population. For these reasons, the indiscriminate use of antimicrobials should be avoided in equine patients. Antimicrobial therapy is not controversial, however, in cases where the suspected etiologic agent is potentially susceptible to antimicrobials. Clostridial enterocolitis, equine monocytic ehrlichiosis, proliferative enteropathy, and possibly salmonellosis are disease processes in which antimicrobial therapy is indicated.

Specific Antimicrobials

Beta-lactams

The beta-lactams include the penicillins, synthetic penicillins, and cephalosporins. Modifications of the basic penicillin or cephalosporin molecule confer differences in antimicrobial activity, as seen with the synthetic penicillins and third-generation cephalosporins, which have a wider gram-negative spectrum. Increased stability against beta-lactamases may also be achieved. The beta-lactam drugs must be present in the tissues at concentrations exceeding the minimum inhibitory concentration (MIC) throughout the entire dosage interval in order to be effective, rendering them "time-dependent" antimicrobials. Penicillin G is the prototypical beta-lactam drug, and is the most widely used antimicrobial in equine medicine. Penicillin G is administered to the horse at a dosage of 20,000 to 60,000 IU/kg, with the procaine suspension being administered IM every 12 hours and the aqueous solutions of Na and K penicillin being administered IV every 6 hours. Toxicity is low for the penicillins, and is mostly due to reactions to intravenous or intra-arterial injection of the procaine form, although anaphylactic reactions have been reported.[161,162] Penicillins are often combined with beta-lactamase inhibitors, such as clavulanic acid, which are believed to protect the penicillin from breakdown by the beta-lactamases by serving as an alternative substrate, but may also serve to increase production of these enzymes. Ampicillin, amoxicillin, and ticarcillin are synthetic penicillins that have been used in the horse, with ampicillin being the most commonly used of the three. The primary cephalosporin administered to horses is ceftiofur, a third-generation drug. Ceftiofur is considered to have a broad spectrum, with the emphasis on gram-negative coverage. It is usually administered at 2.2 to 4.4 mg/kg IM or IV every 12 hours. There are reports of severe colitis associated with ceftiofur administration, but the incidence of this complication appears to be low and ceftiofur remains widely used in equine medicine.[163]

Aminoglycosides

The aminoglycosides are a mainstay in the treatment of gram-negative infections in the horse, due to their rapid bactericidal effects, clinical efficacy, relatively low resistance rates, and synergism with beta-lactam antimicrobials. Aminoglycosides are classified as concentration-dependent antimicrobials because they exhibit peak concentration-dependent bactericidal activity and post-antibiotic effects against susceptible organisms. High peak concentrations of aminoglycosides produce more rapid and extensive bacterial killing than do lower concentrations.[164] High peak concentrations of aminoglycosides (greater than 8 to 10 times the minimum inhibitory concentration) have also been shown to decrease the emergence of resistant strains.[164] Aminoglycosides are typically utilized in an extended-interval dosing regimen, wherein a single large bolus dose is given once every 24 hours. The most commonly used aminoglycoside in the adult horse is gentamicin; the dosage for extended-interval dosing is 6.6 mg/kg intravenously or intramuscularly once daily.[165] Although aminoglycosides are important drugs for the treatment of many equine conditions, these drugs have a low therapeutic index, wherein little difference exists between a therapeutic and a toxic dose, and the toxic potential consists primarily of nephrotoxicity. Toxicity is minimized by the use of extended-interval dosing regimens, but can still occur in patients with decreased renal function. For this reason, therapeutic drug monitoring is recommended in critically ill equines receiving aminoglycosides, to ensure that accumulation of the drug is not occurring and to decrease the risk of toxicity. This monitoring is readily performed by measuring the serum aminoglycoside concentration at 30 minutes and 8 hours after the dose is administered, with the expected concentrations for gentamicin in the adult horse being 25 to 30 μg/mL at 30 minutes and below 4 to 5 μg/mL at 8 hours.

Tetracyclines

Tetracyclines are bacteriostatic and broad spectrum, possessing activity against a wide variety of bacteria and protozoa, as well as rickettsial organisms. These compounds are time-dependent, requiring that concentrations at the site of infection remain at or above the minimum inhibitory concentration for the duration of the treatment interval. The primary indication for tetracycline therapy in equine gastrointestinal disease is for the treatment of equine monocytic ehrlichiosis; the most commonly used compounds are oxytetracycline and doxycycline. Toxicity of the tetracyclines is most often associated with disturbance of gastrointestinal flora associated with the development of colitis. Because oxytetracycline is primarily eliminated via the urinary tract, animals with renal insufficiency are at risk for toxicity from this drug.[166] Rapid intravenous injection of oxytetracycline is associated with collapse in horses, perhaps as a result of chelation of calcium in the blood. Oxytetracycline is administered to horses at 4 to 8 mg/kg slowly IV once or twice daily, usually diluted in 0.5 to 1 L of normal saline and administered over 30 minutes. Doxycycline is administered at 10 mg/kg orally twice daily.[167] It has not been reported to be associated with colitis at this dose. Doxycycline should never be given intravenously, as it is fatal to horses by that route.[168]

Chloramphenicol

Chloramphenicol is highly lipophilic, is widely distributed to the tissues, and reaches high intracellular concentrations. Chloramphenicol has a wide spectrum of action, including gram-positive and -negative bacteria, as well as rickettsia and anaerobes. The use of chloramphenicol in horses with enterocolitis is primarily directed at clostridial organisms, but some *Salmonella* isolates are sensitive to this drug as well. Chloramphenicol is a time-dependent drug, and because of its short half life in horses, it must be administered frequently to maintain adequate tissue concentrations. It is administered to horses at 50 mg/kg orally every 6 hours.[169] Chloramphenicol toxicity is rare, but when it occurs, it is associated with reversible bone marrow suppression or irreversible aplastic anemia. Recent re-evaluation of the association between chloramphenicol administration and the development of aplastic anemia in humans has suggested that the incidence of this complication is extremely low (1 in 3 million to 1 in 20 million).[170-172] Despite this evidence, chloramphenicol may not be used in food animals,[173] and thorough client education is indicated when dispensing this drug. Clients should be advised to avoid exposure to the drug by inhalation or through contact with mucous membranes. Florfenicol should never be administered to horses, as it is associated with fatal reactions.

Fluoroquinolones

Fluoroquinolones have a relatively broad spectrum, with excellent activity against gram-negative organisms. Fluoroquinolones are bactericidal, and achieve higher concentrations in the tissues than in the serum. The fluoroquinolones are concentration-dependent antimicrobials, having peak concentration-dependent bactericidal effects and prolonged post-antibiotic effects similar to those of aminoglycosides. As a result, the fluoroquinolones can be given at relatively high doses at a decreased frequency. Toxicity is primarily manifested through adverse effects on cartilage maturation, resulting in a contraindication to their use in growing animals.[174,175] Enrofloxacin is the most commonly used fluoroquinolone in the horse, although similar compounds, such as orbifloxacin and marbofloxacin, have been used. Enrofloxacin is administered at 2.5 to 7.5 mg/kg orally or IV, with some clinicians preferring lower doses (3-4 mg/kg) given twice daily or higher doses (5-7.5 mg/kg) for once daily administration.[176,177] The fluoroquinolones are primarily indicated in horses with enterocolitis caused by salmonellosis, as their high intracellular concentrations may lead to greater efficacy against this intracellular pathogen.

Metronidazole

Metronidazole demonstrates selective toxicity against anaerobic bacteria and microaerophilic organisms due to its ability to induce an oxidative state within the normally reductive intracellular environment of these organisms. Metronidazole is administered in an inactive form, but after entering the target organism, it is reduced to reactive intermediates that interact with and damage cellular components, resulting in cytotoxicity. Metronidazole is effective against most anaerobes of veterinary importance, with the clostridial organisms being of greatest concern in enterocolitis. Metronidazole is effective against most clostridial strains identified from horses with enterocolitis, but resistant strains have been reported.[178] Metronidazole is administered at a rate of 15 to 25 mg/kg orally or per rectum every 6 to 8 hours; it may be administered per rectum (15 mg/kg) or intravenously (15 mg/kg) in horses with enterogastric reflux.[179-182] The cost of the intravenous form is typically prohibitive in mature horses. This drug will occasionally cause inappetance at higher dosage rates, which resolves with discontinuation of therapy.

Probiotics/Prebiotics

Restoration of the microbial flora of the gastrointestinal tract has been shown in many species to aid in the resolution of colitis. This is most readily accomplished by the administration of live beneficial enteric organisms. These organisms are termed probiotics, which have been defined as live microbial feed supplements that are beneficial to health.[183] A more recent, broader concept is that of "biotherapeutic agents," which have been defined as living microorganisms used either to prevent or to treat diseases by interacting with the natural microecology of the host.[184] Much of the research regarding probiotics has been performed in other species, and the types of organisms used in equine probiotics are generally the same as have been administered to humans. As a result, it is not clear that the organisms present in many equine probiotics *(Lactobacillus, Bifidobacterium, Enterococcus)* are necessarily the most relevant to the equine gastrointestinal flora. The fact that probiotics are marketed as feed supplements also means that there is no requirement regarding the demonstration of efficacy of these products; therefore, any label claims of efficacy should be viewed with caution. This concern is reinforced by the disappointing results of the few trials that have examined the effects of probiotics in equine salmonellosis.[185,186] Further work is clearly required to better define the types of organisms most likely to be beneficial in equine gastrointestinal disorders.

Interest in this area has focused on the administration of beneficial yeasts to horses with colitis, based on the promising reports regarding this type of therapy in humans with clostridial diarrhea.[187,188] The organism with the most apparent promise is *Saccharomyces boulardii*, which has been demonstrated to produce a protease that exerts a proteolytic activity against

the *C. difficile* toxin B molecule. *S. boulardii* also impairs the ability of *C. difficile* toxins A and B to bind to the intestinal mucosa and inhibits the pathogenic effect of both toxins on colonic epithelial cells.[189] Additional protective benefits of *S. boulardii* have been demonstrated in animal studies with *Salmonella typhimurium* and enteropathogenic *E. coli*, although the mechanisms responsible for these effects are not well defined.[189] The safety profile of *S. boulardii* therapy in humans is very good, with the only concern being rare reports of *S. boulardii* fungemia in immunocompromised patients.[190,191] For this reason, *S. boulardii* should not be administered to equine patients with severe neutropenia. The author's clinical experience using S. *boulardii* at the rate of 15 capsules orally every 6 to 8 hours has been promising, but no published studies have defined an appropriate dosage regimen or supported the use of this therapy in the horse.

An alternative means of restoring the normal gastrointestinal flora is the provision of nondigestible oligosaccharides as a "prebiotic." The concept behind prebiotics is that an insoluble fiber that selects for, and stimulates the growth of, beneficial microorganisms in the large intestine can change the microflora to a healthy composition and exert beneficial effects on the host.[192] The substance most studied as a prebiotic is germinated barley feedstuff, which is generated by the brewing industry as a by-product of the brewing process. Germinated barley feedstuff has been shown to have anti-inflammatory effects in animal models of colitis, with one study reporting decreased gastrointestinal and systemic inflammation as well as decreased mucosal injury in association with increased levels of the beneficial short-chain fatty acid butyrate.[193] A similar study demonstrated a superior effect of germinated barley feedstuff, similar to the beneficial effect associated with vancomycin or metronidazole administration, as compared with a probiotic consisting of *Lactobacillus* and *Cl. butyricum* organisms that had no demonstrable effect.[194] Dried germinated barley feedstuff is widely used in dairy cattle feeds and is a component of some commercial horse feeds. Germinated barley feedstuff appears to be a safe feed supplement, although no reports are available regarding germinated barley feedstuff feeding in the horse. The author has utilized fresh and frozen germinated barley feedstuff in horses with colitis at an empirical dosage rate of 0.2 to 0.45 kg 3 to 4 times daily, with variable clinical results. Further work is required to determine the efficacy of this treatment in equine enterocolitis and to identify the most appropriate dosage of germinated barley feedstuff for feeding to horses with diarrhea.

Gastrointestinal Protectants and Adsorbents

An additional means of limiting gastrointestinal inflammation is the administration by the enteral route of products that may exert anti-inflammatory effects on the mucosa or that impair the activity of the enteric pathogens or their toxins.[195] Bismuth subsalicylate has been used as an agent to protect the gastrointestinal mucosa and decrease mucosal inflammation, but there is not much evidence that it has a significant effect in secretory diarrhea in any species.[196,197] This compound has been reported to stimulate intestinal absorption of sodium and water and to have anti-inflammatory and antibacterial effects, including direct binding of bacterial toxins.[196] Bismuth subsalicylate is widely regarded as a safe over-the-counter antidiarrheal, but there are reports of toxicity associated with overdosage in humans.[198,199] Recommended dosages range from 0.5 to 0.45 kg every 4 to 6 hours.[195]

Recent work has examined the possible application of the adsorptive substance di-tri-octahedral smectite (DTO smectite; Biosponge™, Platinum Performance, Los Olivos, CA) in enterocolitis. This product and the related dioctohedral smectite, have been shown to bind *Cl. difficile* toxins A and B, and *Cl. perfringens* enterotoxins in vitro.[200,201] A small study reported that outcome was substantially improved in clostridial enterocolitis with the use of DTO smectite.[202] The recommended dosage is 1.4 Kg of powder in water via nasogastric tube, followed by 0.45 Kg every 4 to 6 hours.

Surgery

Abdominal exploratory surgery is not required in most cases of enteritis and colitis, but there are cases where it may be indicated. The most common indication for surgical exploration is persistent severe abdominal pain (colic). Most horses with enteritis and colitis do not exhibit severe colic signs, and those that do show discomfort often cease to have pain after resolution of gastrointestinal distention secondary to gastric decompression (e.g., in horses with proximal enteritis) or the onset of diarrhea. The persistence of severe pain is a strong indication that the animal may be suffering from a more severe condition that may require surgical correction. Additional diagnostic information may be provided from rectal examination and abdominal ultrasonography, as malpositioning or severe distention of the gastrointestinal viscera is suggestive of more than an inflammatory enteritis or colitis. Early reports indicated that outcome was worsened for patients with proximal enteritis undergoing abdominal exploratory surgery.[2] Although this may have been true, one must consider that some bias may have been involved, as only the more severely affected horses were likely to undergo surgery. Later experience suggested that surgical exploration is not associated with worsened outcome,[5] and it appears clinically that some horses with proximal enteritis may benefit from surgical decompression, with shortened duration of enterogastric reflux and discomfort.

Specific Diseases

Duodenitis-Proximal Jejunitis (Anterior Enteritis)

As no specific etiologic agent has been identified in this disease syndrome, no specific therapy can be prescribed. Aggressive supportive therapy is indicated, consisting of ongoing gastric decompression, intravenous fluids, anti-inflammatory drugs, and analgesics. The volume of fluid lost in the form of reflux can be large, with up to 8 to16 liters being lost every 2 hours in severe cases, and enterogastric reflux can persist for as long as 5 to 7 days. It can be difficult to administer intravenous fluids rapidly enough to correct the initial dehydration and replace ongoing losses in these severely affected individuals. In such instances, the use of large-bore (10 or 12 gauge) intravenous catheters and administration sets aids in delivering adequate amounts of fluids rapidly. The use of colloids in severely affected horses may aid in rapid volume expansion as well as the retention of fluid within the vasculature. Additional therapies may include antimicrobials, surgical bypass procedures, prokinetic therapy, and parenteral nutrition. The efficacy of antimicrobial therapy in this condition is unclear, as no specific bacterial pathogen has been associated with this disease syndrome. Nevertheless, many horses with proximal enteritis receive antimicrobials because of the potential for compromised gastrointestinal mucosal barrier and the risk of bacterial translocation from the gastrointestinal lumen to the bloodstream. Many of these patients are febrile and/or have an increased total peripheral white blood cell count; these abnormalities can represent additional indications for antimicrobial therapy. The choice of antimicrobials is empiric at best, and the most important concern is the avoidance of secondary toxicities arising from the antimicrobials themselves, such as aminoglycoside nephrotoxicity or fluoroquinolone-associated cartilage injury (in growing animals). Severely affected animals that are poorly responsive to medical therapy should undergo surgical explorartion to rule out strangulation-obstruction or other surgical lesions. Bypass procedures can be used in proximal enteritis to allow for the accumulated fluid to drain from the stomach and proximal small intestine into the distal small intestine or cecum; these include gastroduodenostomy and duodenocecostomy.[3, 203] If selected, the created stoma should be made by suturing the seromuscular layer so closure by healing occurs within a few days to weeks.

Salmonellosis

The treatment of equine salmonellosis is primarily supportive. Intravenous fluid therapy is usually required because of the severe fluid losses associated with the profuse diarrhea that occurs in many of these horses. Colloid therapy may be required as well for the systemic hypotension and enteric protein loss secondary to severe gastrointestinal inflammation. Anti-inflammatory therapy primarily consists of flunixin meglumine, although the concurrent administration of polymyxin B may be of benefit because of the possibility of endotoxemia in these patients. Severely affected horses are often inappetant and require nutritional support. The use of gastrointestinal protectants is not well investigated in equine salmonellosis, and their use is not strongly indicated in these patients. Probiotic therapy has proven to have little or no efficacy in the prevention of *Salmonella* shedding in hospitalized equine patients.[185,186,204] Although *S. boulardii* has been reported to have beneficial effects in an animal model of salmonellosis, this has not yet been investigated in the horse.[189]

Antimicrobial therapy is controversial in equine salmonellosis, and many clinicians elect not to utilize antimicrobials in these cases, because of concerns regarding lack of efficacy and the development of antimicrobial resistance. Antimicrobial resistance is common in the *Salmonella* organisms associated with enterocolitis, especially to the beta-lactams, tetracylines, trimethoprim, and the sulfa drugs.[11,205] The intracellular localization of salmonella organisms limits their susceptibility to antimicrobials that fail to penetrate the cell wall, such as the aminoglycosides. In vivo susceptibility is increased to those antimicrobials that are able to reach therapeutic levels intracellularly, such as the fluoroquinolones and chloramphenicol, and these drugs are widely used in humans with salmonellosis.[206] Cephalosporins are also frequently used in humans with salmonellosis, and the third-generation cephalosporin ceftiofur has been reported to be effective in the treatment of calves with salmonellosis.[207] Many equine and domestic animal isolates are reported to be sensitive to ceftiofur and the fluoroquinolones, with slightly higher rates of resistance to chloramphenicol.[11,208] In the author's opinion, the treatment with appropriate antimicrobials of equine patients suffering from salmonellosis is reasonable, despite the concerns regarding this practice, as it may result in an improved chance of survival. Given the presence of multiresistant strains of *Salmonella*, it is important to determine the antimicrobial sensitivity pattern of any equine isolates and utilize this as a guide to ongoing therapy in the individual patient or concurrently affected individuals.

Clostridial Enterocolitis

Supportive therapy with intravenous fluids to correct fluid deficits and replace ongoing fluid losses is often required in equine clostridial enterocolitis. Colloid therapy may also be indicated in more severely affected horses, because of the loss of circulating protein into the gastrointestinal lumen secondary to severe intestinal inflammation. Additional supportive therapy with anti-inflammatory drugs is generally indicated, with flunixin meglumine being the most commonly utilized therapy of this

type. The rationale for using anti-inflammatory drugs is to modulate intestinal inflammation as well as the systemic response to possible endotoxin exposure via the inflamed gastrointestinal mucosa. Polymyxin B may also be a useful therapy in equine clostridiosis due to the potential for endotoxin exposure. The use of *S. boulardii* appears rational because of its reported ability to interfere with the activity of the clostridial toxins and inhibit the binding of clostridial organisms to the gastrointestinal mucosa. Feeding of germinated barley feedstuff as a prebiotic also appears reasonable in an effort to aid in the restoration of the normal gastrointestinal flora and increase the production of beneficial short-chain fatty acids. Most horses with clostridial enterocolitis will continue to eat, and should be provided free-choice hay, but nutritional support may be required in cases where the patient is inappetant. If required, nutritional support may be best delivered parenterally because of the risks associated with enteral feeding of liquid diets.

Specific therapy with antimicrobials is clearly indicated in cases of clostridial enterocolitis, despite the fact that this condition may arise secondary to antimicrobial therapy. Metronidazole is the most widely used antimicrobial in clostridial enterocolitis, as it is broadly effective against clostridial organisms and has few side effects in horses. Because of the possibility of metronidazole resistance, however, other antimicrobials should be considered as primary or adjunctive therapies in horses with a poor response to metronidazole therapy. These drugs include vancomycin and chloramphenicol. Vancomycin is widely used in human medicine for the treatment of clostridial diarrhea, but is rarely used in the horse because of the potential for further alteration of the gastrointestinal flora and the desire to limit the development of resistant strains of bacteria. Chloramphenicol is rarely used in horses because of concerns regarding human exposure, but the author has found it to be a useful drug in equine clostridial enterocolitis cases that are poorly responsive to metronidazole therapy. DTO Smectite has been reported to be effective in the treatment of equine clostridial enterocolitis, and is safe and easy to use, making it a reasonable adjunctive therapy.[202] Germinated barley feedstuff and *S. boulardii* are also potentially beneficial in equine clostridial enterocolitis in decreasing the degree of mucosal inflammation and helping to restore normal function.

Equine Monocytic Ehrlichiosis

Because of the potentially fulminant nature of this disease, aggressive supportive therapy with intravenous fluids is often required. Colloids are also indicated in patients with signs of shock or enteric protein loss. Anti-inflammatory therapy typically consists of flunixin meglumine. *Neorickettsia risticii* is highly sensitive to the tetracyclines, and these drugs are the treatment of choice in this disease. The most widely utilized tetracycline for treatment of this disease is oxytetracycline, typically used at 4 to 8 mg/kg intravenously once or twice daily; this treatment is generally efficacious.[209-211] Doxycycline is reported to be the drug of choice for the treatment of ehrlichial diseases in humans and small animals.[212] There are no studies reporting the efficacy of doxycycline in equine monocytic ehrlichiosis, although efficacy has been demonstrated in a murine model of this disease.[213] Doxycycline has recently come into regular use in horses, at a dosage of 10 mg/kg orally every 12 hours.[167] Doxycycline has been used for the treatment of affected horses by the author and others with anecdotally reported efficacy.

Fatal outcomes associated with equine monocytic ehrlichiosis are often a result of secondary complications, especially laminitis, as the colitis usually resolves with tetracycline therapy. Prevention of these complications is difficult after the development of equine monocytic ehrlichiosis. Therefore, the prevention of complications is best achieved by prevention of clinical disease. The prevention of equine monocytic ehrlichiosis is challenging, however, as the only vaccines available are killed bacterins, which do not induce a consistent or entirely protective immune response.[214] These vaccines also contain only a single strain of the organism, even though several pathogenic strains have been identified.[214] It is widely believed that vaccination, while not entirely protective, does lessen the severity of clinical illness associated with infection and may decrease the incidence of secondary complications such as laminitis, although one report suggests that this is not the case.[215] Recent characterization of *N. risticii* antigens may allow for the development of vaccines that provide cross-strain protection.[216,217]

Viral Enterocolitis

Rotaviral enterocolitis is ultimately self-limiting in most cases, and treatment is fundamentally supportive as there is no specific treatment targeting the etiologic agent. Enteral rest of 24- to 72-hours' duration can be useful, as the damage to the intestinal microvilli impairs the foal's ability to digest lactose in milk. Provision of enteral rest requires that the foal be provided with fluids and nutrition intravenously; this may be accomplished by separating the mare and foal by placement of a barrier within the stall or the use of a stall with a separate area provided for confining the foal. If the foal is to be left with the mare, then a muzzle must be placed on the foal to prevent nursing. The provision of fluid therapy to foals that are housed with their mares is challenging, but this can be facilitated in some cases by use of a "backpack" device that can be placed on the foal and that will deliver up to 250 mL of fluid per hour (IV Backpack, MILA International, Inc., Erlanger, KY). If enteral rest is not possible, then the foal can be administered lactase enzyme orally (Lactaid, McNeil Nutritionals, McNeil-PPC, Inc., Ft.

Washington, PA) at the rate of 1 to 2 tablets (3,000 to 6,000 FCC Units lactase) every 2 to 6 hours to aid in digestion of the ingested lactose. There is no indication for antimicrobial therapy in this condition, and anti-inflammatory therapy is rarely needed or indicated.

Intestinal Parasitism

As the primary intestinal parasites of current concern in equine enterocolitis are cyathostomes, treatment protocols should be targeted toward these organisms.[218] Treatment of cyathostomiasis is complicated by the difficulty associated with killing of the encysted hypobiotic stages (L3, L4) of these organisms.[219] Fenbendazole (7.5 mg/kg PO once daily for 5 days) and moxidectin (0.4 mg/kg PO once) have been demonstrated to have a moderate to high degree of efficacy in the elimination of encysted cyathostomes, while ivermectin is ineffective.[219,220] The 5-day course of fenbendazole therapy is commonly used in the treatment of equine cyathostomiasis, and appears to be clinically effective, although moxidectin may have greater efficacy. Because of the possibility of increased intestinal inflammation associated with the death of encysted small strongyles after anthelmintic administration, some clinicians treat the patient concurrently with corticosteroids, using either dexamethasone or prednisolone.[221] More severely affected animals may develop profuse watery diarrhea and protein-losing enteropathy, and may require intravenous fluid therapy including colloid administration.

Protozoal Enterocolitis

The treatment of cryptosporidial infections is entirely supportive as no specific therapies are available. Fortunately, this disease is ultimately self-limiting, although fatalities may occur secondary to dehydration and electrolyte derangements resulting from severe diarrhea. The profuse nature of the diarrhea in some animals may require aggressive intravenous fluid therapy, including colloid therapy. Enteral rest is typically indicated, as this may be useful in decreasing the volume of diarrhea by decreasing the osmotic load within the intestinal lumen. Nutritional support with partial parenteral nutrition is required in horses placed on enteral rest. Care should be taken in handling these horses, with strict isolation procedures maintained, as the organism is infectious and zoonotic.[222]

Proliferative Enteritis

The typical presentation of animals with proliferative enteritis is one of unthriftiness, weight loss, hypoproteinemia, and peripheral edema. Diarrhea is not always present, and aggressive therapy is usually not indicated. Fluid imbalances and electrolyte disturbances may be present, but rapid administration of intravenous fluids will only cause hemodilution and exacerbation of the hypoproteinemia. The use of enteral fluids may not be appropriate, as the small-intestinal dysfunction associated with this disease may impair fluid absorption. Conservative intravenous therapy is typically the most appropriate approach. The use of colloids is indicated in most cases of proliferative enteritis to restore colloid oncotic pressure and to aid in resolution of peripheral edema. Administration of hetastarch at a dosage of 5 to 10 mL/kg provides rapid colloidal effects and may slow the loss of intravascular protein. Equine plasma may be used as the sole colloid, at a dosage of 12 to 16 mL/kg, or may be used following hetastarch administration at a dosage of 8 to 12 mL/kg. Plasma therapy provides both albumin, for colloid effects, and globulins and other plasma constituents that may have been lost. Repeated doses of colloids may be required, as healing of the intestine may be gradual, resulting in ongoing losses of plasma protein.

As proliferative enteritis from infection with *Lawsonia intracellularis* is a significant disease in swine, but is only rarely reported in horses, much of the knowledge regarding treatment of this disease is derived from experience with swine. One of the primary drugs used for control and eradication of proliferative enteritis in swine is tylosin (a macrolide), however, this drug is not used in the horse. Alternative macrolides have been used for the treatment of equine proliferative enteritis, primarily consisting of erythromycin, which is often combined with rifampin.[223-225] It is not clear that rifampin is required for the treatment of proliferative enteritis, given that tylosin alone is effective in swine, and erythromycin may be used alone. The most commonly used forms of erythromycin are the estolate and phosphate esters, and these are typically administered at 25 mg/kg orally every 8 to 12 hours, while rifampin is dosed at 10 mg/kg orally every 24 hours, divided into 1 or 2 doses.[212] Another widely used compound for the treatment of porcine proliferative enteritis is chlortetracycline, which is reported to have good efficacy with minimal resistance.[226,227] Based on this information, the author and others have used doxycycline (10 mg/kg PO every 12 hours) in the treatment of equine proliferative enteritis with apparent clinical efficacy. Although there are no studies reporting the sensitivity of *L. intracellularis* to chloramphenicol, this drug has been used in the treatment of equine proliferative enteritis based upon its potential intracellular penetration and broad spectrum of action.[212]

NSAID-Associated Right Dorsal Colitis

As horses with NSAID-associated right dorsal colitis can present with variable degrees of severity of disease, the aggressiveness of therapy required can vary widely. The most fundamental aspect of treatment is the cessation of NSAID therapy, to avoid further toxicity. This can be a major dilemma, as the initial problem requiring NSAID treatment is often unresolved, and withdrawal of the drug may result in increased patient discomfort. The provision of analgesia by other means is indicated, if possible, and the opioids are useful drugs in this setting. The author has used fentanyl administered by use of a transdermal patch delivery system in these patients with good results. Fentanyl is particularly convenient as the patches only need to be replaced every 36 to 48 hours, although care must be taken in handling this schedule II narcotic. An alternative to fentanyl is butorphanol, administered as intermittent boluses or as a continuous-rate infusion.

Additional therapy of horses with right dorsal colitis may include intravenous fluids to correct fluid deficits and provide maintenance support, and the use of colloids to attempt to correct the profound hypoproteinemia that can occur in this condition. Sucralfate (20 to 40 mg/kg orally every 6 to 8 hours) has been used clinically in an attempt to facilitate healing of the colonic mucosa, but there is no evidence of efficacy for this treatment. The use of synthetic analogues of prostaglandin E_1 has been advocated for the treatment of this condition, as it may be able to restore mucosal blood flow and aid in the healing of the ulcerated mucosa.[228] Unfortunately, the most common side effects of this drug are colic and diarrhea, which limit its use in horses already suffering from these problems. The most useful medical management in many of these cases, especially the more chronic ones, is dietary management. This consists of the avoidance of long-stem roughage that may further irritate the colonic mucosa, and its replacement with a complete pelleted diet.[229] Supplementation of the diet with vegetable oil (corn, canola, or safflower) has been proposed as a means of providing additional calories and linoleic acid to aid in mucosal healing.[157] Provision of nondigestible oligosaccharides may enhance the production of beneficial short-chain fatty acids that can aid in mucosal healing, and GBF or psyllium may be used to achieve this effect.[157,193] Because of the often unrewarding response to medical therapy, however, surgical resection of the affected region of the colon may be indicated.[230]

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Nonsurgical Management of Nephrosplenic Entrapment of the Large Colon

Chapter 21

Joanne Hardy

Nephrosplenic entrapment (also termed renosplenic entrapment or left dorsal displacement of the large colon) is a form of nonstrangulating large colon displacement in the horse, wherein the left dorsal and ventral colons migrate lateral to the spleen in a dorsal direction to become entrapped in the nephrosplenic space (Figures 21-1A and 21-1B). This condition has been reported in horses of any age, and as young as 9 months.[1] Although one report mentions an increased prevalence in male horses, others have not substantiated that finding.[1-3] The condition has not been reported to occur in miniature horses and pony breeds. It is theorized that excessive gas formation within the left colon, perhaps in association with abnormal motility, causes the left colons to displace lateral to the spleen and dorsally into the nephrosplenic space or to migrate between the stomach and spleen into the renoplenic space. Alternatively, the colon may displace during rolling episodes.[4-7] In most cases, ventro-medial rotation of the left colons also occurs, such that the left dorsal colon is positioned ventral to the left ventral colon (Figure 21-1). The weight of the colon causes the spleen to displace medially and ventrally, and to become congested. Because of impaired flow of ingesta over time, with duration concurrent impaction of the left dorsal colon also occurs (Figure 21-2). With continued gas formation, the sternal and diaphragmatic flexures can migrate cranial and dorsal to the stomach between the stomach and the left liver lobe,[8,9] Nephrosplenic entrapment is a nonstrangulating lesion of the large colon; however, when duration of the condition exceeds 24 hours, colonic congestion and edema can develop, and mural damage can follow.[4] Obstruction to gastric outflow occurs because of pressure of the colon on the duodenum, or tension on the mesentery. Entrapment of the small colon or small intestine in the nephrosplenic space has been described, but these conditions are rare.[10,11] In rare cases, the pelvic flexure courses through a rent in the renosplenic ligament. This can strangulate the entrapped bowel and is not easily relieved at surgery (Figure 21-3).

Figure 21-1A

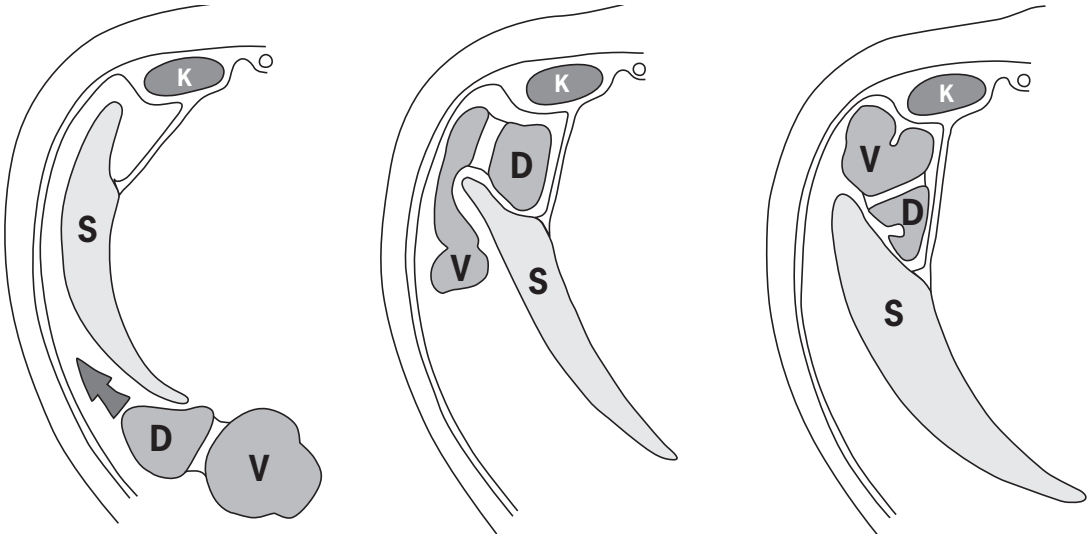
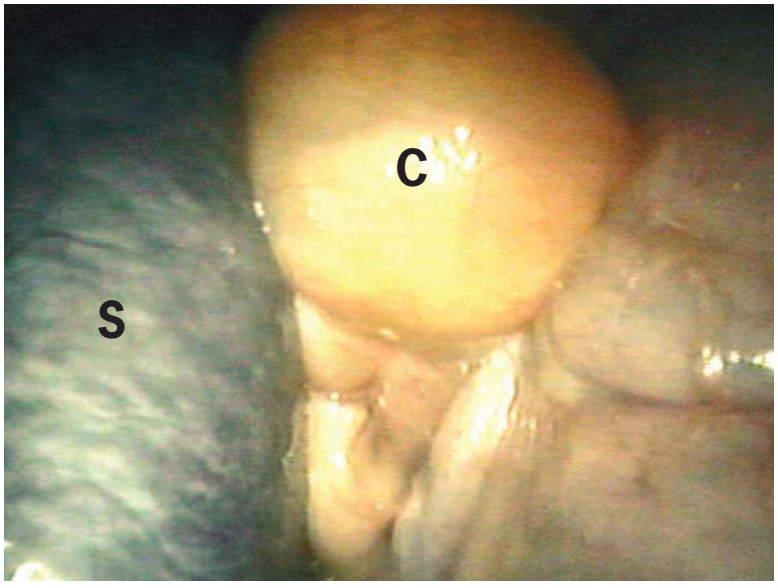


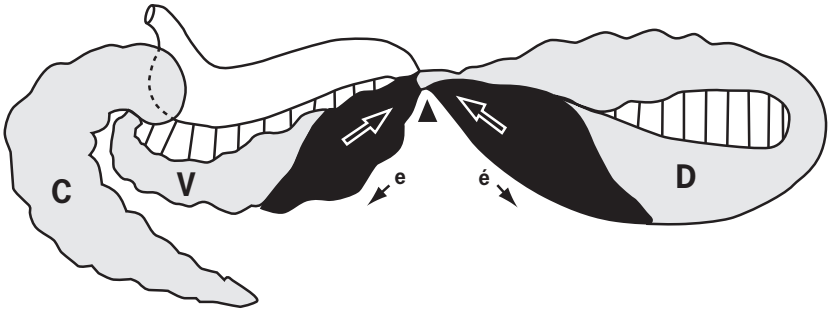
Illustration of the proposed pathogenesis of left dorsal displacement of the large colon into the nephrosplenic space. S: Spleen; K: Kidney; D: Dorsal part of the large colon; V: Ventral part of the large colon. (From: Current Therapy in Equine Medicine, 2nd ed. Robinson NE (ed). Philadelphia: WB Saunders, 1987, p. 62.)

Figure 21-1B



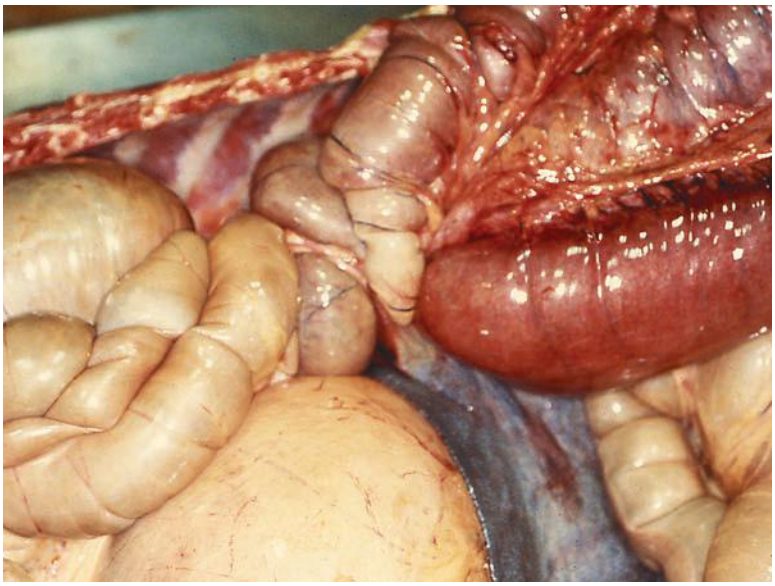
Laparoscopic appearance of a left dorsal displacement of the large colon in a horse. S: Spleen; C: Colon.

Figure 21-2



Accumulation of ingesta that occurs during left dorsal displacement of the large colon. The prestenotic area in the ventral colon and dorsal colon are impacted. Gas accumulation is proximal to the two impactions is. C: Cecum; V: Ventral part of the large colon; D: Dorsal part of the large colon. The black arrows show the direction of peristalsis. The e and é arrows show the effects of peristalsis on the intestinal tube. From Current Therapy in Equine Medicine, 2nd ed. Robinson NE (ed). Philadelphia: WB Saunders, 1987, p. 61.)

Figure 21-3



The pelvic flexure of the large colon is incarcerated in a rent in the renosplenic ligament, which was formed by failure of two parts of the ligament to close during development. To release the colon it must either be passed back through the rent or the incarcerating ligament must be cut, preferably with a stapling device.

Clinical Presentation

Horses with nephrosplenic entrapment show variable degrees of pain depending on the location of the colon, the amount of gas distention, and the presence of secondary gastric distention. Location of the colon lateral to the spleen is associated with minimal to no discomfort, and is found in the resolving stages of the displacement. Entrapment of the colons within the nephrosplenic space with the spleen in a relatively normal position is associated with evidence of severe pain. Affected horses crouch, want to lie down, and often lean to the left. When the spleen is pushed away from the body wall and displaced ventrally, effectively opening the nephrosplenic space, there is less pressure on the colon and horses show only mild signs of abdominal pain.

Diagnosis

The diagnosis of nephrosplenic entrapment is based on the presence of abdominal pain, which can be mild to severe depending on the location of the colon and the degree of gas distention, and relatively normal cardiovascular parameters. These findings are consistent with a simple colonic obstruction. The CBC and chemistry values are usually normal or consistent with mild dehydration. A low packed cell volume (PCV) in the presence of dehydration has been reported as an indication of red blood cell sequestration in the spleen. The results of abdominocentesis are within the normal range; collection of splenic blood (characterized by a PCV exceeding that of the peripheral blood) by abdominocentesis is supportive of a diagnosis of nephrosplenic entrapment, and in one report occurred in 25% of horses at admission.[2] Horses with increased peritoneal fluid WBC counts were more likely to have a long-standing duration of the condition, and more likely to require surgical treatment than horses with normal peritoneal fluid WBC counts.[2] Nasogastric reflux, reported in up to 43% of horses with nephrosplenic entrapment, is commonly obtained as a result of pressure on the duodenum or because of mesenteric

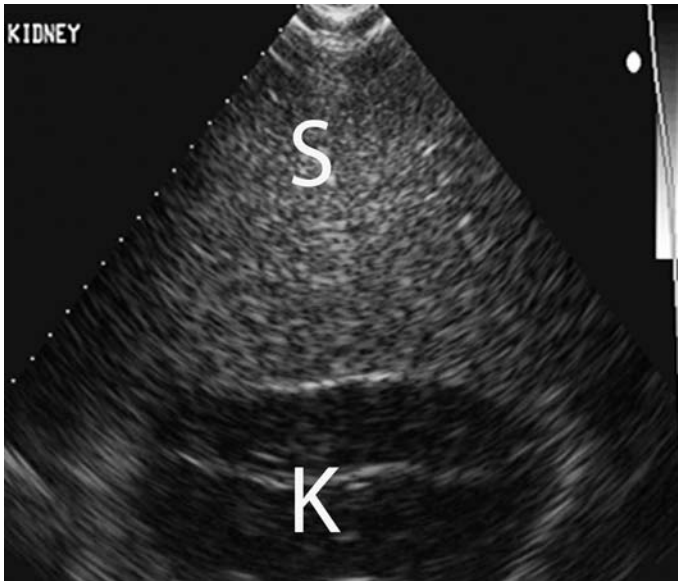
tension.[1] In one study, resistance to nasogastric intubation was encountered in horses with displacement of the sternal and diaphragmatic flexures dorsal to the stomach.[9]

Ultrasound examination of the abdomen can serve as an adjunct to the diagnosis of nephrosplenic entrapment, and in one study was diagnostic in 88% (36/41) of the horses studied.[12] A 2.5 mHz or 3.5 MHz ultrasound probe is placed over the 15th to 17th intercostal space in a direction parallel to the ground, and the spleen is imaged. In the normal horse, the left kidney is imaged deep to the spleen (Figure 21-4a). In horses with nephrosplenic entrapment, the presence of gas-filled colon dorsal to the spleen precludes imaging of the kidney (Figure 21-4b). Evidence of ventral displacement of the dorsal aspect of the spleen is also consistent with nephrosplenic entrapment. If the colons are displaced lateral to the spleen, then imaging of the spleen is obscured. It is important to direct the probe in a horizontal direction; if the probe is angled in a dorsoventral direction, the kidney can occasionally still be imaged, giving a false-negative diagnosis. It is important to realize that the inability to image the left kidney is only supportive of a nephrosplenic entrapment, and should be used in conjunction with rectal palpation. Nonspecific large-colon distention or the presence of small colon in the nephrosplenic space can impair imaging of the left kidney in some normal horses.[13] In addition, if the displaced colon is fluid-filled, imaging of the left kidney is still possible, but the entrapped bowel is also seen.[12]

Rectal palpation remains the mainstay of diagnosis of nephrosplenic entrapment. On palpation, the left colons will most often be gas distended, and the ventral colon will be dorsal to the left dorsal colon; there will often be an impaction of the left dorsal colon. The colons can be followed up into the nephrosplenic space. It is important for correct diagnosis to follow the colons into the nephrosplenic space because in other conditions, ranging from gas colic to large-colon volvulus, the colon can assume a dorsal position within the abdomen, leading to a false diagnosis of nephrosplenic entrapment.[14] This could have dire consequences if nonsurgical management is attempted and the horse has a large-colon volvulus. In three studies, rectal palpation correctly identified left dorsal displacement of the large colon in 61.2%, 68.7%, and 72% of cases,[1-3] although an early study reported a much lower rate of correct identification of only 18%.[9] Rectal palpation can be impeded by patient size, temperament, or in the presence of severe distention.

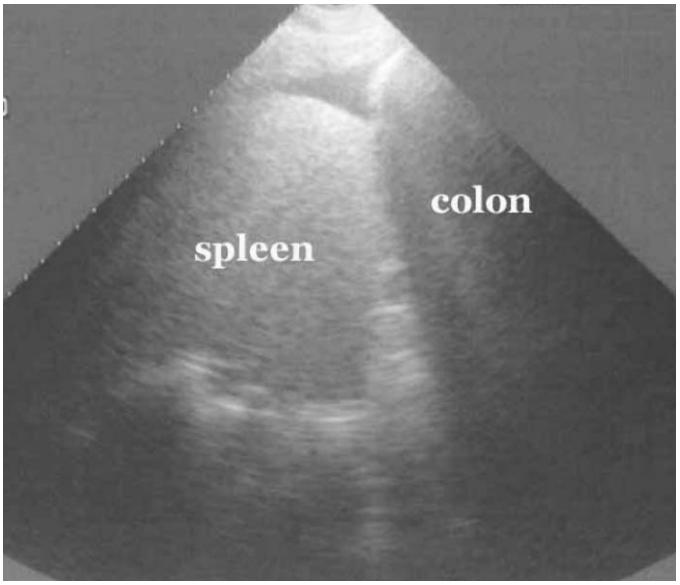
Thorough physical examination, rectal palpation, and abdominal ultrasound should be performed in horses diagnosed with nephrosplenic entrapment because a small number of horses will have another primary lesion involving another segment of the gastrointestinal tract; gastric rupture, small-intestinal volvulus, ileal impaction, large-colon displacement, large-colon volvulus, cecal torsion, and small-colon obstruction have been documented in association with nephrosplenic entrapment.[1-3,12,15]

Figure 21-4A



Normal ultrasonographic appearance of the left flank of a horse, taken in the 17th intercostal space. S: Spleen; K: Kidney.

Figure 21-4B



Ultrasonographic appearance of the left flank of a horse with left dorsal displacement of the left colon. S: Spleen; C: Large colon; dorsal is to the right of the image. Note that the left kidney cannot be imaged.

Nonsurgical Correction

Once a diagnosis of nephrosplenic entrapment has been made and the clinician is confident that no other abnormalities are present, options for treatment are evaluated. These include medical therapy with intravenous fluids and withholding of feed; exercise with or without the use of a vasopressor agent; rolling under general anesthesia with or without the use of vasopressor agents; standing flank laparotomy; and ventral midline celiotomy. This section will describe nonsurgical options for correction of nephrosplenic entrapment.

Medical therapy with intravenous fluids supplemented with calcium gluconate is indicated when the colons are located lateral to the spleen and was successful in 9 affected horses.[1]

When the colons are localized in the nephrosplenic space and the horse is in pain, nonsurgical management can be attempted. In one study, horses that were successfully treated nonsurgically had a shorter duration of clinical signs, lower peritoneal fluid WBC, and a higher blood lymphocyte count than horses treated surgically.[2] In that study, failure of nonsurgical management was also believed to be related to the severity of gas distention, which would also increase with duration. It is important to emphasize that the diagnosis must be certain before attempting this option. With all nonsurgical options, administration of phenylephrine to cause splenic contraction is often used as an adjunct to facilitate correction; bleeding the horse was described in the early literature to reduce splenic size,[16] but this seems unnecessary and possibly detrimental. Phenylephrine (Neo-Synephrine HCl, 10 mg/mL, Winthrop Pharmaceuticals, New York, NY) is an α1-adrenergic receptor agonist that causes vasoconstriction in most vascular beds and splenic contraction. In one study performed in horses, the splenic area was reduced to 28% of baseline, and thickness was reduced to 48% of baseline after administration of phenylephrine at 3 μg/kg/min over 15 minutes.[17] Side effects were minimal at that dose and included hypertension and reflex bradycardia. Currently, the author uses a total dose of 10 mg for horses 450 kg or less and 20 mg for larger horses; the drug is diluted in 50 mL of saline and given slowly intravenously over 5 minutes.

Vigorous exercise is an option for correction of nephrosplenic entrapment providing the horse is not lame. This procedure is more successful when performed early in the course of the disease, before large-colon distention develops.[1,14] If distention of the left colons is significant, the colons can be decompressed before exercise. For percutaneous decompression, an area over the left flank is clipped and prepared aseptically. A 14-gauge over-the-needle intravenous catheter with a catheter extension is used to puncture the flank in a perpendicular direction. The end of the catheter extension is placed in a water container to facilitate observation of gas exiting the colons. Once in place, the trocar portion of the catheter is withdrawn for a few millimeters to avoid laceration of the bowel. The trochar is replaced within the catheter if it needs to be inserted further as the colon is deflated. When doing so, care must be taken not to lacerate the tip of the catheter with the trocar. Rectal palpation can help manipulate the colon to facilitate gas evacuation. Once done, the trocar portion of the catheter is removed and 1 to 2 mL of gentamicin are injected as the catheter is withdrawn. Removal of gas from the colon is useful before an attempt is made to use exercise for the correction of nephrosplenic entrapment; otherwise if the colon is gas distended, it will remain in a dorsal position. Once the decompression is completed, phenylephrine is administered intravenously and the horse is exercised either on a lunge line or in a small paddock for 15 to 30 minutes. Rectal palpation is performed to ascertain the position of the colon. Exercise can be repeated if correction is not achieved.

Rolling the horse under general anesthesia is another nonsurgical option for correction of this disorder (Figure 21-5).[15,16] This procedure has also been reported to be useful in a small number of horses with other large colon displacements.[18] This option is preferred if the horse is lame or if there is large-colon distention. Previous abdominal surgery may preclude the use of this procedure, as splenic adhesions may prevent successful correction of the displacement.[19] For this procedure, the colon is not decompressed unless the distention is severe, as gas translocation is used to achieve correction of the displacement. The horse is prepared for short-term intravenous anesthesia. An α-2 agonist is administered for sedation, followed by phenylephrine infusion as has been described. The horse is then anesthetized and positioned in right lateral recumbency. Using a knee or two-handed fist, the clinician then vigorously shakes the abdomen in the region of the left flank, as the horse's hind legs are being hoisted. If a hoist is not available, the horse is slowly rolled into dorsal recumbency while abdominal compressions are performed. With the hoist, the hind legs are elevated until the horse's body reaches a 60-degree vertical position, while the clinician continues to vigorously shake the abdomen. After 1 or 2 minutes, the horse is repositioned in right lateral recumbency. At this stage, some clinicians prefer to place the horse in left lateral recumbency, roll the horse into a sternal position, and then to right lateral recumbency. The procedure is repeated two more times. After the last manipulation, the horse is returned to left lateral recumbency for recovery. Between manipulations, the clinician can verify the position of the colon. It is the author's experience that it is difficult to determine successful correction of the entrapment, either by ultrasound or rectal palpation, with the horse under general anesthesia. Therefore, this author always allows the

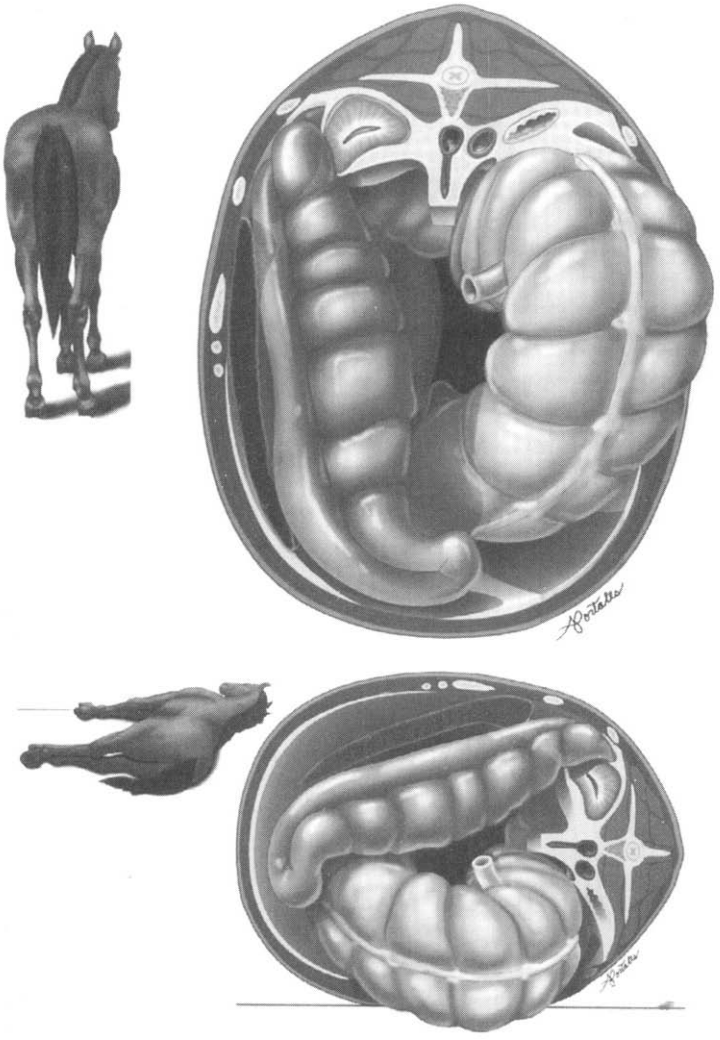
horse to recover from anesthesia before determining whether correction was achieved. Some clinicians prefer to follow immediately with surgical correction without recovery if they believe that correction was not achieved.[14]

One author describes manipulation of the colons per rectum. With the horse in right lateral recumbency, the hand lifts the colons off the spleen as the horse is being turned to left lateral recumbency. The use of muscle relaxants is recommended when this procedure is used to relax the rectum. Rectal manipulation must be performed with extreme caution, as rectal tears are a definite risk of this procedure.[15]

Rectal palpation after manipulation often reveals that the colon is lateral to the spleen and has not completely resumed its normal position. Administration of calcium-containing fluids often results in complete correction within a few hours. Some horses may show mild abdominal pain after manipulation even though correction was thought to be achieved. This is probably a result of residual large-colon distention or impaction and is usually responsive to analgesics.

If nonsurgical manipulations are unsuccessful, then surgical intervention is indicated. Either a standing flank laparotomy or ventral midline celiotomy can be used. The advantages of the standing flank approach are avoidance of general anesthesia, direct access to the displaced colon, access to the nephrosplenic space for closure as an option for prevention of recurrence, and more rapid return of the horse to use. The major disadvantage, as is the case for nonsurgical manipulation, is the inability to correct the underlying problem if an incorrect diagnosis was made. The advantages of the ventral midline celiotomy are that it ensures successful correction, particularly in cases where the colons are dorsal and cranial to the stomach, and allows correction of other unidentified problems. The disadvantages of ventral midline celiotomy include the need for general anesthesia, longer post-operative recovery, and increased cost.

Figure 21-5A, B



Nonsurgical correction of a left dorsal displacement of the large colon. **A**, Caudal view of the standing horse with the left ventral and dorsal colons entrapped over the nephrosplenic ligament. **B**, The patient is anesthetized and placed in right lateral recumbency.

Figure 21-5C

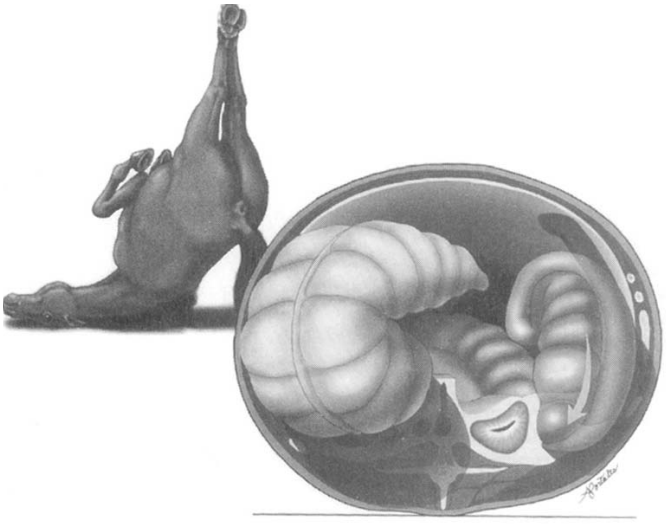


Figure 21-5D

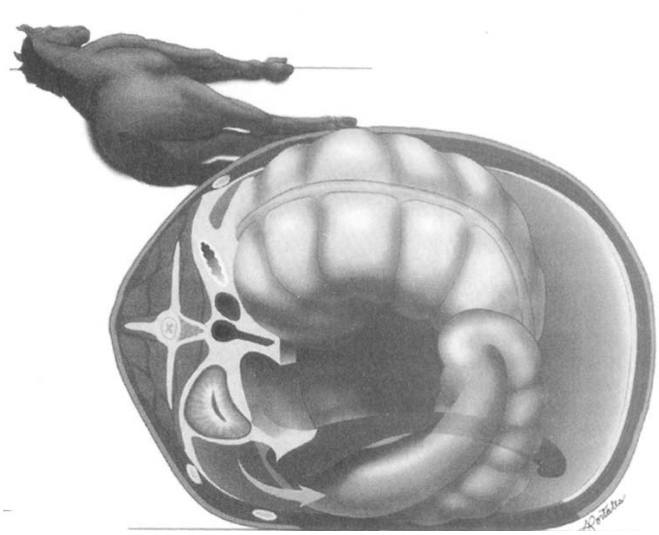


Figure 21-5 (continued) **C**, Hobbles are placed on the hind limbs, and the patient is positioned in dorsal recumbency. The hind limbs are lifted to raise the hind end off the ground. The large colon falls cranially, laterally, and to the right (arrow). **D**, The patient is then positioned in left lateral recumbency. This allows the colon to continue to fall ventrally and laterally to the spleen.

Figure 21-5C

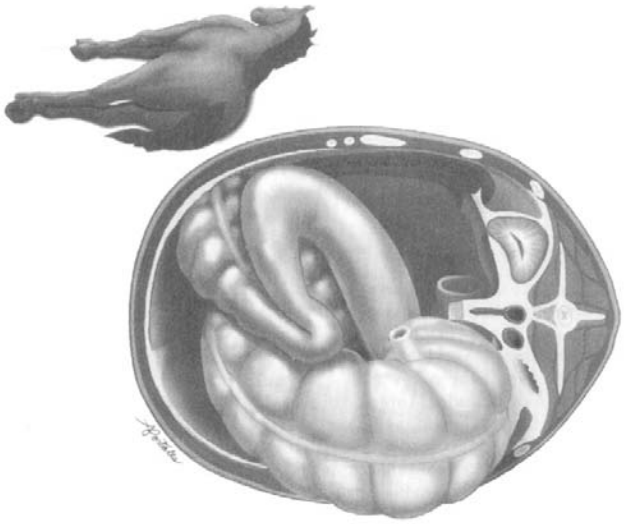


Figure 21-5D

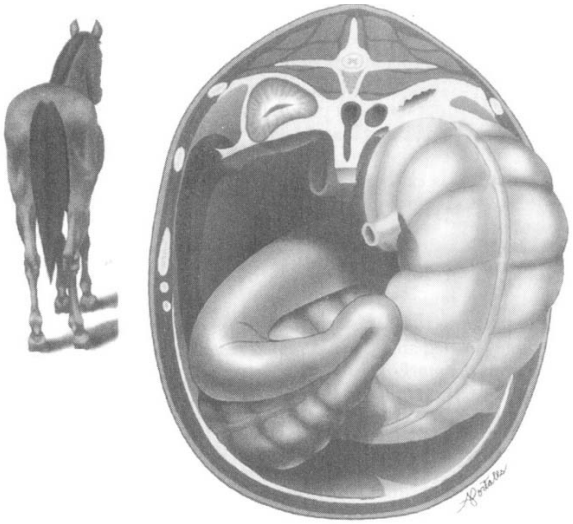


Figure 21-5 (continued) **E**, The 360-degree rotation is completed by rolling the individual into sternal recumbency (not shown) and then back to right lateral recumbency. (This step is omitted by some clinicians). The colon comes to rest in a position medial to the spleen. **F**, The patient is allowed to recover. If the procedure is successful, the colon assumes a position ventral and medial to the spleen. Rectal palpation is performed to assess the position of the colon. (Adapted from: Manual of Equine Emergencies, 2nd ed. Orsinin JA, Divers TJ (eds). Philadelphia: WB Saunders, 2003, pp. 233-235.)

Complications and Prognosis

Complications of nonsurgical correction for nephrosplenic entrapment most often relate to an inaccurate diagnosis, which delays surgical intervention for the correct condition. The presence of other lesions in addition to nephrosplenic entrapment has been reported. The presence of other abnormalities on physical examination, such as signs of cardiovascular compromise, an abnormal abdominocentesis, or other findings on rectal palpation such as small-intestinal distention, should alert the clinician to the possible need for surgical correction.

Complications of needle decompression can occur; these include peritonitis, intestinal laceration, and abscess formation at the site of trocarization. The prevalence of these complications has not been documented.

Prevention of Recurrence

The reported recurrence rates of nephrosplenic entrapment are 7.5% to 8.5%.[1,2] Considering this relatively low risk, surgical intervention for prevention of recurrence is not recommended after a first incidence. However, feeding and management practices should be carefully reviewed to minimize the risk of gas formation in the large colon and subsequent displacement.

Procedures that have been advocated for prevention of recurrence of nephrosplenic entrapment of the large colon include closure of the nephrosplenic space, large-colon colopexy, and large-colon resection. The reader is referred to other sections of this book for reference to large-colon resection and colopexy procedures.

Closure of the nephrosplenic space will not prevent migration of the large colon lateral to the spleen or the occurrence of other forms of large-colon displacement. The procedure can be done through a flank laparotomy or though a minimally invasive laparoscopic approach.[20,21] The flank approach is performed in the standing or laterally recumbent horse. The abdomen is entered either through a modified grid or laparotomy approach. The spleen and nephrosplenic ligament are identified, and the nephrosplenic space is verified to be free of intestine. Cruciate sutures are then placed between the ligament and the tip of the spleen, using a nonabsorbable suture such as 2-polypropylene in a cruciate pattern. Approximately 6 to 12 sutures are pre-placed and then tied. The abdomen is closed in a routine fashion. Alternatively, laparoscopic ablation of the renosplenic space can be performed in the standing horse,[20] and has been reported to be successful in 5 experimental horses. The procedure is performed using three laparoscopic portals and polyglactin 910 suture material in a simple continuous pattern. There are only a few reports in small numbers of horses regarding the long-term efficacy of this procedure.[20,21]

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Colic in the Foal

Chapter 22

Martin Furr

The clinical presentation of foals with colic, with or without abdominal distention, is fairly common in equine practice. Accurate diagnosis is critical for successful management of these conditions. Particularly challenging is the determination of the need for exploratory surgery. No specific findings on clinical examination unequivocally indicate that surgical or medical treatment is indicated, and the synthesis of various diagnostic procedures is important in determining the correct treatment. Many of the diagnostic methods applicable to the adult horse with abdominal pain are not useful in the neonate, and conversely many techniques valuable in the neonate are not used in the adult. A fundamental issue is in attempting to determine whether obstruction is present. If so, surgical exploration is immediately required. Delaying exploration in these cases can decrease the survival as well as increase the risk of adhesion formation associated with distention. It is important to recognize, however, that ileus can be severe enough in foals to cause distention without physical obstruction.

A complete physical examination is imperative because many conditions such as sepsis or congenital abnormalities can lead to ileus, abdominal distention, and colic (Table 22-1). The initial examination should be directed toward determining the nature and extent of all physiologic abnormalities, assessing gastrointestinal patency, ruling out sepsis, and determining the adequacy of passive transfer of immunoglobulins. A complete blood cell count, serum biochemistry profile, and blood culture should be completed on all foals with colic. Abdominal circumference, presence of ascites, cardiovascular and respiratory system function, presence of congenital defects, passage of stool, and urinary tract integrity should all be evaluated.

Abdominal circumference can be measured with a cloth tape measure. Subsequent measurements to determine whether the distention is progressing must be made in the same spot as the initial measure. If abdominal distention exists, determining whether it is the result of peritoneal or gastrointestinal accumulation of fluid or gas is key to the evaluation. Ascites can readily be confirmed by ultrasonography.

Table 22-1
Causes of Colic in the Neonatal Foal

Stomach
Pyloric stricture
Gastric perforation
Gastric ulceration
Gastric abscess
Gastric foreign body

Small Intestine
Enteritis
Volvulus
Peritonitis
Adhesions
Intussusception
Infarction
Impaction (foreign bodies, trychobezoars)
Duodenal stenosis/obstruction
Bowel incarceration (hernia, mesenteric rent)
Mesodiverticular band
Small intestinal displacement
Ovarian stalk obstruction of bowel
Necrotizing enterocolitis

Large and Small Colon
Meconium impaction
Infarction
Colitis
Colonic displacements
Atresia coli/recti/ani
Obstruction (bezoars)
Ileocolonic aganglionosis
Extraluminal obstruction (adhesions)
Intraluminal obstruction

Other
Peritonitis
Hemoperitoneum
Ovarian artery rupture
Ruptured spleen
Fractured ribs
Ascites
Urinary tract disruption
Rectal prolapse
Acute hepatic necrosis
Blunt abdominal trauma

Modified from: Cudd T. Gastrointestinal system dysfunction. In Equine Clinical Neonatology. Koterba A, Drummond W, Kosch P (eds). Philadelphia: Lea & Febiger, 1990.

A digital rectal examination should be performed to determine if a meconium impaction is present. This can cause signs ranging from mild colic to complete obstruction. The absence of fecal passage or the presence of clear, clean mucus on the finger after a digital examination may suggest bowel atresia. The presence of diarrhea makes a diagnosis of enteritis fairly straightforward, but foals can have fairly severe discomfort, ileus, and abdominal distention before passing abnormal stools. Of foals eventually determined to have neonatal sepsis, 30% are presented with diarrhea.

The neonate with colic should also be evaluated thoroughly for metabolic derangements such as hypoglycemia, failure of passive transfer, and electrolyte disorders. Typically, the foal with a ruptured bladder is hyponatremic and hyperkalemic. Similar electrolyte changes can be seen in foals with septicemia, renal failure, and enteritis, necessitating additional diagnostic tests before surgical intervention is initiated. Typically, these tests include abdominal ultrasonography and abdominal fluid collection and evaluation.

Serum IgG concentrations should always be determined in the neonate with colic or abdominal distention to detect failure of passive transfer. Correction of this condition is critical to the overall management of these foals. Concentrations of IgG exceeding 800 mg/dL are considered to be normal, and several different methods, many of them stall-side, are available to determine serum IgG concentrations. It is also necessary to repeat the assessment of IgG concentration sequentially, and particularly postoperatively, as foals that are ill or nutritionally compromised, or have intestinal disease can easily become hypoproteineimic and hypoglobulinemic. It is not uncommon in such foals that repeat treatment with plasma is necessary.

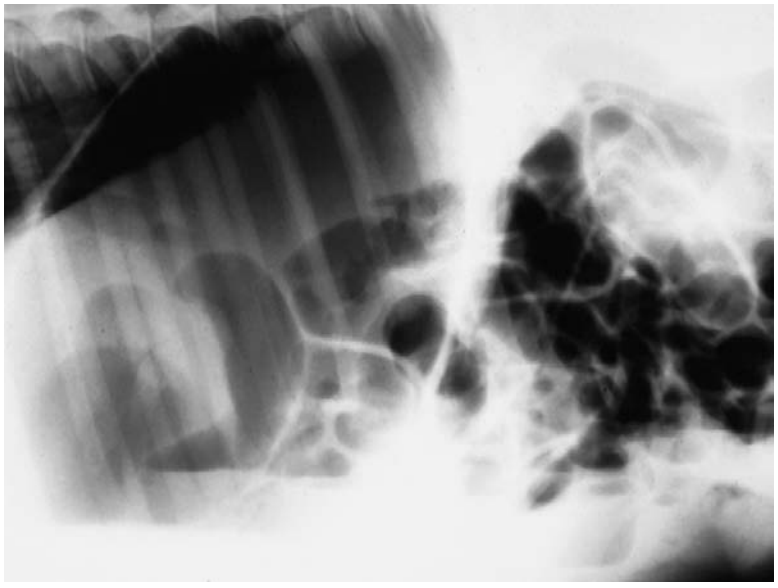
Abdominal Radiography

Abdominal radiography is often helpful in evaluating abdominal distention and colic in the neonate. In one report, radiographic evaluation was proven correct in 25 of 26 cases in identifying the site of the lesion,[1] while radiographic interpretation was correct in 8 of 10 cases in another study.[2] Evaluating abdominal radiographs from foals requires some experience. A lateral view of the abdomen is routinely performed with the foal standing, although views of recumbent foals are often diagnostic. Usually, the abdomen can be imaged on one 14 x 17-inch cassette, and the approximate technique for the typical neonatal Thoroughbred foal is 85 KvP and 20 mAs, using a 10:1 focused grid and a focal film distance of 180 cm. These are guidelines only; the technique may need to be modified based on the specific equipment in use. The stomach is usually noted in the cranial central abdomen and is usually gas- and fluid-filled (Figure 22-1A). Small-intestinal distention with multiple erect and inverted U-shaped loops of bowel is consistent with obstructive disease, whereas ileus produces diffuse and mild small-intestinal distention involving the entire length of the intestines (Figure 22-1B). Gas shadows can be seen in the bowel wall in foals with necrotizing enterocolitis. Large-colon distention (Figure 22-1C) is often noted in foals with ileus, meconium impactions, large-colon displacements, and atresia coli. Serial radiographs may be helpful in determining the significance of specific lesions (see Chapter 15).

Contrast studies that can be performed to further assess the gastrointestinal tract include barium enemas (Figure 22-2) and the upper gastrointestinal series. These should be performed after routine films have been taken to establish a technique. The technique should then be increased by 10% to compensate for the radiodense contrast material. To perform an upper gastrointestinal series, 5 mL/kg of barium sulfate suspension is administered by nasogastric tube after a 4-hour fast. Serial radiographs are performed immediately after administration of the suspension, at 5, 15, and 30 minutes, and then at 2-hour intervals until the contrast medium has reached the small colon. In a normal foal, the stomach should empty within 2 hours. Duodenal strictures, as well as diffuse ileus, markedly delay gastric emptying. Radiographic findings consistent with mucosal erosion and ulceration can sometimes be identified. Filling defects of the stomach suggest gastric abscesses, foreign bodies, or masses. An upper gastrointestinal series is contraindicated in the presence of severe small-intestinal distention. The greatest value of this procedure lies in evaluating gastric emptying and the proximal duodenum for the presence of strictures. More distal lesions are difficult to interpret.

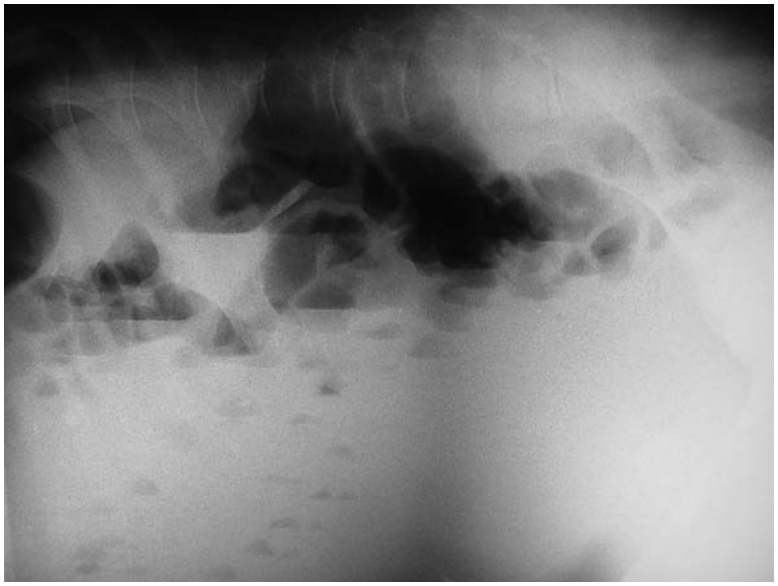
Barium enemas are useful to confirm an obstruction of the rectum or small colon. A well lubricated enema tube should be passed gently into the rectum after evacuation of fecal material. Barium sulfate suspension (180 mL) is slowly infused while the anus is occluded around the tube. A radiograph of the caudal abdomen is performed immediately after instillation of the barium. Filling defects, obstructions such as meconium impactions, and atresia can be diagnosed with this method.

Figure 22-1A



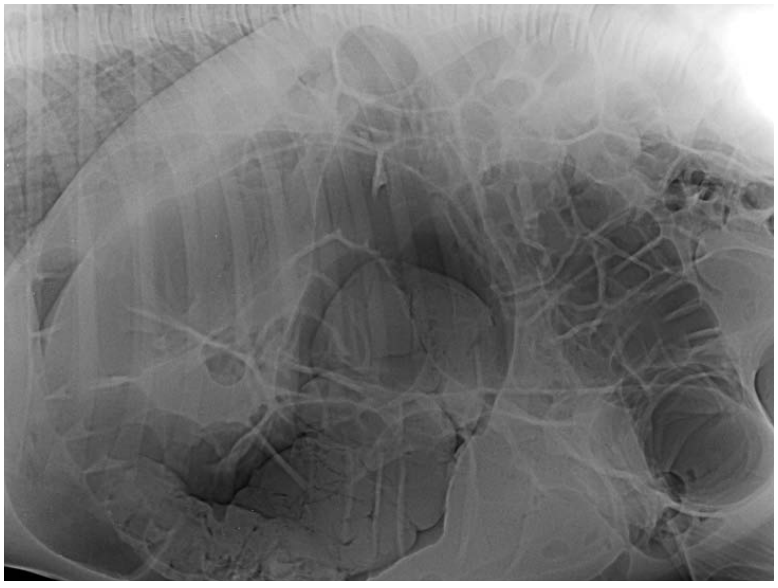
Stomach distention-associated gastric ulcers and poor stomach emptying.

Figure 22-1B



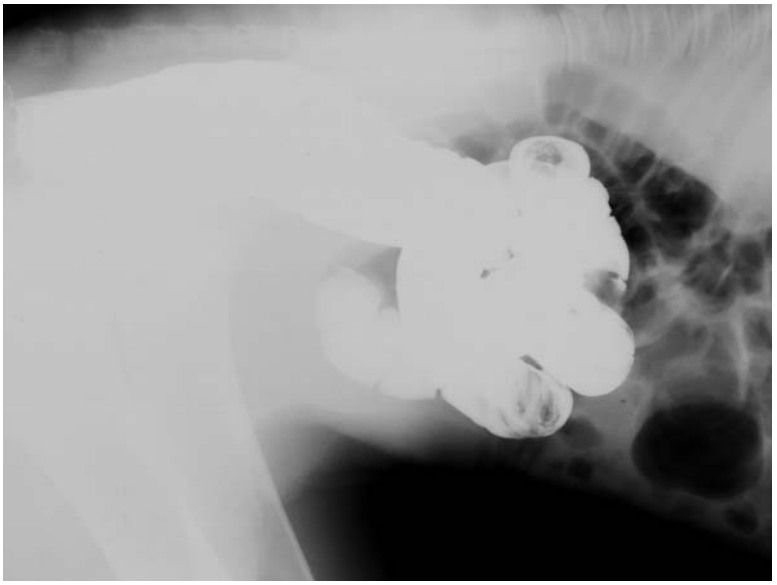
Radiographs of the abdomen of a foal with abdominal distention and colic, demonstrating small-intestinal distention with multiple fluid lines at different levels, suggestive of obstruction.

Figure 22-1C



Radiographs of the abdomen of a foal with colic and abdominal distention demonstrating large-colon distention.

Figure 22-2



Barium enema contrast study of a foal with colic and abdominal distention, demonstrating an abrupt termination of the contrast in the small colon as a result of a meconium impaction.

Gastroendoscopy

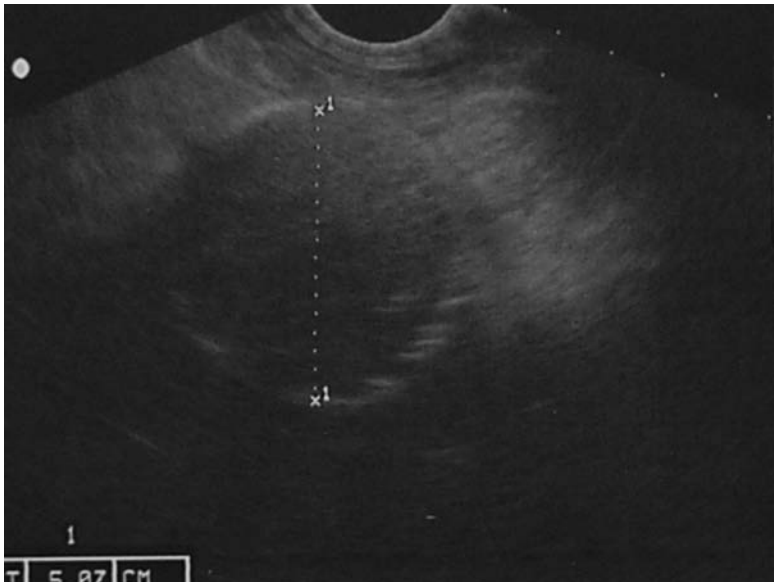
Endoscopy of the proximal gastrointestinal tract is a useful technique in foals with signs of gastric or gastroduodenal ulceration. Signs such as colic, bruxism, excessive salivation, and abdominal pain should prompt gastroendoscopy. Numerous endoscopic systems are available, but in general a system with an insertion tube of 0.9 mm (OD) and 1.5 M working length is adequate to examine the stomach and proximal duodenum of most foals. The stomach is directly observed for ulceration.

Ultrasonography

A 7.5- or 5-MHz scan head, preferably with a built-in standoff, is most useful for the evaluation of colic and abdominal distention in the neonate. The abdomen should be prepared by clipping the hair and applying ultrasound couplant gel. The examination is most productive if the foal is standing, because this allows the small intestine to drop to the ventral body wall. In a routine examination, the urachus, umbilical vein, umbilical arteries, bladder, peritoneum, and segments of the small intestine can be easily visualized via a ventral portal. Segments of the small intestinecan be examined and the thickness of the wall and the presence of distention determined. Normal bowel wall should be 2 to 3 mm thick; bowel thickness more than 4 mm is abnormal, suggesting inflammation, cellular infiltration, or edema (Figure 22-3). Suspicious areas can be compared with other segments of the bowel to determine the presence of focal thickening. Fluid filling, as is noted with diarrhea and enteritis, appears as round areas of bowel filled with composite fluid. Gas-distended bowel has a hyperechoic (echogenic) line at the surface of the bowel with little visualization beyond that surface. Small focal areas of gas may sometimes be seen within the wall of the bowel in foals with necrotizing enterocolitis. Intussusceptions have a characteristic “bulls eye” appearance with concentric rings (see Chapter 6). This observation may be coupled with bowel distention in other small-intestinal segments. Bowel motility can also be assessed using ultrasound. Observing a lack of contractions of small intestine confirms ileus, which can be of physiologic or obstructive origin.

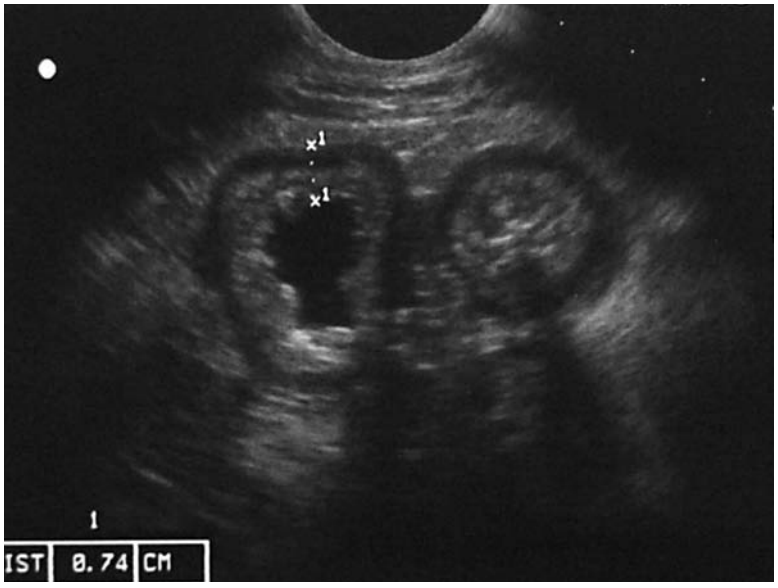
In addition to examination of the bowel, the urinary system can be examined ultrasonographically. The presence of excessive amounts of free fluid should be noted, and the urinary bladder and umbilical remnants examined to ensure there is no urinary tract disruption.

Figure 22-3A



Ultrasound examination of the abdomen of a foal with colic, demonstrating grossly distended small intestine. Observation in "real-time" failed to identify motility in this bowel segment, and at surgery small-intestinal volvulus was found.

Figure 22-3B



Abdominal ultrasound image from a foal with colic, demonstrating grossly thickened small intestinal wall. The thin zone of hypoechogenicity (black) around the periphery is interpreted as a zone of edema separating the muscularis from the serosa.

Abdominocentesis

Abdominocentesis should be performed with caution, because enterocentesis with laceration of the intestine is more likely to occur and cause contamination in the neonate than in the adult horse.[3] Information gained by radiography and ultrasound examination should aid the clinician in deciding whether abdominocentesis is warranted. Often an abdominocentesis is not required to make a decision for or against surgery. The ultrasound examination can detect large volumes of intraperitoneal fluid or localized pockets of fluid that can be retrieved, thus increasing the diagnostic yield and decreasing the risk of bowel penetration. Use of a short teat cannula also reduces the risk of bowel penetration. If a needle is used, the thin bowel can easily be lacerated when the foal moves, resulting in abdominal contamination.

Analysis of abdominal fluid should include assessment of color and clarity, white blood cell count, total protein, and cytologic findings. Normal values for peritoneal fluid of the neonate are similar to those for adult horses, however foals often have slightly lower peritoneal fluid total protein than adults, owing to hypoproteinema being frequently present in neonatal foals. Fluid that is serosanguineous uniformly throughout the collection suggest devitalized bowel. An increased intraabdominal protein concentration and leukocyte count suggests intraabdominal sepsis, which could be due to an abscess, umbilical remnant infection or abscessation, or generalized sepsis. In foals with abdominal distention and/or ascites, peritoneal fluid creatinine should be evaluated to determine whether uroperitoneum is present. A ratio of peritoneal fluid to serum creatinine greater than 2:1 confirms uroperitoneum, which can arise from a ruptured bladder, necrotic urachus, or ruptured ureter.

Blood can be recovered in cases of intraabdominal hemorrhage or when the teat cannula punctures the spleen. In the case of bowel perforation or enterocentesis, cytologic evaluation of peritoneal fluid reveals feed material and a mixed population of bacteria, whereas intraabdominal sepsis may result in the presence of bacteria and degenerative neutrophils.

If enterocentesis occurs during the abdominocentesis, broad spectrum antibiotics should be administered to the foal, preferably including metronidazole (10-15 mg/kg PO or IV every 6 hours). Nonsteroidal anti-inflammatory drugs and heparin (40-50 IU/kg SQ or IV, every 6-8 hours) may be used also, to help minimize the risk of intraabdominal adhesions.

Case Synthesis and Management

If physical obstruction of the intestine is confirmed or suspected, immediate surgical exploration is indicated. Persistent pain and progressive distention are the most common and reliable indications for surgery in the foal and are characterized by distended bowel on ultrasound and/or radiography (see Chapter 5). The decision for surgery should not be delayed, because the neonatal foal's condition deteriorates rapidly, and persistent distention of the bowel can lead to further metabolic compromise and intraabdominal adhesions.

Medical management of the foal with colic or abdominal distention should have the following goals: (1) correction of the primary problem, (2) correction of metabolic or electrolyte abnormalities, (3) decompression of the bowel, (4) relief of pain, and (5) resting the bowel if intestinal distention exists.

In cases of colic in the foal, correction of electrolyte abnormalities, metabolic derangements, and dehydration is vital because any of these conditions can lead to or exacerbate ileus. Specific electrolyte abnormalities should be corrected using the appropriate replacement solutions. Hyponatremia can be corrected using 0.9% sodium chloride (NaCl) solution or hypertonic saline (either 5 or 7.2%). Hyperkalemia can be treated with the administration of fluids that lack potassium combined with intravenous 5% dextrose infusion (see Chapter 17). Simple dehydration can be readily corrected with standard commercial polyionic replacement solutions. These solutions can be administered at 1.5 times maintenance rates (1.5 x 100-120 mL/kg/day), until the hydration status is normalized.

Hypoglycemia, which often accompanies diseases in the neonate, is corrected with an intravenous infusion of 5% to 10% dextrose at a rate of 2 to 4 mg/kg per minute. It is important to give this as a constant infusion rather than a bolus, as bolus administration may lead to a rebound hypoglycemia that is more severe than the original problem.

Decompression of the bowel decreases pain and ameliorates distention-induced ileus. A nasogastric tube should be passed routinely, and gastric decompression attempted. However, intestinal decompression cannot be achieved with a nasogastric tube, and neither the nature nor the amount of reflux obtained has much bearing on the decision for or against surgery. The tube should be left in place and capped to prevent aspiration of air. Gastric decompression followed by treatment with analgesics may alleviate pain sufficiently to diminish ileus. Trocharization of intestine in the neonate is almost never justified and should be performed in only the most extreme circumstances, because severe peritonitis is the sequela. In some foals, if distention and pain continue or progress, surgical decompression may be necessary.

Although decompression of the bowel is important in controlling pain, pharmacologic pain control is also needed. Conservative doses of flunixin meglumine (Flunixamine, Fort Dodge, 0.25 mg/kg IV, every 12 hours) are often adequate for the neonate. Other nonsteroidal anti-inflammatory drugs can be used, but flunixin is probably safest in the foal. Xylazine should be used with caution because of the potential for cardiovascular compromise. Constant-rate infusion of butorphanol or lidocaine has not been described in the neonate and should be used with caution. Because of the risk of gastric ulceration, cimetidine (Cimetidine, Abbot Laboratories, 6.6 mg/kg, IV, every 6 hours) or ranitidine (Ranitidine, Glaxo, 1.5 mg/kg, IV every 8 hours) should be administered intravenously to the foal with colic.

Enteral feeding of foals with colic or abdominal distention is contraindicated. Nursing from the mare can be limited by use of a muzzle or by separating mare and foal with a partition. The foal should be supported with intravenous fluids and dextrose during this period to prevent hypoglycemia and dehydration. If the duration of enteral rest exceeds 48 hours, intravenous nutritional support is highly desirable. The duration of enteral rest necessarily varies with the specific inciting cause, but 24 hours is probably the minimal duration. In foals with enteritis, 3 to 5 days is sometimes necessary before enteral feeding can be tolerated. Findings at surgery dictate the duration of enteral rest in foals that have had a surgical procedure performed. When oral feeding is to be reintroduced, 4 ounces (100 ml) of water or a water and dextrose solution should be given every 2 hours. If this is tolerated, the volume can be increased with subsequent feedings until a volume of 12 to 16 ounces (300-

400 ml) of water or glucose solution is tolerated. Once this is achieved, a 50:50 mixture of water and milk or a milk substitute can be given. If no intolerance is noted after several feedings, the strength of the solution can be increased to normal. Obviously, this process requires some patience, but reintroducing enteral feeding too rapidly often results in relapse of ileus.

Surgical Treatment

The need for exploratory celiotomy is suggested by persistence of pain, progressive abdominal distention, and characteristic changes on radiographs and ultrasound (see Chapter 15). Several conditions require surgical treatment; only a limited number of reviews have summarized the findings of surgical colic in the foal. A summary of 119 cases of foals less than 1 year of age that underwent exploratory celiotomy noted the following results:[4] In foals less than 3 months of age, uroperitoneum was the most common diagnosis (13/53), meconium impaction (8/53) and enteritis (8/53) were the next most frequent diagnoses. Small-intestinal volvulus (3/53), hernia (6/53), gastroduodenal ulceration (4/53), intussusception (3/53), and ileal impaction (2/53) were also noted. In that report, foals less than 3 months of age had a short-term survival of 72%, while foals 3 to 12 months of age had a short-term survival of 53%. Older foals had a greater incidence of large-colon disease, including large-colon volvulus, pelvic flexure impaction, and various displacements.[4] Long-term survival of foals less than 150 days of age was evaluated and a short-term survival (i.e., release from the hospital) was 63%, while the long-term survival (up to 2 years) was 57% for a group of 69 foals.[1] In that study, foals less than 14 days of age were less likely to have long-term survival than older foals (P=0.031). In foals less than 14 days of age, the long-term survival was 10%; however this was based on only 3 foals, 2 of which had been lost to follow-up. This finding is in contrast to an earlier report, in which 13/20 foals less than 14 days of age were dismissed from the hospital.[2] Long-term survival (6 months) in these foals was 41%. Some of the foals lost during the 6-month follow-up period died of unrelated causes, while 3 succumbed to septic peritonitis and 1 was destroyed because of abdominal adhesions.[2]

It is difficult to draw definitive conclusions from the studies cited above, because of variations in study design, ages of animals, and lack of standardized treatments. Obviously conflicting results are reported, making predictions of outcome ambiguous in young foals. In general, clinical experience indicates that foals with uroperitoneum and meconium impactions have good outcomes, while foals with distended and compromised small intestine appear to have more complications. Clearly, young foals have unique problems and responses to surgery, which must be considered in formulating a treatment plan and prognosis.

The surgical approach to the foal's abdomen begins at the umbilicus and extends caudally for 15 to 20 cm. The abdomen is entered in routine fashion. It is important to remember that in the foal the umbilical remnants may be necrotic or contaminated and special care must be taken when entering the abdomen to ensure that contamination of the incision or peritoneum does not occur. The bowel and mesentery should be handled particularly carefully in the foal as the mesentery is easier to tear than in an adult horse. Because of the apparent increased risk of intestinal adhesions in foals, it is important that the bowel is handled minimally and is kept moistened at all times. Bowel should not be left out of the abdominal cavity under surgical lights after exploration. In addition, it may be beneficial for the surgeons to moisten their fingers with diluted hyaluronate when manipulating the intestine.

Exploration of the abdomen proceeds in the same fashion as in an adult horse (see Chapter 10). It is important, however, that the umbilical remnants and bladder are carefully examined for abnormalities and the umbilical remnants are routinely removed, even if they are considered normal, because of the high incidence of umbilical resections necessary in critically ill neonates. Removal during the initial surgery reduces the risk of requiring a repeat laparotomy at a later time.

Closure of the abdomen is performed using #1 synthetic absorbable suture in a simple continuous pattern in the linea alba, followed by closure of the subcutaneous tissues with #00 synthetic absorbable suture in a simple continuous pattern. Skin is most commonly closed with stainless steel staples. Use of a stent bandage or abdominal wrap is not necessary in uncomplicated cases, and use of drains is not recommended unless there is a specific and clear-cut need for them, such as preexisting peritonitis or abdominal abscessation.

Postoperative care of the foal is dictated by the nature of the problem addressed during surgery and the procedures required intraoperatively. In general, foals with small-intestinal distention, enteritis, or intestinal resection, should be given at least 72 hours of enteral rest, followed by slow return to feeding. Nutritional support with intravenous nutrition formulations is important in providing optimal conditions for healing in the postoperative period. Foals with no signs of enteritis or gastrointestinal inflammation generally require less enteral rest. Foals that have had manual breakdown and passage of meconium impactions can have a milk diet immediately in almost all cases.

Gastroduodenal Ulceration

Gastric outflow obstruction is a consequence of chronic gastroduodenal ulceration leading to fibrosis and stricture of the duodenum. Clinical signs include mild intermittent colic associated with interrupted suckle, weight loss or failure to thrive, bruxism, and salivation in the later stages. Medical treatment with anti-ulcer medications such as ranitidine or omeprazole may result in clinical improvement that is incomplete or temporary. Ulceration can progress to gastric perforation, leading to peritonitis or sudden death. Abdominocentesis may reveal peritonitis or the fluid may be normal, and ultrasound evaluation of the abdomen may detect increased fluid or fibrinous exudates around the stomach. Endoscopic examination typically reveals ulceration of the esophagus as well as diffuse and severe ulceration of the squamous region of the stomach. Outflow obstruction can be confirmed with an upper GI series as described above. Treatment for gastric outflow obstruction is surgical bypass of the obstruction by gastrojejunostomy. Extensive and prolonged after-care is necessary in such cases, as it appears that establishing a new gastric emptying pattern develops slowly. Long-term use of anti-ulcer medications is necessary, along with normal postoperative management of ileus. Complications include infection of the surgical site, septicemia, ileus, breakdown of the anastomosis site, and stricture of the anastomosis, leading to persistent colic. Foals should not be fed for at least a week after gastrojejunostomy, and nutritional support must be provided intravenously. Most of the complications can be managed, however, and treatment is often successful.

Small-Intestinal Obstruction

Obstruction of the small intestine occurs in 25% to 45 % of foals with gastrointestinal diseases requiring surgery. These conditions include small-intestinal volvulus, ileus, ascarid impaction, bezoars, pyloric or ileal hypertrophy, and jejunal incarceration through mesenteric rents. Clinical signs and methods of treatment are not substantially different from those used in adult horses.

Large-Colon Obstruction

Meconium impaction is the most common cause of colic in the neonate and may lead to complete obstruction, requiring surgical intervention. Clinical signs of meconium impaction include a failure to pass meconium, progressive colic associated with straining to defecate, and abdominal distention. Digital palpation often reveals the presence of an obstructing fecal mass, but in some cases the meconium may be lodged further orad in the small colon. If meconium impaction is suspected but cannot be determined digitally, then lateral radiographs and/or barium enemas may be diagnostic. In some cases, the obstruction can be observed by ultrasound. Abdominocentesis is not usually necessary, and the peritoneal fluid is normal in most cases. An enema should be administered to affected foals, using either warm soapy water or a commercial phosphate enema (Fleet Enema, C.B. Fleet Company). Fleet enemas work well and are convenient, and the short insertion tube is safe. To perform a soapy water enema, a lubricated soft red rubber stallion catheter can be gently passed to the approximate level of the pelvic inlet and the solution (approximately 1 pint (560 ml)) gently administered by gravity flow. The operator should be careful not to tear the rectum, which is very delicate in the neonate. If the meconium is not passed, the enema can be repeated in 1 to 2 hours. In this author's experience, additional treatments are rarely successful if 2 to 3 enemas have not led to significant improvement.

Additional treatments used for meconium impactions include oral laxatives such as mineral oil (200 mL) or linseed oil (15 to 20 mL). Dioctyl sodium succinate (DSS) (15 mL of 5% solution in water) has also been advocated and can be useful, but should not be repeated because multiple doses can lead to DSS toxicity. The use of an irritant cathartic laxative such as castor oil is not recommended in most cases as these compounds produce severe enteritis and diarrhea if not used judiciously. A retention enema using acetylcysteine has been advocated and reported to be successful in 20 foals in which it was used.[5] Four to 8 ounces (100-200 ml) of 4% acetylcysteine solution are infused into the rectum via a Foley catheter placed into the rectum. It has not been demonstrated, however, that this method is superior to a soapy water enema, and in the author's experience, it has not proven to successfully treat meconium impactions that were resistant to treatment using conventional enemas. Manual removal of meconium using forceps is not recommended because of the risk of rectal trauma or penetration.

If after several enemas there is continued pain and/or increasing distention, surgical removal is indicated, as more enemas are not likely to be curative. Surgical treatment should not be delayed at this point, because of the risk of intestinal rupture with peritoneal contamination. At surgery, the impaction can usually be broken down and "milked out" of the small colon and rectum by massage. Fluid can be injected proximal to the mass to aid in breaking it down, and in severe cases the impaction may be removed through a colotomy in the antimesenteric taenia in a healthy segment of bowel. These procedures seem to be rarely needed. In the author's experience with persistent meconium impactions, surgical treatment is usually uncomplicated and has a high success rate if performed early and prior to the development of significant intestinal distention. If the fecal mass is simply broken down by manipulation and forced out, without enterotomy, then food does not need to be withheld after surgery. If the bowel is compromised, and resection is necessary, then the outcome is likely to be less favorable, and withholding feed becomes necessary.

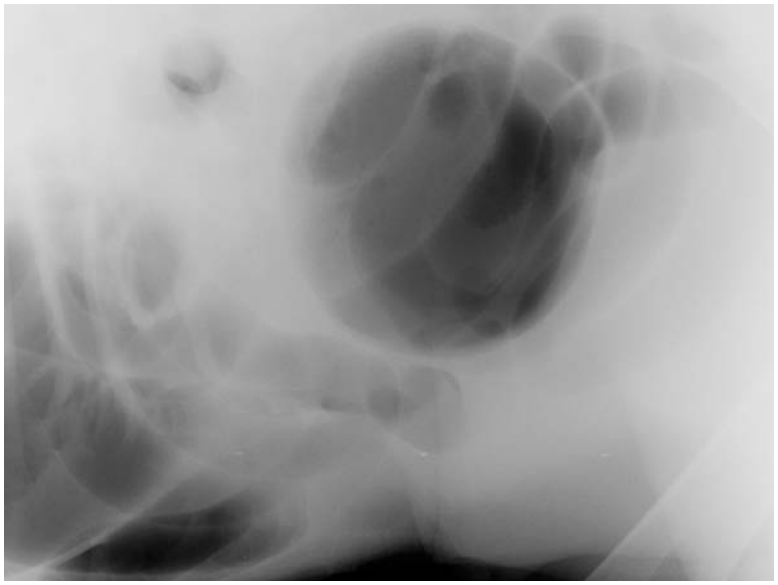
Atresia

Atresia of the colon, terminal ileum, and cecum, in association with an all-white coat color has been referred to as the "lethal white syndrome," because of its association with the recessive gene for white coat color in the progeny of overo-overo breedings. As this is a simple recessive trait, it occurs in 1 out of 4 foals from such matings. The genetic abnormality leads to a failure of migration of the neural crest cells into the bowel during embryonic development. These cells are responsible for myenteric plexus development as well as for forming melanocytes. Most foals are presented at 24 to 48 hours of age with a history of no fecal passage with progressive abdominal distention and colic. The diagnosis is supported by the clinical signs and history, in concert with the observation that the foal has no pigment in the skin.[6,7] Even if surgery to connect proximal and distal segments is possible, the lack of neurons in the myenteric plexus is the reason for a poor prognosis in these cases.

Atresia coli can also occur in foals that is not associated with the recessive lethal white gene. Affected foals have an absence of a segment of bowel, sometimes including the mesentery. The atresia can consist of a total missing segment, an atretic segment consisting of a fibrous band, or a membranous tissue separating two adjacent patent segments of bowel. It is believed that these abnormalities are the result of a loss of blood supply to the affected segment during development. Clinical signs are similar to those described for foals with lethal white syndrome, however these foals have normal pigmentation and are not necessarily the offspring of overo-overo breeding. Radiographs of the abdomen may reveal the absence of a colon, with a blunt gas-distended stump (Figure 22-4A). Surgical correction has been attempted, but results are often disappointing unless the proximal and distal segments are sufficiently formed and can be surgically connected (Figure 22-4B).[8,9]

Atresia ani has been reported in the foal, and can be of variable severity, ranging from nothing more than a simple lack of skin perforation to complete absence of several inches of anus. In foals with an intact anal ring and simple lack of perforation of the skin, surgical correction can be attempted, however results are variable. In more advanced cases, surgical correction is complicated and rarely successful. Prior to attempting surgical correction, it is prudent to fully examine the foal to ensure that other congenital lesions are not present. It has been reported that a number of other conditions occur in association with atresia ani, including cleft palate, renal hypoplasia, coccygeal vertebral hypoplasia, persistent cloaca, and rectovaginal fistula.[10-14]

Figure 22-4A



Radiograph of a foal abdomen with atresia of the pelvic flexure. The large gas-distended viscus on the film represents the blind pouch of the colon.

Figure 22-4B



Atresia coli identified during exploratory celiotomy. Note distention caused by the blind pouch at the site of atresia of the pelvic flexure.

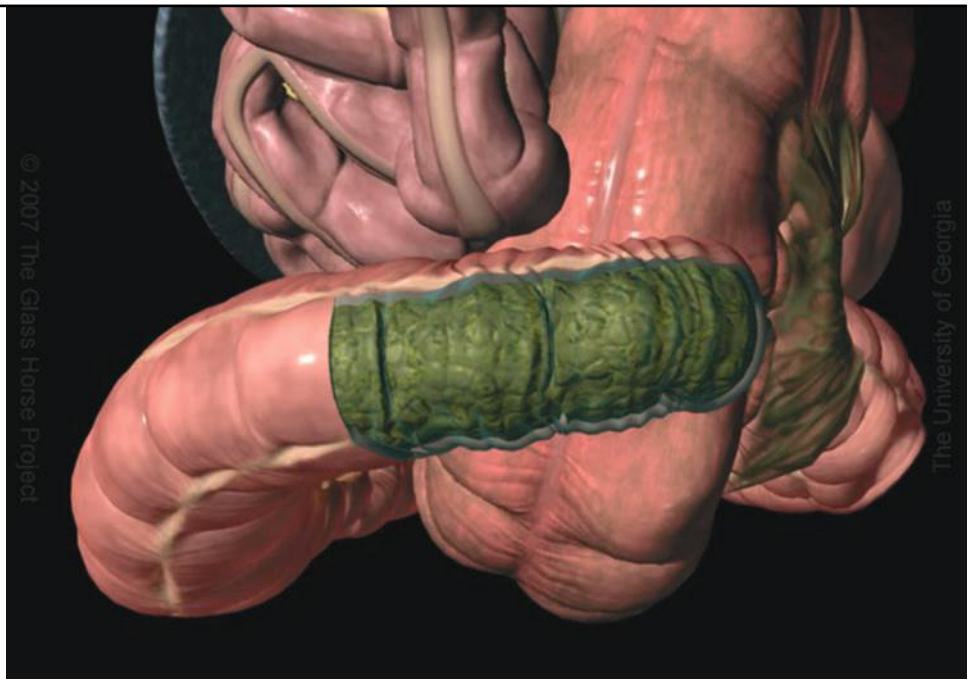
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Nutritional Management

Part 7



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Nutritional Management of the Colic Patient

Chapter 23

Ray J. Geor

In the context of colic, two primary issues are related to nutrition and feeding management. The first relates to the possible role of diet and feeding management in the development of colic in an individual horse. Some epidemiologic studies have provided evidence that changes in diet and feeding practice increase the risk of colic (e.g., changes in the type or batch of hay, sudden exposure to lush pasture, increased amount of grain or concentrate fed, and changes in the type of grain or concentrate).[1-4] Discussions with the owner or manager of the colic patient regarding current feeding management may identify known risk factors for colic and guide development of a feeding program that mitigates risk of future episodes of diet-related colic.

The second issue, which relates to the feeding management of the colic patient during convalescence, is the primary focus of this chapter. Topics covered include the rationale for early initiation of nutritional support in colic patients; estimation of nutritional requirements; strategies for feeding horses after colic and/or celiotomy; selection of diet composition; an overview of methods for delivery of assisted enteral and parenteral nutritional support; and feeding recommendations for specific gastrointestinal diseases (e.g., small-intestinal vs. large-intestinal problems). It should be emphasized that minimal data exist on the nutritional status of horses recovering from colic, and with the exception of a single study that evaluated the effects of parenteral nutrition in horses that underwent small-intestinal surgery, there is no information on the effects of different feeding practices on postoperative complications and long-term outcome after an episode of colic. A number of thorough reviews have been published on the nutritional management of sick horses, including colic patients,[5-10] but many of the recommendations outlined in those articles are based on anecdotal evidence and/or clinician experience rather than the results of controlled clinical trials. Although the present chapter suffers from the same limitation, it is hoped that this review will provide the clinician with a sound basis for selection and implementation of nutritional therapy in horses recovering from colic.

Rationale for Early Initiation of Nutritional Support after Colic and Intestinal Surgery

Withholding feed and water from horses that exhibit signs of colic is normal practice. The duration of feed withholding will vary depending on the cause of the colic and clinician preference. For horses with mild colic that quickly respond to treatment, feeding may be resumed when clinical assessment indicates adequate intestinal motility and/or there is evidence of fecal transit. In these cases, the period of withholding feed may be as short as 4 to 6 hours; however, for horses undergoing colic surgery that involves enterotomy or resection, particularly of the small intestine, the common practice is to restrict feed intake for a substantially longer period. In 30 horses that underwent resection and anastomosis of the small intestine, the mean duration of feed withholding after surgery was 76 hours, with a range of 48 to 91 hours;[11] in another study, some horses were not fed for more than 10 days after colic surgery.[12]

Is this period of starvation after colic surgery beneficial or detrimental to recovery? One rationale for withholding feed appears to be concern that an early resumption of feeding (and water intake) will stress the site of enterotomy or anastomosis, thereby increasing the risk of dehiscence, peritonitis, and other complications. Although no data exist for horses, studies in humans and other species do not provide support for the idea that postoperative starvation is beneficial for healing of wounds and anastomotic integrity. In fact, the results of animal studies have provided evidence that enteral feeding increases wound healing and anastomotic strength, perhaps because of a local enhancement in collagen synthesis,[13-14] while controlled clinical trials in human patients have shown that early feeding leads to a reduction in risk of anastomotic dehiscence.[15]

Evidence exists that nutritional status is an independent determinant of other important outcomes in human patients undergoing major gastrointestinal surgery.[16-18] Nutrient deprivation is associated with immunosuppression and alterations in gastrointestinal function, including decreased motility, villus atrophy, and a decrease in gut barrier function owing to an increase in intestinal permeability. The latter has been associated with bacterial translocation, sepsis, and systemic inflammation. Conversely, postoperative feeding, particularly via the enteral route, is associated with a significant reduction in postoperative complications including ileus, anastomotic dehiscence, and sepsis, and a decrease in the length of stay in hospital. Although these effects are most apparent in patients with preexisting malnutrition,[19-20] considerable evidence now exists that early postoperative enteral feeding is beneficial in well nourished surgical patients. In general, liquid enteral feeding is well tolerated within 6 to 12 hours after intestinal resection in humans. In one study of 650 subjects treated with enteral nutrition starting within 12 hours after major intestinal surgery, only 58 (8.9%) had to be switched to parenteral feeding because of refractory intolerance to enteral feeding.[21]

Whether postoperative nutritional support is similarly beneficial in horses that have undergone intestinal surgery is not known. However, one study of horses treated for surgical colic reported a significant correlation between several serum biochemical

indicators of negative energy balance (e.g., increased serum bilirubin and triacylglycerol concentrations) and incisional complications.[22] This observation suggests that in horses, as in humans, nutrient deprivation may be one factor that contributes to postoperative complications, and provides rationale for initiation of nutritional support early in the postoperative period. Some authors have proposed that the monitoring of changes in serum biochemical variables, particularly bilirubin and triacylglycerol, be used to guide the need for nutritional intervention.[23] Even short periods (24 to 36 hours) of feed withdrawal can result in marked increases in serum bilirubin and triacylglycerol (>1.0 mmol/L; reference range 0.25 to 0.50 mmol/L) concentrations,[24-25] suggesting that the duration of total feed withdrawal should not exceed 24 to 48 hours. Earlier intervention (e.g., as soon as 6 hours after intestinal surgery) should be considered when there is evidence of compromised nutritional status, such as in horses in thin body condition (body condition score less than 3 on a 9-point scale), a history of weight loss and/or inadequate feed intake for more than 24 to 48 hours before the beginning of the colic, or those with evidence of marked hyperlipidemia. Dunkel and McKenzie[26] described the presence of severe hyperlipidemia (serum triacylglycerol concentrations of 6.17 to 18.29 mmol/L) in horses with colic and/or colitis that had clinical and laboratory evidence of systemic inflammatory response syndrome (SIRS). The increase in circulating lipids likely reflects both an increase in mobilization of fat reserves (lipolysis) and a decrease in lipid clearance from blood, with both processes potentially modulated by SIRS and/or endotoxemia. Studies in other species have demonstrated that the activity of the endothelial lipoprotein lipase, the enzyme responsible for tissue uptake of circulating lipids, is decreased by tumor necrosis factor-α,[27] whereas the activity of hormone-sensitive lipase is increased during endotoxemia.[28] In the study of Dunkel and McKenzie,[26] treatment with intravenous dextrose or partial parenteral nutrition resulted in a return of serum triacylglycerol concentrations to normal limits, and improved appetite coincident with the decrease in circulating lipids.

Early nutritional intervention also may be indicated for obese ponies and horses (body condition score=7-9) due to concern that even short periods of negative energy balance coupled with the stress of illness and/or surgery may result in disturbances in lipid metabolism, including hyperlipidemia, hyperlipemia, and hepatic lipidosis. Provision of adequate calories and protein in these animals may lessen the stimulus for lipolysis and mitigate increases in serum triacylglycerol concentrations.

Estimating Nutrient Requirements

The nutritional requirements of horses after colic surgery or other gastrointestinal illnesses have not been determined. Consequently, recommendations are largely based on data from healthy horses with some extrapolation from data in other species. For healthy animals, the first consideration is energy (calories). Negative energy balance because of starvation or underfeeding can compromise immune function, delay wound healing, and result in a marked decrease in lean mass (e.g., skeletal muscle), the latter a result of the breakdown of endogenous protein for use in energy-requiring processes. On the other hand, studies in humans and other species have shown that an oversupply of energy (hyperalimentation) can also be detrimental, with complications such as hyperglycemia, hyperinsulinemia, hypertriglyceridemia, insulin resistance, and increased risk of septic complications.[29] A proposed mechanism for increased complications induced by hyperalimentation is an increase in the expression of tumor necrosis factor receptors associated with an increase in binding of the transcription factor nuclear factor κB to the nucleus.[30] Furthermore, in septic animals, high caloric intake results in an increase in mortality.[31,32] For these reasons, the current thinking in human medicine is to slightly underfeed nonprotein calories (20-25 kcal/kg/day) to minimize risk of septic complications.[29,33]

Daily energy requirements are probably 25% to 40% lower in hospitalized horses compared with healthy horses because of their decreased activity level and feed intake. In normal adult horses, daily digestible energy (DE) needs are calculated by the formula: DE (Mcal/day) = 1.4 + [0.03 x bodyweight (kg)] or approximately 32 to 33 kcal/kg bodyweight (bwt) per day.[34] This equation was derived from the study of horses maintained under extensive conditions, and therefore physical activity accounted for some of the energy requirement. Pagan and Hintz[35] reported that the DE requirement of healthy horses kept in stalls was approximately 22 to 23 kcal/kg bwt per day, or 30% lower than the DE required by horses kept at pasture. This caloric requirement can be estimated by the equation: RER = [21 kcal x bwt (kg)] + 975 kcal, where RER is resting energy requirement (or stall maintenance).[35] Energy requirements are also affected by the level of feed intake. Thermogenesis associated with the digestion, fermentation, and metabolism of feed can account for 15% to 25% of daily energy expenditure.[6] As horses recovering from colic most often consume less feed than normal, some reduction in the energy losses associated with digestion and nutrient processing is to be expected. One author has suggested that stall maintenance energy needs are reduced by approximately 15% to 20% in the situation of decreased feed intake.[6]

Another consideration in the estimation of energy requirements is the effect of disease or surgical intervention on metabolic rate. Evidence from human studies is conflicting regarding the effects of surgery, injury, or illness (e.g., sepsis) on metabolic rate and energy requirements. Some studies have demonstrated that abdominal surgery increases energy needs by as much

as 30%, while others have reported minimal change in energy requirements after gastrointestinal surgery, perhaps a reflection of the decrease in physical activity during hospitalization.[36] On balance, it appears that energy needs are minimally altered by surgery or injury unless there are major complications such as generalized burns or sepsis, in which case energy requirements may increase by up to 40% to100%.[33] The potential effects of underlying disease (e.g., endotoxemia or SIRS) or anesthesia and celiotomy on energy requirements of horses are unknown. However, in sick neonatal foals, resting metabolic rate and energy requirements were considerably lower when compared with healthy foals of the same age,[37,38] while horses that underwent resection of the small intestine gained weight when fed at true maintenance (i.e., 32-33 kcal/kg/day) during the postoperative period.[39] Given the paucity of data on the effects of illness on the energy needs of horses and in light of concerns regarding increased risk of complications during overfeeding, this author recommends that the caloric requirements of horses recovering from colic initially be based on the resting energy requirement or stall maintenance equation (i.e., 22-23 kcal/kg bwt/day). Thereafter, the ration should be gradually increased, although true maintenance DE may not be required until the horse returns to normal management (e.g., field turnout). Importantly, regular measurement of bodyweight or assessment of body condition score should be undertaken during convalescence to judge the adequacy of energy provision and to provide a basis for making adjustments in feeding.

Protein serves an important role in tissue maintenance, immune function, wound healing, and the slowing of endogenous protein catabolism. Protein requirements must be considered in light of caloric intake and the underlying disease process. When energy supply from carbohydrate and fat is limited, endogenous protein will be used for energy, contributing to a loss of lean body mass. Therefore, in developing a nutritional plan one must first ensure that minimal energy needs are met, and then calculate protein requirements. For humans, suggested protein requirements range between 1.2 and 2.0 g protein/kg/day, with the higher end of this range recommended for patients undergoing major intestinal sugery.[40,41] The crude protein (CP) requirement recommended for healthy adult horses, calculated from the equation: CP (grams) = 40 x DE (Mcal DE/day),[34] is an appropriate starting point in the development of a nutritional plan for colic patients. For a 500-kg horse at maintenance that is consuming ~16 Mcal DE per day, this equates to 1.25 g CP/kg bwt. As the efficiency of digestion for most dietary proteins in horse feeds is about 70%,[34] this level of CP will provide approximately 0.9 g available protein/kg/day. For parenteral feeding, a slightly lower amount of protein feeding is reasonable given the higher metabolic availability of amino acids administered via the intravenous route.[11,25,41] In reports of parenteral feeding of horses, 0.6 to 0.8 g protein/kg/day (1 g/40-50 kcal) was administered (as a balanced amino acid solution).[11,25,42] There may be justification for higher levels of dietary protein (e.g., 2 g CP/kg/day), particularly for horses in poor body condition (body condition score less than 3) or those with SIRS, hypoproteinemia, and/or hypoalbuminemia.

Modes of Nutritional Therapy

The mode of nutritional therapy for the colic patient depends on the underlying cause of the colic, the horse's appetite, and complications that arise during convalescence. The three primary modes of nutritional therapy are: 1) voluntary enteral feeding; 2) assisted enteral feeding; and 3) parenteral nutrition.[6,43] The preferred option is a controlled return to normal voluntary intake. Prerequisites are absence of gastric reflux, good intestinal motility, and a willingness to eat. As a general recommendation, horses that have undergone celiotomy without enterotomy and have good gastrointestinal motility can resume feeding within 12 to 24 hours. As discussed, however, some clinicians prefer to withhold feed for a longer period (more than 24 hours) in horses that have undergone enterotomy or anastomosis.[6] Voluntary intake should provide at least 50% to 75% of the horse's resting or stall maintenance DE and crude protein requirements by the second or third day of feeding. For example, 75% of the resting energy requirement of a 500-kg horse (~9 Mcal DE) would be met by the consumption of about 4 kg of first-cut timothy hay that contains approximately 2.3 Mcal DE/kg (as fed). Although labor intensive, weighing the offered hay and the feed remaining in the stall is the only means of determining the adequacy of caloric intake.

More challenging is the nutritional management of anorexic or inappetant horses or horses with severe intestinal compromise that restricts feeding by the enteral route because of ileus or intestinal dysmotility. Inappetant horses should be offered a variety of palatable feedstuffs, including fresh grass, in an attempt to stimulate intake; their failure to consume at least 50% of resting DE requirements for more than 24 to 36 hours is an indication for beginning assisted enteral feeding. Earlier intervention is justified for horses in poor body condition (body condition score less 3) or a recent history of weight loss, for old horses (older than 20 years), horses with suspected or confirmed endotoxemia/SIRS, lactating mares or those in the last trimester, and animals with severe hypertriglyceridemia.[6,43-45] Parenteral nutrition should be considered for horses with ileus and other intestinal conditions that prevent voluntary or enteral feeding, particularly when the withholding of oral feeding is expected to exceed 48 to 72 hours.

In human clinical nutrition, there has been considerable debate on the relative merits of enteral vs. parenteral nutrition. Historically, parenteral nutrition has been associated with several complications including intestinal atrophy, failure of gut barrier function, bacterial translocation, increased incidence of sepsis, and hyperglycemia. In rodent models, intestinal villous atrophy develops within a few days of the start of parenteral nutrition,[46] and withdrawal of enteral feeding has been associated with bacterial translocation, systemic inflammation, and sepsis.[47,48] Early human studies also suggested that complication rates (particularly sepsis) and mortality were higher in patients receiving parenteral nutrition when compared with enteral nutrition. However, a critical review of human studies[29] indicated that parenteral nutrition (i.e., complete bowel rest) is not associated with intestinal atrophy, while the incidence of bacterial translocation is no different between patients receiving parenteral or enteral nutrition. Although enteral nutrition is advocated when the gastrointestinal tract is functional, the weight of evidence from human studies indicates that parenteral nutrition is an important alternative to enteral nutrition when a risk of malnutrition is present and enteral nutrition is not tolerated or not possible because of poor gastrointestinal function. These same principles can be applied when developing a plan for nutritional management of horses with colic.

Voluntary Feeding

For horses with a good appetite, nutritional management is composed of a gradual increase in voluntary intake, with an emphasis on high-fiber feeds. One author has recommended that hay be offered as soon as 12 hours after colic surgery.[7] In one study, feeding grass hay to horses after colic surgery was associated with a decreased incidence of severe diarrhea during the postoperative period.[49] Initially, small amounts (e.g., 0.3-0.5 kg) of good quality forage (e.g., grass hay, alfalfa) should be fed 4 to 8 times daily, with a steady increase in the volume of feedings and a decrease in frequency over a 3 to 5 day period. Limiting the size of feedings during the early phase of re-feeding may reduce the risk of intestinal distention and anastomotic dehiscence.[7] For the same reason, some clinicians prefer to feed processed fiber products (e.g., chopped grass or alfalfa "chaff," alfalfa meal, soaked beet pulp shreds, wheat bran, or combinations) rather than long-stem hay during the early postoperative period. Alternatively, the horse may be allowed to graze pasture for 5 to 10 minutes several times throughout the day, or provided with a highly digestible, low-bulk pelleted feed such as those marketed for use in older horses ("senior feeds").

In general, grain-concentrate feeds (e.g., straight grains or sweet feed) should be avoided for 10 to 14 days postoperatively (or post-colic) because of concern that an excess of hydrolyzable carbohydrate (starch) may disturb an already disrupted hindgut microbial community. Thereafter, grain or grain-concentrate feeding can be resumed, starting at a rate of about 1 kg/day (for a 500-kg or 1100-lb horse) and increasing by no more than 0.5 to 0.75 kg/day. An additional concern with the feeding of grain-concentrates relates to the potential for high glycemic feeds to exacerbate hyperglycemia and hyperinsulinemia during the postoperative period. In humans, uncomplicated abdominal surgery is associated with development of insulin resistance that can persist for up to 2 to 3 weeks after surgery.[50,51] Furthermore, studies in humans have indicated that insulin resistance and hyperglycemia are poor prognostic indicators in critical care patients and that control of glycemia improves outcome.[52,53] The implications of these findings to management of equine colic patients is unknown. However, preliminary studies have demonstrated hyperglycemia and hyperinsulinemia after emergency celiotomy (A. Durham, personal communication 2005), suggesting that insulin resistance also may occur in horses after colic surgery. Avoidance of high-glycemic feeds may be particularly important in overweight horses, ponies, and donkeys in which an association exists between insulin resistance and development of laminitis.[54] This author prefers to feed alternate sources of energy when hay or other forage alone does not meet estimated DE needs, e.g., fat from stabilized rice bran (0.5-1.5 kg/day) or vegetable oil (100-300 mL/day mixed with hay cubes that have been softened in water). The feeding of a small amount of a protein supplement (e.g., 0.25-0.50 kg casein, 93% CP [DM basis]) also may be indicated, particularly in horses with hypoproteinemia.

Assisted Enteral Feeding

Assisted enteral feeding is accomplished by the infusion of a liquid diet through a nasogastric tube. Diet options for assisted enteral feeding include human enteral products, commercial pelleted horse feeds, and homemade recipes. Human formulations that have been administered to adult horses include Vital HN and Osmolyte HN (Ross Laboratories, Columbus, OH).[18-20] Both formulations are devoid of fiber, an advantage with respect to ease of administration through a small diameter nasogastric tube but also a possible reason for the high incidence of diarrhea when these products are fed to horses. There also have been anecdotal reports of laminitis. Risk of these complications may be mitigated by gradual introduction of the liquid diet over a 3-4-day period but diarrhea remains common, perhaps indicating the importance of dietary fiber for maintenance of normal hindgut function.[55,56] It should also be recognized that the mix of energy substrates in these fiber-free human enteral formulas differs from that in typical equine rations.[23] Osmolyte contains approximately 29% of calories from lipid and 54% of calories from hydrolyzable carbohydrate (mostly sugars), while Vital HN provides about 10% calories from lipid and 74% from carbohydrate. The high lipid content of Osmolyte may contribute to digestive disturbances in horses not adapted to

fat-supplemented rations, while use of a high-carbohydrate diet such as Vital HN may be contraindicated for horses with abnormal glucose metabolism.[23] Collectively, these considerations argue against the use of fiber-free human enteral products in horses recovering from gastrointestinal disease. Diets containing a moderate amount of fiber (15% to 20% crude fiber, DM basis) appear to be a more suitable choice for assisted enteral feeding in horses.[23]

A simple approach is to use a commercially available pelleted feed that contains a source of fiber, such as Equine Senior® (Land 'O lakes-Purina Feed, St. Louis, MO) or similar "complete feeds" that contain added fiber and are designed to be fed without hay. These products contain about 14% to 25% crude fiber and provide 2.6 to 3.1 Mcal DE/kg diet (as fed). Therefore, 3.5 to 4.0 kg of diet would be needed to meet the stall energy requirements of a 450-kg horse. Vegetable oils (¼ to 1½ cup or 75 to 375 mL per day) can be added to increase the caloric density of the diet (Table 23-1). One cup (200 g) of oil provides about 1.6 Mcal of DE. Vitamin E (100 - 200 IU per 100 mL of oil) should be added to the ration if supplemental vegetable oil is provided. When providing supplemental fat to a sick horse (450-500 kg bwt), 75 to 125 mL per day (1/4 to 1/2 cup) should be given initially and then gradually increased if no adverse response is seen (e.g., diarrhea, steatorrhea, or lipemia). Feeding vegetable oil may be contraindicated in horses and ponies with hypertriglyceridemia (triglyceride concentration >300 mg/dL) or hepatic lipidosis.

Table 23-1

Enteral Formulation Based on a Complete Pellet Ration and Recommended Feeding Schedule for a 500-kg Horse.[a]

Ingredient	Day 1 (1/4 ration)	Day 2 (1/2 ration)	Day 3 (3/4 ration)	Day 4 (Full ration)
Complete Pelleted Horse Feed (g)[b]	885	1770	2650	3530
Vegetable Oil (mL)	100	177	265	354
Water (L)	8	16	24	24
Digestible energy (Mcal)	3	6	9	12

[a]Energy requirements are at *stall maintenance* for a 500-kg horse (~12 Mcal DE/day). These allowances should be divided and administered into a minimum of 4 feedings daily. (Adapted from Fascetti AJ, Stratton-Phelps M. Clinical assessment of nutritional status and enteral feeding in the acutely ill horse. In. Current Therapy in Equine Medicine, 5th ed. Robinson NE (ed). Philadelphia: Elsevier 2003, pp. 705-710.

[b]Equine Senior® (Land 'O Lakes-Purina Feed, St. Louis, MO), 2.6 Mcal DE/kg as fed).

Variations on the alfalfa/dextrose/casein enteral formulation first described by Naylor et al[57] also can be used for assisted enteral feeding (Table 23-2). The recipe designed by Naylor and colleagues provides about 3 Mcal DE/kg diet and is 33% crude protein and 12% crude fiber. The higher protein content when compared with typical equine diets may be beneficial for debilitated and/or hypoproteinemic horses. In healthy horses, the administration of this diet was reported to maintain body weight and serum biochemical parameters within reference limits; however, occasional diarrhea and laminitis were reported complications.

Suggested feeding protocols for a complete pelleted feed with supplemental vegetable oil and for the alfalfa/dextrose/casein formulation are presented in Tables 23-1 and 23-2, respectively. The rate of diet administration should be gradually increased over a 3 to 5 day period. A suggested rate of introduction is to administer one quarter of the final target volume of feed on day 1, one half total volume on day 2, three quarters of total volume on day 3, and the total volume on day 4 or 5. Clinical signs of intolerance to enteral feeding (see below) dictate a slower rate of introduction. In hospital settings, the enteral diet should be administered in a minimum of 4 and preferably 6 feedings per day with no more than 6 to 8 L per feeding for a 450- to 500-kg horse (including the volume of water used to flush the tube). This volume should be administered over a 10- to 15-minute period. In field settings, a more practical approach is to administer 2 treatments per day although it will not be possible to meet maintenance nutritional requirements with this treatment regimen.

Pelleted feeds should be soaked in warm water to soften before mixing in a blender. A fresh batch of diet should be made before each feeding. The tube with the smallest possible internal diameter should be chosen for diet administration. A tube with a 1/2-inch (12-mm) inner diameter is suitable for most enteral diets that contain fiber. The end of the tube should be open-ended, rather than fenestrated, to prevent the tube from becoming clogged. Fiber-free diets can be administered via a

smaller tube (e.g., 18-Fr, 100-inch feeding tube; NG18100, Mila International). Intermittent nasogastric intubation or placement of an indwelling nasogastric tube can be used to facilitate feeding. In hospitalized horses, feeding tubes can be left in place for up to 7 to 8 days although some degree of nasopharyngeal irritation and mucoid nasal discharge are expected. Softer silicon tubes are less irritating compared with tubes made of polyvinylchloride, do not tend to harden when left in place, and are generally recommended for horses requiring assisted enteral feeding for several days.[23] Before placement of the tube, the clinician should establish that the diet solution flows adequately through the tube. It may be necessary to add more water or to mix the feed in a blender a second time. The tube should be positioned in the stomach rather than the distal esophagus to minimize risk of reflux of feed around the tube. The tube should be secured to the halter; application of a muzzle may be necessary between feedings to prevent the horse from dislodging the tube. A stomach pump is recommended for infusion of fiber-containing diets. After administration of the diet, the tube should be flushed with approximately 1 L of water followed by a small volume of air to ensure that no feed material remains in the tube. The end of the tube should be capped with a syringe case between feedings.

Close clinical monitoring, particularly of gastrointestinal function, is imperative for horses receiving assisted enteral feeding. Repeated ultrasonographic examinations can be useful for evaluation of gastric distention and intestinal motility. The presence of residual gastric fluid should be assessed (i.e., siphoned) before each feeding. Substantial gastric reflux (more than 1-2 L) is an indication to withhold enteral feeding for at least 1 to 2 hours, and to reevaluate before beginning feeding again.[23] Persistent gastric reflux indicates intolerance to enteral feeding and the need for the horse to receive parenteral feeding. Similarly, signs of colic, ileus, abdominal distention, and/or increased digital pulses suggest intolerance to enteral feeding and are indications to discontinue therapy or decrease the volume and frequency of feedings. The passage of loose feces is not uncommon in horses receiving assisted enteral feeding and is of minimal concern if not accompanied by clinical signs of depression, dehydration, ileus, and/or colic.[6,23] It is important to measure the total volume of water administered via the nasogastric tube. Daily water requirements (approximately 50 mL/kg/day) can generally be met during assisted enteral feeding if the horse is fed 4 to 5 times per day. Frequent measurements of hematocrit and plasma total protein concentration also are useful for monitoring hydration status and the adequacy of water administration. Hypokalemia, ionized hypomagnesemia, and ionized hypocalcemia can occur in horses with gastrointestinal disease. Accordingly, frequent measurements of serum electrolytes and ionized calcium and magnesium are recommended during assisted enteral feeding. Supplementation with potassium, calcium, and/or magnesium may be necessary. Horses should also be monitored for development of complications associated with repeated or indwelling nasogastric intubation, including rhinitis, pharyngitis, and esophageal ulceration.[58]

Table 23-2

Alfalfa/Dextrose/Casein Enteral Formulation and Recommended Feeding Schedule for a 500-kg Horse.[a]

	Day						
Parameter	1	2	3	4	5	6	7
Electrolyte mixture (g)b	230	230	230	230	230	230	230
Water (L)	21	21	21	21	21	21	21
Dextrose (g)	300	400	500	600	800	800	900
Dehydrated cottage cheese or casein (g)	300	450	600	750	900	900	900
Dehydrated alfalfa meal (g)	2000	2000	2000	2000	2000	2000	2000
Digestible energy (Mcal)	7.4	8.4	9.4	10.4	11.8	11.8	12.2

[a]Adapted from Naylor JM, Freeman DE, and Kronfeld DS. Alimentation of hypophagic horses. Compend Cont Educ Pract Vet 6:S93-S99, 1984. These allowances should be divided and administered into 3 or 4 feedings daily. Stall maintenance requirements for a 500-kg horse are 12 Mcal DE/day.
[b]Composition of electrolyte mixture: sodium chloride (NaCl) 10 g; sodium bicarbonate (NaHCO3) 15 g; potassium chloride (KCl) 75 g; potassium phosphate (dibasic anhydrous, K2HPO4) 60 g; calcium chloride (CaCl2·2H2O) 45 g; magnesium oxide (MgO) 25 g.

Parenteral Nutritional Support

There have been several reports of the use of parenteral nutrition in colic patients, with ileus, gastric reflux, and gastrointestinal conditions mandating complete bowel rest (e.g., small-intestinal resection, duodenitis-proximal jejunitis) being the most common indications for instigating this form of nutritional therapy.[11,25,42,59] Few studies have evaluated the clinical benefits of parenteral nutrition in colic patients. Durham and colleagues,[11,25] however, examined the effects of postoperative parenteral nutrition in 15 horses (vs. 15 control horses) recovering from resection and anastomosis of strangulated small intestine. These authors reported no beneficial effect of parenteral nutrition on the time elapsed to first oral feeding, the duration of hospitalization, costs of treatment, or short-term survival (up until 5 months after discharge), although the parenteral nutrition protocol did confer improved nutritional status as reflected by lower serum concentrations of triglycerides and total bilirubin and higher concentrations of glucose. However, the duration and volume of postoperative gastric reflux were longer in the parenteral nutrition group than in the control horses, perhaps because of alterations in gastric and/or small intestinal motility, and there was a non-significant trend for catheter-site complications in the parenteral nutrition group. The authors concluded that further study of a larger number of horses is required to determine the clinical benefits and possible harmful side effects of parenteral nutrition in horses recovering from small-intestinal surgery. Studies of the effects of parenteral nutrition in perioperative human patients also have yielded equivocal findings. Several studies have demonstrated that perioperative parenteral nutrition is associated with reduced morbidity and mortality in malnourished patients.[60-62] In contrast, perioperative parenteral nutrition in well nourished human patients has been associated with increased morbidity, particularly septic complications.[63-64] Nonetheless, as discussed above, the current consensus in human clinical nutrition is that parenteral nutrition is an important component of overall case management, particularly in patients with evidence of malnourishment, gut failure, and/or increased nutritional requirements (e.g., pregnancy, lactation, growth). Although further studies are needed to examine the putative benefits of parenteral nutrition in equine colic patients, there is rationale for use of parenteral nutrition in horses that are prevented from eating for more than 48 hours post-colic, particularly those in poor body condition (body condition score less than 3) or with increased nutritional demands (e.g., pregnant or lactating mares).

A detailed description of methods for parenteral nutritional support is beyond the scope of this chapter, and the reader is referred elsewhere for comprehensive discussion of this subject, including methods for preparation of parenteral nutrition solutions.[43,59] The following provides a brief overview on the composition of parenteral nutrition solutions, methods for delivery, and potential complications. As with enteral nutritional support, the goal of parenteral nutrition is to administer calories and amino acids such that loss of body protein (and lean body mass) is minimized. Carbohydrates in the form of a 50% dextrose solution (3.4 kcal/g or 1.7 kcal/mL; osmolarity 2525 mOsm/L) and lipid, as a 10% to 20% emulsion (20% emulsion: 9 kcal/g or 2 kcal/mL; osmolarity 260 mOsm/L), are the primary sources of energy used in parenteral nutrition solutions, while an amino acid solution (e.g., Travasol 8.5% or 10%; Baxter Health Care Corporation) is used to meet protein requirements (e.g., protein synthesis, immune function). Commercial lipid emulsions (e.g., Intralipid 20%; Baxter Health Care Corporation, Deerfield, IL) consist of soybean oil, egg yolk phospholipid, and glycerin. These emulsions provide mainly unsaturated fatty acids (linoleic, 44% to 62%; oleic, 19% to 30%; linolenic, 4% to 11%; palmitic, 7% to 14%). Parenteral nutrition solutions with and without lipid can be used, i.e., dextrose/amino acid or dextrose/lipid/amino acid mixtures. The addition of lipids to the parenteral nutrition formula results in a solution with lower osmolarity when compared with a dextrose/amino acid mixture of similar caloric density. Hence, the lipid-containing solution should be less irritating to peripheral veins. Lipid solutions must be included in the formula if target calorie provision approaches true maintenance (32-33 kcal/kg/day) because this level of calorie delivery from a dextrose/amino acid parenteral nutrition solution often results in marked hyperglycemia and glucosuria. However, when the target daily energy provision is 20 to 22 kcal/kg/day, dextrose/amino acid mixtures can be used. In human medicine, this approach is referred to as partial parenteral nutrition and is often employed in postoperative patients that require only a few days of intravenous nutritional support.[29] A similar rate of calorie provision has been applied in recent reports of parenteral nutrition in postoperative colic patients.[11,25] As discussed previously (see Nutrient Requirements), provision of amino acids (protein) at a rate of 0.6 to 0.8 g/kg bwt per day is one guideline for meeting protein requirements in adult horses, although some authors have recommended 1.0 to 1.5 g/kg/day and provision of amino acids at 0.6 to 2.0 g/kg/day has been used in sick horses without apparent complications.

A suggested parenteral nutrition formula (Table 23-3) is composed of 1 L of 50% dextrose (0.5 g/mL dextrose x 3.4 kcal/g x 1000 mL = 1700 kcal), 1 L of a 10% amino acid solution (0.1g/mL of amino acids x 4 kcal/g x 1000 mL = 400 kcal), and 500 mL of 20% lipid emulsion (0.2 g/mL lipid x 9 kcal/g x 500 mL = 900 kcal). These components are diluted with 4 L of isotonic fluid, yielding a final volume of 6.5 L and a caloric density of approximately 0.45 kcal/mL. A multivitamin supplement (American Pharmaceutical Partners, Los Angeles) may be added this mixture. This solution can be prepared up to 24 hours in advance of administration and stored at 4°C until use. Administration of parenteral nutrition solutions should be through a dedicated intravenous catheter, preferably one inserted into a large vein such as the jugular to minimize risk of complications

associated with the infusion of hyperosmotic solutions. Alternatively, a double lumen catheter can be used, allowing the parenteral nutrition solution to be given through one port and medications and other fluids through the other port. To minimize the risk of thrombophlebitis, nonthrombogenic catheters such those made from polyurethane are recommended. Meticulous attention to sterile technique is needed during catheter placement to further minimize the risk of thrombophlebitis and other septic complications. The fluid lines used for delivery of the parenteral nutrition solution should be changed every 24 hours. An infusion pump is required to ensure accurate delivery of the parenteral nutrition solution.

Table 23-3 provides a recommended rate of parenteral feeding for a 450-kg horse. The initial rate of administration of parenteral nutrition solution should be approximately 35% of target calorie provision, increasing to 60% to 65% after 12 hours and 100% (23 kcal/kg/day) at 24 hours providing there are no complications such as development of marked hyperglycemia, glucosuria, or hyperlipemia. Hyperglycemia and hyperlipemia were the most common complications of postoperative parenteral nutrition in horses. In one report, hyperglycemia was observed in 52 of 79 horses receiving parenteral nutrition,[42] perhaps as a result of insulin resistance, an excessive rate of administration, or both. Urine and blood glucose concentrations should be measured every 4 to 8 hours in horses receiving parenteral nutrition, and the rate of dextrose administration should be decreased if glucose concentrations exceed the renal threshold (approximately 180 mg/dL or 10 mmol/L). A constant-rate insulin infusion (e.g., regular insulin at a starting dose of 0.05 to 0.1 IU/kg/hour) can be instituted if the reduction in the administration rate of dextrose fails to correct the hyperglycemia. Blood glucose concentrations must be closely monitored. Adjustments in insulin dose may be required to achieve glycemic control. As mentioned, tight regulation of glucose concentrations has been associated with improved outcome in critically ill human patients.[52,53] Serum BUN, triglycerides, and electrolytes should be monitored at least daily. Hypokalemia, hypocalcemia, and hypomagnesemia have been reported in horses receiving parenteral nutrition, and it may be necessary to supplement these nutrients if parenteral feeding is used for more than 48 to 72 hours. Finally, body weight should be recorded daily or every second day; maintenance of body weight will provide the best guide as to the effectiveness of nutritional support.

Table 23-3
Parenteral Nutrition Formula and Recommended Administration Rate for a 500-kg Horse.[a]

Formula	1st 12 hours	2nd 12 hours	Day 2 on
Dextrose 50%	1000 mL	1000 mL	1000 mL
Lipid 20%	500 mL	500 mL	500 mL
Amino acids 10%	1000 mL	1000 mL	1000 mL
Isotonic fluids	4000 m	4000 mL	4000 mL
Total volume	6500 mL	6500 mL	6500 mL
Kcal per bag	3000	3000	3000
Kcal per hour	210	333	480
Rate (mL/hour)	470	740	1070
Bags required	0.90 per 12 h	1.4 per 12 h	4.0 per 24 h
Kcals per day	—-	—-	11500

[a]For parenteral nutrition, daily energy needs are estimated at 22 to 23 kcal/kg/day (~11.0-11.5 Mcal per day for a 500-kg horse). (Adapted from Holcombe SJ. Parenteral nutrition for colic patients. In Current Therapy in Equine Medicine, 5th ed. Robinson NE (ed). Philadelphia:Elsevier, 2003, pp. 111-115.)

Transition to Voluntary Feeding

As appetite returns (or when voluntary oral feeding is no longer contraindicated), small amounts of palatable (e.g., fresh grass) feed should be offered. If these feedings are tolerated, the level of tube or parenteral feeding can be gradually reduced as the provision of feed for voluntary consumption is increased. Nutritional support can be withdrawn when voluntary feed intake provides at least 75% of the calorie and protein requirements of stall maintenance. Recommendations for the resumption of oral intake in horses with small- or large-intestinal problems are discussed in the next section.

Feeding Management of Specific Gastrointestinal Conditions

Small-Intestinal Disorders

Disorders of intestinal motility are of primary concern following small-intestinal surgery, particularly in horses requiring resection and anastomosis of the small intestine. Complications include peritonitis, impaction or leakage at the site of enterotomy or anastomosis, and adhesion formation.[65] Little study has been done of the impact of postoperative nutrition on these complications or of the effects of nutritional therapy on short- and long-term survival rates. There have been anecdotal reports that early application of enteral or parenteral nutritional support is associated with decreased incidence and/or severity of postoperative ileus, but there are no data from controlled studies. As discussed earlier, however, parenteral nutrition may be beneficial for the nutritional management of horses after surgery of the small intestine, particularly for the first 24 to 72 hours when there is rationale for restriction of enteral feeding to minimize risk of incisional leakage and dehiscence. Parenteral nutritional support is also advocated for horses with duodenitis-proximal jejunitis because of the protracted nature of the ileus and gastric reflux in these cases. A concern with the feeding of high-bulk feeds, such as long-stem hay, in the early postoperative period is distention at the site of the enterotomy and/or anastomosis. In horses with sutured esophageal wounds, a traditional hay-grain diet can result in development of fatal complications presumably because this high-bulk diet promotes distention at the incision site, increasing the probability for wound dehiscence.[66] On the other hand, horses with esophageal injuries that are sutured closed can make a full recovery if fed a soft diet (e.g., slurry made from pelleted feeds) for 8 to 10 weeks following the injury.[66] These findings may be applicable to the nutritional management of horses following small-intestinal surgery. Specifically, if cost is not prohibitive, the recommendation is to administer parenteral nutrition for 24 to 48 hours after surgery with a subsequent gradual introduction to enteral feeding and concomitant reduction in the level of parenteral feeding. If parenteral nutrition is not feasible, feed should be withheld for 24 to 36 hours. In all cases, enteral feeding should not be started until gastrointestinal function is adequate, as indicated by the presence of borborygmi and the absence of gastric reflux. Initially, small amounts of water should be offered (e.g., 1 L every hour over a 5- to 6-hour period) as a test of intestinal function. If no gastric reflux develops, intake of solid feed can be started. A soft, low-bulk ration is recommended to decrease the risk of anastomosis failure. Fresh grass (hand grazing) and mashes or slurries made from alfalfa pellets or pelleted complete feeds are suitable feedstuffs. Molasses may be added to the mash or slurry to enhance palatability of the ration. Small meals (0.5-0.75 kg) should be fed every 3 to 4 hours in an effort to minimize physical stress at the anastomosis site. In uncomplicated cases of resection and anastomosis, long-stem hay should be gradually introduced after 3 to 4 days of soft-diet feeding. Bran mashes are *not* recommended for horses recovering from surgery of the small intestine.

Resection of more than 50% of the small intestine requires long-term modification of diet. Ponies fed a complete pelleted feed were able to maintain body condition following resection of less than 50% of the small intestine.[67] However, ponies fed the same diet after removal of more than 60% of the small intestine developed diarrhea and substantial weight loss, likely a result of significant malabsorption. Clinical experience has also indicated difficulty in maintaining body condition of horses following resection of 50% or more of the small intestine. A diet based on alfalfa has been recommended (e.g., chopped alfalfa, alfalfa pellets, high quality hay). Beet pulp shreds and stabilized rice bran (a source of digestible fat) also are suitable feedstuffs, and vegetable oil (e.g., 100-500 mL/day divided b.i.d. or t.i.d.) can be gradually introduced to increase the energy density of the ration. Grains should be avoided as the capacity for starch digestion is probably greatly diminished.

Large Intestinal Disorders

Diarrhea is a complication of all types of colic surgery, but the risk appears to be highest in horses undergoing celiotomy for disorders of the large intestine.[49] In one study, the risk for development of diarrhea after surgery was twofold higher in horses with large-intestinal disorders when compared with horses with other lesions.[49] A further increase in risk occurred in horses that had had an enterotomy. Conversely, horses fed grass hay were half as likely to develop severe diarrhea as horses not fed grass hay. Horses should be fed small amounts of grass or soft grass hay at frequent intervals (every 2 to 3 hours) as early as 12 hours postoperatively, providing no evidence exists of gastric reflux or poor intestinal motility. First-cut hay is preferred because of higher dry matter digestibility compared with more mature forages. No grain or concentrate should be introduced until 10 to 14 days after surgery; however, the feeding of a low-bulk pelleted feed such as Equine Senior® may be beneficial during this period.

Longer term dietary modification is required for horses with extensive resection of the large colon, but not when the cecum alone is removed. Bertone and colleagues[68-70] demonstrated that gastrointestinal passage time and fiber, protein, and phosphorus digestion are decreased after resection of more than 90% of the large colon. In one clinical report, chronic diarrhea, weight loss, and hypophosphatemia were complications of extensive resection of the large colon.[71] With appropriate

dietary management, however, these horses can maintain adequate body condition. In the early postoperative period, horses that have undergone extensive resection should be fed small amounts of a low-bulk feed such as alfalfa pellets or a pelleted commercial feed (e.g., Equine Senior). Subsequently, legume forage should be the predominant component of the ration. Following experimental colon resection, a ration of alfalfa hay or an alfalfa-timothy hay mix provided better results when compared with straight grass hay, perhaps because of the higher digestibility and protein content of the alfalfa-based rations.[70] Supplemental phosphorus can be provided in supplement form or by feeding 0.5 kg wheat or stabilized rice bran daily. If additional calories are required for weight maintenance, a "fat and fiber" concentrate rather than grain or sweet feed is recommended.

Horses with impaction of the large colon should be fed soon after resolution of the impaction. Fresh grass, alfalfa pellets, chopped alfalfa hay and other sources of highly digestible fiber are preferred. It has been suggested that pelleted feeds may allow for increased rate of passage because of their smaller particle size when compared with long-stem roughage.[7] Careful dietary management is required for horses recovering from cecal impaction. Affected horses are prone to re-impaction after resumption of feed intake, perhaps reflecting a persistent decrease in cecal motility associated with marked distention of the cecum. Low-bulk pelleted feeds rather than long-stem hay are recommended during the first 10 to 14 days after cecal impaction. Careful clinical monitoring (e.g., repeat ultransonographic examinations and palpations per rectum) is paramount during the first 48 to 72 hours when risk of re-impaction is highest. Thorough oral examination should be undertaken to establish whether inadequate mastication of feed is an underlying cause of the impaction.

Conclusions

Knowledge of the benefits and complications associated with different modes of nutritional support in horses recovering from colic is limited, and further clinical studies are required to facilitate refinement of feeding recommendations. Evidence exists in humans and other species, however, that protein and energy malnutrition can have deleterious effects on recovery from critical illness such as abdominal surgery and, on this basis, there is rationale for early enteral or parenteral support of horses recovering from colic surgery. The mode of nutritional support will depend on the underlying cause of colic, whether or not complications arise during convalescence, and the horse's appetite. Although enteral feeding is the most cost-effective method of nutritional support, parenteral nutrition is required for horses with ongoing intestinal dysfunction (i.e., ileus, dysmotility, gastric reflux). In horses with adequate gastrointestinal function, small and frequent feedings should be offered as soon as 12 to 24 hours after surgery. High-quality grass hay or a low-bulk complete feed should be fed to horses recovering from large-intestinal problems, while horses with small-intestinal problems requiring resection and anastomosis should be fed soft mash or slurry diets for 2 to 4 days postoperatively, followed by a gradual reintroduction to normal diet. Long-term modification of diet is required following radical resection of the small or large intestine.

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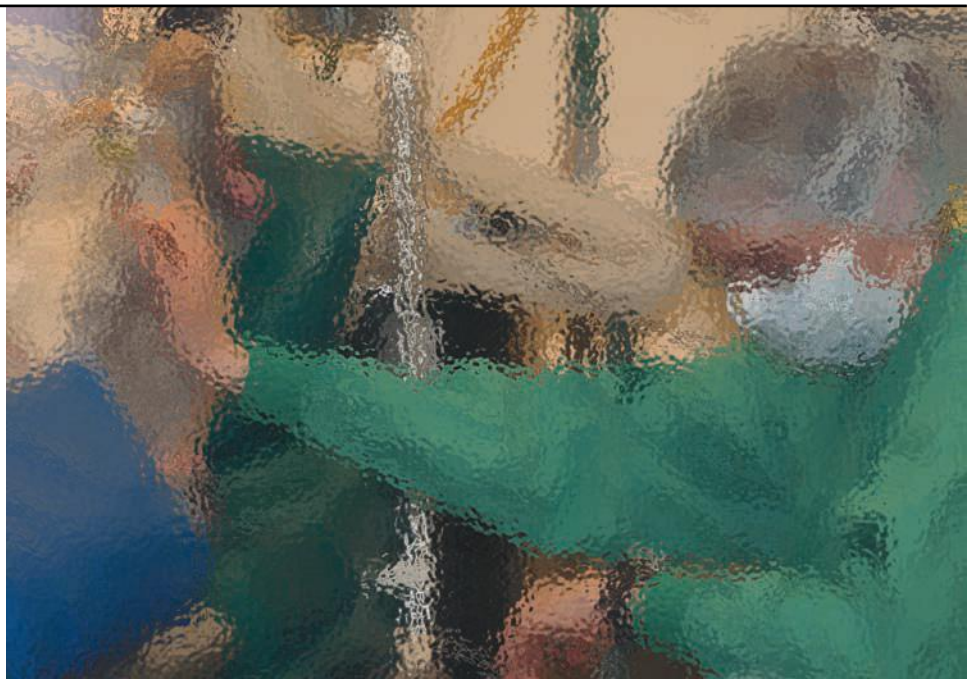
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Anesthesia for Abdominal Surgery

Part 8



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Anesthesia for Horses with Colic

Chapter 24

Cynthia M. Trim

Preanesthetic Assessment

Recognition of abnormalities in a horse with colic allows the veterinarian to manage anesthesia in ways to avoid or limit adverse situations. The goals of pre-anesthetic evaluation are to assess the horse's status regarding: 1) treatments to ensure adequate cardiovascular function after induction of anesthesia, 2) the optimal reduction in dose rates of anesthetic agents, and 3) treatment strategies for complications likely to be encountered. The most relevant aspects of pre-anesthetic evaluation of a colicky horse are its breed, age, and weight, reproductive status, current demeanor, degree of abdominal distention, mucous membrane color and capillary refill time (CRT), pulse strength, cardiac sounds, laboratory test results, and the anticipated surgical lesion.

Indicators of hypovolemia include clinical signs of dehydration, weak peripheral pulses and prolonged CRT, low blood pressure, and values of packed cell volume (PCV), total protein concentration, creatinine, and anion gap that exceed normal values. As hypotension is likely to develop in a hypovolemic horse after induction of anesthesia, restoration of blood volume with an infusion of balanced electrolyte solution, such as acetated or lactated Ringer's solution at 20 mL/kg IV, is advisable before anesthesia. Hypertonic 7.5% saline solution, 2 to 4 mL/kg administered IV over 10 to 15 minutes, can be used to rapidly expand blood volume and promote improved hemodynamic function for about 1.5 hours.[1,2] Hypertonic saline solution should be followed by administration of a balanced electrolyte solution, approximately 30 mL/kg given over 1 to 2 hours, to avoid tissue dehydration (see Chapter 7).

Hypocalcemia and hypomagnesemia are commonly present in horses with colic and in healthy animals with experimentally induced endotoxemia.[3-5] In horses with colic, the serum calcium and magnesium concentrations do not predict survival or length of hospital stay.[3] Further, in a study of endotoxemia in pigs, administration of calcium did not significantly alter survival.[4] However, hypocalcemia can contribute to hypotension during anesthesia. Administration of 23% calcium gluconate, 0.5 mL/kg IV, over 20 minutes before induction of anesthesia appears to provide a temporary but sufficient increase in serum calcium concentration. Anesthesia with halothane, isoflurane or sevoflurane in healthy horses decreases serum calcium concentrations significantly, with the decrease being more pronounced on ionized Ca^{++} than on total Ca^{++}.[6,7] This effect should be taken into consideration when evaluating intraoperative measurements of Ca^{++}.

Should moderate to severe metabolic acidosis be identified during the pre-anesthetic evaluation, it should be at least partially corrected by administration of sodium bicarbonate solution, 1.5 mEq/kg, given IV over 20 to 30 minutes.

Auscultation of the heart should be routinely completed as part of the pre-anesthetic evaluation. Identification of atrial fibrillation or a mitral murmur will forewarn the clinician to the probability that blood pressure will be low and difficult to treat effectively during anesthesia. Premature ventricular depolarizations are occasionally present in horses with endotoxemia and can be treated by intravenous administration of lidocaine when abnormal beats are frequent. Premature ventricular depolarizations may persist for several days after colic surgery and may or may not require specific treatment. Electrolyte abnormalities, such as hypokalemia, hypocalcemia, and hypomagnesemia, occurring in critically ill patients may contribute to the arrhythmias in addition to the direct effect of endotoxin on the myocardium.[8]

Increased intraabdominal pressure not only impairs lung excursion, but also decreases cardiac output. In an extreme case of excessive abdominal distention, where the horse is cyanotic and death is imminent, the dose rates of anesthetic agents for induction of anesthesia may be reduced by 50% or more; endotracheal intubation and controlled ventilation with oxygen must be started immediately after induction of anesthesia.

Intravenous administration of antimicrobial drugs, particularly penicillin and occasionally gentamicin and ceftiofur sodium, may decrease cardiac output and cause hypotension. The hypotensive response to these drugs will further complicate cardiovascular stability during anesthesia.[9] Whenever possible, these drugs should be administered at least 30 minutes before induction of anesthesia, and if administration has to occur during anesthesia, the drugs should be given in small increments while the blood pressure is observed for possible adverse effects.

Anesthetic risk classification is based on a scale of 1 to 5; healthy horses are in category 1. Horses with colic are in categories 3, 4, and 5, where category 3 includes patients with a major systemic disease that is not immediately life-threatening, category 4 is for patients with severe systemic disease and that require life-saving surgery, and category 5 is for horses that are severely ill and cardiovascular collapse is present or imminent. Anesthetic risk categories correlate with the prevalence of anesthetic complications and mortality. Surveys have identified horses to be at a greater risk for death than reported in anesthetized human patients, cats, and dogs. The risk factors associated with anesthesia and surgery in a survey

of 35,978 horses without colic included horses older than 14 years of age, horses that were anesthetized outside normal working hours, a long duration of anesthesia, and foals given inhalation anesthesia without premedication.[10] The mortality rate during anesthesia and for the first 7 days after anesthesia for these horses was 2.4%. Horses that died or were euthanized as a result of perioperative complications constituted 0.9% of the mortality, of which over one third had cardiac arrest, cardiovascular collapse, or were found dead, and one third suffered a fracture or myopathy after anesthesia. In contrast, the overall mortality rate of 5330 horses with colic in this survey was 34.6%, 23% of which had an operable lesion but died or were euthanized because of a problem occurring during anesthesia or postoperatively. Clearly, colic surgery carries a substantial increase in risk for horses, and supportive treatment before and during anesthesia is essential to decrease mortality.

Anesthetic Agents

An anesthetic protocol that best serves the patient is one that combines several agents to produce unconsciousness, analgesia, and muscle relaxation. Pre-anesthetic medication (premedication) often includes xylazine (Sedazine, Fort Dodge Animal Health, Fort Dodge, IA), detomidine (Dormosedan, Orion Corporation, Pfizer Animal Health, Exton, PA) or romifidine (Sedivet, Boehringer Ingelheim Vet Medica Inc., St. Joseph, MO). All of these agents produce mild to good sedation and some analgesia. Low dosages are recommended as these drugs significantly decrease cardiac output and gastrointestinal motility in a dose-dependent manner.[11-18] Addition of butorphanol (Torbugesic, Fort Dodge Animal Health, Fort Dodge, IA) will contribute to sedation and analgesia, but will exacerbate the impairment of gastrointestinal function caused by the other agents, most notably with detomidine.[11,18] Acepromazine (PromAce Injectable, Fort Dodge Animal Health, Fort Dodge, IA) should be omitted from the anesthetic protocol for sick horses as the vasodilation induced by this drug may complicate treatment of low blood pressure during anesthesia.

Induction of anesthesia after premedication is most commonly accomplished by intravenous injection of ketamine (Ketaset, Fort Dodge Animal Health, Fort Dodge, IA), with the addition of either diazepam (Diazepam Injection USP, Abbott Laboratories, North Chicago, IL), midazolam (Midazolam Hydrochloride, American Pharmaceutical Partners, Schaumburg, IL), or guaifenesin (Guaifenesin Injection, Phoenix Scientific Inc., St. Joseph, MO). Guaifenesin is administered at 50 mg/kg, to improve muscle relaxation (Table 24-1). Thiopental (Pentothal, Abbott Laboratories, North Chicago, IL), 2.2 to 4.4 mg/kg, with guaifenesin, 50 to 110 mg/kg, or tiletamine-zolazepam (Telazol, Fort Dodge Animal health, Fort Dodge, IA) are alternative drugs that can be used for induction. Induction of anesthesia with an inhalant administered by mask may not be advisable in foals with colic because pulmonary aspiration of gastric reflux may occur before endotracheal intubation can be achieved.

Table 24-1

A Commonly used Combination of Anesthetic Agents used for Induction and Maintenance of Anesthesia

Stage of anesthesia	Anesthetic agent	IV Dose rate	Dose for 450kg (1000 lb)	Comments
Premedication	Xylazine	up to 1.1 mg/kg	2.5 – 5.0 mL (100 mg/mL)	Dose reduced according to drugs administered in the hour prior to anesthesia
	Butorphanol	0.02 mg/kg	0.9 mg (10 mg/mL)	
Induction of anesthesia	Diazepam or midazolam	0.05 mg/kg	5 ml (5 mg/mL)	Dose of ketamine can be decreased by 20-50% in sick horses
	Ketamine	up to 2.2 mg/kg	10 ml (100 mg/mL)	

Reasons for using an opioid in the anesthetic regimen are that opiods provide minimal cardiovascular depression, that dose rates of other anesthetic agents can be decreased, and that opioids provide analgesia. Although these beneficial effects of opioids have been documented in anesthetized dogs, little published evidence exists that the same benefits occur in horses.[19] In the author's clinical experience, the addition of butorphanol contributes to an efficient induction of anesthesia in horses, and it can lessen tachycardia and high blood pressure during anesthesia presumed to be the result of an inadequate anesthetic plane. Some evidence of analgesia and decreased stress response was observed in horses that had had surgery for colic and were given butorphanol, 0.013 mg/kg/hour, as an IV infusion postoperatively.[20] Improved behavior scores and lower plasma cortisol concentrations were recorded for the horses receiving butorphanol in that study. Opioids decrease

intestinal motility to varying degrees, depending on the drug and dose rate administered, and synergistically prolong the duration of decreased intestinal motility induced by xylazine or detomidine. Healthy horses that had received continuous IV infusion of butorphanol, 0.024 mg/kg/hour for 24 hours,[21] and colic horses given butorphanol 0.013 mg/kg/hour,[20] had a decrease in fecal output. The decrease in intestinal motility was not considered to have significant clinical impact other than introducing the need to include the influence of butorphanol during assessment of the patient's postoperative clinical progress. Morphine (Morphine Sulfate Injection USP, Baxter Healthcare Corporation, Deerfield, IL), 0.1 to 0.17 mg/kg, administered IV after induction of anesthesia has also been used as an adjunct to anesthesia in horses without causing observable adverse effects during recovery from anesthesia in one study.[22] However, in a retrospective study of risk factors for colic in horses after orthopedic surgery, intraoperative systemic use of morphine, median dose 0.1 mg/kg, was associated with a fourfold increase in risk of abdominal pain postoperatively compared with horses receiving either butorphanol or no opioid.[23] Many factors that may affect intestinal motility interact when horses are anesthetized for surgery. Many opioids, including butorphanol, morphine, meperidine, methadone, and fentanyl, have been incorporated into anesthetic protocols for horses, and more controlled studies are needed to evaluate their use and adverse effects.

Induction of Anesthesia

The condition of horses with colic requiring anesthesia varies from relatively healthy to moribund. Consequently, anesthetic administration must be adjusted to accommodate the individual patient.

Many horses with colic have a decreased requirement for anesthetic agents because of CNS depression from multiple administrations of sedatives, electrolyte imbalance, or azotemia. Further, the ability of the horse's cardiovascular system to handle anesthesia may be decreased because of hypovolemia and endotoxemia. Ventilation, cardiac output, and blood pressure decrease as a result of anesthetic administration, recumbency, and change in body position. The dose rates used for sedation and induction depend on which and how many drugs have recently been administered and on the horse's clinical status. Dose rates of the drugs having the most depressant effects on cardiovascular function (i.e., the α-2 agonist sedatives, ketamine, and thiopental) can be decreased by 20% to 50% in some horses. Drugs having less profound effects on the cardiovascular system (i.e., opioids and benzodiazepines) are used at the dose rates used in healthy animals. Horses at risk for cardiovascular collapse at the onset of anesthesia will benefit from dobutamine infusion started before induction and continued through the induction period and as the horse is placed in dorsal recumbency. Horses with considerable abdominal distention can be given oxygen by nasal insufflation during induction of anesthesia until the trachea can be intubated, at which time 100% oxygen can be administered.

Several methods of induction are used in equine anesthesia, including free fall with or without a restraining wall or hydraulic-table induction, manual positioning, or use of a hoist. Regurgitation and pulmonary aspiration of gastric fluid during induction is a concern and may occur despite the presence of a nasogastric tube. This risk can be decreased by removing gastric reflux shortly before induction of anesthesia and by maintaining the horse in sternal position after induction of anesthesia and performing endotracheal intubation and inflation of the cuff before allowing the horse to assume lateral recumbency.

Maintenance of Anesthesia

Maintenance of anesthesia is most commonly provided with a volatile anesthetic agent. Halothane was the mainstay for many years, but isoflurane or sevoflurane are now used more often. Isoflurane and sevoflurane cause less depression of cardiac function, less reduction in intestinal and renal blood flows, and better muscle blood flow than does halothane.[24-28] Many factors influence the outcome in clinical patients; however, analysis of data from many equine clinics indicates that use of isoflurane may be safer in high-risk cases; sevoflurane was not included in the analysis.[29]

Isoflurane and sevoflurane produce similar decreases in arterial blood pressure with increasing depth of anesthesia. Hypotension produced by a deep plane of anesthesia may have an impact on the outcome that may not be readily obvious. Deep anesthesia in healthy horses decreases renal and intestinal blood flows to less than 50% of awake values, and serum creatinine kinase and aspartate transaminase enzymes are increased 19-fold and 4-fold, respectively, the day after anesthesia.[25,30] In a prospective observational study of human patients undergoing general anesthesia and major surgery, independent predictors of mortality in the year after surgery were the disease of the patient, the duration of anesthesia (cumulative deep hypnotic time), and intraoperative hypotension.[31] This information adds incentive to the need to avoid deep anesthesia, to treat hypotension, and to complete the surgical procedure as rapidly as feasible.

Desflurane is another inhalation agent that has been used for anesthesia in horses. Like sevoflurane, the solubility of desflurane in blood is low, thereby facilitating control of the depth of anesthesia. Desflurane may be more sparing to the cardiovascular

system than other inhalation agents, especially during controlled ventilation.[32] Unfortunately, desflurane is unlikely to be in common usage in the foreseeable future because the agent is expensive and requires a specialized vaporizer.

Continuous intravenous infusion of injectable agents, such as guaifenesin-ketamine-xylazine, without any inhalation agent for abdominal surgery raises concerns about the inadequacy of unconsciousness and analgesia. However, injectable anesthetic agents can be administered during anesthesia as intermittent bolus injections or as continuous infusions to provide analgesia or sedation and decrease the percent concentration of inhalation agent delivered. Agents used for this purpose include opioids, α-2 agonist sedatives, ketamine, and lidocaine.

An intravenous injection of butorphanol, 0.02 to 0.024 mg/kg, can be followed by an infusion of this agent at 0.02 mg/kg/hour to maintain steady plasma concentrations; alternatively, supplemental injections of butorphanol, 0.02 mg/kg, can be administered at 45- to 60-minute intervals. The combination of butorphanol and detomidine in conscious healthy horses produces a significant increase in the nociceptive threshold over that for detomidine alone and prolongs the duration of antinociception.[33] Butorphanol has not been documented to significantly decrease the inhalation agent requirement.[34] Continuous infusion of lidocaine during anesthesia has been recommended for four reasons: 1) to provide sedation and decrease the percentage of inhalation agent required, thereby improving cardiovascular performance and decreasing post-anesthetic ataxia; 2) to induce a central anti-hyperalgesic effect (preemptive analgesia) and decrease the amount of analgesic agents required post operatively; 3) to promote early resumption of bowel movements postoperatively, and 4) to provide an anti-inflammatory effect. Lidocaine infusion decreases halothane, isoflurane, or sevoflurane requirement (decreased MAC) in a dose-dependent fashion and with increasing duration of infusion.[35-37] The vaporizer setting can be decreased 10% to 25% for dose rates commonly used clinically. Lidocaine, 1 to 2 mg/kg, given over 15 minutes, followed by an infusion of lidocaine at 0.05 mg/kg/minute has been used successfully for treatment of ventricular dysrhythmias. Large loading doses of lidocaine may result in decreased blood pressure and should be administered over 15 minutes to diminish the impact on the cardiovascular system. Results of a recent study indicate that dose rates of lidocaine in anesthetized horses should be reevaluated. A comparison of serum lidocaine concentrations achieved after infusion of lidocaine 1.3 mg/kg over 15 minutes followed by 0.05 mg/kg/minute for 90 minutes confirmed that serum lidocaine concentrations in horses anesthetized with sevoflurane for arthroscopy were twice the concentrations achieved in awake horses administered the same dose rates.[37] The difference in disposition of lidocaine during anesthesia as compared with the conscious state was probably due to the decrease in cardiac output and organ blood flow caused by sevoflurane. The concentrations in the anesthetized horses were in the range reported to be toxic for horses and, consequently, further investigations are warranted that likely will result in reductions of dose rates during anesthesia as much as 50% from the rate used in this study. It should be noted that this difference in drug disposition caused by anesthesia is similar to that described for gentamicin in anesthetized horses and in critically ill septic and endotoxemic human patients.[38,39]

The contribution of lidocaine to intraoperative analgesia is not fully defined. In one study of healthy horses, infusion of lidocaine at 2.5 mg/kg followed by 0.05 mg/kg/minute during isoflurane anesthesia was accompanied by a 25% decrease in the vaporizer setting.[36] However, in comparing horses that received lidocaine with those that did not, no significant differences were seen in blood concentrations of stress-related hormones or physiologic parameters. Evidence of preemptive analgesia was observed in human patients undergoing general anesthesia for major abdominal surgery by recording observations of nursing staff who were blinded to the intraoperative treatment and by comparing the patients' use of morphine in the 3 days after surgery.[40] Half of the 40 patients in the study received lidocaine 1.5 mg/kg over 15 minutes followed by 0.025 mg/kg/minutes for an average of 6.2 hours. Although no difference in pain scores was observed after anesthesia when the patients were at rest, there was a difference in pain intensity recorded during movement, and in the requests for morphine, especially on the second and third days post-operatively, with maximum effect noted at 36 hours. There was no difference between the two groups in the time to first bowel movement.

Further studies are needed to define the effects of lidocaine on the incidence of postoperative ileus in horses. In one investigation of lidocaine infusion in colic horses given 0.65 mg/kg lidocaine followed by 0.025 mg/kg/minute during anesthesia and then at twice that rate after anesthesia, no differences were detected in the presence of gastrointestinal sounds or the time to first passage of feces compared with horses not given lidocaine.[41] Percutaneous ultrasonography identified similarities and differences in intestinal wall thicknesses and cross sectional area in horses with or without lidocaine. Investigations in clinical patients may be unable to accurately assess the impact of lidocaine as many other factors are involved in the development of ileus. The results of one study identified that horses at risk for ileus are those with small intestinal lesions, high preoperative PCV, and duration of anesthesia exceeding 3 hours.[42] Administration of adjunct agents during anesthesia may also have an impact on postoperative gastrointestinal function. Hypertonic saline decreases mucosal injury and ileus in

laboratory animals subjected to intestinal ischemia and reperfusion and improves survival rate in animal models of shock and sepsis.[43,44] Increased intestinal permeability to endotoxin is prevented in anesthetized endotoxic pigs by administration of a combination of lactated Ringer's solution, hetastarch, and dobutamine.[45] The mechanism for this effect was attributed to maintenance of mesenteric perfusion, with the greatest effect achieved by the combination of blood volume expansion and dobutamine administration.

Both lidocaine and hypertonic saline modulate the inflammatory response to tissue injury by altering polymorphonuclear neutrophil activity, and may have a beneficial influence in horses with colic when given early and within 12 hours of onset.[46,47]

Anesthetic Agents in Foals

Anesthetic agents can be titrated to preserve a light plane of anesthesia more easily in young foals because of their small size and ease of restraint. Physiologic immaturity in foals less than 3 months of age has a significant impact on their responses to anesthesia. Requirement for anesthetic agents is less in foals than in adult horses because of increased permeability of the blood-brain-barrier and decreased plasma protein concentration. Arterial blood pressure is lower and heart rates and cardiac output are higher in young animals compared with adults as a result of decreased myocardial compliance and contractility.[48] Foals are at greater risk for hypotension as a consequence of bradycardia or small decreases in blood volume, such as may occur after administration of an α-2 agonist sedative, dehydration, or blood loss.

Preanesthetic sedation can be provided by combination of 2 or all of the following drugs: xylazine, 0.1 to 0.4 mg/kg; butorphanol, 0.01 to 0.02 mg/kg; and diazepam, 0.05 to 0.1 mg/kg. Pentazocine (Talwin, Abbott Laboratories, North Chicago, IL), 0.3 mg/kg, can be used as an alternative to butorphanol and appears to provide greater restraint but for only 30 minutes compared with approximately 60 minutes obtained from butorphanol. Induction of anesthesia should be achieved with the lowest possible dose of ketamine, 0.5 to 2.0 mg/kg, and anesthesia maintained with isoflurane or sevoflurane in oxygen. Foals accommodating an endotracheal tube up to 16 mm (internal diameter) may be connected to a small-animal anesthesia circle. Larger foals intubated with an 18-mm endotracheal tube or greater should be connected to a large-animal circle to avoid resistance to breathing created by the small diameter of the hoses used in small animals.

Monitoring

Arterial blood pressure should be measured as soon as possible after the horse is connected to the anesthesia machine (Figures 24-1 and 24-2). An electrocardiogram (ECG) is useful to diagnose abnormal cardiac rhythms so that appropriate treatment of dysrhythmias can be instituted. Administration of anesthetic drugs and positioning the horse in dorsal recumbency frequently result in a dramatic decrease in mean arterial blood pressure (MAP). Furthermore, the inhalant agents cause substantial vasodilation and further decreases in MAP in the first 20 minutes of anesthesia. Indirect measurement of blood pressure with a Doppler ultrasound probe or oscillometric method is useful, but direct measurement of blood pressure with a catheter in an artery and displayed on an oscilloscope provides more information.[49] The values obtained from direct blood pressure monitoring include accurate values for systolic, mean, and diastolic pressures that can be observed without delay. Acceptable values for heart rates are 24 to 46 beats/minute and greater than 70 mm Hg for MAP. Mean arterial pressure equal to or less than 65 mm Hg is defined as hypotension, and MAP of 55 mm Hg or less is life-threatening. Observation of the pulse waveform on the monitor or recorded on paper reveals rate and rhythm of cardiac beat, and the steepness of the upsweep of the wave is related to contractility (Figure 24-3). The presence of "cycling" (marked fluctuations in systolic pressure) in sequence with the ventilator has been correlated with low cardiac output.

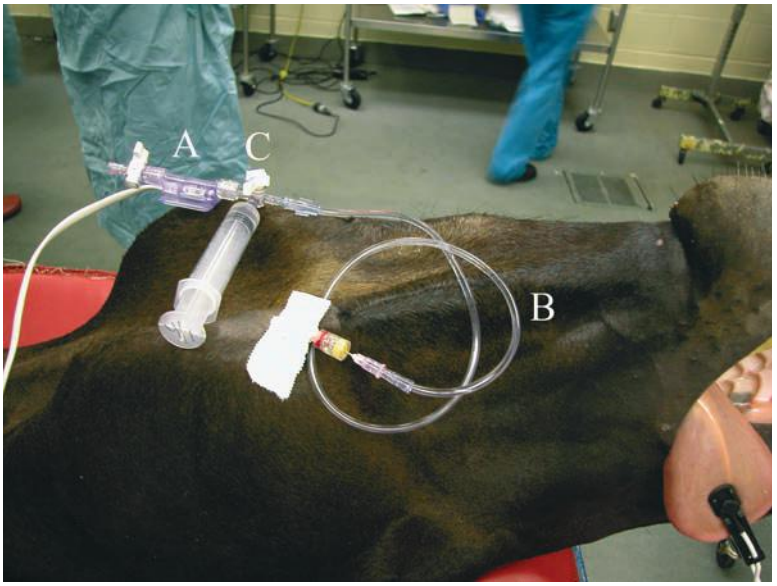
Placement of a catheter in the facial artery of foals may be difficult at the level of the curve of the mandible. Catheterization may be easier adjacent to the rostral border of the masseter muscle on the side of the face. An alternative site for foals is the dorsal metatarsal artery on the lateral side of the leg distal to the hock; this vessel is more easily catheterized before the foal is turned into dorsal recumbency. The transducer must be placed level with the thoracic inlet and extra length in extension tubing is needed between the transducer and the metatarsal artery.

Satisfactory peripheral perfusion may be indicated by a clear pink mucous membrane and a CRT less than 1 second. Prolonged CRT will occur when the cardiac output is decreased. White, bluish, deep red, or fuchia-colored membranes are present when peripheral perfusion is decreased.

Monitoring ventilation of anesthetized horses is directed at determining the severity of hypoventilation and identifying horses that are hypoxic. Unless the respiratory rate is less than 5 per minute, indicating a strong likelihood of significant hypoventila-

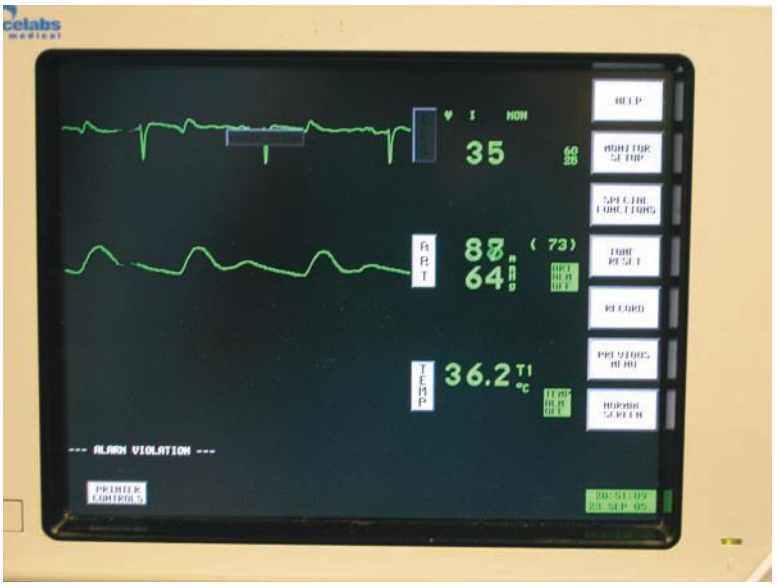
tion, respiratory rate is not a useful measure of adequacy of ventilation. Hypoventilation can be monitored noninvasively using capnography (Figure 24-4) or invasively by collecting arterial blood and performing blood gas analysis. The Y-piece of the anesthetic circuit must have an outlet to which a sampling line for the gas analyzer is connected (Figure 24-5). Capnography provides continuous measurement of end-tidal carbon dioxide concentration ($ETCO_2$). The measurements obtained in horses are generally reliable and useful when artificial ventilation is employed. The $ETCO_2$ may differ considerably from actual arterial carbon dioxide pressure ($PaCO_2$) when horses are breathing spontaneously because of ventilation-perfusion mismatch caused by lung collapse. In healthy horses during controlled ventilation, arterial PCO_2 is 4 to 6 mm Hg higher than $ETCO_2$. The difference is greater in horses with colic, and is on average 10 to 13 mm Hg (range 5-30 mm Hg).[49,50] Normal $PaCO_2$ in horses is approximately 40 mm Hg and values up to 50 mm Hg are considered as evidence of mild hypoventilation. A blood gas analysis done early in the anesthetic period will determine the difference between $ETCO_2$ and $PaCO_2$, and capnography can be used subsequently to assess adequacy of ventilation. Controlled ventilation will achieve satisfactory $PaCO_2$ for most horses when $ETCO_2$ values are in the low to mid 30s.

Figure 24-1



Measurement of arterial blood pressure with a 20-gauge catheter in the facial artery. The pressure transducer (A) is connected by a saline-filled extension tube (B) to the catheter in the artery. The transducer must be filled with saline by gently back-flushing with saline and then closing stopcock (C) permanently. The transducer must be calibrated to zero pressure at room ambient pressure before measuring the patient's pressure for the first time. The transducer must be placed at a level corresponding to the right atrium, which is at the level of the thoracic inlet or point of the shoulder or lateral tuberosity of the humerus when the horse is in dorsal recumbency.

Figure 24-2



A pressure waveform of the arterial pressure pulse and digital values for systolic (87 mm Hg), diastolic (64 mm Hg), mean (73 mm hg) pressures, and heart rate (35 beats/min) are observed on the monitor screen.

Figure 24-3A

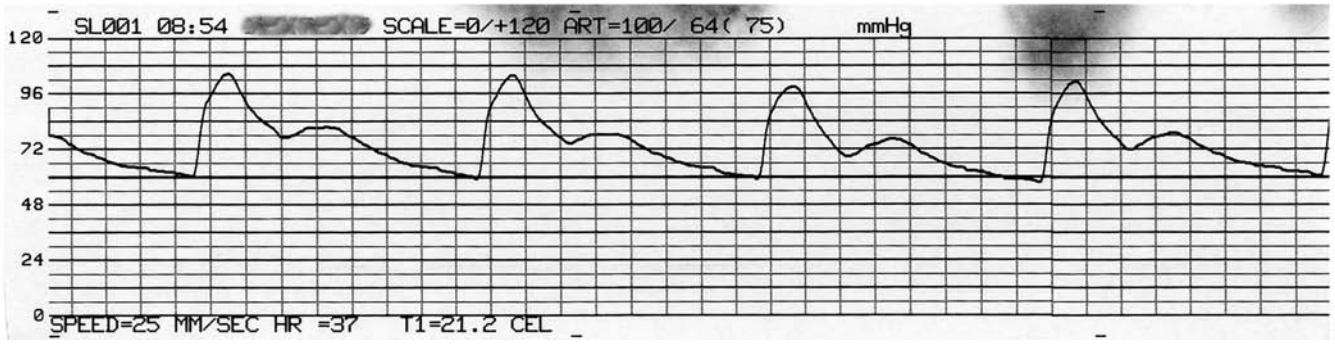
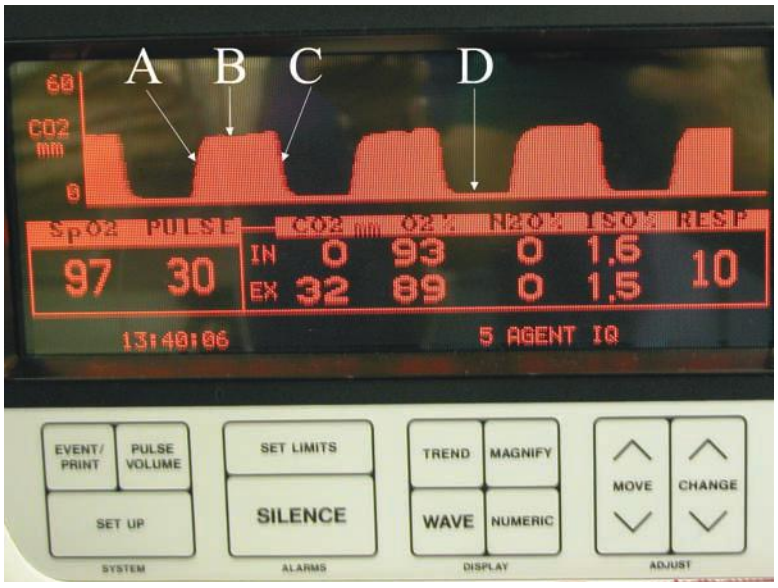


Figure 24-3B



ECG and blood pressure traces can be used to evaluate cardiovascular function. ECG electrode placement was RA on right side just cranial to scapula, LA approximately 6 inches to the left of midline over the 5th costochondral junction, LL midline over the neck. Arterial pressure was recorded from the facial artery. **A.)** Acceptable values in an anesthetized horse; systolic pressure 100 mm Hg, diastolic pressure 64 mm Hg, mean pressure 75 mm Hg, heart rate 37 beats/min. **B.)** Blood pressure trace in this horse has a slow upsweep indicative of decreased contractility. The blood pressure waveforms that occur after inspiration are severely decreased (arrows) and indicate a significant decrease in cardiac output, probably related to insufficient blood volume. The ECG was recorded on Lead III.

Figure 24-4



Photograph of a gas analyzer screen. Upsweep (A) of the carbon dioxide waveform is exhalation, the plateau (B) is end-tidal carbon dioxide concentration, and downsweep (C) is inhalation. The trough (D) is inspiratory concentration and should be zero. This horse has an end-tidal CO_2 of 32 mm Hg (within normal limits).

Figure 24-5A

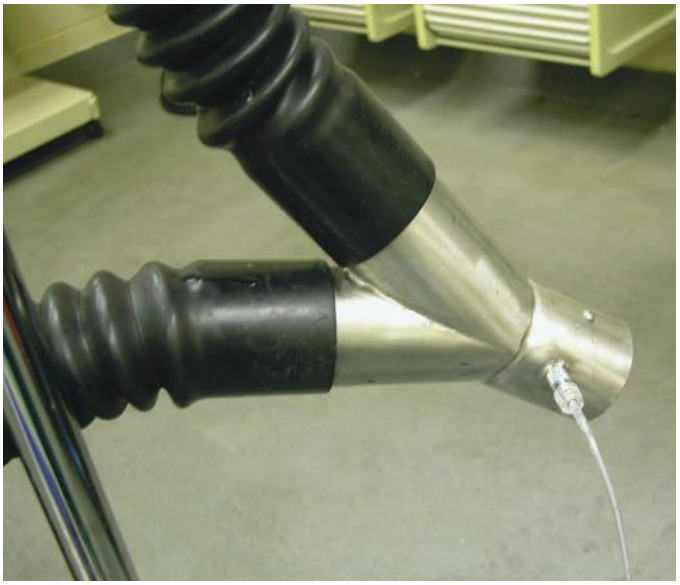
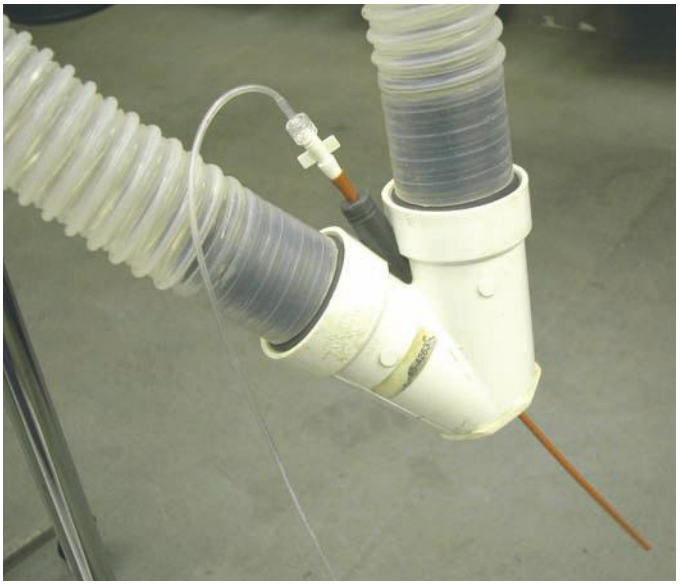


Figure 24-5B



The sampling line for the capnograph or gas analyzer can be connected at the Y-piece of the circle circuit adjacent to the endotracheal tube. The Y-piece (B) has an adapter port through which a red rubber feeding tube has been inserted so that several inches project into the endotracheal tube (Hallowell EMC, www.Hallowell.com).

Hypoxemia can be difficult to identify using clinical signs. Mucous membranes of horses that are hypoxemic (arterial oxygenation less than 60 mm Hg) are frequently dusky pink rather than cyanotic, and horses may not increase their respiratory rates or attempt to breathe against the ventilator despite the presence of hypoxia. Pulse oximetry using a clip on the tongue, lip, or nostril fairly accurately identifies hypoxemia when the monitor displays an O_2 saturation equal to or less than 90%. Almost all pulse oximeters fail to produce a reading some of the time as well as performing differently on different species.[51] Nellcor Puritan Bennett-290 and -395 monitors performed the most consistently in horses in one study. Ambient light may cause erroneous pulse oximeter readings and so the probes should be covered to avoid this problem. Moistening the tongue with water and moving the clip periodically may be necessary to restore a reading. Blood gas analysis with an automatic analyzer (Radiometer; CibaCorning; Boehringer; Hitachi) provides accurate measurement of arterial oxygenation (PaO_2) (Table 24-2).

Table 24-2

Arterial pH and blood gas analysis, capnography and pulse oximeter readings in 2 anesthetized horses with colic. Horse A: 430 kg American Saddlebred with small-intestinal volvulus has a low—normal pH, mild respiratory acidosis, and mild metabolic alkalosis. Horse B: 500 kg Quarter Horse with sand colic. All values are within the normal ranges.

	Horse A	Horse B	Normal values
pHa	7.38	7.43	7.38 – 7.44
$PaCO_2$ (mm Hg)	48.2	39.2	38 - 44
PaO_2 (mm Hg) breathing oxygen	320	523	up to 500 + (< 60 = hypoxemia)
HCO_3 (mmol/L)	29.0	26.0	24 - 29
Base Excess (mmol/L)	+ 3.1	+ 2.0	0 - + 5
$ETCO_2$ (mm Hg) Capnography	39	27	30 – 35 (Add average 13 in colics = $PaCO_2$)
SaO_2 (%) Pulse oximeter	98	99	> 90

Hand held or portable analyzers (i-STAT Corporation, East Windsor, NJ; IRMA TRUpoint, ITC, Edison, NJ; Nova Biomedical, Waltham, MA) are available to provide point-of-care analyses of pH and blood gases that are sufficiently accurate for management of clinical patients.[52-55] PaO_2 was reported to be overestimated by 2 to 9 mm Hg and $PaCO_2$ overestimated by 2 to 5 mm Hg by these analyzers. Discrepancies have been noted for potassium and ionized calcium concentrations, blood glucose and PCV measurements. For example, in one study the iSTAT underestimated the ionized Ca^{++} at normal-to-high values although the low measurements were closer to the real measurements and glucose values were substantially overestimated.[53] Hematocrit values were measured as substantially lower than actual values by several portable analyzers.

Monitoring depth of anesthesia is based on absence of movement, presence or absence of a palpebral reflex, eyeball position, and presence or absence of sympathetic nervous system stimulation. Eye signs can be difficult to assess when the horse is on its back, and rotating the head to one side may expose one eye for evaluation (although the eyes often differ in their positions). A light plane of anesthesia during inhalation anesthesia is judged when the eye is rotated rostroventrally and a weak palpebral reflex is present. The horse may be too deeply anesthetized when the eye has rotated into a central position and the palpebral reflex is absent.

An accurate evaluation of anesthetic depth can be obtained using an anesthetic gas analyzer. The analyzer draws a continuous stream of gas from the circuit at approximately 150 mL/minute and measures both inhaled and exhaled concentrations of the anesthetic agent. The inhaled concentration is usually substantially less than the vaporizer setting because exhaled gas, which has a low anesthetic concentration, dilutes the inflow of anesthetic gas from the vaporizer. The exhaled concentration can be used to assess depth of anesthesia. The anesthetic concentration at the end of exhalation (alveolar, end-tidal) that will maintain anesthesia in 50% of healthy horses is known for each anesthetic agent. This measurement is referred to as the Minimum Alveolar Concentration or MAC. MAC values for halothane, isoflurane, and sevoflurane are 0.9%, 1.3%, and 2.3%, respectively. Satisfactory maintenance of anesthesia is usually achieved in healthy horses having end-tidal anesthetic concentrations between 1.0 and 1.5 times the MAC value. Horses with colic that are endotoxemic and have received analgesic drugs can often be maintained at an end-tidal anesthetic concentration of MAC or less. Monitoring with a gas analyzer (Figure 24-4) allows adjustment of the vaporizer to maintain the plane of anesthesia within a narrow range of anesthetic concentrations and avoids depths of anesthesia that are either too light or too deep.[56]

Hypothermia is a complication of colic surgery performed in an air-conditioned room. Horses appear to be more ataxic in recovery when their rectal temperatures are less than 35.5°C (96°F). Attempts to slow the rate of the decrease in body temperature include use of a warm-water mattress under the horse (New World MFG Inc., Cloverdale, CA), intravenous administration of warmed replacement fluids, and application of a hot-air blanket (Bair Hugger, Augustine Medical Inc., Prairie, MN) over the head, neck, and shoulders of the horse. Heat loss may be increased if the horse's back becomes wet after lying in water left from preparation of the surgical site.

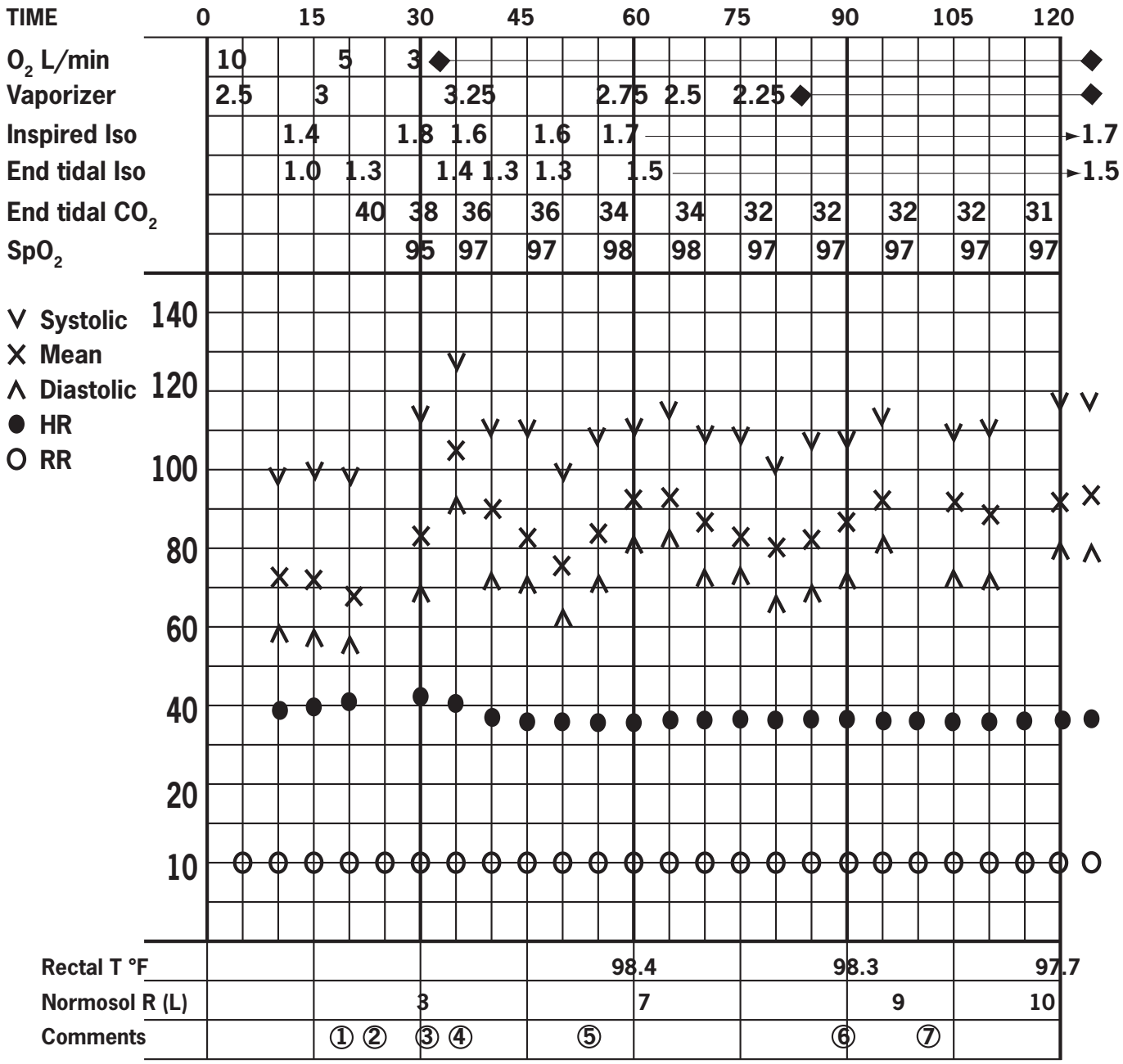
Monitoring blood glucose concentrations in foals less than 3 months of age should be routine; infusion of 5% dextrose in water at 3 mL/kg/hour is recommended as a precaution against hypoglycemia. Depending on the individual foal's blood glucose concentration, the infusion rate can be adjusted to maintain blood glucose above 100 mg/dL.

Cardiovascular Support

Adequate blood volume and venous return are essential to maintain a satisfactory cardiac output. Ideally, blood volume should be restored with balanced electrolyte solutions or expanded by administration of hypertonic saline solution before anesthesia. Infusion of acetated or lactated Ringer's solution, 10 mL/kg/hour, should be continued during anesthesia. Unsatisfactory circulation may be recognized by a MAP less than 65 mm Hg, capillary refill time longer than 1 second, and white, bluish, or deep red mucous membranes. All available cardiovascular measurements should be assessed in conjunction with knowledge of the concentration of the anesthetic agent administered, duration since induction of anesthesia, and the status of surgical manipulations (Figure 24-6). This makes it easier to determine the cause(s) of suboptimal circulation and select appropriate therapies. The variety of causes for decreased circulation fall primarily into two physiologic abnormalities: decreased venous return and decreased cardiac function (Table 24-3). Low blood pressure at the start of anesthesia occurs as a result of decreased venous return to the heart in horses that are hypovolemic and have vasodilation or decreased cardiac output induced by anesthetic agents. The low MAP present immediately after induction of anesthesia may respond to infusion of hypertonic saline, 2 to 4 mL/kg, and dobutamine 1 to 5 μg/kg/minute. Dobutamine (Dobutamine USP, Abbott Laboratories, North Chicago, IL) is a synthetic catecholamine that stimulates β1-receptors to increase cardiac contractility and cardiac output, thereby increasing MAP.[57] Heart rate may be unchanged, increased or decreased by infusion of dobutamine. Limited β2- and α1- receptor activity causes vasodilation or vasoconstriction, respectively. A convenient dobutamine solution concentration (200 μg/mL) is made by

adding 8 mL of 12.5 mg/mL dobutamine to 500 mL N-saline. The infusion rate can be regulated by counting drops per minute or per second through a 10-, 15-, or 20-drop/mL administration set or by administration using a volume pump that is programmed in mL/hour (Baxter Flo-Gard 6201, Volumetric Infusion Pump, Baxter Healthcare Corporation, Deerfield, IL). Selected calculated infusion rates are listed in Table 24-4. Inappropriate bradycardia or tachycardia occurring during administration of dobutamine is managed by a decrease in the dobutamine administration rate and addition of alternative cardiovascular support such as ephedrine.

Figure 24-6



Anesthetic record of a 3.5-year-old 465-kg Appaloosa cross mare with ileal impaction. Ventilation is controlled. Comments on record: 1. Started 1 L hypertonic saline solution, upsweep of arterial wave excellent. 2. Started dobutamine infusion at 0.5 μg/kg/min; surgery start. 3. Started lidocaine infusion at 0.65 mg/kg over 15 min followed by 0.025 mg/kg/min. 4. Dobutamine off. 5. Restart dobutamine infusion. 6. Starting abdominal closure. 7. Dobutamine off, removed nasogastric tube, stop lidocaine. Recovery was good and quiet with horse showing no movement for 50 min and then standing at second attempt 67 min after isoflurane discontinued.

Table 24-3

Flow Chart to Aid Diagnosis and Management of Hypotension (Mean Arterial Blood Pressure < 65 mm Hg).

Evaluation	Rule outs	Management
Obvious initiating event	Recent administration of antimicrobial drug	Preop delay anesthesia for 30 min; hypotension during anesthesia requires treatment for decreased cardiac contractility
	Blood loss	Balanced electrolyte solutions at 3 times the volume lost, dobutamine, transfusion
	Change in body position: impact varies from minor to severe	Decrease anesthetic administration, may need dobutamine
	IV anesthetic agent (guaifenesin, lidocaine, butorphanol)	Dobutamine
	Release or manipulation of ischemic bowel	Dobutamine, decrease anesthetic administration, hypertonic saline solution, may need sodium bicarbonate
Heart rate abnormal	Bradycardia < 24 beats/min (identify sinoatrial block or atrioventricular heart block)	Atropine or glycopyrrolate and/or dopamine or ephedrine
	Tachycardia > 55 beats/min (hypercarbia, hypoxemia, endotoxemia, catecholamine administration, measurement artifact)	Identify and treat cause
Heart rhythm abnormal	Premature atrial depolarization	Treatment may be unnecessary
	Atrial fibrillation	Treat hypotension initially with fluid volume and dobutamine; quinidine if support therapy fails
	Atrioventricular heart block	Atropine or glycopyrrolate and/or dopamine or ephedrine
	Premature ventricular depolarization (hypercarbia, endotoxemia)	Controlled ventilation if hypercarbia, treat with lidocaine if contributing to hypotension
Depth of anesthesia using eye signs, anesthetic agent gas analyzer	Excessive inhalation agent causing vasodilation	Decrease administration, fluid volume, dobutamine
Check for mechanical cause	Increased airway pressure from closed pop-off valve; check circle pressure gauge	Correct machine malfunction
	Increased intraabdominal pressure from intestinal distention	Abdominal incision, intestinal decompression
	Caudal vena cava compression by fetus, intestinal impaction, enterolith	Surgical elevation of mass
Check for other causes	Hypocalcemia	Calcium borogluconate
	Hypoglycemia	5% dextrose in water

Table 24-4

Infusion Rates of Dobutamine Calculated using a Solution Concentration of 200 μg/mL and an Administration Set Delivering 15 drops/mL.

Bodyweight		Infusion 2 μg/kg/min		Infusion 5 μg/kg/min	
Kg	or lb	mL/hour	drops/sec	mL/hour	drops/sec
100	220	60	1 drop/5 sec	150	~1 drop/2 sec
227	500	136	~1 drop/2 sec	340	3 drops/2 sec
350	770	210	~1 drop/sec	525	2.2 drops/sec
454	1000	273	~1 drop/sec	681	~3 drops/sec
550	1210	330	4 drops/3 sec	825	3.4 drops/sec

Injection of ephedrine (Ephedrine sulfate USP, 50 mg/mL, Taylor Pharmaceuticals, Decatur, IL) may be an effective treatment of hypotension in anesthetized horses.[58] Ephedrine is a plant alkaloid that increases cardiac contractility through release of norepinephrine from neurons and a mild direct agonist effect on α-, β1- and β2-receptors. Cardiac output and blood pressure are increased, heart rate may be slightly increased, some vasoconstriction is induced, and blood volume is mobilized from viscera, especially the spleen. Ephedrine is administered IV as a bolus, 0.03 to 0.06 mg/kg (Table 24-5). The onset of action is slow, generally taking several minutes to be evident, and the duration is 30 to 40 minutes. When tachycardia is unwanted, the initial dose of ephedrine should be 0.03 mg/kg. Ephedrine also can be used when splenic contraction is needed to facilitate surgical manipulation.

Dopamine (Dopamine HCl Inj. USP, Abbott Laboratories, North Chicago, IL) is another catecholamine that can be given to improve cardiovascular performance. Dopamine is a natural precursor of norepinephrine. Consequently, part of dopamine's cardiovascular effects are mediated through norepinephrine and part are mediated by stimulation of dopamine DA1, α1-, β1- and β2-receptors. Effects of dopamine are dose- and time-dependent. Low dosages of dopamine, 1 to 3 μg/kg/minute, increase renal and mesenteric blood flow, may increase MAP, and produce a mild increase in cardiac output. Moderate dosages of dopamine, 3 to 10 μg/kg/minute, increase cardiac contractility, cardiac output, and heart rate at the higher dose. Vasodilation observed with a moderate dose slows the rate of rise of MAP and may result in a decrease of MAP in the first 5 to 7 minutes. Over 15 to 30 minutes, plasma concentrations of norepinephrine increase and cardiac contractility and blood pressure continue to increase. High dopamine dosages, more than10 μg/kg/minute, cause vasoconstriction and are not often warranted in horses. Dopamine infusion has been documented to increase cardiac output and blood pressure in healthy and endotoxemic anesthetized horses and to increase intestinal and renal blood flow.[59-61] Despite evidence that administration of dopamine increases oxygen delivery to the gastrointestinal tract and attenuates the endotoxin-induced decrease in intestinal villus blood flow, there is evidence that distribution of blood flow is modified, resulting in a disproportionate decrease in mucosal blood flow.[62,63] Dobutamine may be administered first as treatment for hypotension, but an improved effect may be obtained by the combination of dobutamine and dopamine in some horses where an unsatisfactory response is obtained from dobutamine. Dopamine is the drug of choice in life-threatening hypotension and for treatment of advanced atrioventricular heart block. The infusion rate for these conditions is 6 to 10 μg/kg/minute.

Infusion of calcium gluconate during anesthesia significantly increases cardiac output and MAP and decreases heart rate in healthy horses.[6]

Occasionally hypotension occurs as soon as the horse is positioned in dorsal recumbency and treatment to improve cardiovascular performance is unsuccessful. In these patients, increasing the infusion rate of catecholamines results in tachycardia but does not increase blood pressure. The hypotension may be caused by high intraabdominal pressure or to compression of the aorta or caudal vena cava (aortocaval syndrome) from the weight of the gastrointestinal tract. This condition frequently occurs in horses with impaction of the transverse colon. The arterial pressure increases only after the pressure in the abdomen is decreased by incision and intestinal decompression or when the intestines are lifted by the surgeon. The impact of such severely impaired circulation on cerebral function depends on its duration. Although severe hypotension after induction of anesthesia may have other causes, incision of the abdomen with decompression and exteriorization of distended intestine is urgent when aortocaval syndrome is suspected. Sometimes, tilting the horse 10 to 15° to one side results in sufficient repositioning of intestines and less pressure on the caudal vena cava to allow the blood pressure to be restored.

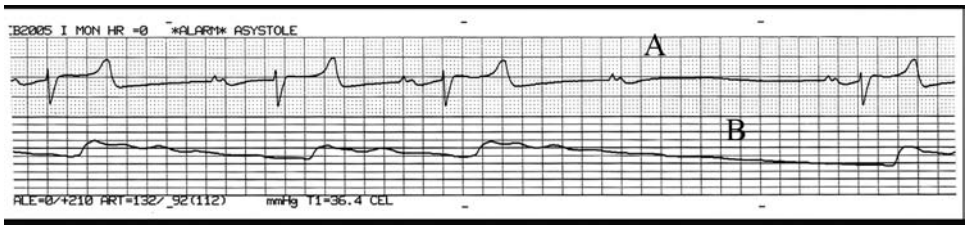
Table 24-5
Drug Dosages for Treatment of Complications.

Drug	Indication	Dosage
Atipamezole[1] (5 mg/mL)	Detomidine antagonist	0.006-0.2 mg/kg IV Inject slowly in increments
Atropine (0.5 mg/mL or 15 mg/mL)	Bradycardia with hypotension, atrioventricular heart block	0.005-0.02 mg/kg IV Time of onset may be several minutes
Calcium gluconate 23%	Serum Ca ≤ 9.5 Not for cardiac arrest	0.5 ml /kg IV over 20-30 min
Dobutamine	Hypotension	1-5 μg/kg/min using 100, 200, or 500 μg/mL solution, decrease rate as BP rises
Dopamine	Hypotension	3-5 μg/kg/min using 100, 200, or 400 μg/mL solution, decrease rate as BP increases
	Advanced AV heart block or cardiac arrest	7-10 μg/kg/min
Ephedrine (50 mg/mL)	Hypotension, to induce splenic contraction	0.06 mg/kg IV bolus, divided dose. Duration 30-40 min
Epinephrine[2] (1 mg/mL)	Cardiac arrest	0.015 mg/kg IV = 6-7 mL for 450 kg (1000 lb)
Glycopyrrolate[3] (0.2 mg/mL)	Bradycardia	0.0025 – 0.005 mg/kg IV
Hetastarch[4]	Hypovolemia	5-10 mL/kg over 30 min IV (small/large animals)
	Cardiac arrest	2 mL/kg with hypertonic saline
Hypertonic saline 7.5%	Acute treatment of hypovolemia or hemorrhage, cardiac arrest	2-4 mL/kg over 10-15 minutes. Must be followed by LRS 30 mL/kg if patient is dehydrated
Lidocaine	Premature ventricular depolarizations, ventricular tachycardia, ventricular fibrillation	1-2 mg/kg IV bolus, 0.02-0.06 mg/kg/min IV infusion
Naloxone[5] (0.4 mg/mL)	Opioid antagonist	0.01-0.02 mg/kg IV; usually 2 mL per large horse
Quinidine[6] (80 mg/mL)	Atrial fibrillation	1.0-1.5 mg/kg at 10 min intervals up to total of 11 mg/kg. Administer when atrial fibrillation is causing hypotension and treatment with dobutamine is unsuccessful
Sodium bicarbonate[7]	Metabolic acidosis	1.5 mEq/kg (mmol/kg) over at least 20 min (treats a deficit of 5); or Base excess X 0.3 X kg bodyweight = mEq given over at least 1 hour. Do not treat a deficit of more than 10 mEq/L in less than 1 hour; repeat pH/blood gas analysis first
Tolazoline[8] (100 mg/mL)	Xylazine antagonist	1-2 mg/kg IV in divided dose; must be given over several min to avoid hypotension

[1]Antesedan, Pfizer Animal Health, Exton, PA.
[2]Epinephrine USP, IMS Limited, So El Monte, CA.
[3]Glycopyrrolate Injection USP, American Regent Laboratories, Shirley, NY; Robinul, Baxter Healthcare Corporation, Deerfield, IL.
[4]Hespan, B. Braun Medical Inc., Irvine, CA.
[5]Naloxone HCl Inj., Abbott Laboratories, North Chicago, IL.
[6]Quinidine Gluconate Injection, Eli Lilley & Company, Indianapolis, IN.
[7]Sodium bicarbonate 7.5% 50 mL, American Regent Laboratories, Shirley, NY; 5% Sodium bicarbonate, Abbott Laboratories, North Chicago, IL.
[8]Tolazine, Lloyd Laboratories, Shenandoah, IA.

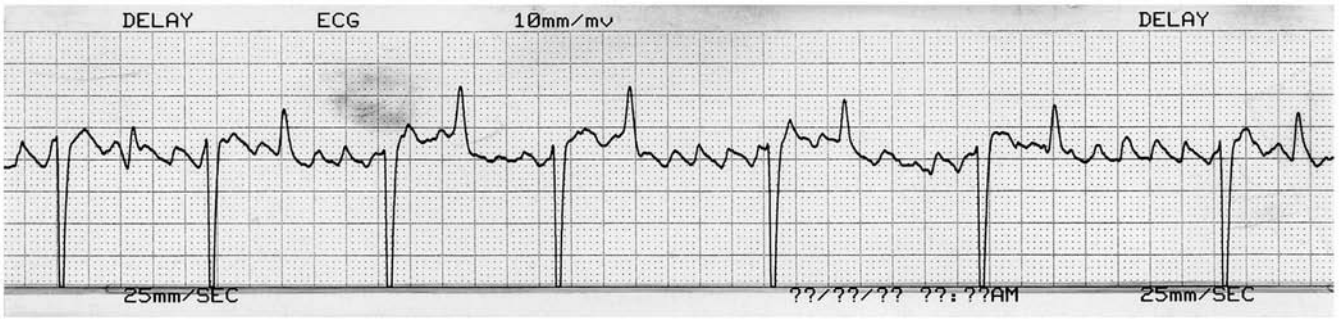
Abnormal cardiac rhythm may be responsible for decreased cardiac output in some horses. Second-degree atrioventricular (AV) heart block is characterized by the presence of a P wave without a QRST complex on the ECG and loss of a corresponding peripheral pulse (Figure 24-7). Administration of xylazine, detomidine, and romifidine may initiate this rhythm and no treatment is indicated. Blood pressure may decrease when this rhythm is initiated by dobutamine, and this effect is usually reversed by decreasing the rate of dobutamine infusion. The presence of AV block on other occasions is cause for concern because it may progress to advanced heart block or cardiac arrest. Second-degree AV block may be treated with infusion of dopamine, 6 μg/kg/minute, or a bolus injection of atropine, 0.005 to 0.02 mg/kg, IV. Atrial fibrillation is an occasional complication that may be responsible for hypotension during anesthesia (Figure 24-8). In horses with atrial fibrillation, the premedication dose rate for xylazine should be kept as low as possible, and isoflurane or sevoflurane should be used in preference to halothane anesthesia. Treatment with dobutamine may maintain adequate MAP. Quinidine has been recommended by IV administration at 1.0 to 1.5 mg/kg at 10-minute intervals up to a total of 11 mg/kg when adequate arterial pressure cannot be supported by other means.[64]

Figure 24-7



Second-degree atrioventricular heart block at A and subsequent loss of pulse at B.

Figure 24-8



Atrial fibrillation. Ventricular rate may be normal or fast.

Surgical manipulation of poorly perfused intestines can result in release of vasoactive substances that cause an abrupt decrease in cardiovascular function, a decrease in blood pressure, tachycardia, and metabolic acidosis. Endotoxin has been detected in the circulation after manipulation or enterotomy of the large colon in colic horses.[65] Even before significant changes occur in cardiovascular measurements, counter measures can be instituted that include a decrease in the vaporizer setting and preparation for administration of dobutamine or ephedrine.

Rupture of a large blood vessel may occur during intestinal manipulation and cause hypotension. Treatment involves decreasing the concentration of the inhalant anesthetic and increasing the rate of intravenous fluid administration. Hypertonic saline will maintain cardiac output and blood pressure in the presence of severe hemorrhage, but the blood loss must be augmented if the source of the bleeding cannot be stopped. Blood transfusion, if feasible, should be considered if blood loss exceeds 20% of blood volume. Blood volume of most horses is 100 mL/kg, and of draught horses and ponies is 72 mL/kg. In the absence of whole blood, plasma, hetastarch, or dextran 70 can be infused to maintain colloid osmotic pressure.

When the horse with colic is known to have the hyperkalemic periodic paralysis gene, serial measurement of serum potassium concentration during anesthesia will identify development of the syndrome. Mild muscle fasciculations on the face or body may be observed during anesthesia at the onset of the syndrome, which can occur at any time during anesthesia. Tachycardia, hypertension, and dysrhythmias are not always features of this syndrome in anesthetized horses. Treatment that should be available includes normal saline, calcium gluconate, 5% dextrose solution, and sodium bicarbonate to treat acidosis.

Hypercapnia and Hypoxemia

Controlled ventilation is advisable for most horses with colic as abdominal distention caused by either ingesta or gas causes cranial movement of the diaphragm and lung collapse. Hypercarbia may cause sympathetic stimulation, tachycardia, and increased MAP or decreased cardiac contractility and decreased MAP. A variety of respiratory rate and tidal volume values can be used to achieve a $PaCO_2$ of 40 to 44 mm Hg. A combination that will result in $PaCO_2$ within normal range is a frequency of 10 breaths per minute and volume per breath of 10 mL/kg for adult horses. Foals need a higher minute volume, such as a respiratory rate of 12 breaths/minute and tidal volume 15 mL/kg. In adults or foals, the tidal volume must be greater when a slower respiratory rate is used. Blood gas analysis will accurately determine the efficiency of ventilation.

A mechanical ventilator should ensure consistent adequate ventilation, thereby allowing the anesthetist to attend to other functions. Two anesthesia machines with ventilators that are available in North America are marketed by Mallard Medical and Surgivet (Figures 24-9 and 24-10). In each case, a separate source of oxygen or compressed air is used to drive the ventilator. Additionally, each of these ventilators has an exhaust outlet separate from the circle pop-off valve that must be scavenged. Each ventilator has a control panel (figure insets) used to control the respiratory rate (frequency), the tidal volume (flow rate), the duration of inspiration, and the inspiratory pressure. The duration of inspiration should be 1.5 to 2 seconds; longer inspiration than this impedes venous return to the heart by increasing intrathoracic pressure and decreasing cardiac output. The inspiratory time is controlled on the Mallard by the I:E ratio (inspiration:expiration); for 10 breaths per minute, a satisfactory I:E ratio is 1:2 or 1:2.5. The inspiratory time is controlled on the Surgivet using the inspiratory time knob. The peak inspiratory pressure can be read from the pressure gauge on the circle. Peak inspiratory pressure in healthy horses at a respiratory rate of 10/minute is 20 to 24 cm H_2O. Higher pressures are needed in horses with colic because of increased abdominal pressure on the diaphragm. A maximum pressure of 40 cm H_2O is recommended to minimize the risk of alveolar rupture. However, even this maximum pressure may not sufficiently expand the lungs to yield normal $PaCO_2$ values at the start of anesthesia, before the abdomen is opened and the bowel decompressed or emptied. In this situation, hypercarbia is permitted until surgery can begin and bowel decompression allows better expansion of the lungs.

Figure 24-9A



Figure 24-9B



A.) Large-animal anesthesia machine (Mallard Medical Inc., Redding, CA). **B.)** Ventilator control panel. Respiratory rate is adjusted with the rate knob and the volume per breath (tidal volume) is increased or decreased with the flow rate knob.

Figure 24-10



Large-animal anesthesia machine (Surgivet, Waukesha, WI). The circle circuit is stacked above the ventilator. The tidal volume is adjusted by increasing or decreasing the inspiratory flow rate (inset). The volume of the ventilator bellows can be adjusted using a hand crank on the side of the ventilator to raise or lower the base of the bellows.

Hypoxemia may develop during anesthesia as a consequence of lung collapse. Although cyanosis is uncommon, the mucous membranes appear muddy red or pale. Hypoxemia may be suspected when dark colored blood is observed during placement of the arterial catheter for blood pressure measurement. Although pulse oximeters may or may not be able to confirm low hemoglobin saturation, analysis of arterial blood for PaO_2 will confirm the abnormality. In the event of hypoxemia, controlled ventilation should be started if the horse is breathing spontaneously. The expectation is that artificial ventilation will open collapsed regions of lung. Occasionally, the PaO_2 will decrease at the onset of ventilation because pressure on the diaphragm is so great that only parts of lung already ventilated are further distended. In these instances, the ventilation-perfusion inequality is worsened because the cardiac output is decreased as a consequence of increased intrathoracic pressure. If circulation is poor, improvement of cardiovascular function with dobutamine infusion occasionally will increase PaO_2. Imposition of positive end-expiratory pressure of 10 cm H_2O (PEEP) may increase oxygenation. Results are variable and the further decrease in cardiac function that occurs as a consequence of PEEP must be treated with vasoactive support. Occasionally, PaO_2 increases after the abdomen is opened and an improvement in ventilation is achieved. Many times hypoxemia persists throughout anesthesia and into recovery. A retrospective study of 582 colic cases identified the incidence of hypoxemia at 17%; however, the discharge rate of these horses from the hospital was no different from horses that were not hypoxemic during anesthesia.[66]

Airway Management

An endotracheal tube is inserted for delivery of oxygen and inhalation agent. The cuff is inflated to produce an airtight seal to prevent leak of anesthetic gases into the room and entrance of any refluxed gastric fluid into the lungs. Over-inflation of the endotracheal tube cuff to 100 mm Hg causes tracheal epithelial damage.[67] Consequently, the cuff should be inflated just enough to prevent an air leak during inflation of the horse's lungs. A cuff pressure of 80 mm Hg (Cufflator, Mercury Medical, FL) in silicone endotracheal tubes, combined with a thin film of K-Y lubricant gel on the cuff, has been shown to prevent leak of fluid around the cuff with minimal tracheal damage.

Although airway obstruction is a complication that must be dealt with during recovery, the problem originates during anesthesia. Congestion and edema of the nasal mucous membranes will develop when the horse's head is positioned level with the thorax; consequently, it is important to elevate the horse's head during anesthesia to prevent the occurrence of nasal mucosal swelling (Figure 24-11). Reflux of gastric fluid into the nostrils around the nasogastric tube appears to irritate the mucosa and cause nasal mucosal swelling. When reflux has been observed to occur, the horse should be allowed to recover from anesthesia with the orotracheal tube in place and the cuff inflated to prevent pulmonary aspiration of fluid. The mouth speculum is removed and the endotracheal tube positioned so that it exits the mouth through the interdental space. The tube

is secured in place with tape or a length of gauze. This method must also be used when removal of the nasogastric tube has resulted in hemorrhage. The endotracheal tube is removed when the horse is standing and can lower its head and expel blood clots.

Alternative techniques for management of nasal obstruction by mucosal swelling include replacing the orotracheal tube with a nasotracheal tube, or topical application of phenylephrine to the nasal mucosa (5 mL 0.15% phenylephrine solution for a 500-kg horse).[68] It is important to ensure a clear airway as the excessive inspiratory effort caused by airway obstruction or hypoxia can generate sufficient negative intrathoracic pressure to initiate pulmonary edema.[69] In the absence of nasal swelling or gastric reflux, use of the endotracheal tube during recovery is the clinician's preference.

Figure 24-11



The horse's head should be elevated above the level of the spine to decrease the risk for nasal mucosa swelling and airway obstruction in recovery.

Recovery from Anesthesia

Management of colic horses for recovery from anesthesia should be similar to that applied to healthy patients: recovery in a warm, darkened, and padded recovery area with a foam- or air-filled pad for the horse to lie on, and nasal insufflation of oxygen at 15 L/minute. Continued application of controlled ventilation using a demand valve (Demand/Resuscitator Valve HU-034-112, Mercury Medical, Clearwater, FL) with oxygen in the recovery stall for the first 10 minutes should prevent hypoxemia and speed elimination of the inhalation agent. The IV administration of xylazine, 0.1 to 0.2 mg/kg, or romifidine, 0.008 mg/kg, approximately 5 minutes after the inhalation anesthesia is discontinued may provide sufficient sedation to promote a smooth transition from inhalation anesthesia to conscionsness and improve the quality of recovery.[70] The sedative appears to induce the horse to remain recumbent longer and exhale more of the anesthetic before attempting to stand. In one experimental study utilizing healthy horses, recovery from sevoflurane anesthesia, with or without postanesthetic administration of xylazine, was better than recoveries observed from isoflurane anesthesia.[71] Additional sedatives may be unnecessary in horses that have received supplements of injectable agents during anesthesia. Intravenous administration of lidocaine up to the end of anesthesia appears to prolong the duration of recumbency.

Foals are easily managed because of their size and may not need additional drugs during recovery from anesthesia. Foals may be left connected to the anesthesia machine and breathing oxygen after the end of surgery or may receive nasal insufflation of oxygen using a small-diameter tubing.

The need for assistance using ropes attached to the head halter and tail will be determined primarily by hospital routine, but should be considered for those horses that are likely to have weakened muscle function. Factors influencing muscle strength include endotoxemia, hypocalcemia and hypokalemia, body temperature below 96°F (35.5°C), anesthesia time exceeding 3 hours, old age, major blood loss, and hind limbs maintained in the flexed position. Assistance with ropes is facilitated by metal rings high on the walls of the recovery box. A halter is placed securely on the horse and a rope tied to the noseband, passed through a metal ring on the wall, and then through a hole in the wall to the outside where it can be held by one person. A second person holds onto a rope that has been attached to the horse's tail and passed through a ring on the inside wall before passing through a second hole in the wall. Several variations on this system are in use. The horse must make the

effort to stand but tension applied to the ropes restrains the horse, preventing forward movement that could lead to stumbling. The head rope must not be too tight as the horse attempts to stand, but traction on the tail rope can provide some lifting action.

Attempts to provide analgesia after surgery have included use of a nonsteroidal anti-inflammatory agent with continuous administration of butorphanol, fentanyl, or lidocaine. Evidence of decreased stress response associated with butorphanol administration was present in an investigation of 27 horses with colic.[20] A group of horses receiving butorphanol infusions, 0.013 mg/kg/hour for 24 hours after celiotomy, had decreased plasma cortisol concentrations compared with the group not receiving butorphanol. Heart rates and respiratory rates were not affected by the administration of butorphanol, but the time to first passage of feces was significantly delayed and the total fecal output in 24 hours was decreased.

Pharmacokinetic studies of transdermal administration of fentanyl (Duragesic 100 μg/hour, Janssen Pharmaceutica, Titusville, NJ) in healthy horses have determined that distribution of fentanyl in horses differs from that in other species. Application of two 10-mg patches to the lateral side of the antebrachium or gaskin of adult horses after clipping or shaving off the hair results in rapid absorption, with peak plasma concentrations of fentanyl occurring in 8 to 15 hours, and then a gradual reduction in concentrations until the presumed analgesic concentration is reached at 48 hours.[72] In a second study of transdermal application of fentanyl in 9 clinical patients with a variety of illnesses, fentanyl absorption was slower in the ill horses and serum fentanyl concentrations were more variable.[73] Pain scores were significantly decreased by the administration of fentanyl, but the drug appeared to be more effective for horses having soft tissue rather than orthopedic procedures. Further controlled studies are needed to determine the effective use of transdermal administration of fentanyl in horses.

Anesthesia for Surgery in the Standing Horse

Flank laparotomy or laparoscopy can been performed in standing horses with colic, using sedation in combination with infiltration of local anesthetics, such as lidocaine, at the incision site. Sedative combinations frequently used are butorphanol, 0.02 mg/kg, with either xylazine, 0.3 to 0.5 mg/kg, or detomidine, 0.005 to 0.01 mg/kg, and sedation maintained by continuous infusion of detomidine, 0.0001 to 0.0002 mg/kg/minute (total infused detomidine 3 to 6 mg/hour for a 500-kg horse). The infusion can be achieved by adding 12 mg detomidine to 500 mL saline and administering the solution at a rate of 2 to 4 mL per minute. Local infiltration of skin and subcutaneous tissues with local analgesic solution at the incision sites is easily performed. The anesthetic protocols for standing surgery that include sedation with detomidine and either butorphanol, 0.02 mg/kg, or buprenorphine, 0.006 mg/kg, followed by a continuous IV infusion of detomidine have been reported as satisfactory for abdominal surgery in standing horses.[74,75] Despite satisfactory immobilization for the procedure, analgesia may be insufficient because metabolic and physiologic changes occur in response to surgical manipulation.[75] Other suggested anesthetic techniques have combined sedation and epidural analgesia with lidocaine/xylazine or lidocaine/detomidine; however the value of including an epidural nerve block for analgesia for flank incisions in standing horses is unknown.[76] The impact of epidural administration of these agents on intestinal motility has not been fully documented. One investigation of the effects of epidural morphine and detomidine deposited at the lumbosacral region through an indwelling epidural catheter every 12 hours for 14 days in conscious healthy horses was unable to document adverse systemic effects.[77] No significant changes in gastrointestinal motility were identified by auscultation of intestinal sounds twice daily and records of hay and water intake.

Conclusion

As more knowledge is gained about the pathophysiology of endotoxemia, sepsis, ischemia, and multiple organ failure, it is increasingly obvious that physiologic changes occurring in these patients are exceptionally complex. At present, a prime goal in management of anesthesia should be to maintain mean arterial pressure, perfusion, $PaCO_2$, and depth of anesthesia within a tight range of values. Blood volume expansion is essential to maintenance of normal cardiovascular parameters and is best done before induction of anesthesia and maintained during the surgical procedure. Additional controlled studies are needed to support the use of individual anesthetic agents, opioids, and adjunct drugs such as lidocaine.

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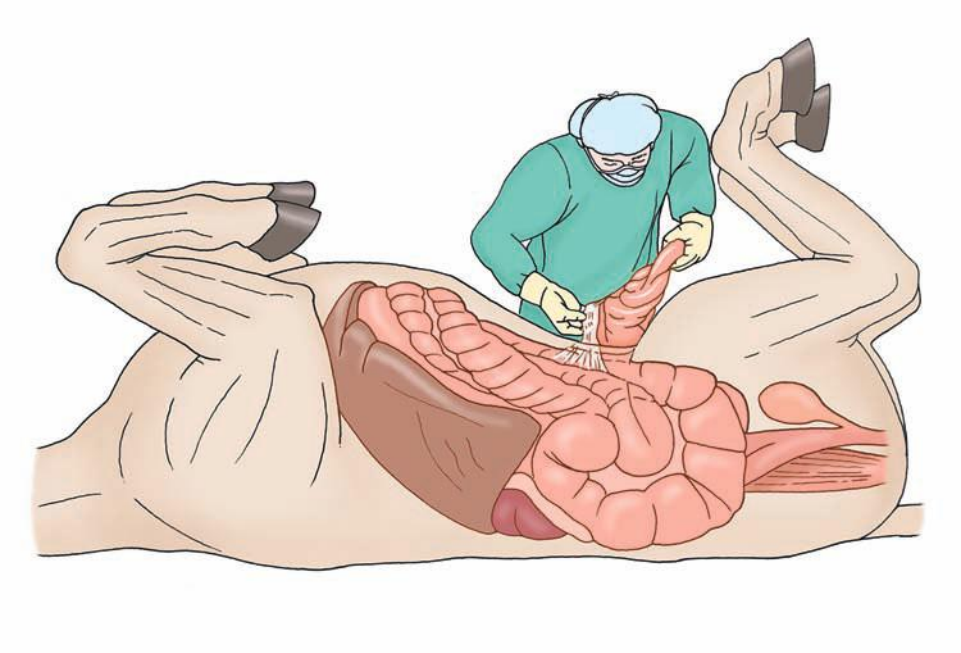
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Surgery for Acute Abdominal Disease

Part 9



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Preparation of the Patient

Chapter 25

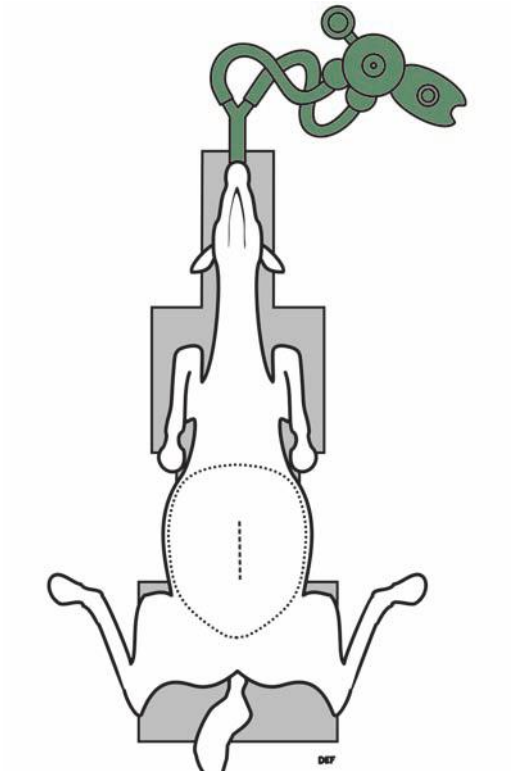
David E. Freeman

Positioning, clipping, and scrubbing of the patient and draping the surgery site are all critical preparatory steps for any surgery, but specific features of colic surgery, such as a large incision, long duration of surgery, emergency conditions, and a compromised patient, demand special attention to patient preparation. The following will focus on the steps up to and including draping, using the most common ventral median approach as the example. Other approaches have been described (see Chapter 26), and the same procedures and principles can be used as applicable.

Patient Preparation

Horses that have a heavy coating of dirt, as from rolling and lying down on wet soil, should be bathed before surgery, because any attempt at cleaning after surgery risks contamination of the abdominal incision. Ideally, the abdomen should be clipped as soon as the decision is made for surgery, and before or during anesthetic preparation. This will make good use of the time before the horse is anesthetized and will shorten the total anesthesia time. The latter advantage probably outweighs any risk of increasing the risk of infection through skin damage caused by clipping at this short interval before anesthesia.[1] A #40 blade is used to clip hair from a large area around the proposed incision from the inguinal region to slightly cranial to the xiphoid, laterally to the level of the flank fold and around the costal arch (Figure 25-1). The clipped site can receive a final clip when the horse is anesthetized, especially around the proposed incision, but shaving with a razor blade is usually unnecessary,[2] and is associated with an increased risk of wound infection.[3] A heavy-duty vacuum is used to remove all clipped hair.

Figure 25-1



Clipped site on ventral abdomen (dashed line) and its relationship to the abdominal incision (broken line).

After a male horse is anesthetized, its penis is packed into the prepuce with a handful of 4 x 4 gauze sponges, and the external ring of the prepuce is sutured securely with size 2-0 or 0 monofilament suture in a simple continuous pattern (Figure 25-2). If the surgery may involve an inguinal approach or an approach to the bladder, packing the sheath in this way can force the penis to lie over and interfere with access to the inguinal canal and caudal abdomen. An alternative in such cases is to exteriorize and clean the penis, catheterize the bladder, and draw the penis to one side of the abdomen or caudad where it can be secured to the table or the horse's tail. The shoes are removed so that they cannot damage the recovery stall floor or injure the horse during recovery, although this step can be omitted if it will delay surgery. Instead, the foot should be picked clean; the foot and shoe can be wrapped with an adhesive tape with sufficient layers to provide adequate protection (Figure 27-2). A rectal sleeve is then placed over each limb to restrict contamination from that source and to act as an additional layer between the foot and the surgical drape (Figure 27-2). These steps and the following preliminary scrub are completed outside the surgery room.

The clipped skin undergoes a preliminary or gross scrub for approximately 5 minutes with surgical soap or until a wipe with a moist sponge fails to pick up any visible dirt, before the final 5-minute surgical scrub in the surgery room. The scrub is

started at the proposed surgery site and should move out from there in concentric circles until the periphery of the clipped area is reached (Figure 25-2). The sponge used for that application is discarded after it reaches the periphery of the clipped site and is replaced with a new sponge to repeat the process. The surgery site is then coated with a layer of antiseptic solution while the horse is moved into the surgery room. Once in the surgery room, sterile containers of scrub material and sponges are used for the final scrub; the scrub nurse wears sterile surgeon's gloves for this step. After the preliminary and final scrubs are completed, all pools of solution are removed to prevent subsequent strike-through in draped areas. Special attention is paid to the inguinal regions, which are drained by depressing the flank fold and soaking up the remaining fluid with sterile towels or sponges.

Figure 25-2



Scrubbing the ventral abdomen in concentric rings that start at the proposed incision line and then move outwards. Note that the penis is sutured within the sheath, the feet are wrapped in tape to include the shoes, and the feet and lower limbs are covered with a rectal sleeve.

Antiseptic Agents

Either povidone-iodine or chlorhexidine is suitable for both the preliminary and final scrubs, because both are effective against the most common types of pathogens. Differences between them can determine choice of antiseptic; these are discussed further on. No agent or application technique will render the field sterile, but careful application of appropriate agents will produce the closest to the ideal environment for aseptic surgery.

Chlorhexidine diacetate (2%; Nolvasan Solution and Surgical Scrub, Fort Dodge Laboratories Inc., Fort Dodge, IA) and chlorhexidine gluconate (4%; Hibiclens, Stuart Pharmaceuticals, Division of ICI America, Inc, Wilmington, DE) have a rapid onset of action and a persistent effect,[4] the latter attributed to binding to protein of the stratum corneum to form a persistent residue that can kill bacteria emerging from adnexal elements during surgery.[5] An approved antiseptic for preoperative skin preparation, 2% chlorhexidine gluconate and 70% isopropyl alcohol (ChloraPrep®, Medi-Flex, Inc., Leawood, Kansas), provided significantly more persistent antimicrobial activity at 24 hours than either of the components used separately.[6]

Iodophors are complexes of elemental iodine with a carrier, such as polyvinylpyrrolidone (PVP), which forms povidone-iodine (Betadine solution and scrub, The Purdue Frederick Company, Norwalk, CT). The complex retains the bactericidal activity of iodine, while reducing tissue irritation and staining. However, iodine is so tightly bound to PVP that the standard 10% solution contains insufficient free iodine to kill bacteria.[7] Addition of detergents, as in surgical scrubs, and any remaining hair and organic debris further reduce the release of iodine and hence the bactericidal activity.[7] Dilution of the 10% solution of povidone-iodine and at least 2 minutes of scrubbing liberate more free iodine and render it more bactericidal.[3,7]

A one-step surgical preparation with Dura-Prep Surgical Solution, which is 70% isopropyl alcohol in an iodophor-polymer complex (3M Health Care, St Paul, MN), is as effective as a two-step povidone-iodine preparation.[8] This solution forms a water-insoluble film with sustained chemical and physical barrier properties on skin.[8] In a study on ventral midline incisions in horses undergoing celiotomy, Dura-Prep applied after hexachlorophene scrub was as effective as povidone-iodine followed by alcohol in reducing colony-forming units up to time of skin closure. Both methods had comparable rates of incisional drainage.[9] However, preparation time was significantly shorter for Dura-Prep compared with the routine skin preparation technique.[9]

Although chlorhexidine's wider range of antimicrobial activity, longer residual action, minimal inhibition by organic material, and greater tolerance by skin should render it superior to povidone-iodine, both agents perform comparably in the surgical setting.[10,11] Chlorhexidine might be more suitable for a long surgical procedure because of its greater residual activity. Povidone-iodine and 4% chlorhexidine gluconate scrubs rinsed with 70% isopropyl alcohol decreased skin microflora in cattle and had similar frequencies of surgical wound infection.[4] Colony-forming units were less with chlorhexidine and alcohol immediately postscrub, but there was no difference in residual effect between the two scrubs.[4] Chlorhexidine is more expensive than povidone-iodine.[12]

Either alcohol or sterile saline can be used to rinse the surgical scrub solution from the surgery site.[12] Alcohols have higher and more rapid kill rate than chlorhexidine, followed by povidone-iodine,[13] but are effective only against vegetative bacteria.[14] Alcohols have a mild defatting effect but are inactivated by organic debris and lack residual activity after evaporation.[14] Alcohol does not inactivate chlorhexidine gluconate in vitro and has no significant effect on its protein-binding property in vivo;[3] however, isopropyl alcohol rinse can reduce the residual antimicrobial activity of chlorhexidine.[10,11] Because isopropyl alcohol potentiates the antimicrobial efficacy of povidone-iodine by increasing the release of free iodine, it should be used as a rinse after this surgical scrub.[8,15]

Antimicrobial film drapes with adhesive backing (Ioban™ 2, 3M Animal Care Products, St. Paul, MN) contain an iodophor and come in a range of sizes suitable for colic surgery. The scrubbed skin is prepared for application by rinsing it with isopropyl alcohol. Drying with a sterile towel and application of a medical grade adhesive spray (Medical Adhesive, Hollister Inc, Libertyville, IL; EZ Drape Adhesive, Clinipad Corp, Rocky Hill, Conn) can be used to improve adherence,[9] but this is not essential. Based on results of clinical trials on human patients, the value of antimicrobial adhesive drapes is questionable.[16,17] Because this drape must be applied directly to the surgery site when the entire horse is uncovered, the largest sheet available should be used so that the surgeon can stand as far as possible from the horse to prevent contact with limbs and other unprepared areas (Figure 25-3). For the same reason, an operating room nurse can help with the application by drawing the backing sheet from the adhesive surface as this sheet is stripped from the drape (Figure 25-3).

Figure 25-3



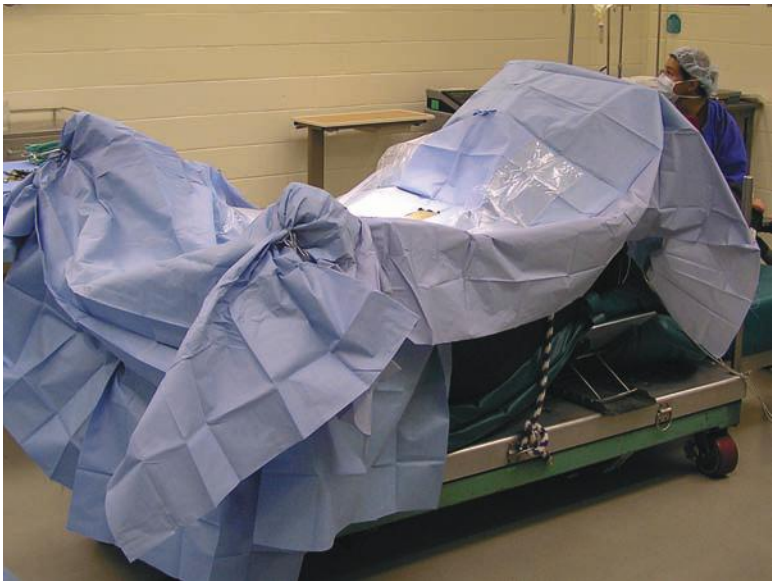
Method of applying an adhesive iodophor-impregnated drape to the ventral abdomen. Note that the surgeon must stand as far from the horse as possible to prevent accidental contact; an operating room nurse or scrub nurse can detach the plastic packing in a way that helps with drape placement.

Draping the Surgery Site

Disposable waterproof paper drapes (General Econopak, Inc, Philadelphia, PA) will be described in Chapter 27, Surgical Techniques. This chapter will discuss their application. The entire horse can be covered with a single drape (Figure 25-4) that has a center fenestration with inner edges that adhere to the underlying plastic drape or skin (Figure 25-5). This seals the operative site from sources of contamination beneath the drape. Other variations are several single drapes applied in different arrangements (Figure 25-6) or a large nonfenestrated drape that covers the entire horse. The latter can be fenestrated as needed by cutting an appropriately sized window over the proposed surgery site; the edges of this fenestration are secured at the corners by towel clamps.

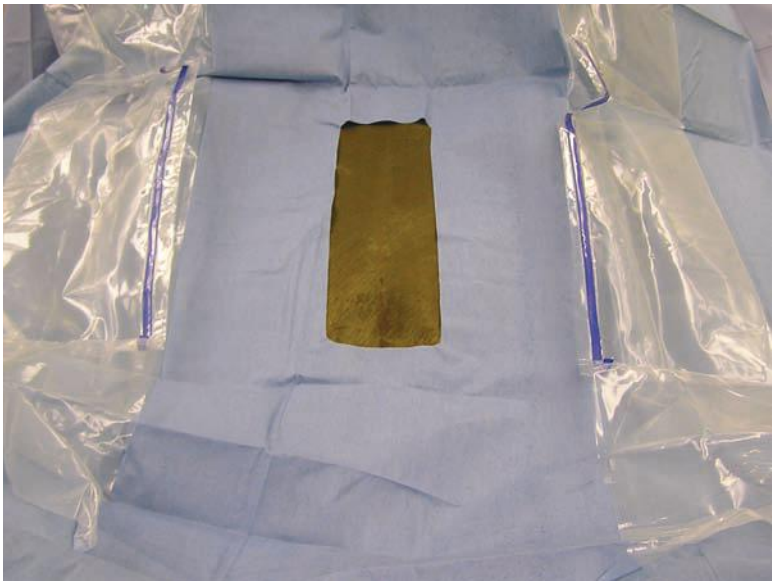
If single drapes are used, one technique requires that the areas most likely to cause contamination be covered first, such as each individual hind foot and hind limb, followed by the front limbs to the cranial edge of the ventral abdomen (Figure 25-6).

Figure 25-4



A large fenestrated drape that covers the entire horse. Single drapes have been used to cover the hindlimbs. Part of the lateral aspect of large horses cannot be fully covered with this system.

Figure 25-5

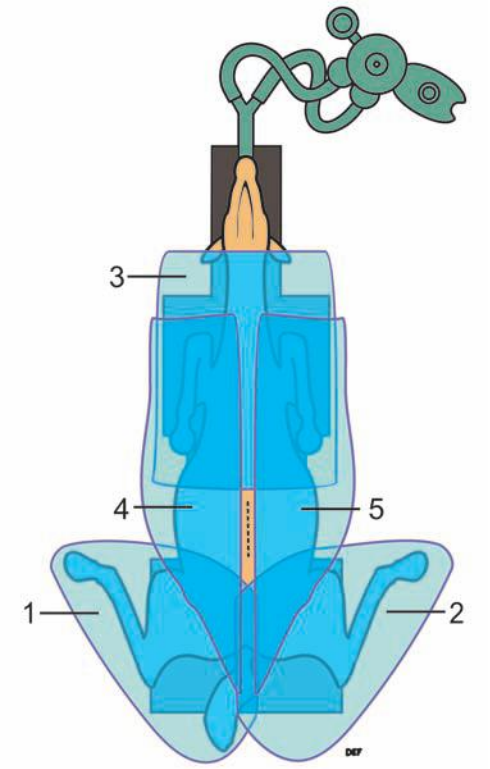


Close-up view of the fenestration in place. The inner edge is adhered to the underlying adhesive drape. The clear pouches on the sides can be used to retain suction equipment and instruments.

Then the side drapes can be applied more safely because the surgeon can stand close to the abdomen to complete fine adjustments to the edge that will border the incision (Figure 25-6). All edges applied around the proposed incision should be doubled back at the first fold from the edge to place the folded portion underneath and give a smooth doubled edge to this critical part of the drape. The surgeon should roll the hands into the drape corners (above the drape edge) during application to protect them from contact with unprepared areas on the horse's body and limbs.

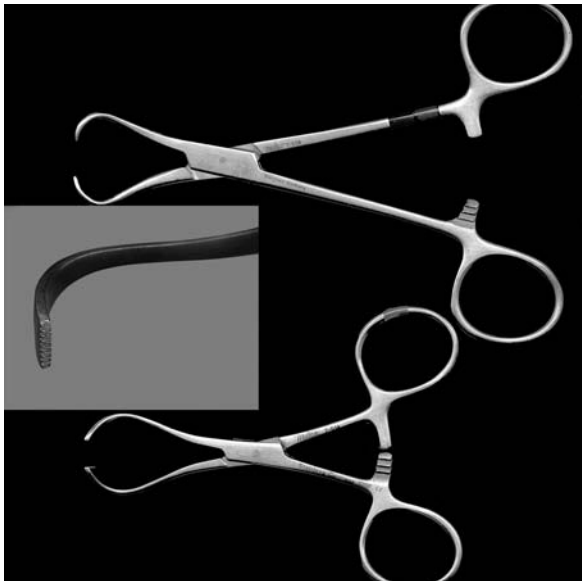
Once a drape is applied, the edges furthest from the surgeon should not be handled because they might have come in contact with nonsterile areas. Ideally, the drape should not be moved once it is placed on the surgery site, but as a precaution the drape is placed too close to the proposed incision site and then withdrawn from that site as needed. The opposite maneuver will drag the underside of the drape from a nonprepared area onto the prepared field and thereby contaminate skin that is close to the incision. Typical towel clamps applied to the drape over sterile fields can penetrate the drape (Backhaus and Roeder clamps), but nonpenetrating clamps (Lorna clamps) should be used at sites distant to the prepared area (Figure 25-7) or to help secure tubing and cautery leads to the drapes. If penetrating towel clamps are applied to unprepared areas on the horse, they and the sites of drape puncture should be regarded as contaminated. A sponge count can be conducted by having the anesthetist record the known count of sponges in each package as it is opened, and then all used sponges are thrown onto a drape placed on the floor behind the horse (Figure 25-8). These are then counted and the numbers compared with the count for each opened pack. If each sponge is discarded immediately after it is used without leaving the operators hand or forceps, a sponge count is not needed.

Figure 25-6



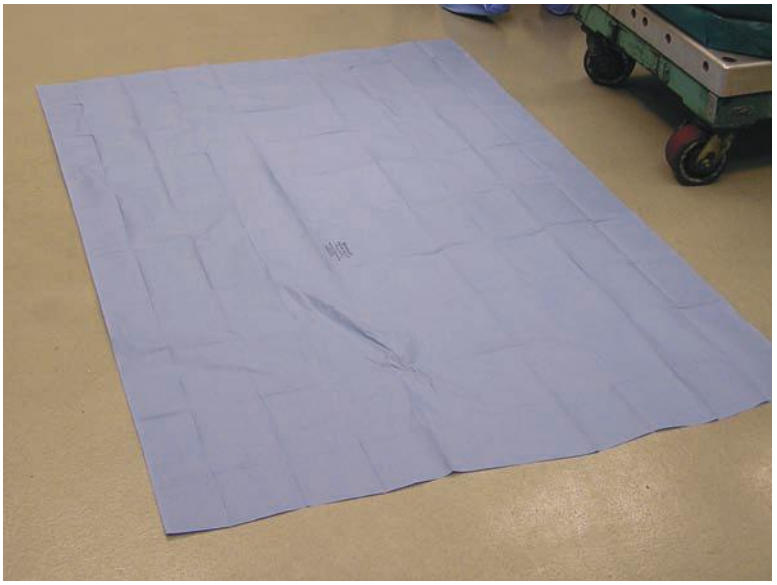
Method of applying several single drapes around a proposed ventral median approach (broken line). The numbers represent the order in which the drapes are applied.

Figure 25-7



Close-up view of Backhaus towel clamp (top) and a nonpenetrating Lorna towel clamp (bottom). The inset is a closer view of the grasping surface of the jaw of the Lorna clamp. This clamp is not suitable for application to skin and does not secure drapes as well as the Backhaus or Roeder clamp, but it leaves the drape intact, which is preferred over nonsterile areas.

Figure 25-8



A drape placed on the floor behind the horse to catch sponges as they are discarded immediately after use.

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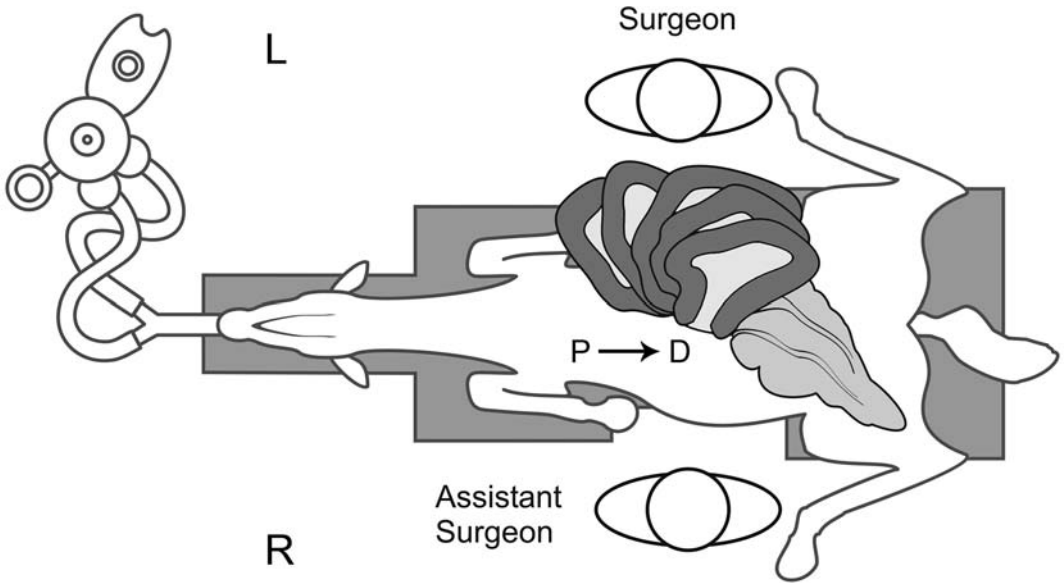
Surgical Exploration and Manipulation

Chapter 26

David E. Freeman

In horses with colic, the abdomen is usually explored through a ventral midline incision, although other approaches can be indicated according to the location of the lesion and anticipated procedure. It is critical that the surgeon develops a system for the approach and subsequent abdominal exploration that is simple and consistent, so that familiarity with normal anatomy is acquired, deviations from the norm are easily recognized, lesions can be corrected quickly, and normal anatomic arrangements are preserved. This involves standing on the same side of the abdomen for every surgery, which is usually the left side of the horse for right handed surgeons, following a consistent order of exploration, and arranging exteriorized bowel so that it can be readily traced in its normal anatomic relationship, and then replaced easily and correctly in the abdomen (Figure 26-1).

Figure 26-1



Arrangement of exteriorized small intestine and cecum in a horse with a small intestinal strangulation, arranged so that the normal orientation of the bowel is preserved. R and L refer to the right and left sides of the horse respectively, and the proximal (P) to distal (D) direction is indicated. This arrangement prevents any confusion in bowel orientation during correction of the lesion and subsequent surgery.

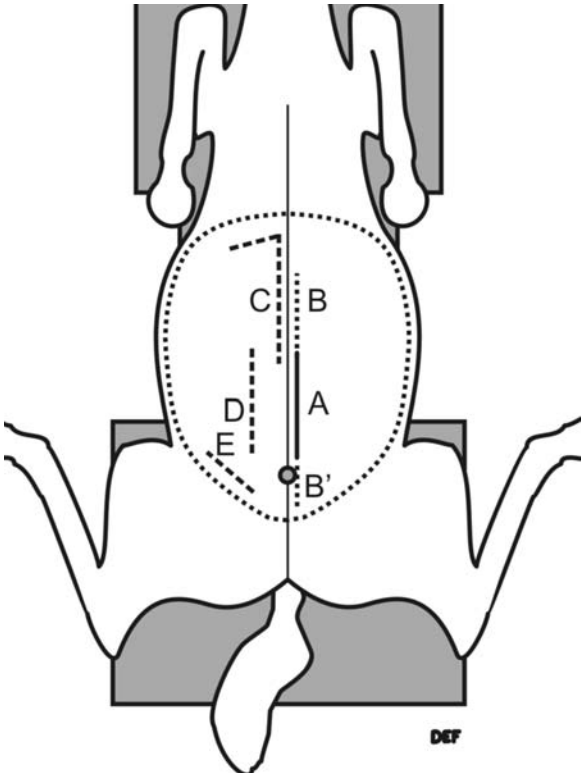
Ventral Midline Incision

Popularity of the ventral midline celiotomy (laparotomy) for correction of gastrointestinal lesions in the horse can be attributed to direct access to most of the abdomen, simplicity of opening, familiarity, and ease of closing compared with other incisions. This incision extends cranially from a point 2.5 cm cranial to the umbilicus (Figure 26-2). The length of the incision depends on the requirements of the surgery, with less than 25 cm being sufficient for many small intestinal lesions and more than 25 cm being necessary in some instances to correct diseases of the large colon. Although long incisions will take longer to close, a short incision can delay the surgery if it hampers bowel manipulation and is vulnerable to trauma by repeated intraabdominal manipulations.

A more cranial location of the incision (Figure 26-2) facilitates correction of a large-colon volvulus, places a colopexy in a more favorable location in the pregnant mare, and would allow a more caudal approach if a second procedure were required later.[1] A more cranial approach would also be indicated if preoperative information suggested a lesion in the cranial part of the abdomen, such as a diaphragmatic hernia, gastroduodenal lesion, liver lobe torsion, cholelith, and renal or ureteral lesion in a foal. To improve access, the cranial end of a cranial incision might need to be extended laterally in a paracostal fashion for approximately 12 to 15 cm at an angle of 60° to 90° to form a J-shaped incision (Figure 26-2). A more caudal incision is required for cesarean section, surgery of the bladder and umbilical components, and for access to lesions in the distal part of the small colon and rectum (Figure 26-2). Caudal incisions in male horses require a paramedian skin incision around the prepuce and reflection of the skin edge laterally to expose the ventral midline on the body wall. A more caudal approach has a greater thickness of fat in the subcutaneous and retroperitoneal layers than in a cranial incision; however, the linea alba is thicker caudally than cranially, which makes it more difficult to open cranial incisions precisely on the midline.

Scalpel incision of all tissue layers from skin to linea alba is recommended (Figure 26-3a), guided by the ridge of the linea alba, which is sometimes palpable on the ventral midline or, after the linea alba has been incised, on the dorsal aspect of this layer. Careful sharp incision of the linea alba with the belly of the blade is required and may be guided by the jaws of a thumb forceps to direct further extension and protect underlying structures (Figure 26-3b). A variable but usually thick layer of retroperitoneal fat will be encountered under the linea incision (Figure 26-4a). The peritoneum can be punctured with a finger and

Figure 26-2



Approaches to the ventral abdomen. A, is the typical midline approach cranial to the umbilicus; B and B' are cranial and caudal extensions or variations; C, Cranial J-shaped incision; D, paramedian incision; and E is the inguinal approach.

Figure 26-3A



Figure 26-3B



Method of making an incision in the linea alba. The skin and subcutaneous tissue are incised **(A)**. If bowel is distended, the body wall can be elevated and underlying bowel protected with thumb forceps or fingers used to direct the scalpel blade **(B)**.

torn longitudinally, or can be opened by cutting along the falciform ligament with a scissors or a scalpel (Figure 26-4B). Although bleeding from small skin or subcutaneous vessels is initially observed, this normally stops after opening the abdominal wall. Although cautery for skin bleeders is time-consuming and, therefore, not used routinely, incisional hemorrhage can increase postoperative swelling, provide an environment for bacterial proliferation in the wound, and facilitate transfer of bacteria from the stall floor to the wound interior. In fat horses, some surgeons excise the retroperitoneal fat, but no attempt should be made to undermine or separate the skin or subcutaneous fascia from the abdominal tunic during incision or subsequent closure. Such undermining is traumatic, creates dead space, and could reduce vascular perfusion of wound margins.

Figure 26-4A

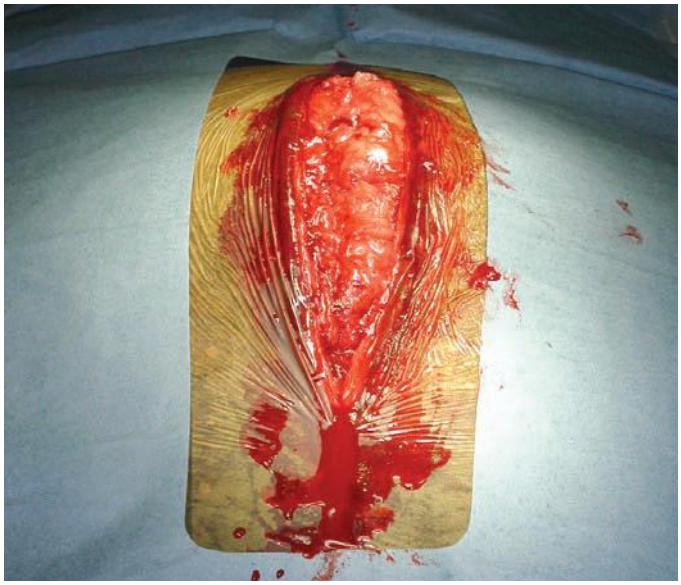
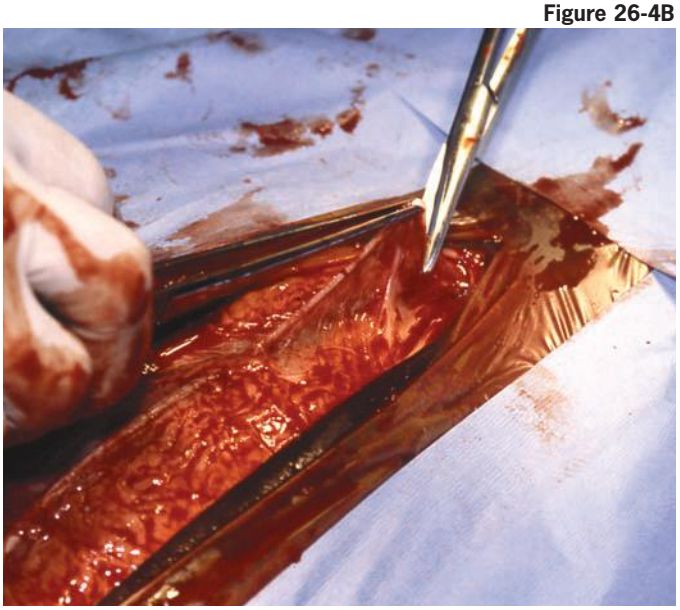


Figure 26-4B

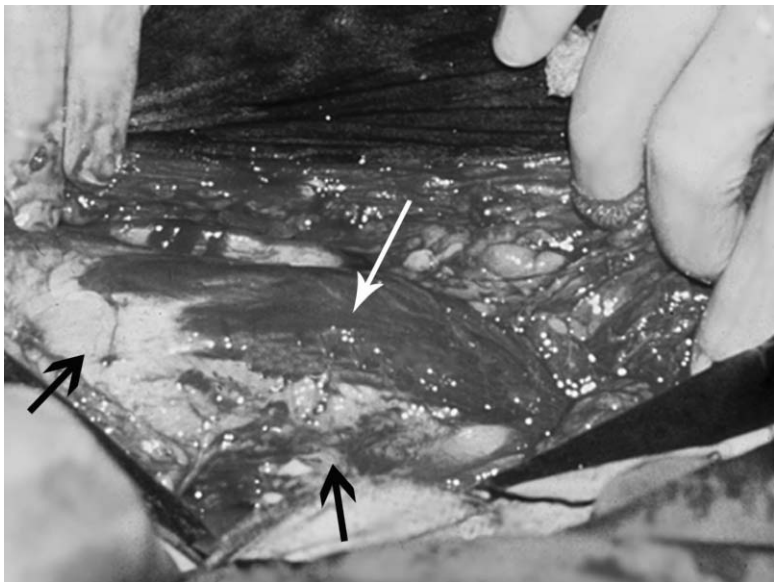


A.) Typical appearance of retroperitoneal fat bulging between edges of the incision in the linea alba. **B.)** Incision of the falciform ligament maintains the peritoneum for closure in cases where this is necessary.

Inguinal Approach

For correction of a nonreducible inguinal hernia, an 8- to 10-cm skin incision is made over and along the external inguinal ring, followed by blunt separation of the subcutaneous fascia and superficial fascia to expose the spermatic cord (Figure 26-5). The superficial or external inguinal ring in the horse is a 10-cm long slit in the aponeurosis of the external abdominal oblique that runs parallel to the direction of the tendon fibers.[2] The inguinal canal is an oblique passageway around the caudal edge of the internal abdominal oblique and directed ventrally and caudally to the level of the superficial inguinal ring. In the male horse, the canal contains the spermatic cord, the vaginal tunic, the external cremaster muscle, the external pudendal artery, inguinal lymph vessels, and nerve branches. A small vein may accompany the external pudendal artery through the inguinal canal but, in the horse, the external pudendal vein proper passes through a separate foramen that is caudal to the inguinal canal.[2] However, this vein and its branches are prominent in the area of the superficial inguinal ring and care must be taken to avoid them during surgery. The parietal layer of the vaginal tunic and its contents form the spermatic cord and follow an oblique 10-cm long course from the lateral angle of the deep ring to the medial angle of the superficial ring. The surgical procedure for correction of inguinal hernia has been described elsewhere (see Chapter 27).

Figure 26-5



Inguinal approach in a horse with an inguinal hernia showing the cremaster muscle (white arrow) and the vaginal tunic (black arrows) exposed. The next step is to make an incision into the tunic to release the entrapped bowel.

Flank Laparotomy

The flank or paralumbar incision is infrequently used in colic surgery because it allows limited access to the abdomen, but could be indicated for specific diseases and when necessitated by financial constraints (see Chapter 38).[3] When surgery is indicated but not economically possible, yet the horse's condition does not appear to justify euthanasia, a flank laparotomy may allow the surgeon to make a more precise diagnosis, plan treatment more effectively, or even provide supporting evidence to recommend euthanasia.[3] Many of the procedures that were once amenable to diagnosis and treatment by standing laparotomy are now handled better by laparoscopy.

Surgical Technique

For standing flank laparotomy, the horse is restrained in stocks with the tail bandaged and tied to prevent contamination of the sterile field.[3] Xylazine with or without butorphanol provides sufficient sedation for most horses (see Chapter 9). The suspected disease process or the affected organ will determine whether the left- or right-sided approach is performed. The surgery site is prepared for aseptic surgery and local anesthesia is provided by a paravertebral block,[4] an L-block, or a line block, with some additional blocks at sites for towel clamps.[3] The paravertebral block often requires additional local block in the distal aspect of the incision.[3] Draping is routine, except that the drape is folded to create a pocket to support the exteriorized bowel. The standard surgical approach is midway between the last rib and the tuber coxa, starting approximately 2-cm above the prominent ridge of the internal oblique muscle. In the standing horse, the modified grid is preferred because the intact internal oblique muscle edges can help keep the intestines within the abdomen.[3] In the modified grid, the external oblique muscle is incised but the internal oblique and transverse abdominal muscles are bluntly separated by fingers.[3] If needed, topical anesthetic solution may be applied before perforating the peritoneum.

From the left side, the spleen is the first organ palpated as the abdomen is examined, and the left kidney and nephrosplenic ligament are located medial to it.[3] The small colon is identified within or close to the pelvic inlet and its mid section can be exteriorized and examined. The mesocolon prevents access to the right side of the abdomen. After palpation of the small colon, the surgeon's hand is then passed under the small colon to reach for the right side of the abdomen, where the cecum and right kidney can be located at the level of the 15th to 17th ribs. The duodenum is ventral to the right kidney and dorsal and caudal to the cecum, and it loops behind the root of the mesentery, which should be palpated for enlargement or fremitus.[3]

The duodenum can be traced to the jejunum, which can be exteriorized in sections, taking care to prevent mesenteric stretching, which is painful to the horse.[3] When the ileum is reached, the ileocecal junction can be palpated, followed by the cecum and large colon, which can be checked by tracing the ventral aspect of the right ventral colon.[3] In smaller horses, the stomach and pylorus can be palpated medial and cranial to the spleen.

For closure, the transverse abdominis and peritoneum are sutured as one layer in a simple continuous pattern with size 1 or 2 absorbable material. The internal oblique is apposed with simple interrupted sutures that take large bites, spaced 1 to 2 cm apart and tied without tension. The external oblique muscles are apposed with absorbable size 1 or 2 sutures in a simple continuous pattern, and the subcutaneous tissues and skin are closed routinely. Horses are stall rested with daily walking in hand for 3 weeks, followed by controlled activity for 3 more weeks.

Indications

Diseases that are difficult to diagnose preoperatively, but are suitable for definitive diagnosis and treatment through a flank laparotomy include right dorsal colon impactions, nonstrangulating adhesions, intraabdominal masses, large-colon displacements, some lipomas, small-colon impactions, small-colon fecaliths, mesenteric rents, and uterine torsion.[3] This approach also allows the surgeon to close the nephrosplenic space to prevent recurrence of a large-colon entrapment.[3,5] The flank laparotomy is well suited for evaluation of weight loss and for biopsies of intestinal lesions and abdominal masses, especially in horses too debilitated for general anesthesia.[3] A pelvic flexure enterotomy can be performed in the standing horse, but is difficult by this approach and requires a colon tray to relieve tension on the colon wall.[3]

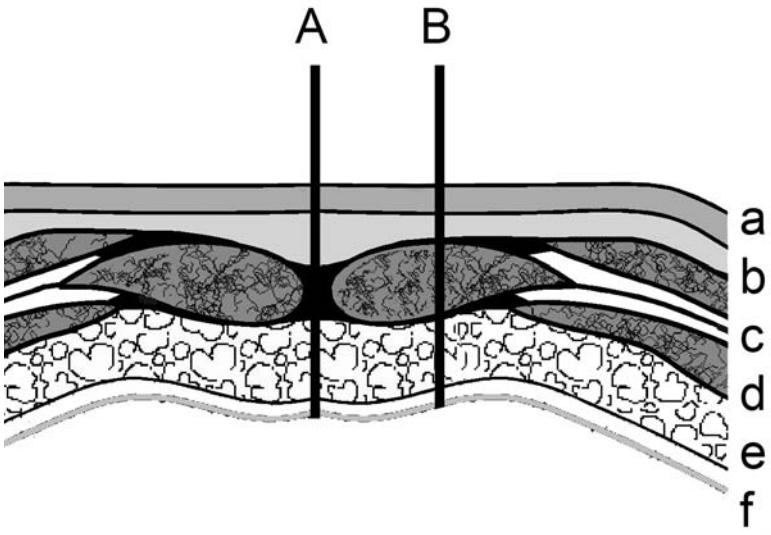
Alternative Approaches

Some surgeons use a paramedian approach (Figures 26-2 and 26-6) rather than a standard midline approach, because their surgery table restricts access to the ventral midline.[6] This approach could be useful also to avoid going through a previous ventral midline incision that has adhered to bowel, is the site of a colopexy, or is infected. With the paramedian approach, the major body wall layers incised are the thick ventral fascia, the rectus abdominis muscle, and the dorsal fascia (Figure 26-6). Several sizeable blood vessels can be encountered, so bleeding can be greater than with a linea alba incision.

The abdomen can be approached after a rib resection to access structures too far cranial for a flank approach, but care must be taken to remain caudal to the diaphragmatic attachment.[7] At the last rib, the line of attachment is 10 to 12 cm dorsal to the ventral end of the rib.[2] An approach through the right 18th rib has been used for total typhlectomy,[7] correction of cecocolic intussusception by partial typhlectomy (Huskamp B and Scheidemann W, personal communication, 2003), and enlargement of the cecocolic orifice in horses with recurrent cecal impaction.[8] To decompress the small intestine and salvage large volumes of fluid accumulated in it in horses with duodenitis-proximal jejunitis, a temporary duodenocecostomy has been performed through a 25- to 30-cm long incision between the right 17th and 18th ribs.[9] The duodenum can also be approached to remove a foreign body by enterotomy through a dorsal paracostal incision, 3 cm caudal to the right 18th rib.[10]

For the approach through the right 18th rib, the incision follows the rib and extends from the ventral end of the iliocostal muscle for 25 to 30 cm in the ventrocranial direction.[7] The muscles over the rib and the periosteum are incised, the rib is separated from its attachments, and transected dorsally and ventrally in the angles of the incision with an oscillating saw or obstetrical wire. The abdominal cavity is opened by an incision through the underlying periosteum and peritoneum, at which point the abdominal wall at the flank will sag. This opening provides a good access to the cecal base, the caudal duodenal flexure, and the beginning of the right ventral colon. Closure of this incision is in layers from peritoneum and periosteum, through to subcutaneous tissues and skin.[7]

Figure 26-6



Difference between layers incised through a ventral midline approach (A, through linea alba) and paramedian approach (B, through muscle sheaths and rectus abdominis muscle). a, skin; b, external abdominal oblique; c, internal abdominal oblique; d, transverse abdominis muscle; e, retroperitoneal fat; and f, peritoneum. The external abdominal oblique and internal abdominal oblique muscles from the external rectus sheath and the transverse abdominis muscle forms the internal rectus sheath.

Abdominal Exploration

Before exploring the abdomen, the surgeon applies waterproof sleeves to both arms if the gown does not include them, and sterile saline is poured onto the sleeves to lubricate them and remove glove powder before the arm is inserted in the abdomen. Exploration of the abdomen is largely dictated by the preoperative findings, which are usually accurate in determining whether small or large intestine is involved, but not at identifying the specific lesion.[11] Once the ventral abdomen is opened, the affected bowel is often immediately evident, and, in some horses with advanced intestinal strangulation, the odor of necrotic tissue will emanate. Obvious intraabdominal gas and odor will escape in horses with a ruptured viscus. Any abnormalities in peritoneal fluid should also be noted at this time, such as evidence of peritionitis (fibrin and excess serosanguinous or purulent fluid), rupture (excess sanguinous fluid, vegetable material), and hemorrhage.

If the lesion cannot be seen or palpated immediately through a ventral midline incision, it is located by the following methods, combined with a sound knowledge of the abdominal anatomy of the horse in dorsal recumbency (Figure 26-7). Manual palpation of intraabdominal contents is used locate the following: 1) tight band, bowel distended with gas, fluid, impacted digesta, or foreign material; 2) bowel drawn tightly across the abdomen; 3) an intraabdominal mass or enterolith; 4) mesenteric mass or abscess; thickened bowel wall; or 5) distended bowel that can be traced into an internal site of strangulation. This part of the examination should be brief, and, if it fails, the next step is to trace from fixed or easily located segments to all contiguous parts of the gastrointestinal tract.

Figure 26-7A

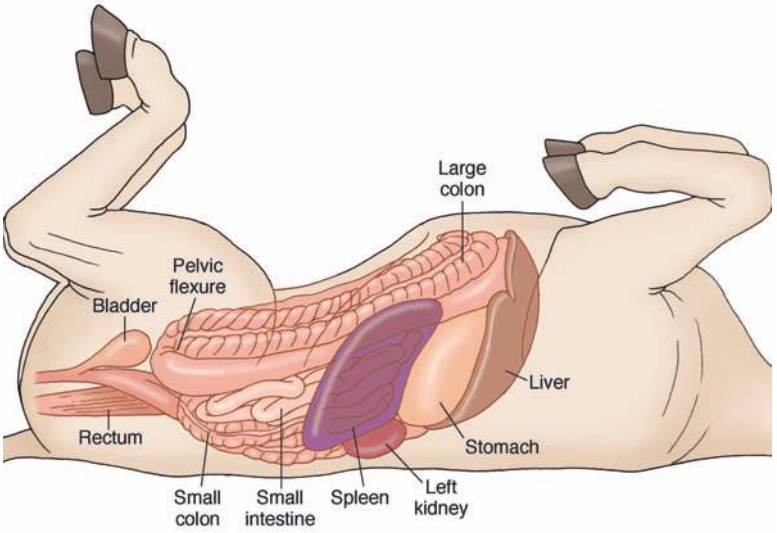
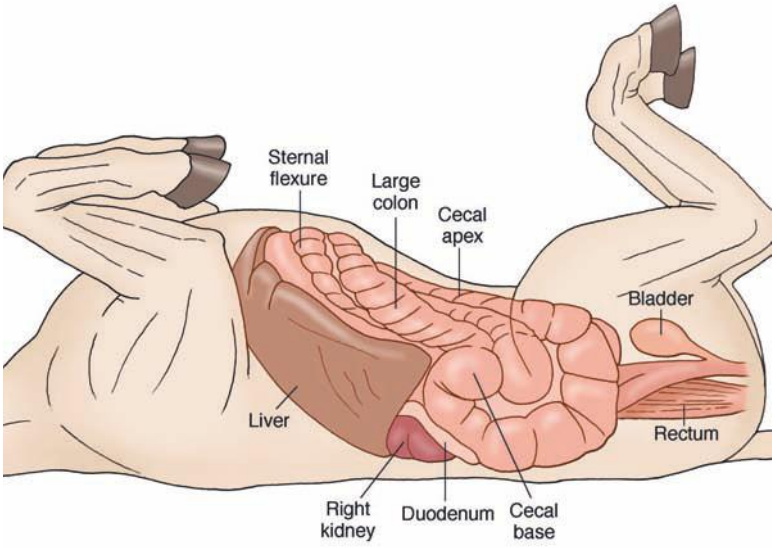


Figure 26-7B



The structures in the abdomen stay relatively fixed even when the horse is turned on its back. Structures on the left **(A)** include the stomach, left kidney, spleen, left colon, and small colon. Structures on the right **(B)** include the liver, duodenum, right colon, and cecum. (From White NA. Surgical exploration of the equine intestinal tract for acute abdominal disease. Proc Vet Sem, 1:52-57, 1986.)

The apex of the cecum is exteriorized, which is usually the first structure found where it lies on the midline or to right of midline with the apex directed cranially (Figure 26-8). The portion exteriorized is followed to the body and base of the cecum. In horses with small-intestinal lesions, the cecum is empty and usually more to the right side, where it can be difficult to find. If the cecum cannot be found, it might be involved in a displacement.

The lateral band of the cecum can be traced to the cecocolic fold and its attachment on the ventral aspect of the right ventral colon (Figure 26-8). From this point, the large (ascending) colon can be followed and exteriorized (Figure 26-9). Failure to find the cecocolic fold could indicate a colonic displacement (Figure 26-10). Parts of the large intestine can be recognized readily by location and characteristic longitudinal bands or tenia. The cecum, and right and left ventral colons have four bands, the left dorsal colon has one band that is buried in the mesenteric attachments and close to the mesenteric lymph nodes and colonic vasculature, and the right dorsal colon has three bands.

The easiest method for examining the large colon is to trace along the left parts toward the pelvic inlet where the pelvic flexure can be located (Figure 26-11). This part should be carefully cupped in the hand and then drawn back to the incision. The remainder of the colon is then worked out of the abdomen in segments and cradled over the surgeon's arm to elevate it away from the incision (Figure 26-11). It is critical that tension not be applied to the dorsal colon as it is elevated, especially if it is impacted, because it is prone to rupture close to its attachments to the dorsal body wall.

Figure 26-8A

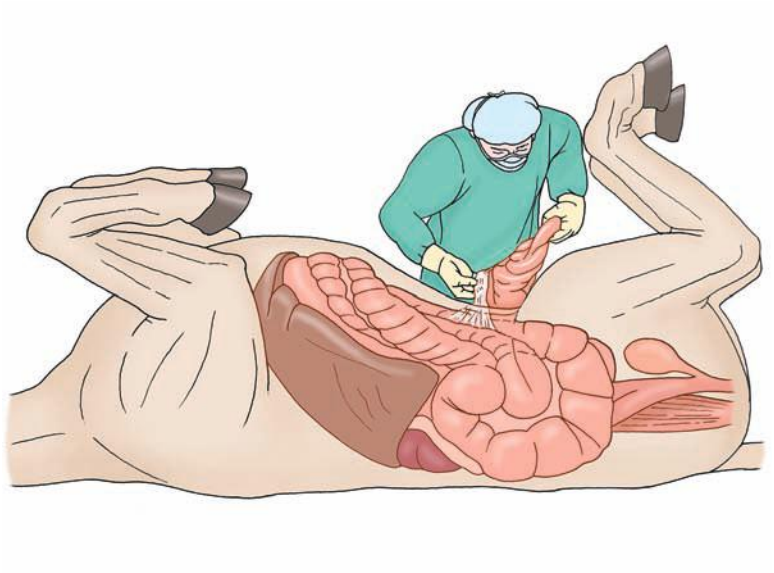
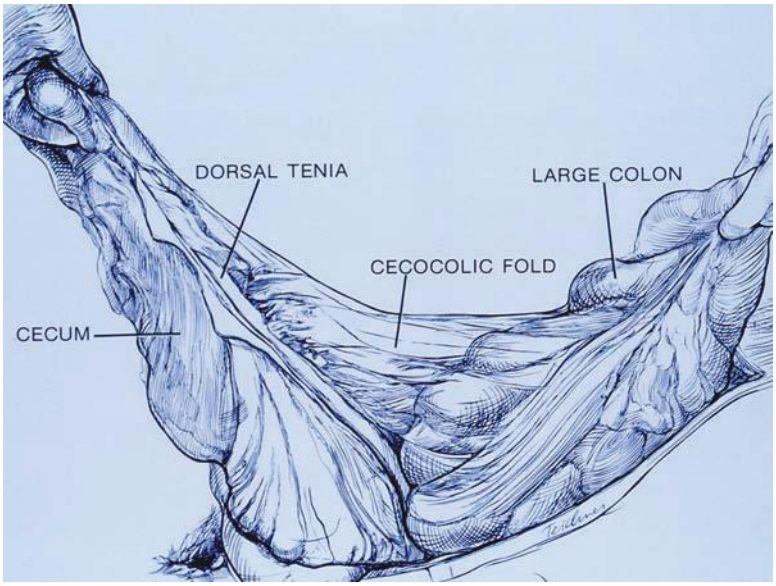
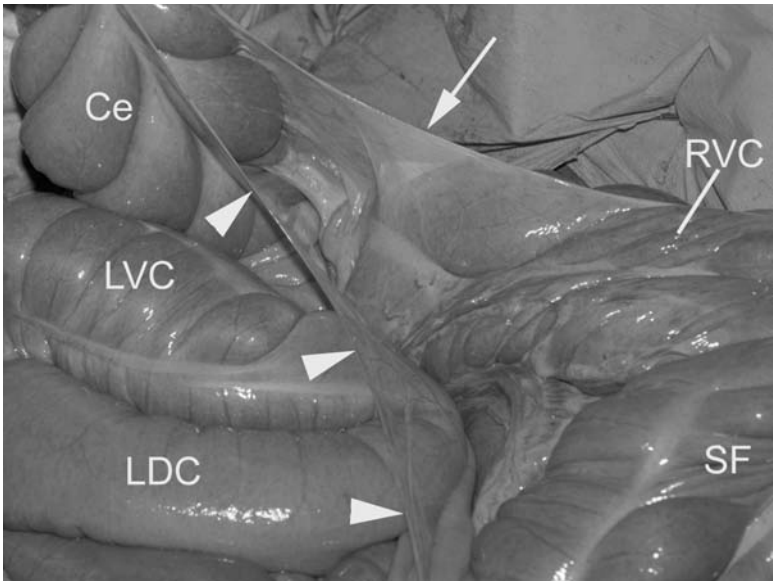


Figure 26-8B



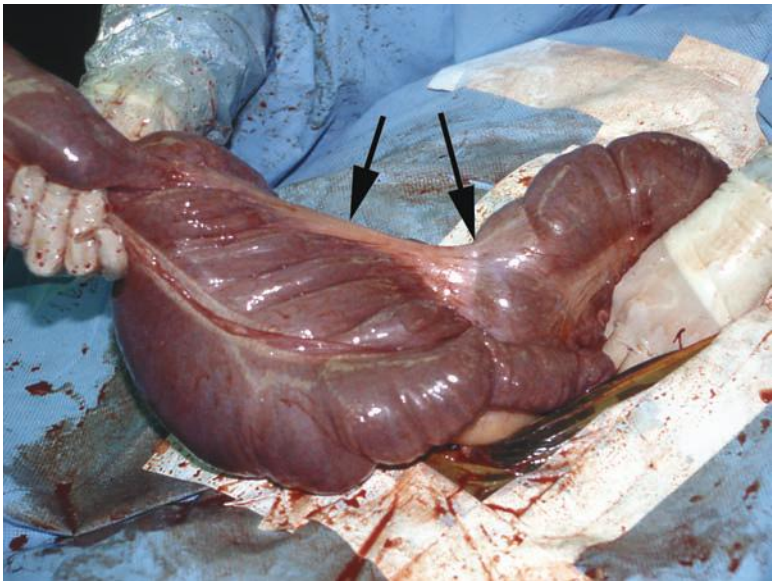
The apex of the cecum is grasped and brought out of the abdomen and pulled caudally **(A)**. The lateral band of the cecum is followed to the cecocolic fold which attaches to the right ventral colon **(B)**. (From White, NA. Surgical exploration of the equine intestinal tract for acute abdominal disease. Proc Vet Sem 2:52-57, 1986.)

Figure 26-9



Important anatomic landmarks exposed through the ventral midline in a weanling, as viewed from the left side, with cranial to the right. RVC, right ventral colon; SF, sternal flexure; LVC, left ventral colon; LDC, left dorsal colon, and Ce, cecum. Arrow points to the cecocolic fold and arrowheads point to the ileocecal fold, which is draped over the pelvic flexure.

Figure 26-10



Cecocolic fold fully displayed to confirm correction of a displacement in a mature horse, showing attachment to the lateral band of the cecum (left arrow) and to the ventral aspect of the right ventral colon (right arrow). Cranial is to the right.

Figure 26-11A

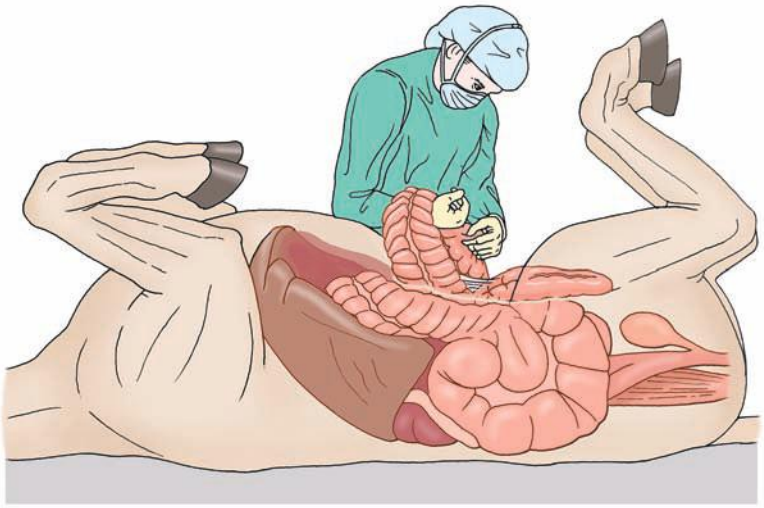
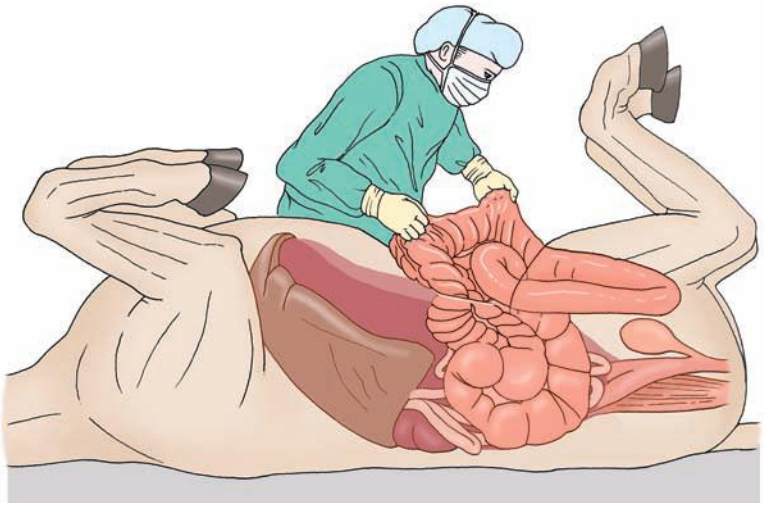


Figure 26-11B



The large colon should be lifted carefully. Laying the colon over the forearm helps to elevate it out of the abdomen **(A)**, decreasing the risk of seromuscular tears or rupture. The colon should be exteriorized and examined during the exploratory celiotomy **(B)**. (From White NA. Surgical exploration of the equine intestinal tract for acute abdominal disease. Proc Vet Sem, 1:52-57, 1986.)

To examine the small intestine, the cecum is partly exteriorized, the apex is drawn upward to display the ileocecal fold as it traces from the dorsal band to the ileum (Figure 26-12). Traction on the cecum should tense the band so that it becomes more obvious. From that point, the ileum (about 50 cm) is followed to the jejunum (20 m) to the duodenocolic ligament, which attaches the duodenum to the proximal small colon. The most proximal 25 to 30 cm of jejunum, the distal 25 to 30 cm of ileum, and ileocecal junction cannot be exteriorized.

Figure 26-12A

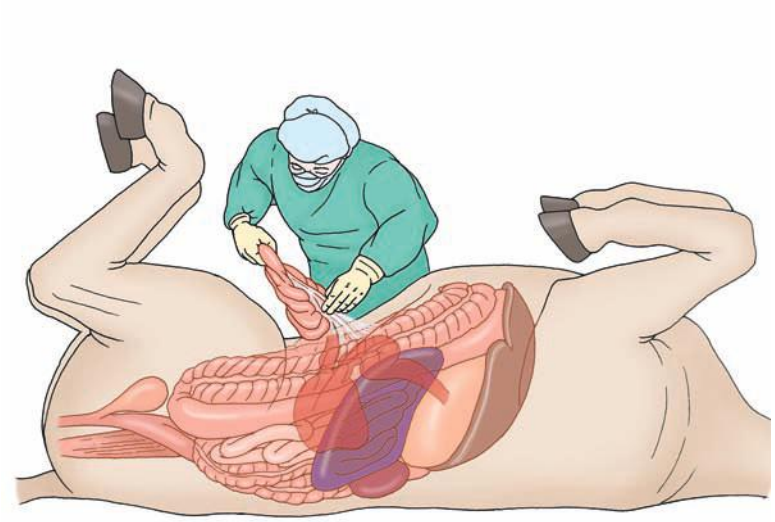


Figure 26-12B



Figure 26-12C

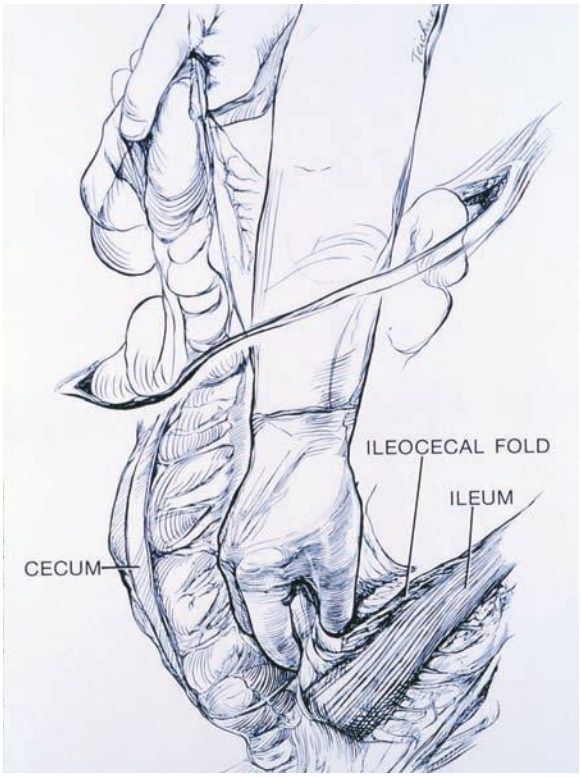
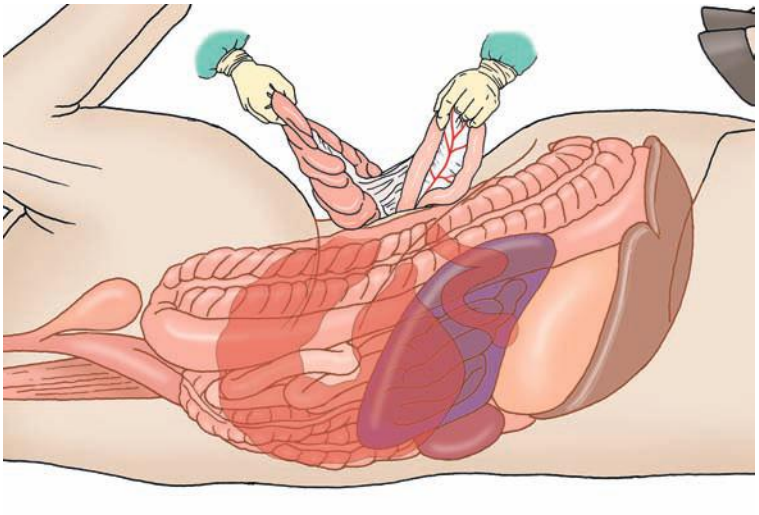


Figure 26-12D



To find the ileum, the cecum is pulled caudally and the dorsal band is grasped and followed into the abdomen **(A)**, where it forms the ileocecal fold on the antimesenteric surface of the ileum **(B)**. Palpating the ileocecal fold helps to locate the ileocecal junction **(C)** and leads to the ileum, which is brought out of the abdomen to initiate examination of the small intestine by tracing it orally **(D)**. (From White NA. Surgical exploration of the equine intestinal tract for acute abdominal disease. Proc Vet Sem, 2:52-57, 1986.)

The ileum is distinguished from the jejunum by its thicker wall, less obvious vascular pattern on its wall, the ileocecal fold, the single ileal artery along the mesenteric attachment, and, in some horses, typical raised hemorrhagic hemamelasma ilei on the surface (Figure 26-13). The cause of hemamelasma ilei is unknown, although this lesion does not seem to create clinical problems. In the horse in dorsal recumbency, the small intestine is located in the middle of the abdomen, dorsal to the large colon. If the distal part of the small intestine is empty and collapsed, a more proximal strangulation should be suspected and sought by tracing proximally. A segment of jejunum and a fold of associated mesentery are elevated from the abdomen, and the mesenteric edge thus formed is traced to the cranial mesenteric artery and right kidney (Figure 26-14). Any abnormality in the cranial mesenteric artery, mesenteric volvulus, or abscesses and enlargements in the lymph nodes in the mesenteric root can be found by this technique (Figure 26-14).

Figure 26-13



Typical appearance of a hemamelasma ilei lesion on the distal jejunum, proximal ileum. Note the ileocecal fold being extended in the lower left.

The small (descending) colon has two longitudinal bands, one in the mesenteric attachment and the other on the antimesenteric surface. The mesentery of the small colon contains abundant yellow fat, except in severely underweight horses (Figure 26-15), and the small colon can be readily identified by fecal balls in the lumen. The pronounced sacculations disappear when the small colon becomes distended. The major mesenteric vessels of the small colon are obscured in the mesenteric fat, but the terminal branches are obvious for a short distance from the mesentery on the bowel wall and are closely spaced (Figure 26-15). Sacculations or haustra that are obvious on the cecum and ventral parts of the large colon disappear at the pelvic flexure and along the left dorsal colon and are sparse and shallow in the right dorsal colon. The medial and lateral cecal bands contain cecal vessels and lymph nodes, but the dorsal and ventral bands are free of any vasculature. The ventral band does not extend as far as the others and ends close to the medial band.

In the horse in dorsal recumbency, the small colon is located in the middle of the abdomen, further caudally than the small intestine. A portion of the small colon is exteriorized and followed aborally to the rectum (Figure 26-16) and then orally to the transverse colon (Figure 26-17) and right dorsal colon. The transverse colon is too deep in the abdomen to see, but can be located running transversely across the middle of the abdomen by tracing the small colon proximally or the right dorsal colon distally (Figure 26-17). The transverse colon should always be palpated by a surgeon on the left side of the horse, for example, with the right hand coming from the right dorsal colon and the left hand from the small colon simultaneously to ensure that it is not obstructed by an enterolith along the intervening portion.

Against the left body wall, the caudal edge of the spleen is traced manually to the dorsal edge, and then medially to the renosplenic (nephrosplenic) ligament, and left kidney (Figure 26-18). The dorsal edge of the spleen forms a sizable notch, dorsal to its line of attachment to the renosplenic ligament, that can trap the large colon when it is displaced into this area. Both kidneys should be palpated for enlargement or renal calculi. When the small intestine becomes strangulated through a rent in the gastrosplenic ligament, the entrapped bowel can be palpated in the left cranial part of the abdomen, cranial to the spleen.

Figure 26-14A

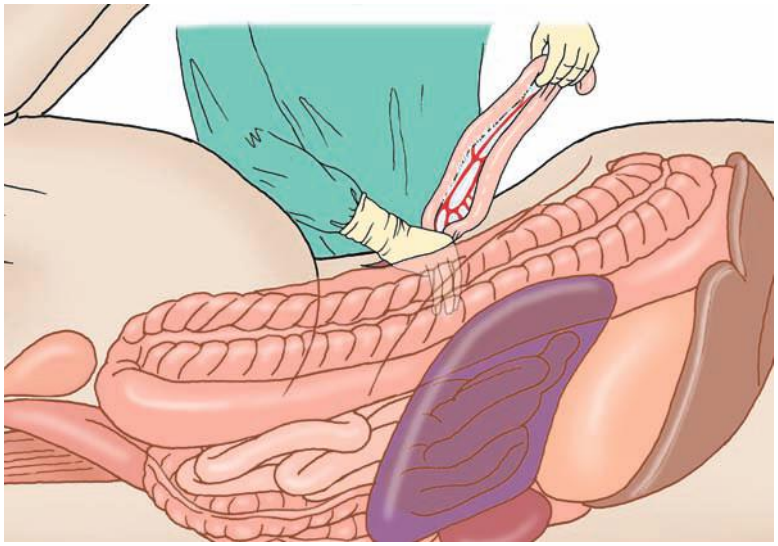


Figure 26-14B



Figure 26-14C

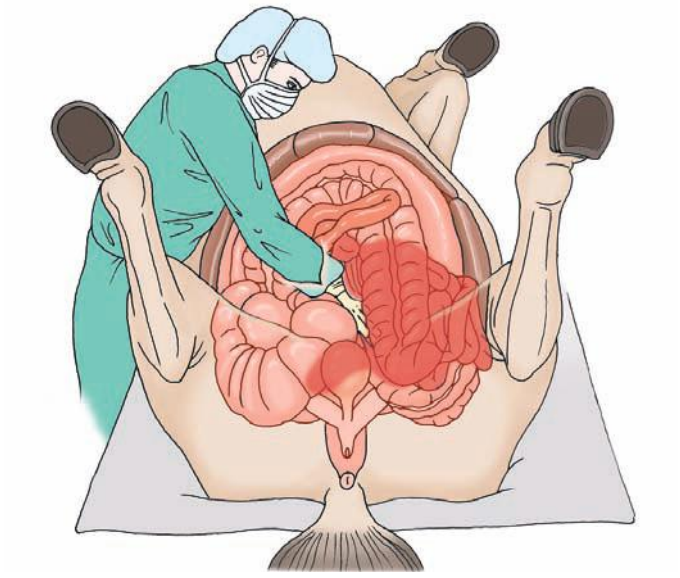
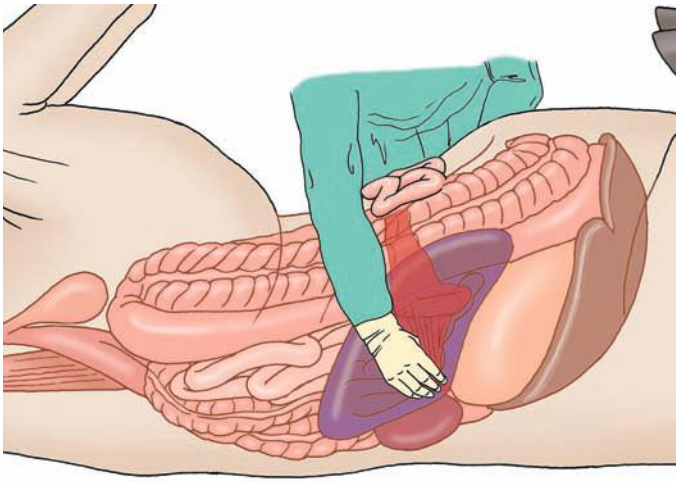
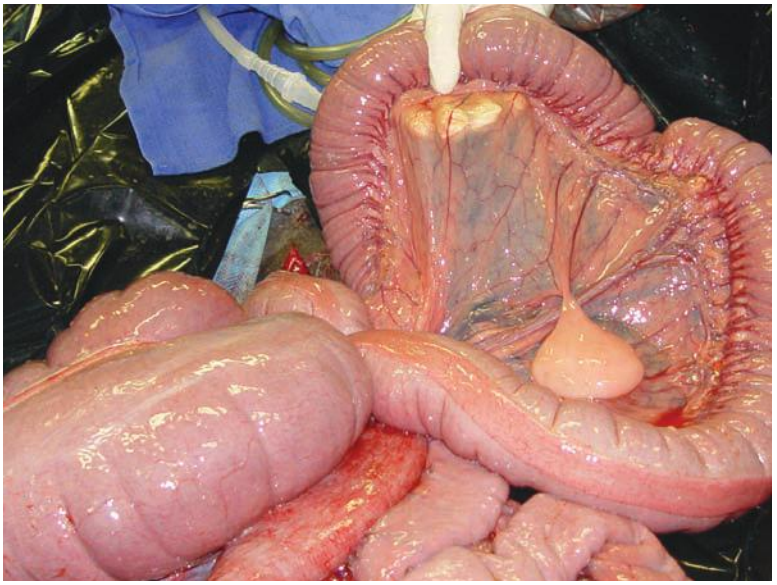


Figure 26-14D



To examine the small intestine and the mesenteric root, one hand stretches the small intestine from the abdomen **(A)** while the other hand is slid down the mesentery to the dorsum of the abdomen **(B)**. The mesentery is felt for any thickening and twisting that would indicate a volvulus. The attachment of the mesentery is on midline at the level of the first lumbar vertebra **(C and D)**. (From White NA. Surgical exploration of the equine intestinal tract for acute abdominal disease. Proc Vet Sem 1:52-57, 1986.)

Figure 26-15



Intraoperative demonstration of a large lipoma in the mesocolon of a horse that had a segment of small intestine strangulated by a similar lipoma. This lipoma was removed to reduce the risk of strangulation. Note the typical mural vasculature, tenia, and sacculations of the small colon. This is an underweight horse with a small amount of fat in the mesocolon, suggesting that factors other than body condition played a role in its tendency to lipoma formation.

Figure 26-16A

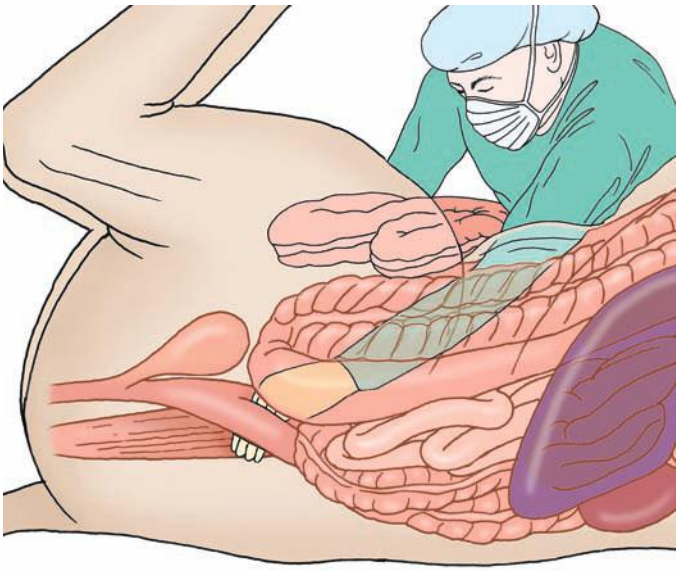
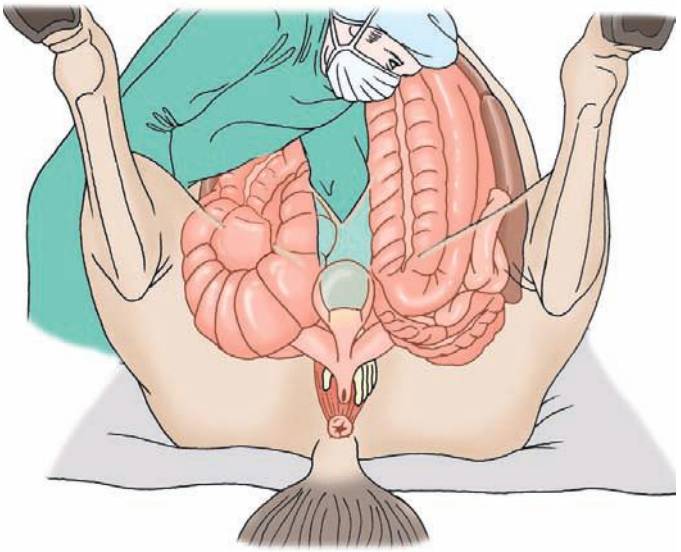


Figure 26-16B



The rectum can be located in the pelvic inlet or by following the small colon distally, **(A and B)**. The right-handed operator will find it easiest to palpate the rectum from the left side of the horse. (From White NA. Surgical exploration of the equine intestinal tract for acute abdominal disease. Proc Vet Sem 1:52-57, 1986.)

Figure 26-17A

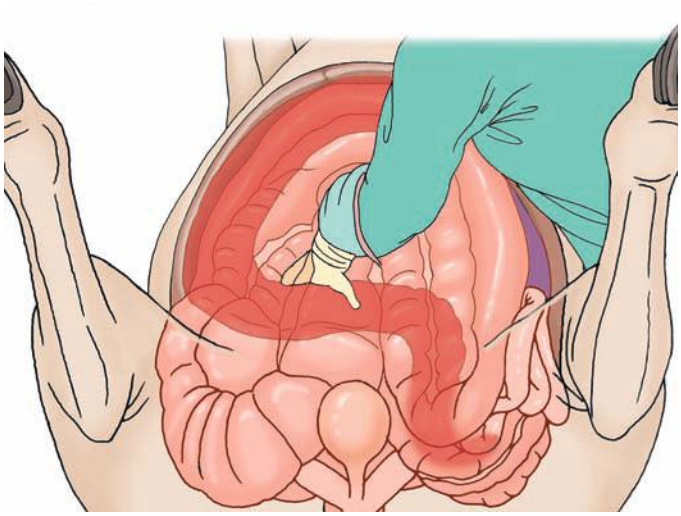
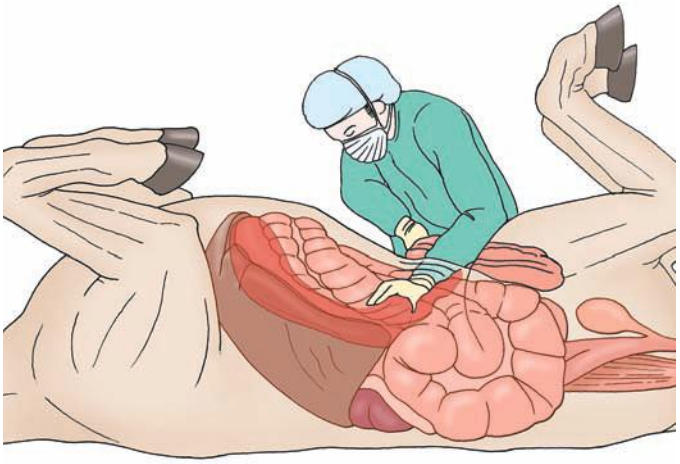


Figure 26-17B



The transvere colon is palpated by following the right dorsal colon aborally **(A)** or the small colon orally. It is found in the center **(B)** of the abdomen just cranial to the mesenteric stalk and cannot be exteriorized. (From White NA. Surgical exploration of the equine intestinal tract for acute abdominal disease. Proc Vet Sem 1:52-57, 1986.)

Figure 26-18A

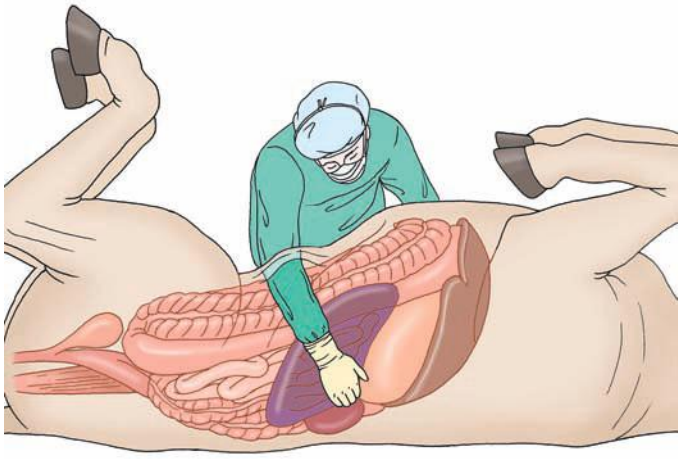
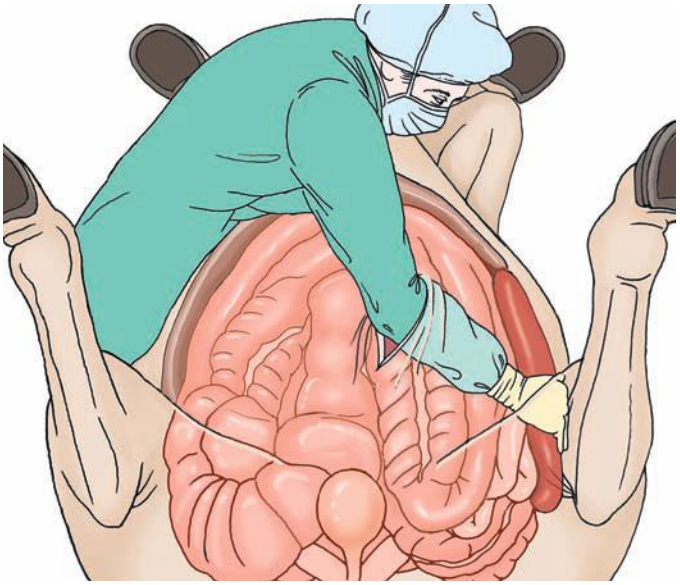


Figure 26-18B



The spleen and renosplenic space are palpated on the left side lateral to the incision by passing the hand dorsally along the caudal edge of the spleen **(A and B)**. The renosplenic space and the gastrosplenic ligament should always be checked for intestinal entrapment or incarceration. (From White NA. Surgical exploration of the equine intestinal tract for acute abdominal disease. Proc Vet Sem 2:52-57, 1986.)

The vaginal ring is the point at which the peritoneum is evaginated into the inguinal canal to form the parietal layer of the vaginal tunic, and is different from the internal inguinal ring (Figure 26-19). The deep or internal inguinal ring is an approximately 15-cm line of separation between the muscular edge of the internal abdominal oblique and the inguinal ligament. The vaginal rings, on both sides of the abdomen, are slightly ventral and cranial to the brim of the pelvis and caudal to the muscular edge of the internal abdominal oblique muscle. Each ring is evident as a small ventrally directed slit that will accommodate one or two finger tips, and is bound medially by a 2- to 4-cm long flap with the free edge dorsal to the opening. The rings are more obvious and larger and penetrated by well formed testicular vessels in a stallion compared with a gelding. The small intestine can be palpated entering the vaginal ring in a horse with an inguinal hernia. In this part of the abdomen in a mare, the uterus should be checked for torsion and the broad ligaments for a hematoma from ruptured uterine artery or for a tear that has strangulated small intestine. The bladder can also be examined in this area (Figure 26-20).

In the cranial abdomen (Figure 26-21), the surgeon can palpate the stomach just left of midline, pylorus to right of midline,

Figure 26-19A

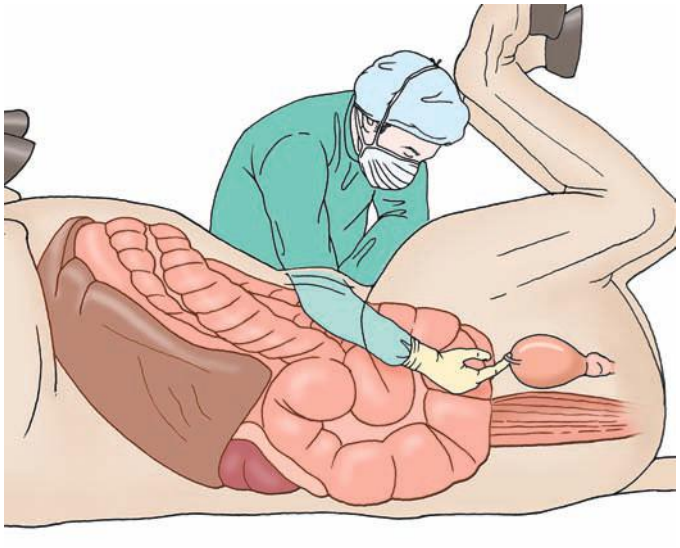
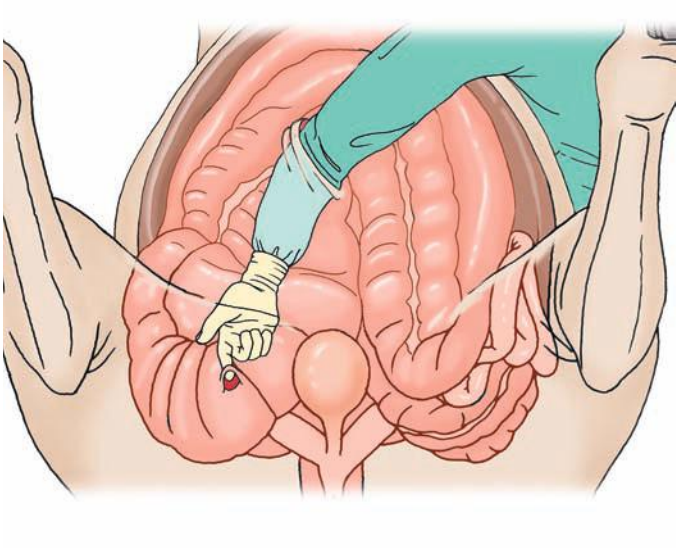


Figure 26-19B



The vaginal rings are found on both sides of the pelvis at the level of the pubis. The surgeon uses a forefinger to check the thin vaginal ring for entrapped intestines or adhesions **(A and B)**. The ductus deferens can be followed from the bladder to its entry into the rings. The vaginal ring will vary in size in the stallion and will be closed in the gelding. (From White NA. Surgical exploration of the equine intestinal tract for acute abdominal disease. Proc Vet Sem 2:52-57, 1986.)

Figure 26-20A

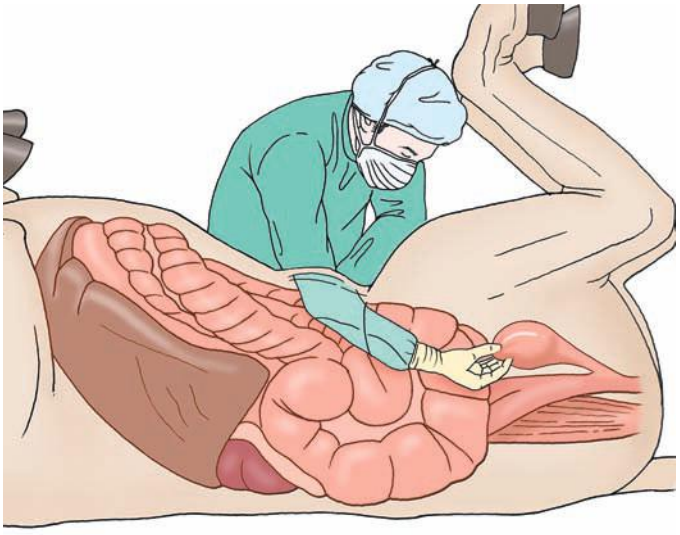
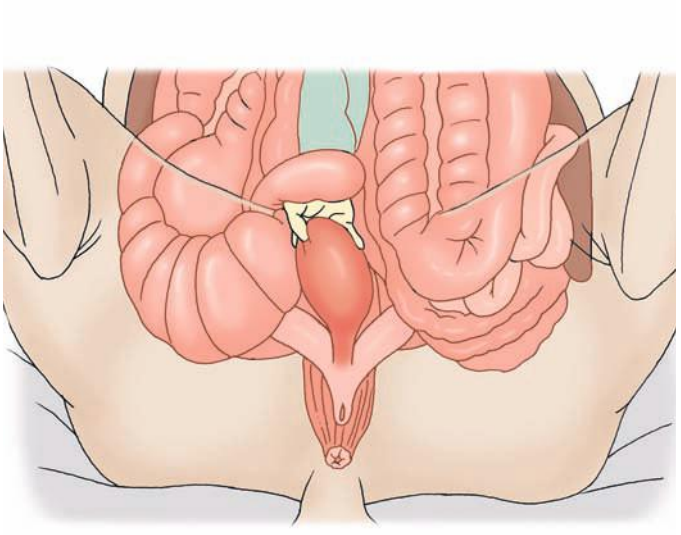


Figure 26-20B

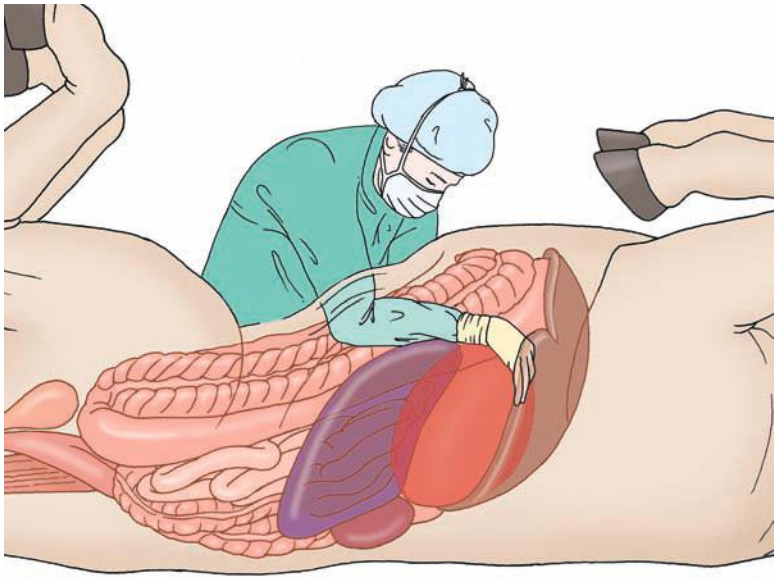


The bladder is easily palpated if distended and if empty feels like a thick elastic sac. The bladder is in the pelvic canal and can be identified on midline and ventral to the rectum (the uterus in the mare) **(A and B)**. The bladder can be exposed for inspection, but the incision must be made caudal to the umbilicus up to the pubis. (From White NA. Surgical exploration of the equine intestinal tract for acute abdominal disease. Proc Vet Sem 1:52-57, 1986.)

the duodenum (1 m long) along the right dorsal abdomen, the liver (right and left sides), and the diaphragm (Figure 26-22). The stomach is readily apparent when distended and can be recognized by the omental attachment and the prominent gastric veins and superimposed arteries that branch extensively toward the greater curvature. When empty, the stomach is flaccid, thick-walled, and difficult to locate because it is not visible through most incisions and is difficult to distinguish by palpation from the large colon. The pylorus is readily palpated as an approximately 8-cm long thickening in the transition zone between antrum of the stomach and duodenum to right of midline (Figure 26-23). The duodenum, pylorus, and antrum can be exposed in foals but are rarely visible in adults through a ventral median incision, without some modification such as converting it into a J-shaped incision (Figure 26-2). The diaphragm should be carefully palpated to detect any defects in it (Figure 26-22). The surface of the tendinous portion of the diaphragm is normally rough on palpation. On the left dorsal and cranial part of the abdomen, the left liver lobe can be found and part of it can be seen, so hepatic disease and enlargement can be determined by this means. The liver should be palpated for any evidence of rounding of the normally smooth and sharp edges; a biopsy can be taken from the left lobe if needed.

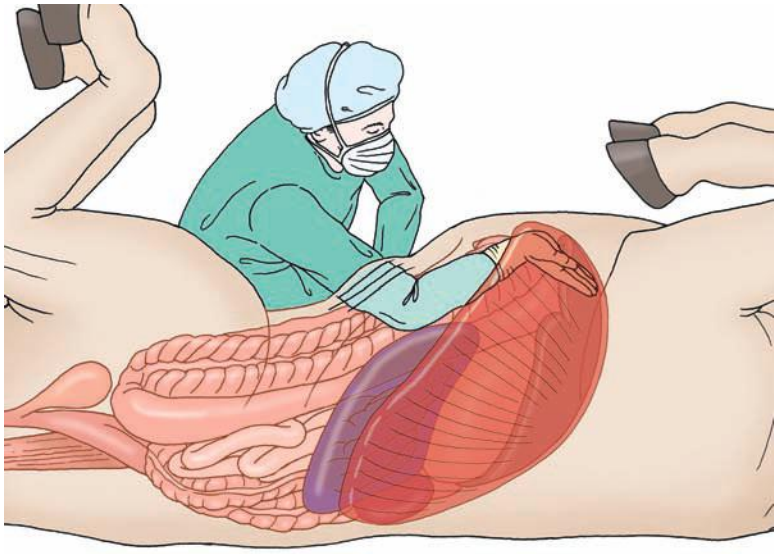
To find the epiploic foramen, the surgeon stands on the left side of the horse and inserts the right hand through the most rostral commissure of the incision, to direct it with the arm at right angles to the incision along the right body wall (Figure 26-24). When the fingertips encounter the edge of the liver, the fingers are traced medially along the visceral surface of the right lobe of the liver, until the caudate process and lobe are encountered. The fissure separating the right lobe from the caudate lobe is ignored and the back of the fingertips are traced medially along the caudate lobe until a slit-like passageway (1 to 3 fingers or 4 cm wide in a 450-kg horse) is encountered between the caudate lobe and the portal vein (Figures 26-24 and 26-25). This is the epiploic foramen, and intestine usually passes through this from left to right (Figure 26-25).

Figure 26-21



The stomach and liver are palpated on the left side in the cranial part of the abdomen. The greater curvature of the stomach can be seen in the abdomen if the incision is made on ventral midline just behind the xiphoid or if the stomach is severely distended. (From White NA. Surgical exploration of the equine intestinal tract for acute abdominal disease. Proc Vet Sem 2:52-57, 1986.)

Figure 26-22



The diaphragm is palpated cranial to the stomach and liver. Most lesions occur in the ventral central portions of the diaphragm and in the central region at the musculotendinous junction. (From White NA. Surgical exploration of the equine intestinal tract for acute abdominal disease. Proc Vet Sem 2:52-57, 1986.)

Figure 26-23A

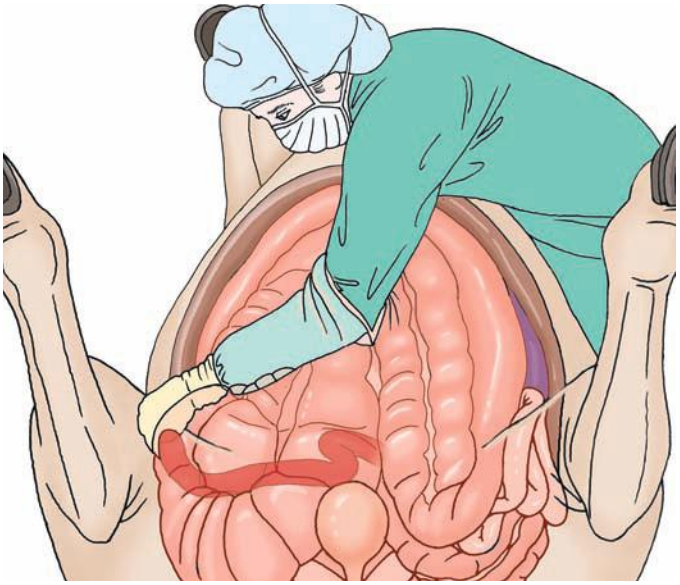
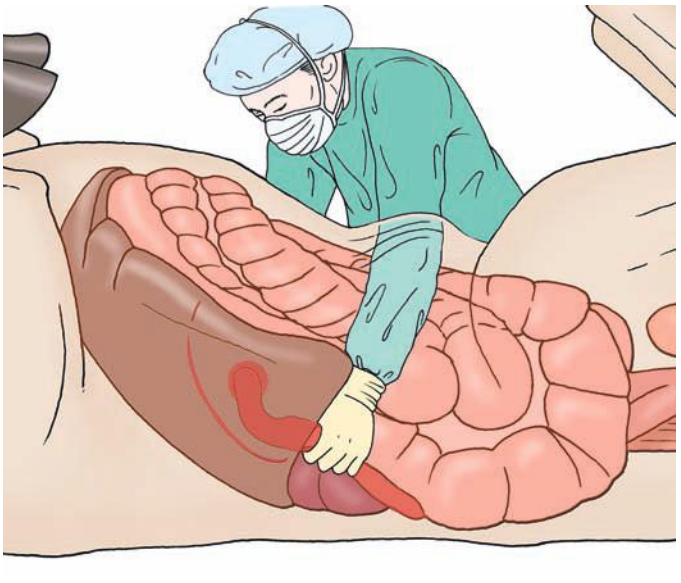
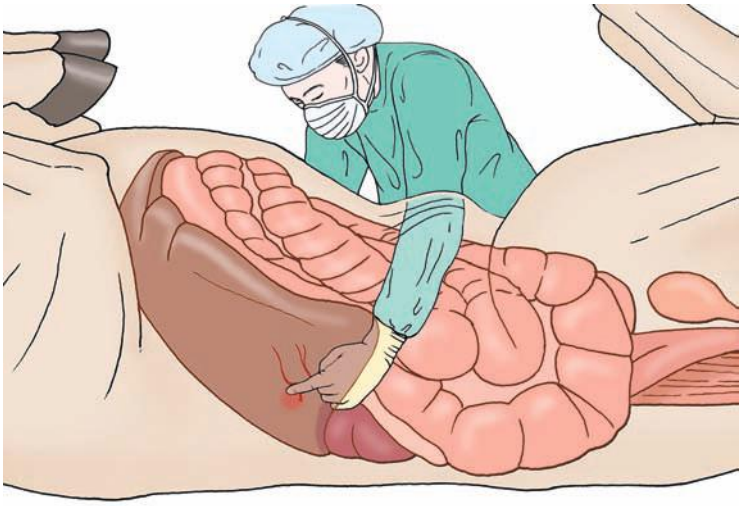


Figure 26-23B



The duodenum and pylorus are palpated from the left side, reaching to the right with the left hand **(A and B)**. The duodenum is attached to the body wall by the mesoduodenum and is normally thin and pliable. The pylorus is normally muscular and thick and can be seen through a ventral midline incision just behind the xiphoid, but only by retraction of the intestine and the stomach. (From White NA. Surgical exploration of the equine intestinal tract for acute abdominal disease. Proc Vet Sem 3:52-57, 1986.)

Figure 26-24



The epiploic foramen is palpated on the right side of the abdomen on the visceral surface of the liver between the vena cava and caudate lobe of the liver dorsally and the portal vein and gastropancreatic fold ventrally. This space should always be checked for incarcerations of the small intestine. (From White NA. Surgical exploration of the equine intestinal tract for acute abdominal disease. Proc Vet Sem 1:52-57, 1986.)

Figure 26-25A

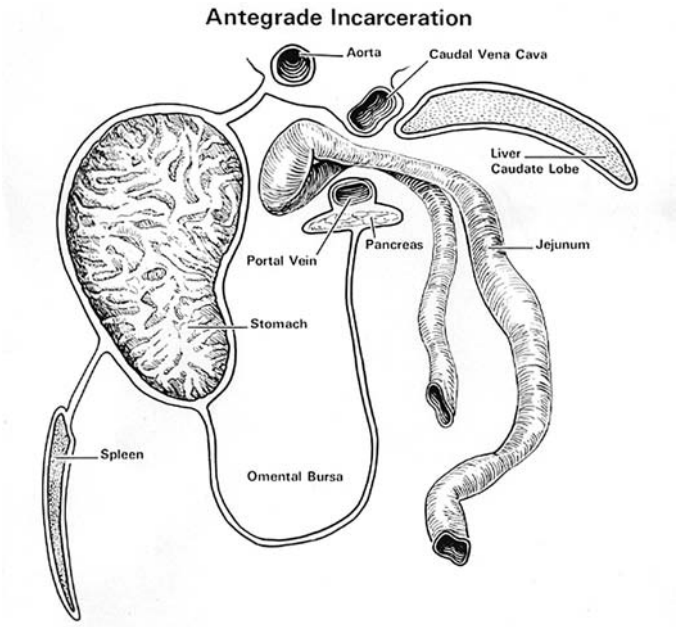
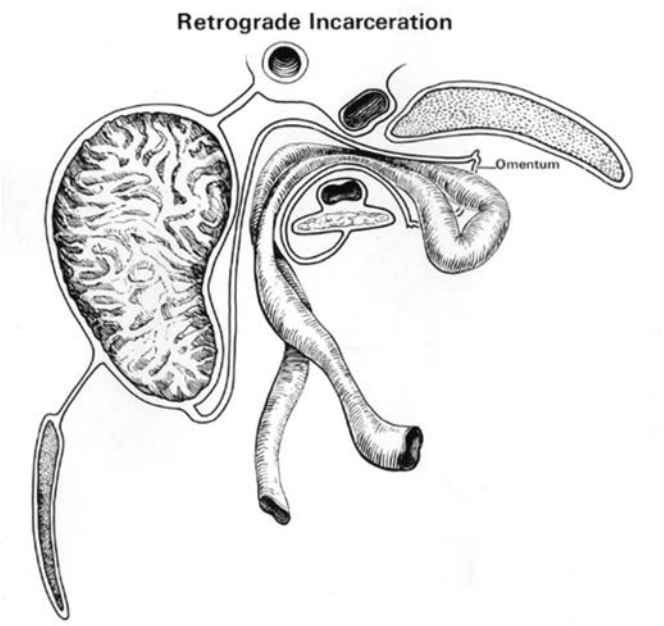


Figure 26-25B



A schematic representation of the incarceration of small intestine in the epiploic foramen as viewed from caudal to cranial. The intestine rarely enters the space from the right to left direction **(A)** and the left to right direction **(B)** is the more common. (From Turner TA, Adams SB, White NA. Small intestine incarceration through the epiploic foramen of the horse. J Am Vet Med Assoc 184:731-734, 1984.)

Examination and Handling of Small Intestine

In a horse with extensive small intestinal strangulation and distention, loops of distended small intestine can emerge from the abdomen as soon as it is opened (Figure 26-26). The surgeon should resist exteriorizing several discontinuous loops if possible, because these will only create taut mesenteric bands that will trap other fluid-filled loops as they are drawn from the abdomen, and slow the process considerably. Instead, the surgeon should exteriorize the affected loops in an orderly fashion, arranging them on the left side of the horse and maintaining their proximal to distal alignment (Figure 26-1). In this way, if jejunocecostomy is required, the bowel is positioned to facilitate flow of contents from proximal to distal during decompression, and the risk of disorientation and incorrect positioning is reduced. For example, small-intestinal volvulus (Figure 26-27A) usually involves several feet or most of the small intestine that need to be exteriorized to allow rotation of the bowel in the direction required to correct the mesenteric twist. By exteriorizing all of the small intestine, the mesentery can be followed to its attachment. The direction the surgeon's hand turns when following the mesenteric twist is the direction the entire small intestine must be rotated to correct the volvulus. Once the volvulus is corrected, the ileocecal ligament can be exposed, aligned with the cecum and with all of the small intestine to the left side of the horse without a twist in the mesentery (Figure 26-27B).

Figure 26-26



Typical appearance of distended small intestine emerging though the incision in a horse with a small-intestinal obstruction or strangulation. This can represent a physical obstruction or strangulation.

Procedures for correction of specific lesions are described in Chapter 36. Small intestine must be handled carefully to prevent the finger tips from tearing intestinal wall and mesentery, especially in foals. For this purpose, the author prefers to grasp the distended small intestine with the back of the fingers, while the finger tips are curled back to the palms. Before intestine is manipulated, the serosal surface is lubricated with sterile saline delivered from a spray bottle, a bulb syringe, or a rotary fluid pump. Some surgeons coat the bowel wall with sterile 1% sodium carboxymethylcellulose to facilitate handling.

Figure 26-27A

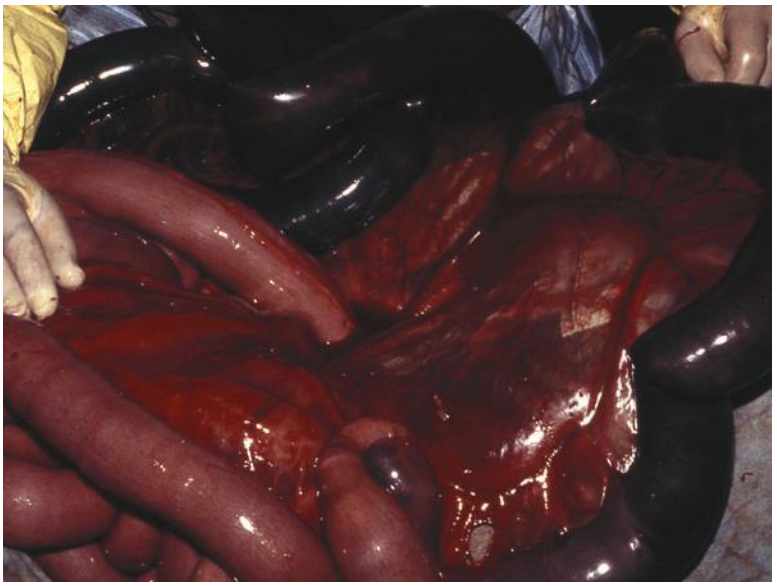


Figure 26-27B



A 360-degree volvulus of the small intestine with separation of the ileum from its normal position adjacent to the cecum **(A)**. The entire intestine is withdrawn from the abdomen to determine the direction of the mesenteric twisting. Once untwisted, the entire small intestine can be aligned to the left of the cecum and ileum and the ileocecal fold is in alignment with the cecum and ileum **(B)**.

Examination and Handling of Large Intestine

Correction of large-colon displacement requires recognition of the abnormal bowel orientation and return of the bowel to its normal anatomic position (see Chapter 38). The colon usually must be exteriorized and decompressed to accomplish this. Gas might need to be removed by needle aspiration from an accessible portion of the colon before the abdomen can be adequately examined and before the colon can be exteriorized. Needle decompression is completed using a 14-gauge needle directed into the submucosa and tunnelled several centimeters prior to penetrating the mucosa (Figure 26-28). After aspirating all the gas from the colon, the needle is withdrawn and the puncture site wiped with a saline-soaked gauze sponge. If there is a risk of leakage because of continued distention or a friable colon wall, a purse string or cruciate suture is used to close the decompression site.

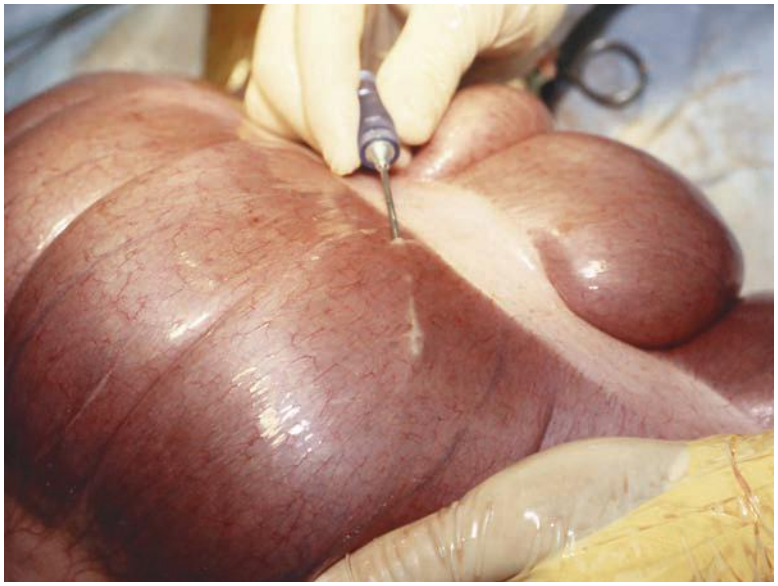
Prior to correction of a displacement or after incomplete correction of a colon displacement, the cecocolic fold might be difficult to exteriorize. If it can be exteriorized, but is directed caudally, further correction is required. When the cecum and

large colon are in proper position, the cecocolic ligament can always be brought out of the abdomen. The ligament should be straight, extending from the cecum caudally to the right ventral colon cranially (Figure 26-10).

To correct large-colon volvulus, the direction of the twist must be determined; this is usually clockwise as viewed from the back of the horse (the ventral colon rotates in a medial and dorsal direction). As much colon as possible is exteriorized, both arms are placed deep in the abdomen, and the bowel is manipulated as close to the twist as possible with open flat hands. From the surgeon's perspective through the abdominal incision, the direction for derotation of large-colon volvulus is clockwise in most cases (see Chapter 38). As the twist is corrected in the abdomen, the correction should then be applied to the exteriorized portion to eliminate resistance from this against further rotation of the intraabdominal segment. The most difficult part of correction is to turn the fluid-filled right dorsal colon around the right ventral colon.

To prevent rupture of the bowel during manipulation and exteriorization, the surgeon must not grab the wall with fingertips and should relieve distention if necessary by needle decompression or by enterotomy. Rupture is more likely to occur during surgery as the intraabdominal pressure equilibrates with atmospheric pressure so that the gas-distended bowel can then expand to its limit. Some surgeons partly fill the abdomen with sterile saline before they exteriorize the colon to help it float to the incision with minimal handling. The abdominal incision should be enlarged as needed to allow more room for manipulation of heavy bowel, to release entrapment of a heavy intraabdominal portion as it is drawn out of the abdominal incision, and to relieve some of the abdominal compression that holds the colon in place. The healthy colon is more likely to tear from tension than is the strangulated colon, because the wall is thinner and more likely to stretch to its limit than the wall that is splinted by congestion and edema. Congested colon wall is more susceptible to tearing by finger penetration. Partial-thickness tears, usually through the seromuscular layer (submucosa and mucosa intact) are common and should be sutured, preferably after tension in the wall is reduced by removal of gas, fluid, or an impaction.

Figure 26-28



A 14- to 16-gauge needle is directed through the seromuscular layer and tunnelled for 2 to 3 cm prior to entering the bowel lumen. Once the gas has been removed, the needle is withdrawn while holding a saline-soaked gauze sponge over the puncture site to prevent contamination. If continued distention or bowel friability increase the risk of leakage through the puncture, a purse string or cruciate suture is used to close the site.

Special Circumstances

A mare in advanced pregnancy can pose a considerable challenge to complete exploration of the abdomen, because the gravid uterus can occupy a large space and hinder access to many areas; however, thorough and complete examination and correction of the lesion may still be possible. Caesarean section should not be used as a means of facilitating the exploration and surgery, because this imposes another major procedure on the mare and jeopardizes the life of the foal if it is premature. In addition, it should be possible to complete the procedure under these conditions, and the abdominal incision can be bolstered with retention sutures to protect it during a rough recovery from anesthesia (see chapter on Abdominal Closure).

Enteroliths are usually located in the right dorsal colon, transverse colon, and small colon, where they become tightly impacted and easy to identify as solid objects covered by stretched intestinal wall. Less solid foreign materials, such as plastic bags and matted rubber or fiber, can be less obvious when incorporated into a mass of intestinal contents. Also, an enterolith that has a flattened surface is a strong indication that others have formed in the colon, but these can be difficult to locate, especially smaller ones that are hidden in the intestinal contents. Therefore, a thorough search through the large colon is indicated while its contents are drained through an enterotomy.

It is not unusual to find a segment of strangulated small intestine lying free in the abdomen, apparently displaced spontaneously after being strangulated. The cause of the strangulation is rarely found and usually little is to be gained by searching for it. Exceptions are diaphragmatic defects, inguinal hernias, and some tears in the small intestinal mesentery; these should be sought because strangulation in them can recur. Diaphragmatic defects and obvious mesenteric tears should be repaired immediately, although with difficulty in many cases, and the owner should be allowed the option of surgical prevention of an inguinal hernia as an elective procedure. In all horses that have evidence of a released small intestinal strangulation, the diaphragm must be examined carefully because a tear in this structure would be easy to implicate in the lesion, and repair would be strongly indicated.[12] If the horse fits the age category for a lipoma, the small intestinal mesentery should be examined closely. A strangulating pedunculated lipoma that detached spontaneously and thereby released the bowel might be located by a manual sweep of the abdomen or might float to the surface during abdominal lavage. Failure to find a detached lipoma does not appear to cause problems in the abdomen in most cases.

Although lipomas less commonly strangulate the small colon compared with the small intestine,[13] the small colon mesentery should be examined for lipomas if a strangulating lipoma is found in the small intestinal mesentery (Figure 26-15). More importantly, the remainder of the small intestinal mesentery should be searched for other lipomas, and those that have an obvious stalk or are close to the intestinal attachment should be removed, regardless of size. If time permits, the small intestinal mesentery should be examined for lipomas in any horse over 10 years, and certainly over 20 years, that has undergone gastrointestinal surgery for an unrelated lesion. The long-term prognosis is good enough after colic surgery that remaining lipomas will have time to enlarge, acquire a stalk, and strangulate the bowel.

In some horses with clinical signs consistent with large-colon volvulus or some strangulating lesion of the large colon, the colon is found in its normal position, but is obviously edematous and congested, as if it had experienced a recent compromise of blood flow. It is fairly common to find no abnormality in a horse that had evidence of a surgical lesion beforehand that then improved dramatically after surgery, suggesting spontaneous correction of a displacement. Relaxation of the abdominal muscles under general anesthesia, rotating the horse into dorsal recumbency, and elevating the horse onto the table are all procedures that could lead to spontaneous correction before the abdomen is opened.

Rarely, a horse may suffer from two, apparently unrelated, strangulating lesions of the small intestine[14,15] or from a strangulating lesion (inguinal hernia) and a secondary small-intestinal volvulus.[16,17] More commonly, a small intestinal lesion and a large intestinal lesion can develop concurrently in the same horse.[18] However, the extent to which a thorough search is made for a second lesion varies according to the surgeon's preference. There are no guidelines on this issue, but if the exploration reveals a lesion that would be fully consistent with preoperative findings, thorough examination of the remaining intestine would most likely be unproductive. However, a horse with a strangulating lesion of the small intestine could have a second concurrent strangulation of the small intestine[14,15] or a displacement of the large colon, neither of which might be suspected based on preoperative findings. The author does not routinely "run" the small intestine in a horse with a large-intestinal lesion that would explain the horse's preoperative status, but does examine the ileum and distal 2 to 4 m of the jejunum. The ileum is readily accessible, and approximately 50% of abnormalities of the small intestine involve the ileum; in addition, the ileum is prone to unique lesions, such as ileal impaction, muscular hypertrophy, and intussusception (see Chapter 36). History and known risk factors (sand ingestion, previous surgery) should also prompt examination of the structure most likely affected when the primary surgical lesion is not related.

Not all causes of colic are related to the gastrointestinal tract, and this should be considered when the abdomen is explored. For example, splenic infarction has been reported to cause mild colic and intraabdominal hemorrhage,[19] subcapsular splenic hematoma can cause mild colic, anemia, and anorexia,[20] and splenomegaly has been documented as a rare cause of recurrent colic.[21] Torsion of the liver involves the left liver lobe and should be suspected based on preoperative ultrasonographic findings and changes in liver enzymes, and by finding hemoperitoneum and a necrotic odor during surgery.[22] In normal horses, the common hepatic duct is 1.0 to 1.5 cm wide and 5 cm long and not readily located,[23] but in horses with cholelithiasis, this duct is enlarged and can be palpated on the right side of the abdomen, close to the duodenum, about 12 to 15 cm from the pylorus.[23-25] Usually, preoperative elevations in liver enzymes, preoperative ultrasonographic findings, and marked liver enlargement at surgery will direct the surgeon to examine this area. In the same location, swelling and hemorrhage might be evident in those rare cases of pancreatitis.[26,27] The adrenal glands are rarely the site of disease in horses, although ruptured pheochromocytoma can cause nonspecific signs that can be confused with colic and lead to exploratory celiotomy.[28] These glands are embedded in retroperitoneal fat on the medial and cranial poles of the kidneys and measure approximately 8 cm long, 3 to 3.5 cm wide, and up to 1.5 cm thick.[29]

Intestinal Placement

After surgery is completed, the bowel is returned to the abdomen and replaced according to its normal anatomic position in the dorsally recumbent horse (Figure 26-7). The large colon is replaced first, usually by elevating the left parts and using gravity and manipulation to place the sternal and diaphragmatic flexures in the cranial part of the abdomen. The left parts are then positioned to the left of the incision, while the pelvic flexure is grasped gently in one hand and worked back into the caudal abdomen. The small colon is positioned in the caudal part of the abdomen and the small intestine is placed in the middle of the abdomen, between the right and left parts of the large colon. The cecal base and body are positioned as far caudally as possible, and the apex is the last part to be replaced so that it can be laid under the abdominal incision and thereby act as a means of retaining loops of small intestine in the abdomen. If lesions have been corrected and all bowel arranged and replaced according to the recommended system, no special attempts need be made to prevent any error in placement.

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Surgical Techniques

Chapter 27

David E. Freeman

Colic surgery is one of the most commonly performed procedures in clinics that offer a comprehensive range of equine operations, and is the second most expensive surgery after repair of long-bone fractures in most clinics. Colic surgery places enormous demands on hospital resources, especially when complications develop. Therefore, adequate facilities, personnel, equipment, and expertise must be in place beforehand to facilitate the surgery, prevent complications, and ensure a successful outcome at a reasonable cost.

The purpose of this chapter is to address the technical and planning aspects of colic surgery. It will also cover surgical techniques involving the small intestine that are not covered in the chapter on resection and anastomosis (Chapter 29). Various surgical instruments will also be described, with emphasis on those used specifically in colic surgery, although most are applicable to a wide range of gastrointestinal procedures.

Requirements for emergency abdominal surgery in horses include (1) a surgical team; (2) induction, surgery, and recovery areas and systems; (3) proper surgical attire and instruments; and (4) proper anesthesia (see Chapter 24).

Surgical Team

The surgical team should consist of at least four persons: the primary surgeon, an assistant surgeon, an operating room nurse, and an anesthetist (Table 27-1). Although one surgeon can sometimes complete the surgery, two surgeons can reduce surgery time and contamination in difficult cases. An operating room nurse or technician can speed the delivery of instruments and materials, help with the surgical preparation, contain areas of contamination, and oversee and orchestrate functions of other team members.

Table 27-1

Primary Responsibility of the Surgical Team Members

Surgical Team Member	Primary Responsibilities
Surgeon	1. Directs all other members of the team. 2. Responsible for draping. 3. Incision, exploration, bowel manipulation, decompression, resection and anastomosis, decontamination and lavage, abdominal closure. 4. Selection of approach, suture type, and instrument use. 5. Diagnosis and selection of appropriate surgical manipulation including determination of bowel viability, site of enterotomy, resection, or bypass. 6. Decision for euthanasia in cases of terminal disease 7. Client communication during surgery.
Assistant Surgeon	1. Assists surgeon as requested. 2. Maintains a sterile field and removes material from the incision area to the instrument table. 3. Retrieves instruments and maintains an organized table in the absence of a scrub nurse. 4. Retracts, holds, performs lavage, suture preparation and primary enterotomy closure.
Circulating Operating Room Nurse	1. Completes skin preparation at the incision site. 2. Opens sterile packs. 3. Assists in gowning. 4. Responds to surgeon's requests for equipment and supplies. 5. Acts as scrub nurse to temporarily hold bowel or contaminated bowel during evacuation, lavage, resection, and closure. 6. Assists the anesthetist during anesthetic emergencies.
Anesthetist	1. Selects proper anesthetic agents. 2. Induces anesthesia. 3. Maintains anesthesia. 4. Treats shock and pulmonary failure. 5. Monitors for cardiac depression and arrhythmias. 6. Ensures proper positioning to prevent myositis. 7. Oversees recovery of animal from anesthesia.

During surgery, the anesthetist should be positioned at the head of the horse with all materials readily available to change ventilation or drug administration with minimal movement (Figure 27-1). The surgeons work best across from each other according to the primary surgeon's preference for the side at which he or she wishes to stand. For most right handed surgeons, the left side of the horse is preferred, as this provides the greatest access to most lesions and facilitates bowel manipulation. However, the most critical issue is that the primary surgeon works from the same side consistently so that he or she can follow the same sequence for abdominal exploration and can become comfortable with the abdominal anatomy from the same perspective. The assistant surgeon should have access to the instruments to hand them to the surgeon. Ideally, additional persons would include a scrub nurse to assist during the surgery with instrument delivery and to continually moisten bowel, lavage an enterotomy, or stabilize tissue, and a second circulating nurse to help with bowel manipulation, anesthesia induction, positioning of the horse, and recovery from anesthesia.

Figure 27-1

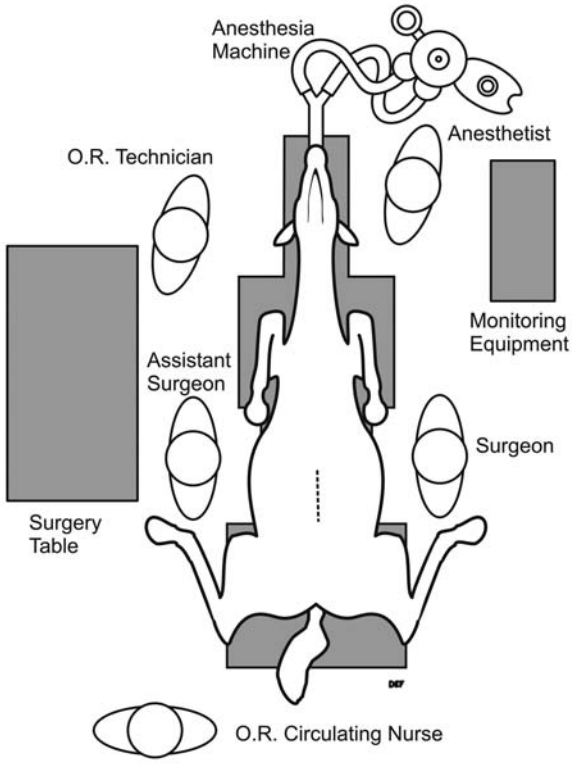


Diagram of the horse on the surgery table and the relative positions of the personnel involved in the surgery. The anesthetist, surgeon, and OR nurse are critical. A second surgeon is always desirable to reduce surgery time.

Surgical Environment and Equipment

The success of colic surgery depends on a proper environment for efficient completion of anesthesia and aseptic surgery. The operating complex should be a closed, well lighted room. Ideally the ventilation system should be filtered and should force the air from the room at the normal exits. Although the same room can be used as an induction/recovery area, this area should be separate from the surgery room. Ideally, the floor of the surgery room should have an impervious coating that allows easy cleaning, but without being slick. All drains that are expected to handle large volumes of intestinal contents should have a flushing mechanism that can prevent clogging of the drains.

Several labor-saving methods used for moving the horse include hoisting the horse on the table by its legs or in a sling, lifting the entire table by hoist, rolling the horse onto the table from a raised induction area, and having the table rolled in as part of the induction stall floor. Whichever method is chosen, it should require at least three persons to anesthetize and position the horse. The surgery table should be capable of raising the horse, rotating it to one side or the other, and elevating either the head or tail. The need for such versatility in a table arises when access to a diaphragmatic tear or the pelvis can be enhanced by elevating one end or the other so that bowel gravitates away from the lesion. The surgery also may be facilitated by rotatng the horse to one side or another, as for typhlotomy, cesarean section, or colotomy in the right ventral or dorsal colons. An exact dorsal position with adequate padding helps to prevent development of myopathy and facilitates incision placement and closure. The table should be made of rust-resistant material, be easy to clean, and if portable, be easily moved by one or two people (Figure 27-2). Padding for the surgery table can be foam mattresses or a waterbed that is filled once the horse is in the desired position. The waterbed is filled with warm water just below body temperature (35 to 36°C) until the horse is floating. Foam mattresses and air mattresses can also be used effectively for positioning and protective padding. When a water bed is filled to the appropriate level, it has superior cushioning characteristics compared with foam mattresses.[1]

Figure 27-2



Horse positioned in dorsal recumbency for colic surgery. The shoes have been wrapped to protect the horse and recovery stall floor, and rectal sleeves have been placed on the feet to limit contamination form this source. The horse is placed so that padding is evenly distributed. In this system, minimal use of side poles improves surgeon access to the abdomen, but demands that the horse be well restrained with padding and side supports.

Gowns, Drapes and Accessories

Unique features of colic surgery, such as a large incision, long duration of surgery, an extensive surgical field, large segments of bowel exteriorized at any time, and an environment soaked with blood, peritoneal fluid, lavage solutions, and intestinal contents, demand that special gowns, drapes, and accessories be developed to preserve sterility. Specialty colic packs are provided in 36” x 36” outer wrappers and include combinations of such items as a 44” x 80” table cover, 80” x 140” laparotomy sheets, 60” x 80” drape sheets, 52” x 60” Split Sheet with 24” adhesive split (Saranex/Tyvek or Polyethylene), 36" x 36" sponges, colic gowns, hand towels, and tape strips (General Econopak, Inc, Philadelphia, PA). Inventory for such supplies should be based on the need to always reglove, sometimes regown, and even redrape or add drapes after bowel has been opened and closed and before abdominal wall closure.

Gowns and Accessories

Colic gowns come in different designs that include a sterile back, fluid-repellent laminated Sontara® body, impervious body and sleeves, a Tyvek front shield, and impervious blue or yellow heat-sealed polycoated Tyvek sleeves with stockinet wrists (General Econopak, Inc, Philadelphia, PA). The basic pattern is a heavy duty construction that allows the arm to be inserted into the abdomen and exposed to body fluids without the risk of leakage or strike-through. Sleeves and/or arm covers are also available separately as sterile, Tyvek, elbow-length sleeves with an elastic wrist, or the same as a full-length sleeve with interlocking thumb hole (General Econopak, Inc, Philadelphia, PA). A lightweight plastic sleeve of similar construction and design as a rectal palpation sleeve, but with an elastic retainer around the upper arm and with the finger and thumb tips removed, is also available (Surgical Resources, Inc, Darlington, MD). Another alternative is a gas-sterilized rectal palpation sleeve with tips of fingers and thumbs removed. Both these types of sleeves will allow fluid to leak through the open tips and soak into the gown if not secured with tape strips or with an additional surgeon’s glove (Figure 27-3). The author prefers the latter, although the additional glove can reduce sensitivity and be uncomfortable if it is too tight around the fingers. Protection of footwear from soiling and preservation of an appropriate operating room environment can be achieved with polypropylene, blue, fluid-resistant non-skid shoe covers or Tyvek boots with high- or low-cut and nonskid soles.

Drapes

The first layer of draping can be an adhesive iodine-impregnated plastic drape with low memory that will stick tightly to clipped skin and provide a protective aseptic barrier (Ioban, 3M, St. Paul, MN). Disposable paper drapes that are waterproof can be custom made to fit the table and cover the entire horse (General Econopak, Inc, Philadelphia, PA). An example is a Dexter material, center laminated, 80” x 140” drape (Tullener's Drape) with embossed polyethylene, with a 4” x 13” center fenestration (General Econopak, Inc, Philadelphia, PA). Variations on this include an adhesive center fenestration that adheres to the plastic drape or skin and thereby seals the operative site from sources of contamination beneath the drape. Other variations are smaller (80” x 90”, with 3” x 9” center fenestration) and larger versions (140” x 220”, with 4” x 13” center fenestration). A special foal drape measuring 60” x 80”, with 4” x 6” center fenestration is also available. A wound protector, held in place by a flexible plastic ring, can also be inserted into the abdomen once the incision is made. Unfortunately, the

plastic ring can restrict manipulation or exteriorization of bowel and limits the size of the incision to the dimensions of the ring itself. Wound protectors offer little if anything in preventing incisional complications, and are not recommended unless conditions demand protection of the incision from a nearby focus of contamination or sepsis that is difficult to contain.

Figure 27-3



A lightweight plastic sleeve similar to a rectal palpation sleeve, but with an elastic retainer around the upper arm and with the finger and thumb tips removed (Surgical Resources, Inc, Darlington, MD). An additional surgeon's glove is applied over this to prevent fluid leaking through the open tips.

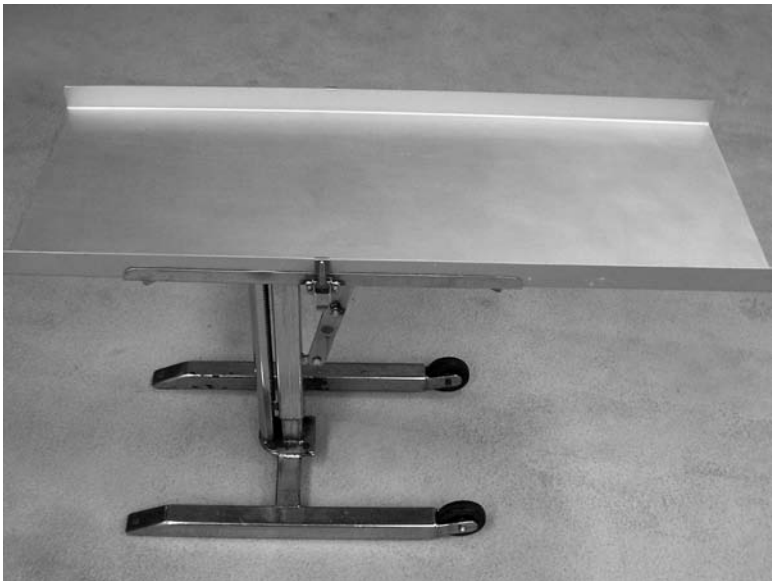
Decompression and Drainage

Colic surgery frequently requires decompression of distended and impacted bowel. This can be accomplished by different methods, depending on the segments involved and the cause of distention, but needle decompression to remove gas and enterotomy to remove solid and liquid contents are often used. Equipment that can expedite these procedures are suction, lavage delivery systems, and a colon or colotomy tray to support open intestine away from the abdomen.

Colon Tray

The colon or colotomy tray (Figure 27-4) holds the intestines, usually the large colon, away from the operative field so that colon contents cannot contaminate the sterile environment. It allows the colon to be exteriorized to the greatest extent possible, while placing less tension on the mesentery or the overstretched colon wall than if it were to be hung from the abdomen without support. A tray placed beside the horse's abdomen eliminates the possibility of a surgeon working from that side (Figure 27-5A), whereas one placed between the horse's hind legs causes less crowding and places the source of contamination further from the sterile field (Figure 27-5B). Another disadvantage of a tray placed against the side of the abdomen is that the abdomen will fall progressively below the edge of the tray as intraabdominal intestine is emptied by the decompression procedure. More bowel must then be exteriorized to prevent bowel on the tray being drawn towards the abdominal incision as the incision drops away from the tray.

Figure 27-4



Top of the moveable colotomy or colon tray is stainless steel and can be tilted to improve positioning between the hindlegs.

Figure 27-5A



Colon tray in use between the horse's hindlegs, where it can direct the colon contents away from the surgical site while placing little mesenteric tension on the exteriorized bowel.

Figure 27-5B



Colon tray used on the side of the abdomen, as for drainage of the cecum. Note that this reduces space for a surgeon on this side. The tray has been covered with a paper drape and an impervious plastic drape will be applied over this before bowel is placed on it.

Most colon trays are separate units (Figure 27-4) that can be wheeled into place and adjusted to fit against the horse (Kimsey Welding Works, Woodland, CA) or attachments designed for insertion to the rear of the table (Shank's Veterinary Equipment, Inc, Milledgeville, IL). The tray should be covered with a sterile and completely impervious sheet with a smooth surface that does not retain bowel contents, that is easy to flush clean, and that does not adhere to or abrade bowel wall (Figure 27-5). Sterile specialty drape sheets that can be used to cover a colon tray include a polyethylene, semitransparent, lint-free, fluid-proof 36" x 48" colon tray/bowel drape; a 44" x 72" bowel drape; and a blue polyethylene 24" x 48" pull-over, Mayo-stand cover (General Econopak, Inc, Philadelphia, PA). A split sheet of embossed polyethylene, 52" by 60", and a 24" U-shaped split with adhesive edges, can also be used to cover a colon tray (General Econopak, Inc, Philadelphia, PA). The U-shaped split can be applied around bowel as it exits the abdomen in a way that protects the abdominal incision, and can be adhered to other drapes to provide a secure seal and attachment. However, an ideal drape should be one that can be drawn away from the abdomen if more bowel needs to be exteriorized, so that the contaminated portion of drape can be kept away from the body wall; this cannot be done easily with a well attached adhesive U drape. An inexpensive method of draping a colon tray is to use a gas-sterilized, large heavy-duty trash bag that has been cut on one side and the bottom to form a flat sheet. These improvised drapes and similar plastic drapes can also be sutured to bowel wall around a proposed enterotomy site to provide a more complete seal against leakage from segments that cannot be completely exteriorized from the abdomen (Figure 27-6).

A pull-over polyethylene clear 26" x 40" sheet has been designed to allow a cleaner enterotomy (General Econopak, Inc, Philadelphia, PA), but it is not widely used. This drape has a stockinet collar that can be sutured or clamped to the wall of the pelvic flexure to isolate an elliptical field around the proposed enterotomy site. Another method to obtain a cleaner enterotomy is a modified colon tray with a funnel-shaped accessory that creates a mechanical separation between the sterile and nonsterile parts of the tray.[2] Sterile hooks are used to stabilize the open portion of bowel and keep it separated from the sterile field. Use of this tray nearly eliminates the need for lavage, and it is less labor-intensive than traditional methods. For enterotomy in segments that cannot be easily drawn onto a colon tray, such as small colon, small intestine, cecum, and right portions of the large colon, the segment can be hung over the side of the abdomen and then isolated from the surgical field with sterile plastic drapes.

A receptacle, such as a plastic garbage can, can be used to catch colon contents as they drain off the colon tray (Figure 27-5), and tubing from the bottom of the container can divert the liquid contents to a drain at a distance from the operative site. A

hole can be placed in the bottom of the garbage can in place of an efflux tube and positioned directly over or close to a flushable drain to allow the can to empty. A perforated steel insert can be placed in the bottom of the garbage can to retain solid material at 6 inches or so above the efflux tube, so that only liquid material can drain from the container. An alternative approach is to use a strainer made from 1.2-cm^2 galvanized steel mesh, reinforced with stainless steel bands (2.5 cm wide), and formed into a large basket that fits into the trash can.[3]

Figure 27-6



A sterile trash bag sutured to the right ventral colon before doing a colotomy to correct a cecocolic intussusception. The incision has been partly opened only to demonstrate its relationship to the drapes. Large laparotomy sponges are applied close to the incision, especially on the lower edge to trap material leaking from the bowel.

Suction

Indications for suction in colic surgery are gas decompression of bowel, removal of contents from an open segment of bowel (Figure 27-7), and drainage of lavage fluid from the abdominal cavity. The vacuum system should be of sufficient strength (100 mm Hg) to remove large volumes rapidly. Medical grade silicon tubing or any thick-walled tubing that is stiff enough to resist collapse and can be sterilized is suitable. A disposable needle (14- to 16-gauge) is readily inserted into the tubing for gas decompression. Since the needle will be a source of contamination after bowel puncture, a holder that isolates the needle away from the sterile field should be used, or the needle and hose should be discarded once they are no longer needed.

Commonly used suction tips are the Yankauer, Frazier-Ferguson, and Poole, but the type most useful for colic surgery is the Poole suction tip, because this tip has several small holes along the outer cover that allow fluid to enter the inner suction tip while omentum, mesentery, and solid material are kept away from it (Figure 27-7). To remove large volumes of peritoneal fluid or lavage solutions from the open abdomen, the suction tip can be carried into the abdomen protected within the surgeon's

Figure 27-7



Poole suction tip inserted into the completed incision in Figure 27-6 to remove liquid colon contents and blood. The intussusceptum formed by the cecum fills most of the lumen.

hand and directed into spaces free of small intestine and omentum, such as the right dorsal quadrant, along the visceral surface of the liver. Not only should the suction tip that was used to remove bowel contents be replaced before suction is used for sterile abdominal contents, but the tubing should be replaced also. Otherwise, contaminated contents of the tubing could reflux into the sterile abdominal fluid if flow through the suction tube is arrested, even briefly.

Needle Decompression

Gas can be removed using a 2- to 3-inch 14-gauge needle tunneled beneath the seromuscular layer for at least 1 cm and then inserted through the mucosa and connected to a suction device. The tunnel staggers puncture sites in the different layers so suture closure is unnecessary. If leakage is a concern, especially if a larger bore needle is used, the puncture site should be placed between the two parallel bites of a preplaced cruciate suture of size 2-0 absorbable material. Regardless of method, the needle should be withdrawn into a dry sponge at the entry site to collect any solid material dragged out by the needle, while a saline-soaked sponge is used to grasp the bowel wall (Figure 27-8). The needle is then placed in a dry sponge and wrapped in a towel for future use.

A focal impaction with dehydrated intestinal contents can be softened by injection of saline through an 18-gauge needle tunneled through the bowel wall and then connected to a large syringe through an extension set (Figure 27-9). The extension set is used so that an assistant can disconnect and refill the syringe as often as necessary without disturbing the bowel at the site of needle puncture. Without having to be concerned about the weight of the syringe, the surgeon can more easily direct the needle throughout the substance of the impaction until it is completely softened.

Figure 27-8



Method of removing a needle used to suction gas from bowel. The puncture site is held with a moist sponge so that it can be inspected and cleaned, and the needle is withdrawn into a dry sponge to collect any material trapped at the tip.

Figure 27-9



Small colon impaction being injected with saline. A 20-gauge or 18-gauge needle can be tunneled between the seromuscular layer and mucosa and inserted into the bulk of the mass. The extension set allows independent manipulation of syringe and needle. (From Bartmann CP, et al. Diagnosis and surgical management of colic in the foal: Literature review and retrospective study. Clinical Techniques in Equine Practice 1:125-142, 2002, with permission.)

Intraluminal Lavage

An inexpensive and readily available method for intraluminal lavage of bowel is delivery of a moderate flow of tap water through a large-bore nasogastric tube connected to a garden hose. In one system described for colon lavage during colotomy, two hoses connected to a single hose through a Y-piece (Figure 27-10) are handled by an unscrubbed surgical nurse to deliver warm (37°C; 98.6°F) water.[3] One hose is a flexible nasogastric tube that can be gently advanced through the colotomy and into the dorsal or ventral colon so that colonic contents can be softened and removed (Figure 27-10). Although sterile polyionic fluid is preferred, water from the extraluminal hose can be directed onto the serosal surface of the colon toward the trash can to keep the serosa wet and free of particulate matter. It also can be directed onto the sterile plastic drape beneath the colon to remove solid contents that could adhere to the underside of the bowel. The serosal surface of the colon is thoroughly lavaged with warm water during closure and then finally rinsed with 0.9% sterile saline or lactated Ringer's solution.

Figure 27-10



Two stomach tubes connected through a Y-piece to a hose so that one tube can be used to flush the bowel interior and the other to flush the enterotomy site and surface of colon tray with tap water.

An advantage of this system is that tap water is an inexpensive, readily available source of lavage in large volumes; disadvantages are that it is nonsterile and hypotonic. Excessive use of water on the serosal surface of the colon causes a mottled appearance and blanching of the serosa, possibly from intramural edema induced by a hypotonic solution. Although this does not appear to have clinically significant effects, water lavage should be restricted to areas of the colon in which the potential for contamination is greatest. However, there is no evidence that warm tap water is harmful to the gastrointestinal mucosa, although thorough intraluminal lavage with water has been blamed, along with other confounding factors, as a possible cause of postoperative diarrhea.[3] The temperature of the water is not critical, provided that extremes, especially high temperatures, are avoided. A thermostat on the water source set just below body temperature is recommended to prevent temperature changes during the lavage.

Lavage of the serosa with a sterile polyionic fluid is preferable to tap water to remove contamination during enterotomy or anastomosis, because this fluid is sterile and isotonic. Large fluid sources such as carboys, 1-liter plastic bottles, or 5-liter plastic fluid bags are easiest to use. Fluid can be delivered by gravity flow, but a rotary pump (Cole-Parmer Instrument Company, Chicago, IL) with sterile tubing can deliver up to 2280 mL/minute, and the rate of flow can be controlled manually at the pump (Figure 27-11). For intermittent lavage to prevent serosal dehydration of bowel surfaces exposed for long periods, smaller volumes can be delivered by a spray bottle or bulb syringe, or by pouring directly from a 1-liter bottle or from a saline bowl. The bottles and fluid bags can be warmed in a microwave oven, fluid warmer, or sink full of hot water. The fluid of choice is lactated Ringer's solution, although saline probably is the most commonly used.

Systems that rapidly deliver large volumes of sterile fluid can also be used to lavage the abdominal cavity at the end of surgery. Another method of abdominal lavage is for an unscrubbed nurse to suspend a 5-L bag of fluids by one hand while holding a bottom corner of the bag with the other hand. Another unscrubbed nurse can then cut off a portion of the free bottom corner and the person holding the bag can direct gravity flow from the open corner into the abdomen. Care must be taken to ensure that the fluid does not contact any unscrubbed person or nonsterile surface as it flows to the abdomen, and difficulties in directing flow by this method can lead to fluid loss; however, this is a rapid means of delivering large volumes of sterile fluid.

Figure 27-11



A rotary pump (Cole-Parmer Instrument Company, Chicago, IL) with sterile tubing that can deliver high volumes of sterile fluids and allows the rate of flow to be controlled manually at the pump.

Laparotomy Sponges

Large laparotomy sponges soaked with sterile saline are used to pack off bowel and thereby contain contamination during procedures involving the intestinal lumen (Figure 27-6). The sponges can be secured to the bowel with Babcock forceps or to drapes with Allis tissue forceps. Sponges of 4-ply 100% US cotton gauze are absorbent, soft, vacuum-delinted to minimize lint and particulate matter, and have colored radiopaque markers that remain visible when saturated with blood (General Econopak, Inc., Philadelphia, PA; Tyco Healthcare Kendall, Salem, CT). They are packaged for easy stacking and storing, are sterile, ready to use, and come in a variety of sizes. However, the 12" x 12" (5 per pack), 18" x 18" (5 per pack) and 36" x 36" (1 or 2 per pack) are particularly well suited for colic surgery. They are preferable to reusable hand towels that have been washed, because they are more pliable, softer than tissues, more absorbent, and free of any soap residue that might not rinse out during the wash. Large sponges are safer than small ones because they are less likely to get lost in the abdominal cavity. Regardless of its original size, however, a blood-soaked sponge can compress to a size that can be difficult to locate if it is packed into a recess. Unused sponges should be removed from the surgical field as soon as the abdomen is open, and used sponges should be discarded immediately. Small sponges rapidly become engulfed in omentum and can easily be lost from the surgical field. Although not always practical in equine surgery, a sponge count can be conducted by having the anesthetist record all sponges in each package as it is opened, and then all used sponges are thrown onto a drape placed on the floor behind the horse (see Chapter 25). These are then counted and the numbers compared with the count for each opened pack.

Surgical Instruments and Suture

Basic surgical instruments are similar to those used for most soft tissue procedures in horses (Table 27-2), but some special instruments should be included in the pack or readily available in the surgery suite. Instruments should span a range of fine and delicate for handling viscera to large and robust for body wall closure. At least one extra set of instruments should be available in a smaller pack, because it is often necessary to use new instruments for abdominal closure once the original set of instruments becomes contaminated during enterotomy or bowel resection. At the very least, clean instruments should be partitioned away from the dirty instruments on the same table, although this does demand strict surveillance of instrument handling and carries a high risk of contamination.

Intestinal Clamps

Intestinal clamps or forceps are essential elements of colic surgery, although soft rubber Penrose drains, 1/4 to 1/2 inches wide, can be used for atraumatic occlusion of segments of small bowel (see Chapter 30). Several types of specialty clamps

Table 27-2

Basic Instruments Required for Equine Abdominal and Intestinal Surgery

Categories	Types
Towel clamps	Backhaus Roeder
Scalpel handles	#3 and #4 scalpel handles and blades
Thumb forceps	Brown-Adson Rat teeth (2) De Bakey Russians
Scissors	Mayo scissors (straight and curved) Metzenbaum scissors Suture scissors
Needle holders	Mayo-Hegar (2 – 3)
Hemostats	Mosquito hemostats (4) Kelly hemostats (10)
Lavage and decompression	Saline solution bowl Bulb syringe (or spray bottle) Decompression tubing and needle Poole suction tip
Cautery	One disposable/reusable unit
Sponges	4 x 4 sponges Laparotomy sponges*
Tissue forceps	Babcock intestinal forceps* Allis tissue forceps
Intestinal clamps*	Carmalt forceps* Fogarty intestinal clamps*

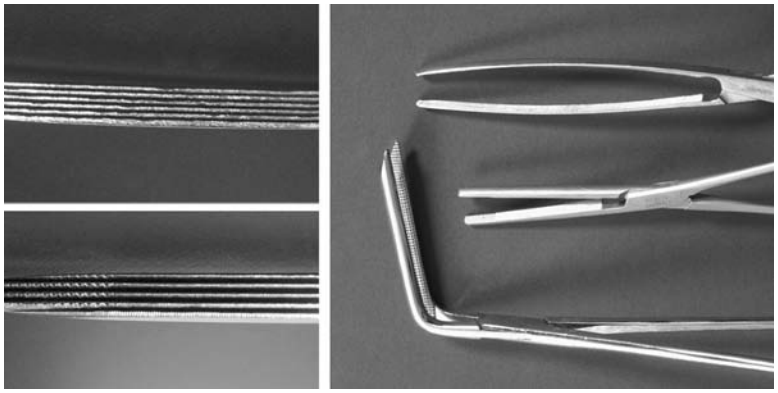
*Because these are not required for every colic surgery, they can be packed separately to save on labor and wear and tear.

are available (Figure 27-12). Although the Doyen or Robinson clamps are atraumatic, they can be damaging to intestinal tissue, partially because of an inability of these instruments to accommodate thickness of equine bowel. If the Doyen clamps are applied tightly enough to engage the last ratchet, the jaws close to the joint will compress the bowel wall, but the tips will spread and fail to engage the bowel wall at that end. Use of rubber tubing over the jaws does not reduce the pressure applied, because they can interfere with jaw closure and thereby allow slippage. Clamps with flexible jaws and replaceable inserts, such as Fogarty intestinal clamps, can grasp securely and yet apply even pressure without slippage. Carmalt forceps or Payr Pyloric clamps are traumatic and do not slip, and are therefore used to clamp bowel that will be removed (Figures 27-12 and 27-13). Right-handled clamp, such as Glassman clamps or Best colon clamps, allow placement on bowel deep to the incision, such as an ileal stump (Figure 27-12). The TA 90 autosuture instrument with a sterile, previously discharged cartridge can also be used as a right-angled clamp. Sullins-Scudder intestinal clamps (Scanlan Instruments, Englewood, CA) are of sufficient size to occlude the lumen of the equine large colon for resection.

Babcocks are the preferred tissue forceps for elevating bowel wall for incision or closure. They have a triangular open-tip shape with longitudinal lines on the grasping surface and come in lengths from 13 to 24 cm (Figure 27-14). Babcock forceps might be more suitable for colon than for small intestine, because they can cause some tissue compression that could be a focus for adhesion formation in the small intestine.

Bowel edges can be handled during suturing with Brown-Adson, DeBakey, Cooley, or Russian forceps. The author prefers the first three. The Brown-Adson forceps can be regarded as atraumatic because its fine serrations allow the bowel to be grasped with minimal pressure and low risk of tissue tearing. The Russian forceps lack teeth, but require some pressure to maintain a purchase and likely cause serosal injury.

Figure 27-12A



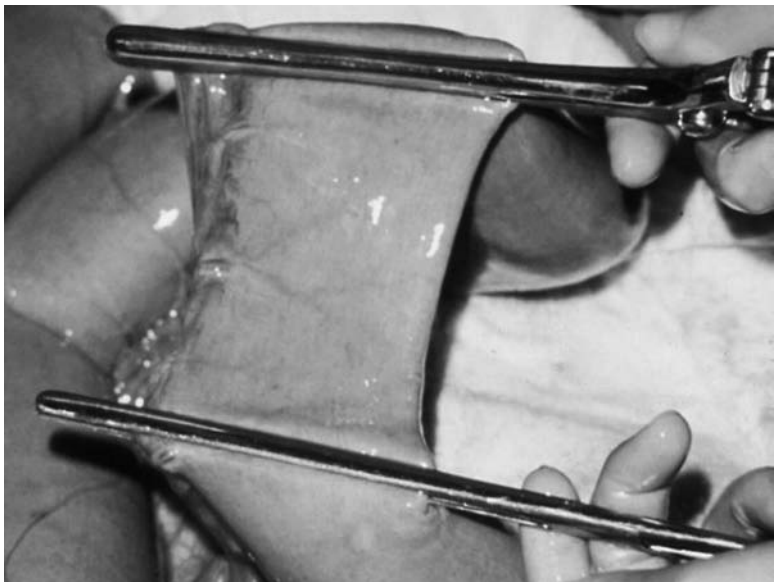
Assorted bowel clamps on the right, top to bottom: Doyen clamps, Carmalt clamps, and Best right angle clamps. Close up view of the interior of the jaws on the left shows the longitudinal grooves on the slightly bent and malleable jaw of the Doyen (top) and the more rigid, straight jaw of the Carmalt (bottom) with longitudinal grooves and cross hatching at the tip to improve purchase on the bowel.

Figure 27-12B



Fogarty clamps with one soft and one apposing gripping insert. These are atraumatic and are recommended. The right angled handles allow an assistant to manipulate the bowel for the surgeon.

Figure 27-13

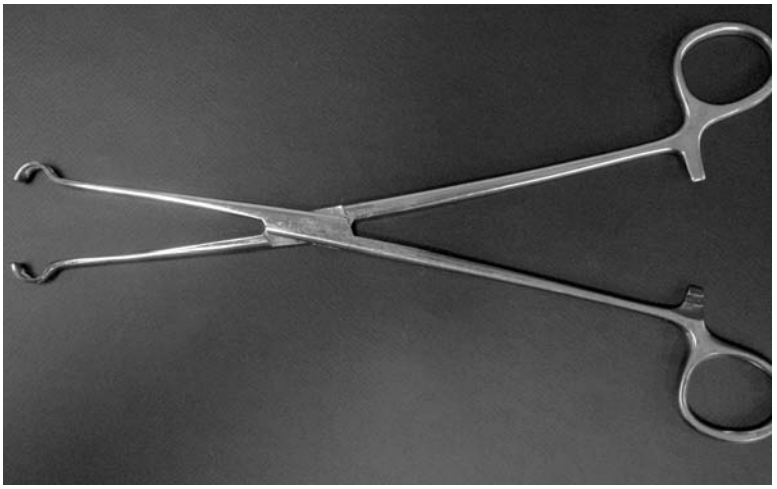


Typical placement of traumatic and atraumatic clamps on jejunum for resection. The bottom clamp is a Doyen and the top is a Payr clamp that has a robust and rigid jaw that crushes tissue on closure and provides an excellent seal on bowel to be discarded.

Suture Material

Several sizes and varieties of suture can be used for the different procedures usually encountered during colic surgery (Table 27-3). The specific recommendations are made in other sections of this chapter where the techniques are described. The most common sutures used for intestinal suturing and abdominal closure are the synthetic absorbables. Polyglactin 910 (Vicryl) is a braided multifilament suture commonly used in colic surgery, with moderate tissue drag and excellent knot security. Its rapid rate of absorption is not a disadvantage in bowel wall, although it could be in the body wall. Polydiaxanone (PDS II) is a monofilament suture with great strength, good handling properties, but slower absorption than is needed in bowel wall. Polyglecaprone 25 (Monocryl) is a newer synthetic absorbable monofilament, with less memory, and better handling characteristics than other monofilaments, such as PDS and Polyglyconate (Maxon). Needles should be swaged, curved, and taper point for most applications in the bowel wall.

Figure 27-14



Babcock forceps opened to display typical appearance of the atraumatic jaws.

Table 27-3
Commonly Used Suture Materials and Sizes for Adult Horses

	000	00	0	1	2	3
Polyglycolic acid (Dexon)	X	X	X	X	X	
Polyglactin 910 (Vicryl)	X	X	X	X	X	X
Polydioxanone (PDS)	X	X	X			
Polyglecaprone 25 (Monocryl)	X	X				
Nylon		X		X	X	

Stapling Instruments

Stapling instruments are expensive, and little if any evidence exists that they can shorten anesthesia time sufficiently in clinical use to offset the cost of the instruments. The best explanation is probably that the anastomosis makes a small contribution to the total surgery time, the surgeon, not a nurse, usually loads the instruments, and only a small number of staple lines are applied for most equine procedures. Most prices are negotiable for universities and private practices, and many instruments are for multiple use, so their costs can be distributed over many cases. It is also possible to rent stapling instruments, provided that a sufficient number of cartridges is purchased concurrently.

Despite these limitations, stapling instruments have contributed enormously to intestinal surgery in the horse and are essential under certain circumstances, such as application of a suture line to a segment of bowel that is inaccessible for handsewn methods. They also facilitate side-to-side anastomosis, because they produce a stoma that is consistent in length and easy to create in the desired region of the bowel. Contamination can be decreased with proper use of stapling instruments. The decision to oversew staple lines is dictated by the surgeon's preference, because this step will extend surgery time but could provide added security.

Linear Cutting Instruments

These stapling instruments place two double-staggered rows of B-shaped staples and cut between the middle rows of staples simultaneously, thereby creating a stoma. Examples used most commonly in equine gastrointestinal surgery are the GIA 50 Premium stainless steel instrument, the GIA 90 Premium stainless steel instrument (Figure 27-15), the Multifire GIA 80 disposable stapler, and the ILA 100 reusable stainless steel stapler (Figure 27-15) with stainless steel staples. These are all produced currently by the United States Surgical Corporation and the number on each instrument indicates the length of the staple line.

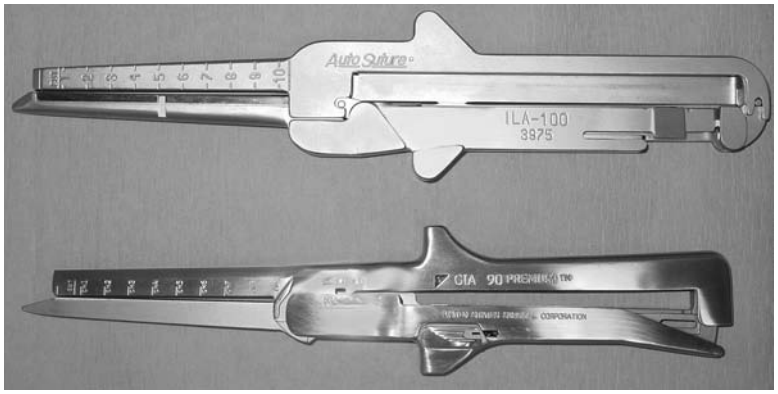
All stapling instruments suitable for anastomosis (GIA and ILA) are used with bowel placed in side-to-side manner and can also be used for bowel transection and simultaneous closure, although the GIA 50 Premium is too short to span the width of adult horse intestine. When used for bowel transection, the GIA and ILA can be applied in a partially coupled scissor-like position (Figure 27-16); but to join 2 bowel segments, it is easier to insert the forks separately into the bowel lumens before alignment of the back hinge and closure of the locking lever. The ILA 100 can be reloaded with disposable units that

discharge 3.8 mm (blue) and 4.8 mm (green) stainless steel staples, but the GIA 90 Premium can only use the 3.8 mm long staples. The Multifire GIA 80 disposable can be reloaded with 3.8 or 4.8 titanium staples and can be used 8 times. The staples with the longer legs compress tissue to 2 mm and are more suitable for adult equine intestine, whereas the shorter staples compress to 1.5 mm, and might be better suited for use in foals.

Ethicon Endo-Surgery (Johnson & Johnson, Cincinatti, Ohio) produces the Proximate Linear Cutters that are similar to the GIA and ILA, and produce stomas of 53 mm (Product code 55), 73 mm (Product code 75), and 98 mm (Product code 10). They have titanium staples in two lengths, a blue cartridge for tissue that compresses to a thickness of 2 mm and a green cartridge for tissue that compresses to 1.5 mm. Cartridges or reloads do not contain a knife replacement, but the instrument can be used with the original and 7 reloads (8 applications). The instrument's safety lock-out feature is designed to prevent a used reload from being accidentally discharged and also prevents the instrument from opening, thus exposing the knife if the instrument is only partially discharged. A mechanism at the back of the handle forces the forks together as the staples are being discharged; this prevents jaw misalignment and resulting staple misdirection.

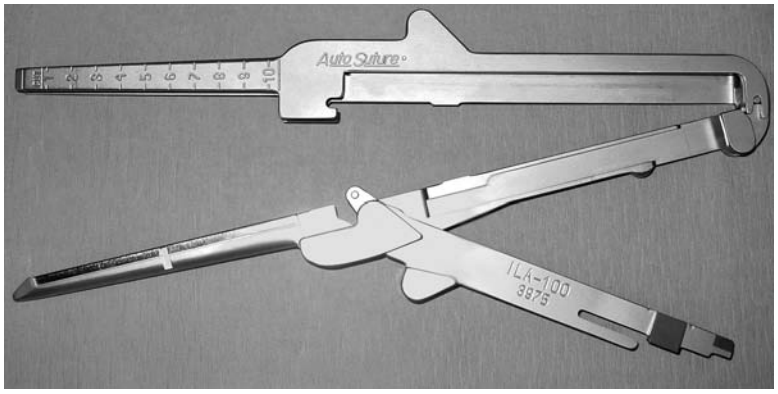
As with all linear cutters, any "bunching" of tissue at the proximal end of the forks may result in an incomplete staple line. The alignment/locking lever is closed completely when the tissue is fully in place. After this instrument is discharged, the firing knob is returned to the original "Return Knob Here" position until a click is heard, and the instrument halves are separated by pulling open the alignment/locking lever. Failure to properly follow the instructions for any stapling instrument may lead to leakage or disruption.

Figure 27-15



The ILA 100 (top) and GIA 90 (bottom), are linear anastomosing/cutting instruments for equine intestine.

Figure 27-16



The ILA 100 opened in the scissors configuration as it would be when applied to bowel for transection.

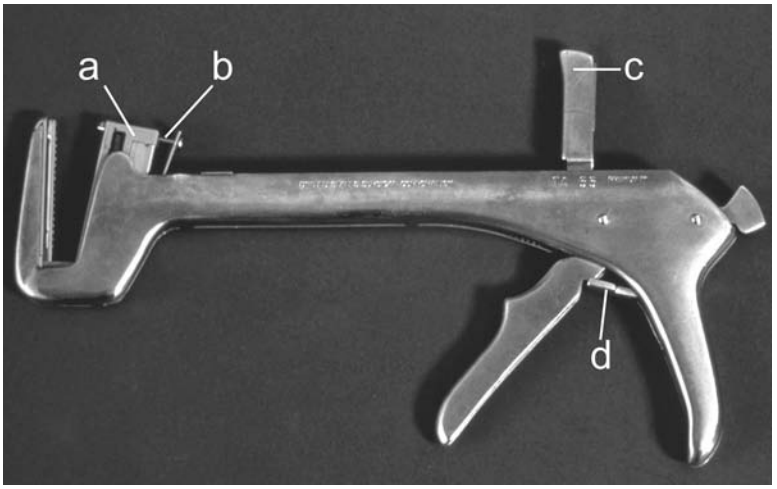
Thoracoabdominal (TA) Staplers

The TA instruments place two staggered staple lines and the TA Premium 55 and the TA Premium 90 stainless steel instruments fire 3.5-mm and 4.8-mm-long staples (United States Surgical Corporation, Tyco Healthcare, Salem, CT). The Multifire TA staplers can be used up to 4 times during a single surgical procedure and should not be resterilized. The Proximate Linear Stapler is the equivalent instrument from Ethicon; this has an adjustable knob that allows the surgeon to adjust the depth of the bend in the "B" of the staples according to a thickness gauge on the instrument.

When closing the instrument jaws on TA instruments, the approximating lever must be depressed completely, or staples may not form properly when the handle is squeezed (Figure 27-17). If considerable force is required to close the approximating

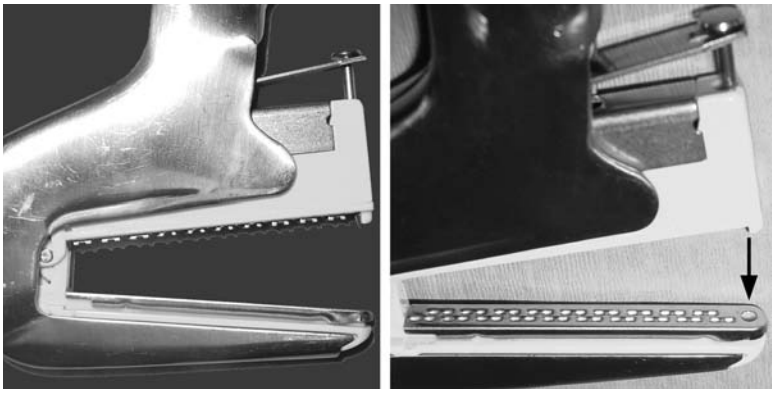
lever, the tissue is too thick for the staple size selected. The retaining pin must be pressed firmly into place to ensure proper alignment of the cartridge and anvil; failure to do so could result in improperly formed staples (Figures 27-17 and 27-18). The safety catch is released when ready to discharge, and the instrument handle must be squeezed as far as it will go to discharge the staples and have them form completely. The instrument edge then is used as a cutting guide to place the incision at a proper distance from the staple line. After the instrument is removed, the staple line always should be inspected for hemostasis. The safety catch should be replaced immediately after discharging, and must be in the locked position during all reloading steps. As with any stapler that has been discharged, the drivers used to push the staples out of the pocket, through the tissue and into the forming anvil, will be visible (Figure 27-18). Failure to recognize this can be a potential source of fatal error, because empty cartridges can be mistaken for unused cartridges and can be resterilized.

Figure 27-17



A TA 55 loaded with a cartridge and ready to apply to intestine, showing a) the disposable loading unit; b) the retaining pin; c) the approximating lever; and d) the safety catch.

Figure 27-18



Close-up view of a discharged TA 55, showing the drivers used to push the staples out of the pocket, through the tissue, and into the forming anvil (left). This feature allows a discharged stapler to be used as a right angle clamp to hold bowel deep in the incision. The example on the right shows the direction the retaining pin must follow to enter the slot on the cartridge to ensure that the staples meet the anvil correctly.

End-to-End Anastomosis (EEA) Instrument

The EEA can be used to create a stapled end-to-end anastomosis, but the small size of the stoma produced limits its use to gastroesophageal and jejunojejunal anastomoses in foals and American Miniature Horses. The EEA stapler advances a cartridge over the central shaft along a grooved track, and the anvil is screwed onto the tip of the central shaft. Within the cartridge are two staggered rows of stainless steel staples surrounding an inner circular cutting blade, which surrounds an inner plastic cushion that accommodates the “doughnut” rings of tissue produced when the instrument is discharged. Grooves within the anvil direct the fired staples into a “B” formation. Disposable sizers of 21/25 mm to 31/34 mm allow the surgeon to decide which size cartridge will be appropriate. Disposable loading units for the EEA instrument come in three sizes, 25 mm, 28 mm, and 31 mm. A disposable Premium Plus instrument is available with a 34-mm stapler.

The instrument is introduced into one segment of bowel through a small longitudinal enterotomy and advanced until the cartridge carrier is at the end of one segment and the anvil is advanced into the other. Before insertion, a purse-string clamp is used to rapidly apply purse-string sutures to the bowel ends. The series of interlocking serrations on the purse-string clamp grip the bowel end and provide a channel through which a straight suture is easily run. Alternatively an “over and over” stitch is placed over the transected bowel ends with bites 7 mm apart. The sutures so placed are tightened over the segment of shaft that spans the space between the separated anvil and cartridge carrier. Tissue closure around the shaft must be secure

enough to place apposing segments of bowel wall completely between staples and blade, or staples might miss a segment of bowel and leakage can follow.

The wing nut at the proximal end of the instrument controls separation and approximation of the anvil and cartridge. The safety catch is removed and the trigger fired to drive the staples through the full-thickness of the bowel ends, while the circular knife simultaneously trims the inverted bowel wall. The instrument is then rotated and withdrawn through the enterotomy and the doughnut rings of bowel ends are checked for completeness. The safety catch should be in place at all times except during discharging of the staples.

Other Staplers

The Ligate Divide Stapler (LDS-2) stainless steel instrument (United States Surgical Corporation) both ligates the vessel with staples that compress into a letter C and cuts simultaneously between each staple (Figure 27-19); additional ligatures are usually not necessary. Each cartridge allows 15 ligations. The CO_2-powered LDS disposable stapler (Figure 27-20) accomplishes the same with titanium staples, but cannot be reloaded. In a comparison of different methods of vascular ligation of mesenteric vessels in adult horses, mean ± SEM bursting pressure after 2-0 polydioxanone ligation (1,014.50 ± 279.05 mm Hg) was significantly greater than mean bursting pressure after ligation with the LDS (373.25 ± 183.69).[4] Failures with the LDS were mostly at the staple.[4] For this reason, the use of a suture to ligate mesenteric vessels should accompany staple LDS ligation.

Figure 27-19



Application of the LDS to a mesenteric vessel. The number indicates the total number of staples and the arrow points to the line of vessel transection. Though not needed for ligation with this instrument, an additional ligature should be applied if added security is required.

A variety of staplers can be used for skin closure in the ventral midline incision, but the staples can be difficult to remove and cause discomfort in the process, despite the use of the special staple remover. The Autosuture Multifire Premium skin stapler and the SFS (Reusable Skin Stapler) each place one staple each time the instrument handle is squeezed. There are different sizes of staples, each contained in its own single-use loading unit that can discharge from 12 to 35 staples. The Royal single-use skin stapler also places stainless steel staples in two sizes. In the closed position, the regular staple has a width/crown of 4.8 mm and leg length of 3.4 mm, and the wide staple (with W after the number) has a width/crown of 6.5 mm and leg length of 4.1 mm. This skin stapler comes preloaded with 12, 25, or 35 staples, and can be gas sterilized between surgeries. Disposable 3M staplers come in two types, the patented arcuate staple in the DS Disposable Skin Stapler encompasses tissue similar to a suture, whereas the MS Disposable Skin Stapler places the familiar standard box-style staples.

For skin closure, the skin edges are approximated with tissue forceps or a tissue-approximating device, making certain the edges are everted. The instrument nose is placed on the approximated tissue with the directional arrow in the middle of the

incision, and the trigger is squeezed completely, then released. Failure to completely squeeze the handle can result in incomplete staple formation and insufficient wound approximation. This procedure is repeated, taking care to space the staples evenly at approximately 0.7 to 1 cm intervals.

The skin stapler was applied in one study to create an anastomosis in canine jejunum.[5] The approximating end-to-end intestinal anastomosis with the stapler was found to be equivalent in bursting strength, lumen diameter, lumen circumference, and healing characteristics to the traditional hand-sewn technique, but could be performed in significantly less time.[5] This application of the skin stapler has not been tested in the horse.

Figure 27-20



Gas-powered LDS. This instrument cannot be resterilized for repeated use.

Directional Stapling Technology

Directional Stapling Technology (DST) was developed because existing technologies (both Ethicon and Auto Suture) have limitations in thick tissue, caused by cartridge to anvil deflection or misalignment. The DST technology incorporates two components, a new staple wire that bends more consistently and reliably in the plane that it is supposed to, and a new anvil geometry that provides a larger target area for the staple to form. The result is more consistent and reliable staple formation. The DST Series TA Staplers have been launched and the DST Series GIA Staplers will be launched after completion of a field test.

Miscellaneous Instruments

In one study, the LigaSure vessel-sealing device (LigaSure Atlas Laparoscopic Sealer/Divider Instrument, Valleylab, Boulder, CO), was evaluated for occlusion of mesenteric vessels of less than or equal to 7 mm diameter during small-intestinal resection and anastomosis in horses.[4] Benefits included reduced time required to provide hemostasis and acceptable arterial bursting pressure (less than a ligature but more than LDS), without leaving foreign material in the tissues.

The Hemoclip Ligation System (Teleflex Inc, Limerick, PA) can be used for rapid occlusion of mesenteric vessels during resection, but the author has only used this system in equine mesentery in conjunction with another occlusion device. The system includes a reusable ring-handled applier that is easy to reload with an individual clip from a cartridge base. The clip is made from stainless steel or tantalum and has a heart-shaped design that provides a firm grip on a vessel. In the open position, the clip has a preformed chevron shape that encloses the vessel so that it becomes entrapped by the tips and ensures precise tip-to-tip closure. The wire is annealed for softness to allow complete closure along its length, and transverse grooves make the clip resistant to slippage across the vessel. Larger sizes are applicable to horses and each clip size requires its own applier.

The Hem-o-lok Ligation System (Teleflex Inc, Limerick, PA) is an innovative cold-ligation system suitable for open and laparoscopic surgery. The 4 sizes of clips span vessels or tissue bundles from 2 mm to 16 mm. The unit places a locking clip made from an inert nonabsorbable polymer. Though this system might be applicable for the equine mesentery, it has not been tested for this purpose.

Surgical Procedures in the Small Intestine

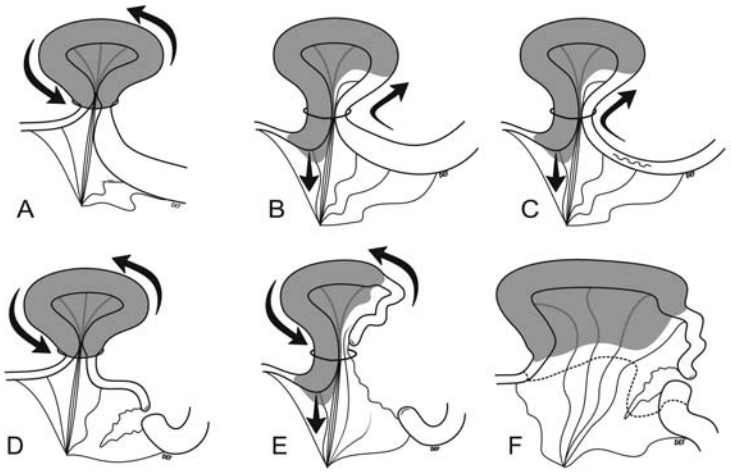
Small-intestinal strangulation obstructions that can be difficult to correct are strangulation in the epiploic foramen, inguinal hernia, diaphragmatic hernia, and intussusceptions. The following procedures can be used to treat these and other challenging lesions.

Strangulation in the Epiploic Foramen

In most cases, it is possible to correct strangulation of small intestine in the epiploic foramen by gentle traction on the efferent (distal) limb of the strangulation, with the line of traction in a horizontal plane across the abdomen. Traction vertically towards the incision runs the risk of drawing thick-walled bowel across the portal vein, which can tear and cause fatal hemorrhage. Careful milking of fluid from the strangulated bowel into the empty and collapsed distal segment might be necessary to decompress the strangulated segment. This is easier than milking fluid into the proximal distended bowel. Alternatively, strangulated bowel can be decompressed by drawing nonincarcerated bowel through the foramen to allow fluid from the strangulated segment to be distributed into the nonedematous bowel.[6]

In a small number of horses, bowel cannot be drawn back through the epiploic foramen by the preceding methods, and the strangulated segment usually cannot be brought up to the incision for resection.[7] Under such conditions, the jejunum approximately 1 meter proximal to the obstruction can be drained through an enterotomy (Figure 27-21). Alternatively, the proximal jejunum can be emptied by milking fluid further proximally; it is then transected proximal to the emptied segment (Figure 27-21). Because transection replaces one strangulated segment of bowel with mesentery, and enterotomy replaces a strangulated segment with empty healthy jejunum, reduction of the strangulated segment becomes considerably easier (Figure 27-21). After reduction, abnormal bowel is resected to include the transection or the enterotomy sites.[7]

Figure 27-21



In an epiploic foramen entrapment (viewed from the ventrum and left side), the following options are used for correction, if simple traction is not sufficient (from easiest to most difficult; A-F). A. Fluid is milked in the direction of arrows to decompress strangulated bowel. B. Nonincarcerated bowel is drawn through the foramen to allow fluid from the strangulated segment to be distributed into it and thereby empty the strangulated segment enough so that it can be drawn through. C. Proximal jejunum is drained through an enterotomy so that it can be drawn into the foramen and, thereby, provide more room. D. Intestine is transected to allow it to pass into the foramen. E. Empty nonstrangulated intestine is pulled through the foramen to provide more room for reduction. F. After reduction, resection is completed along the dotted line. (From Freeman DE. Surgery of the small intestine. Vet Clin North Am Equine Pract 13:261, 1997, with permission.)

Diaphragmatic Hernia

Diaphragmatic hernia is an uncommon cause of intestinal incarceration in the horse and it can be challenging to treat. If the defect is large, correction can usually be accomplished by careful traction on the bowel, but a small diaphragmatic defect might have to be enlarged with scissors[7,8] or a curved fetotome[9] to release the bowel. Ideally, a respirator should be used to provide controlled positive pressure ventilation and correct the compromised pulmonary function.

An advantage of preoperative diagnosis of diaphragmatic hernia is that the abdominal incision can be placed further cranially than the standard approach. Access to ventral defects in the diaphragm is not difficult, but access to more dorsal defects can be impossible through a standard ventral median approach. Access can be improved by extending the ventral midline incision to the xiphoid cartilage and then directing the incision laterally for approximately 12 to 15 cm at an angle of 60 to 90 degrees to the ventral median incision. This will produce an L-shaped incision that transects muscle bellies and several large vessels in the paracostal component. Access can be enhanced also by tilting the table so that the cranial end of the horse's abdomen is elevated and abdominal contents fall away from the diaphragm. The diaphragm should be repaired before or at the same time as performing a resection and anastomosis because failure to close the diaphragm adequately could result in repeat herniation.

A continuous pattern with heavy absorbable or nonabsorbable material can be used for closure of the defect, with completion of the suture line at full inspiration to reduce pneumothorax. Mesh coverage will be required for defects that cannot be sutured because of their large size or because the edges are too firm to allow apposition. In one report, a dorsal rent that

was inaccessible for suture placement was repaired by blind fixation of a doubled polypropylene mesh (Marlex Mesh #1266, Dowd Inc, Providence, RI) with 4-mm stainless steel staples (Disposable Skin Stapler, Richard-Allen Medical, Richland, MI).[10] A thoracic rib resection that was placed by guidance from thoracoscopy and manual palpation through a flank incision allowed repair of an inaccessible dorsal defect in a standing horse.[11] After the surgery is complete, an indwelling 28 to 30 French Argyle catheter can be placed at the 10th intercostal space in the dorsal thorax to correct pneumothorax. All air can be evacuated through a vacuum with a 3-bottle suction system, with the aid of a respirator to expand the lungs. The tube should be left in place in case it becomes necessary to repeat air removal.

Unrepaired diaphragmatic defects can partly seal by adhesion of adjacent stomach and liver to the edges,[11] although recurrence of intestinal incarceration immediately after anesthetic recovery is also likely.[10] One horse with a small defect that was inaccessible for repair returned to a full athletic career.[9] Successful repairs in adult horses and foals have allowed successful performance in various forms of competition and delivery of foals.[8-10]

Ileocecal Intussusception

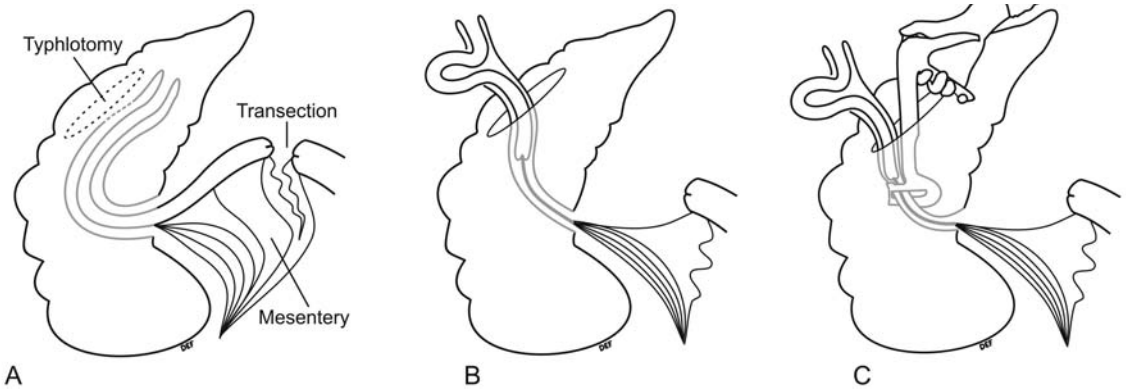
Ileocecal intussusception is common as an acute or chronic disease in young horses. Short segments of ileum (≤ 10 cm) are usually involved with chronic ileocecal intussusceptions, and treatments of choice are reduction, if possible, and bypass by ileocecostomy without transection. The latter works well, although it does carry the risk of anastomotic obstruction by an impaction extending from the ileocecal orifice. This is more likely if the intussusception cannot be reduced. Because the small intestine proximal to the lesion is so thickened from chronic recurrent obstruction, a handsewn anastomosis with size 0 absorbable material is recommended over stapling instruments.

Reduction of a chronic intussusception by traction can be difficult and carries an increased risk of rupture and contamination. Although the involved bowel is not edematous, it forms longitudinal webs of seromuscular layer at the reflection of the intussusceptum and appears to become permanently folded. In such cases, the author prefers to place a thumb on the cecal wall on each side of the ileocecal junction and apply pressure simultaneously with fingers against the leading point of the intussusceptum, under the wall of the cecum. This can force the intussusceptum between the thumbs as they push against the ileocecal orifice.

When the entire ileum and a long segment of jejunum become strangulated, as in acute intussusceptions, the bowel can be too edematous and hemorrhagic to allow correction by traction. In such cases, one option is to leave the strangulated segment in place in the cecum, transect and oversew the jejunum close to the intussusception, and perform a jejunocecostomy. Complications after this type of bypass are severe postoperative hemorrhage[12] from the intussuscepted segment and possible migration of the intussusception through the cecocolic orifice with obstruction of that opening.

Preferably, the nonreducible intussusceptum should be removed through a typhlotomy.[13] For this purpose, the jejunum proximal to the intussusception is closed with a TA 90 stapling instrument and transected so that the staples are on the distal segment[13] (Figure 27-22). The cecum is then draped off from the abdomen with saline-soaked towels and plastic drapes sutured to the cecal wall, and a 10-cm incision is made in the cecum over the intussusceptum (Figure 27-22). An incision through the outer wall of the intussusceptum exposes the inner loop (Figure 27-22). The inner loop of intussusceptum is then

Figure 27-22



Correction of a nonreducible strangulated ileocecal intussusception. A. Transection and typhlotomy. B. Oversewn end is pulled back so that the ileum is empty at the proposed site of transection. C. Application of the TA90. (Redrawn From Beard W, Byrne BA, Henninger RW. Ileocecal intussusception corrected by resection within the cecum in two horses. J Am Vet Med Assoc 200:I978, 1992, with permission.)

pulled through the incision in the outer layer until the stapled end can be palpated in the outer layer of the ileum at a point distal to the proposed site of transection (Figure27-22); if too much bowel is drawn through this incision, mesenteric vessels will be torn and subsequent hemorrhage can be fatal. The stapling instrument is then applied across the inverted ileum within the cecum and the necrotic bowel is removed by incision along the edge of the TA90 (Figure 27-22). Unless the preceding precautions are taken, this procedure can be associated with extensive contamination, especially if cecal contents enter the incision in the intussusceptum and thereby drain into the abdomen.

Inguinal Hernia

In adult horses, most acquired inguinal hernias are indirect, in which small intestine passes through the vaginal ring into the vaginal tunic, and most are irreducible. When jejunum and, occasionally, the testicle escape through a rent in the vaginal tunic and lie in the subcutaneous space of the scrotum and prepuce, the less common direct hernia results. Unlike indirect hernias, direct hernias constitute surgical emergencies in foals. Both types are surgical emergencies in adult horses. When a loop of intestine enters the vaginal tunic in adult horses and becomes strangulated, it compresses the testicular vessels and causes testicular congestion.

Nonsurgical Treatment

A direct hernia in an adult horse can be corrected by external massage or by gentle traction to the bowel per rectum, with or without external massage of the scrotum.[14-16] With these noninvasive methods, laparoscopy can be used simultaneously to determine completeness of correction and assess intestinal viability,[15] or laparoscopic inguinal herniorrhaphy may be performed approximately 1 week later to prevent recurrence, using either a mesh onlay graft[14] or a cylindrical mesh plug.[17]

Surgical Treatment

A nonreducible inguinal hernia is corrected through an inguinal approach with the horse in dorsal recumbency and prepared and draped for aseptic surgery (see Chapter 25). The abdomen should be prepared for a ventral midline celiotomy, which might be needed to allow intraabdominal traction on the bowel, to assess viability of the released bowel, to decompress or examine proximal bowel, to correct an associated volvulus proximal to the hernia,[18,19] and to allow performance of an end-to-end anastomosis, and particularly a jejunocecal anastomosis, if needed. If sufficient healthy bowel can be drawn through the inguinal approach to permit resection of the strangulated segment, the transected ends are then oversewn and returned to the abdomen for resection and anastomosis through a ventral midline incision. This avoids the long incision in the tunic and the associated difficulty in closure.

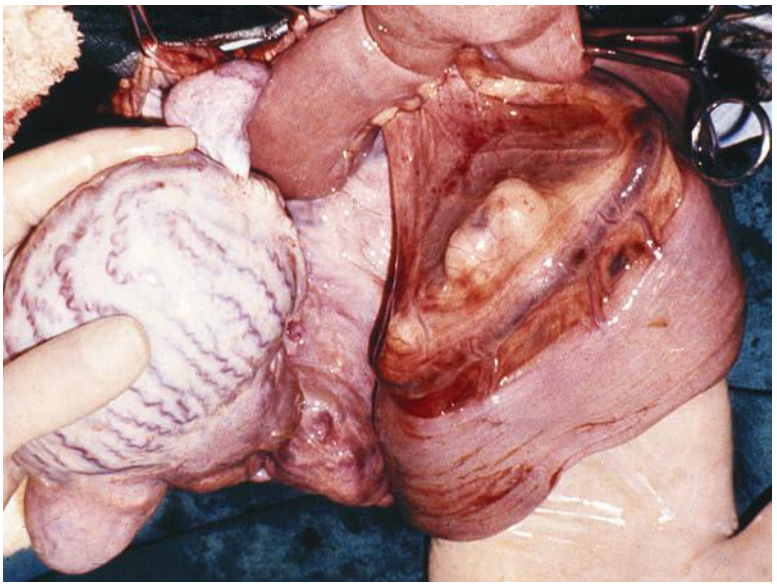
A 6-cm skin incision is made over the external inguinal ring, and the underlying subcutaneous fascia and superficial fascia over the external inguinal ring are bluntly separated. The tunic is dissected from the surrounding tissues, with care taken to not damage the pudendal vein and branches. To release the strangulated intestine, a cranial incision is made in the vaginal tunic with a scalpel. Using digital guidance to protect contents of the tunic, this incision is then extended parallel to the cremaster muscle with Metzenbaum scissors, a teat knife or similar narrow, curved tenotome, to cut the constricting ring of internal spermatic fascia and connective tissue in the neck of the vaginal process.[15,20] This fascial ring is distal to the vaginal ring and is the actual structure that strangulates the entrapped bowel. The incision is continued until both the incarcerated edematous bowel (Figure 27-23) as well as any end-to-end anastomosis performed subsequently can be returned to the abdominal cavity.[20] Any excess fluid in the proximal intestine can be massaged into the poststenotic intestine before replacement of the strangulated bowel.[20] The incision in the vaginal trunk is sutured using a continuous technique, starting at the proximal extent of the wound. The tunic edges should be grasped with hemostats to maintain them within access for closure. Medial and cranial retraction on the edge of the internal abdominal oblique muscle with a Deaver retractor will improve exposure to the tunic edges, while bowel is directed away from the suture line by a finger.

The least traumatic and easiest method for transecting the constricting ring of internal spermatic fascia is to pass a curved Kelly hemostat under the ring to elevate it from the vaginal tunic.[20] Then the ring can be cut under visual control, without the need for an additional incision in the vaginal process.[20] With this approach, the incarcerated bowel can be returned to the abdomen, but cannot be examined, so that tissue viability cannot be determined.[20]

Because short segments of intestine are usually involved (less than 25 cm) and external appearance of the bowel usually improves markedly after correction, resection is rarely needed (Figure 27-23). Castration is not necessary if the strangulation is recent and the testicle is not irreversibly damaged,[20] but such cases are candidates for imbrication procedures[21,22] or delayed mesh herniorrhaphy[14,17] to prevent recurrence. Castration allows more complete closure of the vaginal tunic by transfixation ligatures of size 0 or 1 absorbable suture and abolishes the risk of recurrence. In some horses that have not

undergone castration, the involved testicle can atrophy or become cystic or nonfunctional in time, and postoperative swelling in the affected testicle can cause chronic pain. In some cases, a hernia can occur some time later on the contralateral side, and this would jeopardize the breeding potential of a stallion that underwent a unilateral castration for treatment of the first occurrence of an inguinal hernia.

Figure 27-23



Small intestinal strangulation released from an inguinal hernia through an incision in the vaginal tunic. The short segment of bowel in this case is viable.

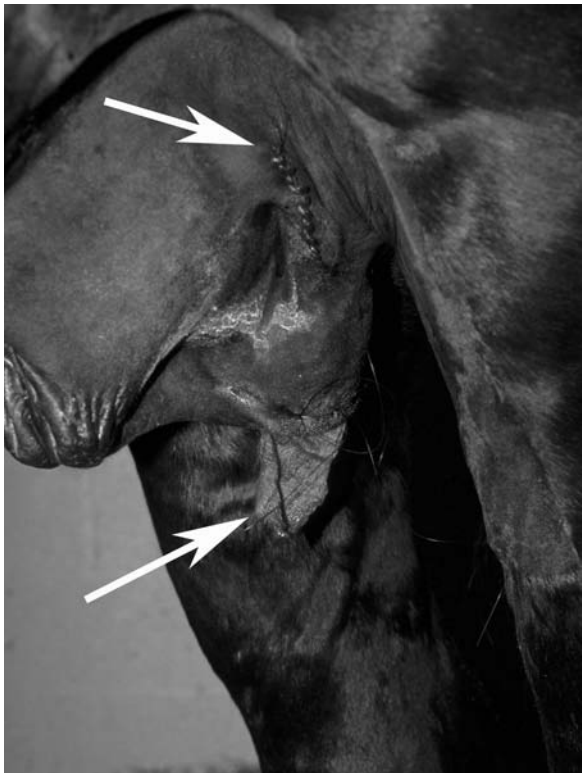
If the vaginal ring can be closed, closure of the external inguinal ring is not essential and does not ensure against evisceration.[23] If there are any doubts about security of the vaginal tunic closure, then the pelvic and abdominal tendons of the external oblique abdominal muscle can be sutured together, using continuous or interrupted absorbable sutures. It is important not to include the external pudendal artery or vein or the genitofemoral nerve in the sutures.[20] In addition, sutures placed too tightly can cause lymph stasis.[20]

Regardless of the technique used, after the vaginal tunic is closed, the thick subcutaneous fascia is closed with size 0 or 1 Polyglactin 910 suture in simple continuous fashion. The skin incision is closed with a simple continuous pattern of the same suture but using size 2-0 or smaller. A skin suture of heavier material pulled tight enough to imbricate the skin edges and reduce the wound to about one third its original length is also described, as this could make the wound sufficiently strong to withstand the pressure of an intestinal prolapse.[20] After surgery with unilateral castration, the scrotum on the castrated side usually lies against the prepuce, and swelling is minimal (Figure 27-24).

Surgical correction can be accomplished in foals with congenital hernia through an inguinal approach with exposure of the tunic and its contents, removal of the cremaster muscle, twisting of the testicle and tunic to force the bowel into the abdomen (Figure 27-25), and then closed castration combined with a transfixation ligature of 0 polydioxanone through the tunic. Closure of the external inguinal ring is not essential and will not prevent reherniation.[23,24] Alternative methods are laparoscopic repair with[25] or without castration,[17] an inguinal approach without castration,[21] or a midline celiotomy with closure of the vaginal ring. The latter 2 methods can cause atrophy of the testicle.

For repair of a direct or ruptured inguinal hernia in foals, the torn edges of the common vaginal tunic are identified and drawn upward to create a funnel through which the bowel is returned to the abdomen. Digital manipulation or grasping the bowel in unclosed sponge forceps can be used for bowel replacement; the torn tunic should be repaired as much as possible to the level of the vaginal ring. Usually, the intestine is viable and not resected, and delayed necrosis is rare.[24] Castration will facilitate the repair and closure of the vaginal tunic.

Figure 27-24



Inguinal incision after an inguinal herniorrhaphy and castration on the left side, demonstrating the suture line in the skin (top arrow) and packing inserted in a separate open incision in the bottom of the empty scrotum (bottom arrow). The packing is not necessary and not recommended.

Figure 27-25



Correction of an indirect scrotal hernia by a closed castration technique with twisting of the tunic to force intestinal contents into the abdomen. The cremaster was removed to facilitate this procedure. (From Bartmann CP, et al. Diagnosis and surgical management of colic in the foal: Literature review and retrospective study. Clinical Techniques in Equine Practice 1:125-142, 2002, with permission.)

Miscellaneous Conditions

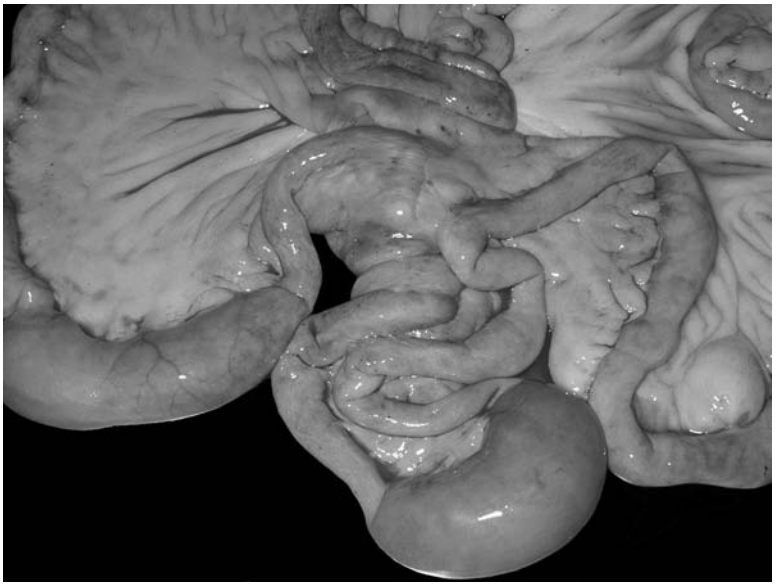
In volvulus nodosus, the ileum typically forms a knot-like wrap around contiguous small intestine and correction can be difficult in foals and adult horses.[26,27] The strangulation can be reduced by massaging the contents of the entrapped loop into the proximal segment, thereby allowing the bowel to be pulled through the ring formed by the ileum.[27] If the bowel involved in a volvulus nodosus is necrotic, time can be saved by resecting the entire lesion without reduction, followed by a jejunocecostomy.[27]

At surgery, a strangulating pedunculated lipoma can be found wrapped around intestine close to the mesenteric root, which, therefore, can be difficult to exteriorize. Blind resection of the pedicle is often necessary, but carries the risk of creating a mesenteric rent and mesenteric bleeding. Incidental lipomas with distinct pedicles should be removed with the LDS stapling instrument or by ligation and transection. Small, broad based tumors are more difficult to remove but they are less likely to cause problems in the near future.

Mesenteric rents can be difficult to correct because of the long segments of bowel involved in some horses and because of hemorrhage from the affected mesenteric vessels.[28] Closure of the entire defect can be difficult or impossible through a ventral midline approach; therefore, elective laparoscopic closure of the full defect is indicated as a standing procedure shortly after correction of the strangulation through a ventral midline celiotomy.[29] Both sides of the abdomen might need to be examined to locate the tear, although many are in the distal duodenal or proximal jejunal mesentery on the right side.[29]

Obstruction from adhesions can be difficult to treat in many cases (Figure 27-26) because not all the adhesions and involved bowel are accessible, the adhesions can be extensive, and the configuration of the involved loops can be too complicated to determine the course of bowel through them (Figure 27-26). The risk of recurrence of lysed adhesions always exists, so bypass procedures are preferable and often the only procedure possible.

Figure 27-26



Mature adhesions of bowel to bowel, bowel to mesentery, and mesentery to mesentery in the midjejunum. This would be impossible to correct by adhesiolysis, and would require bypass, which would be complicated by the manner in which the adhesions have drawn some segments deep into the abdomen.

Surgery of the Duodenum

Duodenal impactions can be caused by a variety of ingested objects or formed concretions, and can be treated successfully by massage of the intestinal contents into the stomach for removal by gastrotomy[30] or into the jejunum for manual disruption or removal by enterotomy.[31,32] If the obstruction cannot be dislodged, an enterotomy can be made through an incision in the dorsal paralumbar space, 3 cm caudal to the 18th rib,[33] placed with some guidance by ultrasonography. The duodenum can be elevated in some horses sufficiently close to a ventral median incision to allow removal of an impaction through an enterotomy in the duodenum, provided that the bowel is packed off well. In a 2-year-old horse with a leiomyoma involving the duodenum, the tumor was excised without penetration of the lumen of the small intestine, and the horse recovered without complications.[34]

Duodenal and Jejunal Bypass Procedures

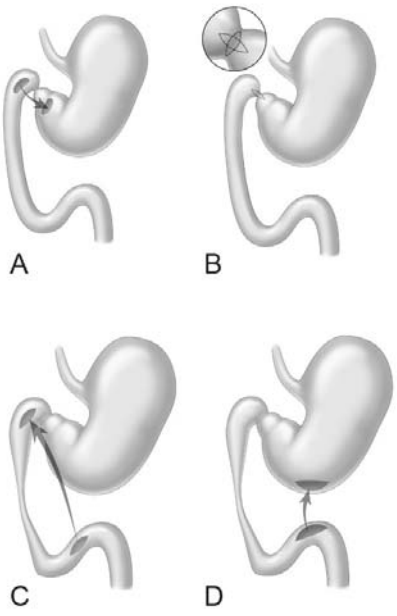
Access to the duodenum for bypass procedures is considerably easier through a ventral median celiotomy in a foal than in an adult horse.[35,36] The abdominal incision should be extended to the xiphoid cartilage; an L shaped incision is required in an adult horse, along with elevation or tilting of the table as needed to displace bowel from the surgery site.[36] Access can be improved by retraction, deep packing of the abdomen with saline soaked towels, and suction to remove some unavoidable contamination.[36]

Pyloromyotomy, Heineke Mikulicz pyloroplasty, gastrojejunostomy, or gastroduodenostomy have been used successfully to correct pyloric stenosis in foals (Figure 27-27).[35,36] For a side to side gastroduodenostomy, a hand sutured anastomosis is preferred over the GIA instrument[35,36] because stapled incision edges can heal together at the commissures of the stoma and, thereby, occlude the stoma.[35] Also, stapling instruments are difficult to use in the limited space available.[35] In one foal, a focal duodenal stricture was corrected by transverse closure of a full thickness longitudinal incision that spanned the lesion.[37] Choledochojejunostomy and duodenojejunostomy have been used successfully in foals with obstruction of the common bile duct and duodenum at the level of the hepatopancreatic ampulla.[35] A duodenojejunostomy can be used to bypass a duodenal stricture beyond the hepaticopancreatic ampulla.[35] A side to side jejunojejunostomy can be performed distal to bypass procedures to prevent intestinal contents from stagnating in the blind loop between the obstruction and the stoma.[35] The contents of this loop can pass aborally through this stoma, without entering the stomach.

In horses with duodenitis-proximal jejunitis that fail to respond to medical treatment, bypass procedures can drain the affected segment of small intestine into more normal distal segments, so that the large volumes of accumulated fluid can be absorbed by healthy intestine. In one method, a temporary duodenocecostomy is performed through a 25- to 30-cm-long incision between the 17th and 18th ribs[38] to approach the duodenum before it turns through its caudal flexure behind the base of the cecum. Duodenum and cecum are then joined by the "cutting thread" technique that creates a stoma of 2 cm in diameter. The goal is to allow the distended duodenum to drain into the cecum, after which the fistula closes spontaneously when the condition has resolved. A carbohydrate absorption test can be used during the recovery stage to determine whether the stoma has healed completely. A duodenojejunostomy through a ventral median celiotomy is an alternative procedure, and is effective in reducing gastric distention and reflux.[39]

A side to side gastrojejunostomy has been used to bypass affected bowel in an adult horse with duodenitis-proximal jejunitis.[40] This horse developed signs of the "dumping syndrome," a metabolic consequence of rapid influx of gastric contents into the jejunum, that was evident as lethargy lasting for 1 to 2 weeks after the horse ate oats.[40] Although this horse had trouble maintaining body weight for the first year after surgery, it did well for a follow up period of 8 years.[40]

Figure 27-27



A. Gastroduodenostomy to bypass a pyloric or proximal duodenal stricture. B. A Heineke-Mikulicz pyloroplasty, in which a 4-cm long, longitudinal incision over the pyloric stenosis is closed transversely to maximize the pyloric lumen. C. Duodenojejunostomy to bypass a duodenal stricture. D. Gastrojejunostomy to bypass a duodenal stricture. (From Bartmann CP, et al. Diagnosis and surgical management of colic in the foal: Literature review and retrospective study. Clinical Techniques in Equine Practice 1:125-142, 2002, with permission.)

A modification of the Roux-en-Y anastomosis procedure was used to bypass a pyloroduodenal mass in a 12-year-old Arabian stallion that presented with a 4-week history of ventral and hind-limb edema, hypoproteinemia, fecal occult blood, intermittent abdominal pain, weight loss, and gastric reflux.[41] On exploratory celiotomy, an inaccessible obstructive mass was located in the pylorus and proximal portion of the duodenum,[41] and was successfully bypassed by gastrojejunostomy and duodenojejunostomy with a stapled side-to-side anastomosis.[41]

In addition to medical treatment, two horses with small intestinal obstruction by abdominal abscesses underwent surgical procedures to bypass the lesions.[42] In one horse, the small intestine was transected proximal to the abscess and an end-to-side anastomosis performed distally. In the other horse, a side-to-side anastomosis was performed without bowel transection.[42] The results suggested bowel transection with an end-to-side anastomosis is the preferred procedure.[42]

Parker-Kerr Technique

The purpose of this procedure is to close a segment of intestine with a) minimal contamination, b) excellent serosal apposition, and c) a watertight seal. It is ideal for closure of an ileal stump in horses that need a jejunocecostomy or to prepare ends of small intestine for side-to-side anastomoses with small intestine, stomach, cecum, or ventral colon. An intestinal clamp is applied at right angles to the long axis of a segment of intestine, and any arcuate vessels that run along that segment are ligated at two points 1 cm apart at the level of the clamp. The mesentery is incised between the ligatures and this incision is continued across the intestine along one edge of the clamp. If the intestine is of a thickness that places too much stress on the clamp or appears in any way to be at risk of becoming dislodged, approximately 2 to 3 mm of transected tissue can be left beyond the jaws. This projecting tissue can be grasped at each end with Allis tissue clamps or with Kelly hemostats to retain the bowel in the jaws until the first suture line is completed.

A Cushing suture pattern is placed with alternate bites on each side of the clamp and close to it, while the assistant holding the clamp rotates each side toward the surgeon to facilitate suture placement (Figure 27-28). The free end of the suture is not tied at the start, but is secured with a hemostat. When this first row is completed, the two ends of the suture are grasped by the surgeon and pulled taut. As these ends are pulled taut, the assistant releases the clamp, opens it slightly, and withdraws it, directing the tip slightly toward the intestinal lumen in the process (Figure 27-28). These steps are coordinated so that the intestinal edge is carefully inverted as the clamp is withdrawn (Figure 27-28). The suture will bind on the clamp as it is withdrawn, but, with care, the process can be completed. When completed satisfactorily, the intestinal edges will be apposed in an inverted fashion without exposing the lumen, although the ends or corners of the closure might resist inversion. The second row is then placed immediately to maintain this inversion, and it continues in a Cushing pattern to the start of the first row, to end by tying the needle end to the free end (Figure 27-28). Any points of eversion can be corrected by gently grasping the everted edges in atraumatic thumb forceps or tips of hemostats and pushing them into the lumen. A Lembert bite can be used if necessary to keep the bowel inverted at these points. If a Parker-Kerr technique is performed to prepare bowel for a side-to-side procedure, the final suture line can be pulled tightly to accordion the end of the bowel and produce a narrow, blunt end rather than a broad flat end (Figure 27-28). The latter can become displaced and thereby obstruct the nearby stoma.[7]

Doyen forceps have the advantage for the Parker-Kerr procedure in that they have pliable jaws and longitudinal serrations that allow them to be easily drawn off the bowel when needed (Figure 27-12). However, for the same reasons, they can slip off prematurely and, therefore, are not recommended. Carmalt forceps are preferable because they do grasp the bowel ends more securely (Figure 27-12), but the jaws might be too short to fully span a wide intestinal segment in some horses. The suture material of choice is monofilament absorbable, such as polydioxanone, and size 0 or 1 should be used on the ileum. For thin-walled bowel, size 2-0 is suitable.

Figure 27-28A

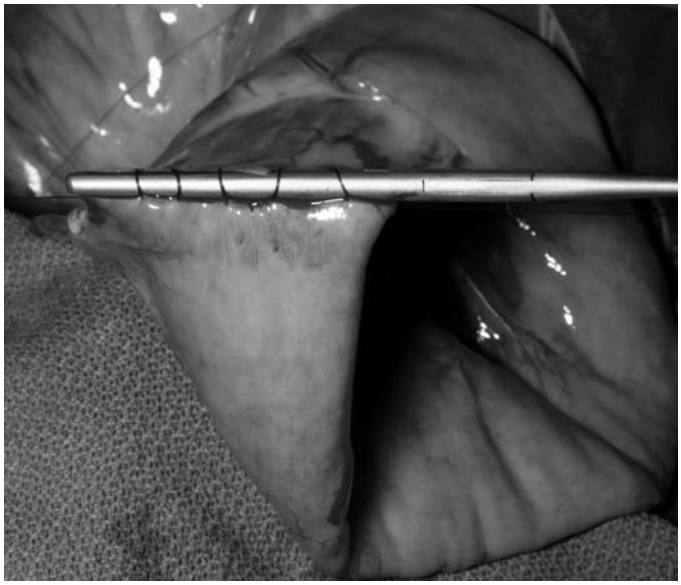


Figure 27-28B



Figure 27-28C

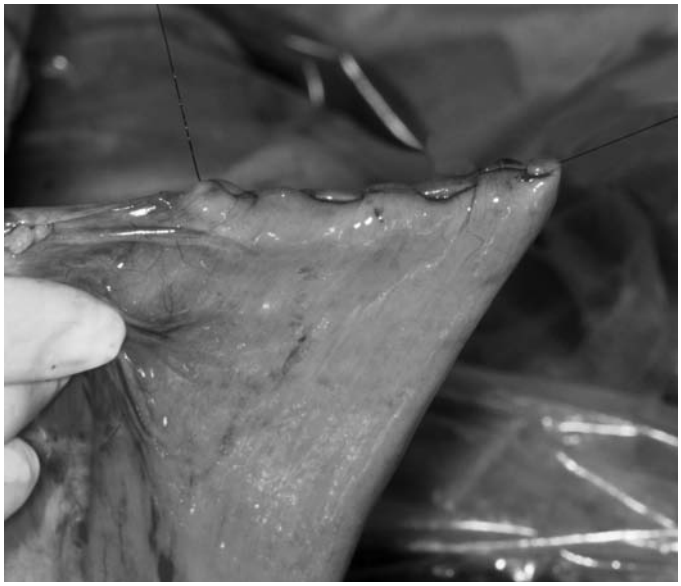


Figure 27-28D

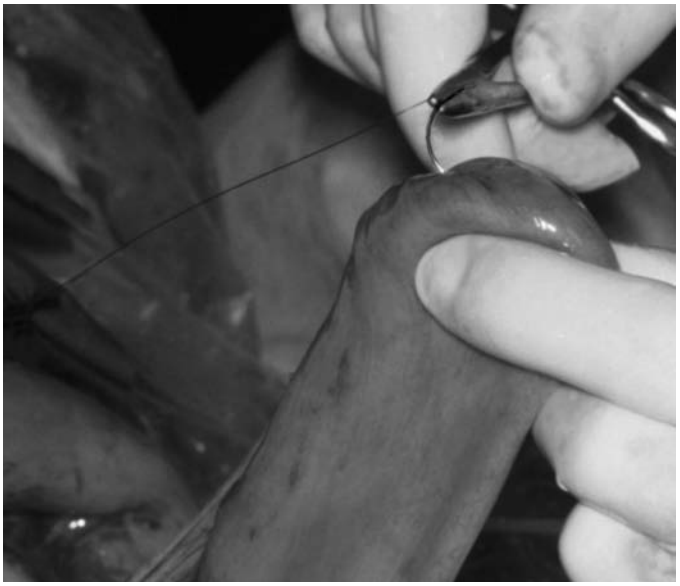
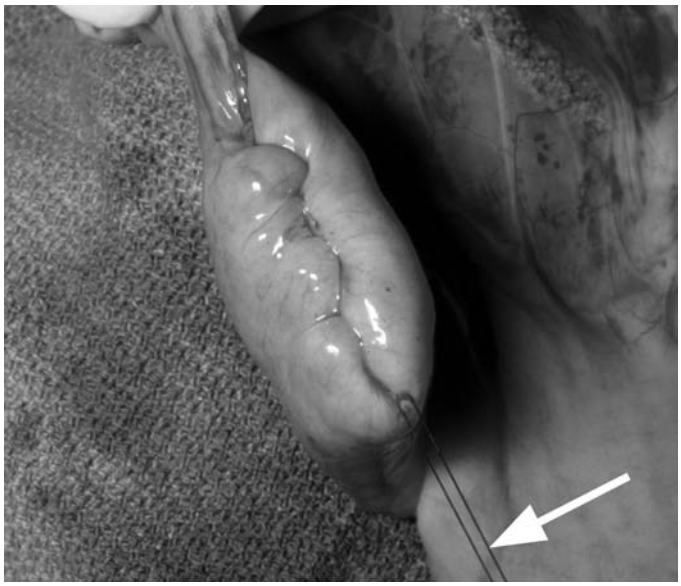


Figure 27-28E



Parker-Kerr technique. **A.** First row of suture over the Carmalt intestinal clamp that is holding the cut end of bowel. **B.** Removing the clamp while simultaneously tightening the first row and directing the bowel edge into the lumen with the clamp. **C.** Appearance of the first row of suture. **D.** Application of the second row by using the same suture in the opposite direction to the first row. **E.** After the second row is completed, the two suture ends are on the same side of the bowel (arrow) and traction on them should shorten the suture line before the knot is tied.

Small Intestinal Enterotomy

Enterotomy is indicated to a much lesser extent in small intestinal surgery than in colon surgery, and should be avoided if other options are available, because the healing incision could be a focus for adhesion formation (see Chapter 7). For example, viability can be assessed by seromuscular changes without need for mucosal inspection. Extensive strangulating lesions can be corrected without removing fluid contents beforehand. A focal impaction with dehydrated intestinal contents can be softened by injection of saline through an 18-gauge needle (see earlier) or by massaging the impaction into the more proximal liquid contents. If a resection is not indicated, distended small intestine can be decompressed by massage of contents into the cecum, from where they can be drained through a typhlotomy (Figure 27-29).

A longitudinal enterotomy on the antimesenteric surface of the small intestine can be required for removal of impactions with food components, foreign material, or ascarids, or to empty a segment of distended bowel to facilitate reduction of a strangulation in the epiploic foramen. Methods to prevent adherence of intestinal contents to the serosa around the incision include constant lavage of the bowel with warm saline or precoating the proposed enterotomy site with sodium carboxymethylcellulose. The enterotomy can be closed with single or double inverting layers (Lembert or Cushing pattern) or with a mucosal closure or an appositional layer and inverting layer, using 2-0 polydioxanone on a taper needle. If the end of the first row is left untied, the end of the second row can be tied to it to reduce the amount of foreign material in the knots. The advantage of the Cushing pattern for the final row is minimal inversion and less suture material exposed to the peritoneal cavity. Any closure method should be close to the cut edges to minimize lumen reduction and should be of fine material (size 2-0 to 4-0) to reduce risk of adhesions.

Many options are available to stabilize the bowel before the enterotomy, as for a segment that cannot be exteriorized, or afterward during enterotomy closure. Stay sutures can be placed approximately 1 cm away from each end of the proposed incision on the antimesenteric surface of the bowel and along its long axis. Each stay suture should include a substantial thickness of seromuscular layer in an 8- to 10-mm bite; its ends are long and secured in hemostats rather than tied. An assistant gently elevates the wall of the intestine with these sutures to prevent leakage of contents, and any leakage is wiped off with moist sponges. It is not necessary to oversew the stay suture sites, but if this is done, the short end of the first knot for the first layer can be used as a stay suture during closure. Less traumatic and simpler methods for stabilizing the intestinal wall include Babcock forceps and assistant's fingers. The latter are the least traumatic and are preferred for most instances in the small intestine.

Figure 27-29



Method of emptying the distended small intestine by stripping its contents into the cecum, which will be drained through a typhlotomy.

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Intestinal Viability

Chapter 28

David E. Freeman

Surgeons have learned through experience or research that the consequences of leaving nonviable bowel *in situ* may include continued tissue necrosis, perforation, abscessation, adhesion formation, obstruction, loss of intestinal function and motility, endotoxemia, peritonitis, and death. Even an experienced clinician may find that viability of intestine subjected to subtle ischemic changes is difficult to detect at the time of surgery. Rarely, an intestinal segment that appears normal after release of strangulation at surgery deteriorates because of undetected vascular thrombosis or reperfusion injury; such segments can be impossible to recognize.

It has been proposed that improved methods of assessing viability could improve long-term survival after colic surgery by reducing the need for resection.[1] Most surgeons who follow the "if in doubt, cut it out" tenet are at risk of taking an overly pessimistic and harmful approach to intestinal viability. This approach could lead to euthanasia in horses in which the option of resection is eliminated by prevailing conditions, such as lack of expertise, equipment, financial constraints, inaccessibility of the affected segment, or involvement of too much bowel to allow normal intestinal function.

Small Intestine

In horses, a small-intestinal segment judged as viable and left *in situ* is more at risk of adhesion formation than it is of progressive necrosis. This risk must be balanced against the risks of small-intestinal resection, such as the expense and complications (especially adhesions, anastomotic complications, and short bowel syndrome) and the duration of surgery. A short surgery without intestinal resection, that is less expensive and that has a relative lack of complications, is a favored approach compared with a high-risk anastomosis, such as jejunocecostomy, if this were the only other alternative for treatment.[2,3] It would also eliminate performing a resection in horses that would be at risk for malabsorption if a large amount of intestine was resected, or euthanasia, if affected bowel was inaccessible.[2] The expense of resection, from longer anesthesia time, more complicated surgery, and intensive aftercare, could force an owner to elect intraoperative euthanasia. Increased duration of surgery needed for resection could extend anesthesia time beyond safe limits for horses of large body size or mares in advanced pregnancy. In such cases, leaving damaged bowel in place and recovering the horse might be a reasonable option. Interpretation of intestinal viability becomes critical in deciding which approach will increase the chances of survival.

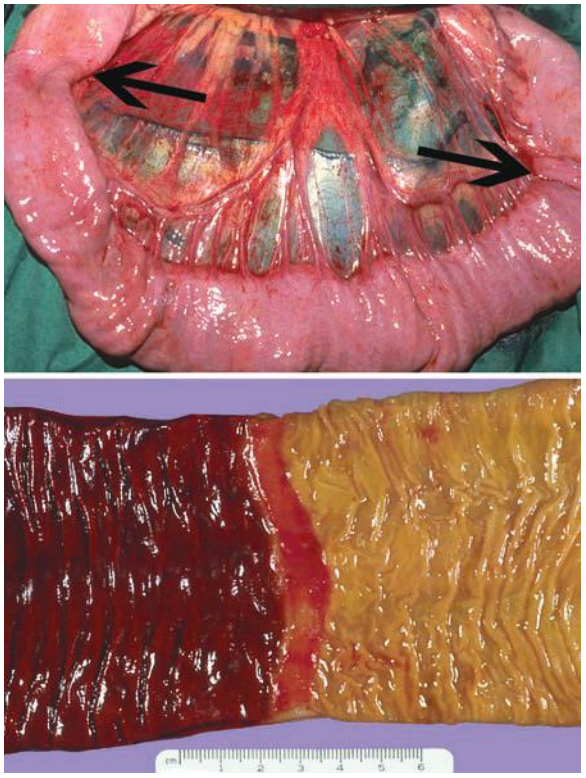
Clinical Judgment

Clinical criteria of viability are serosal color, bowel wall thickness, presence or absence of mesenteric arterial pulses, spontaneous motility or motility evoked by snapping a finger against the intestinal wall, and improvement in color after correction of the strangulation. In normal bowel, snapping a finger against or pinching the bowel wall will induce muscular contractions, and also create a transient focal, blanched, raised plaque on the intestine. Spontaneous or evoked motility will appear sluggish in viable strangulated bowel because edema and hemorrhage "splint" the muscle wall. Edema and hemorrhage in the intestinal wall is not unusual after strangulation and does not signify an irreversible change, because both are caused by occlusion of thin-walled veins. Short intestinal segments with these changes can survive without forming adhesions so that resection leads to high false-positive results (unnecessary intestinal resections). Enterotomies are not recommended to assess viability of the small intestine because of the risk of adhesions to the suture line and because mucosal appearance is usually severe enough to lead to false assessments (Figure 28-1).

Methods of assessing viability in equine (pony) jejunum have been compared with clinical judgment in only one study.[4] In that study, all intestinal segments were recovered from different types of ischemia without developing complications, including adhesions, although clinical judgment and fluorescein fluorescence predicted otherwise.[4,5] In another study, the results were different, with jejunal segments that were subjected to identical types and durations of ischemia forming adhesions, even when the bowel yielded a viable fluorescent pattern.[6] Differences between the studies that could have favored adhesion formation included strangulation of four segments versus one segment per animal, more traumatic methods for inducing ischemia, and omission of antibiotics and flunixin meglumine in the postoperative management.[5,6]

A retrospective evaluation of short- and long-term outcomes in horses after surgery for strangulating lesions of the small intestine led to the development of a clinical grading system for small-intestinal viability (Table 28-1).[2,3] In that study, horses with segments scored as grades I, II, and III (Figures 28-2 to 28-4) did not undergo a resection and had a more favorable outcome than horses that had undergone resection.[2,3] Although the former horses had milder intestinal lesions than the horses that required resection (Figures 28-5 and 28-6), they were also allowed to recover from surgery with those lesions in situ, which could have placed them at risk for development of adhesions[6]; however, they did not appear to be at any greater risk of adhesions than those that had a resection. Factors that tended subjectively to worsen the prognosis for these horses were prolonged surgeries, failure to decompress distended bowel at surgery, and failure to distinguish accurately between grade III and grade IV lesions (Figure 28-7).

Figure 28-1



Segment of jejunum 15 minutes after it was subjected to 3 hours of arterial and venous occlusion (between arrows, top). Although the bowel appears viable based on appearance of its serosal surface, the mucosal surface of a segment treated in a similar manner has undergone more severe changes (bottom).

Table 28-1

Grades of Mucosal Injury Used to Decide on Need to Resect Strangulated Small Intestine.

Grade I
Improves within 15 minutes after correction of the lesion and is similar to healthy adjacent bowel, but slightly darker pink, with mild edema and ecchymoses (Figure 28-2). Motility spontaneous or induced by snapping a finger against the intestinal wall.

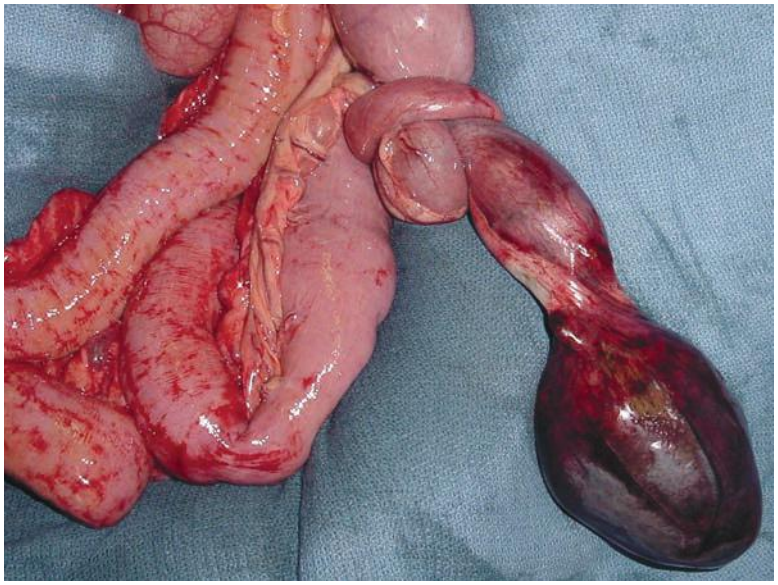
Grade II
Improves within 15 minutes after correction of the lesion and has marked edema, with extensive ecchymoses, coalescing into diffuse patches of red against a background of dark pink, and no circumferential constrictions at points of strangulation (Figure 28-3). Motility is weak or induced by snapping a finger against the intestinal wall.

Grade III
Similar to Grade II, with some circumferential constriction in the wall and/or black patches or stripes against a red background (Figure 28-4).

Grade IV
Improves slightly or not at all within 15 minutes after correction of the lesion, and predominantly dark red, blue, or purple (Figure 28-5), with bowel wall thickness ranging from thin to thick, a flaccid wall, and presence or absence of black striations, a necrotic odor, or constrictions at points of strangulation.

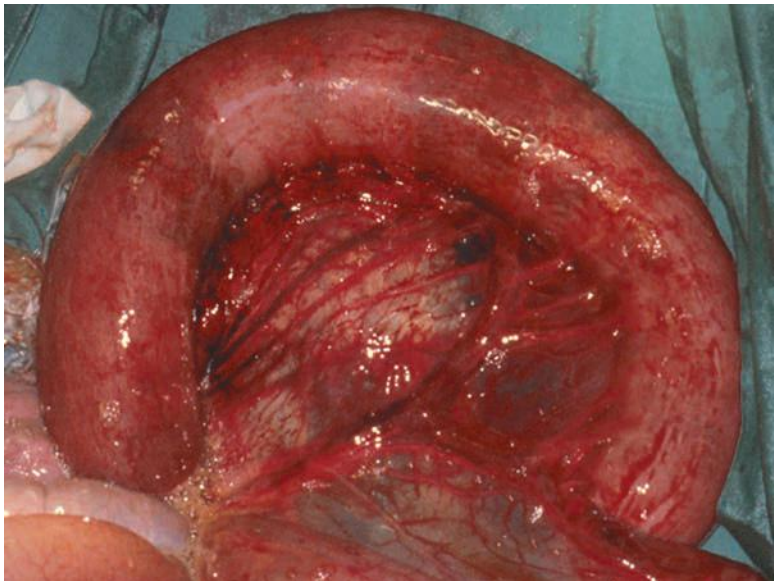
Grade V
As Grade IV, except diffusely gray, black, or green discoloration (Figure 28-6).

Figure 28-2



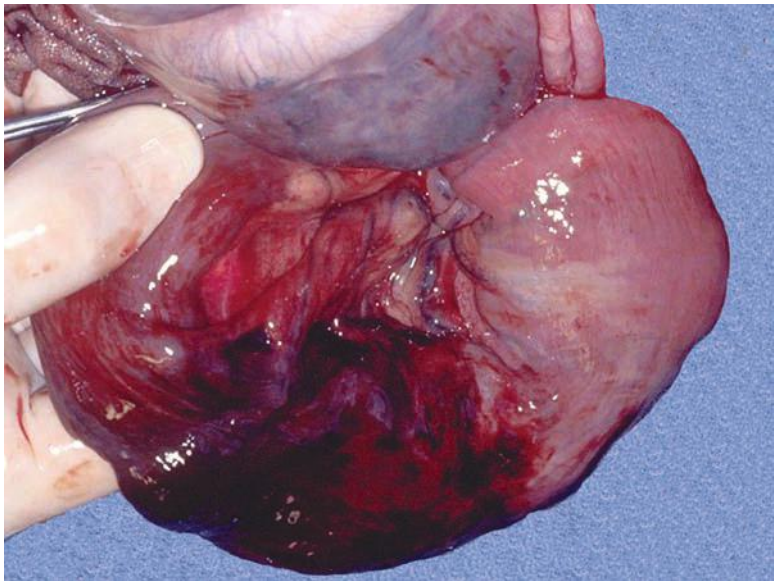
Grade I changes in a segment of foal jejunum and ileum (to the left) involved in strangulation by a Meckel's diverticulum.

Figure 28-3



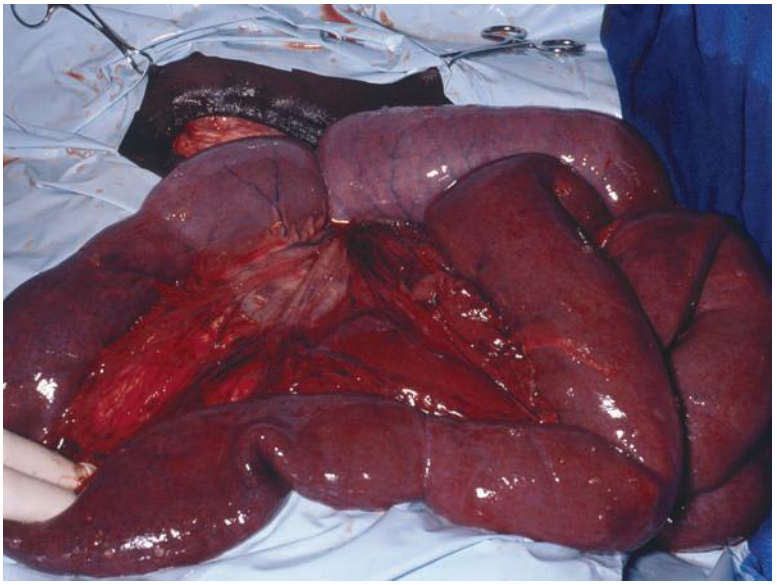
Grade II changes in small intestine that was strangulated in the epiploic foramen and was not resected. The horse recovered and did not develop any known problem over a 2-year follow-up.

Figure 28-4



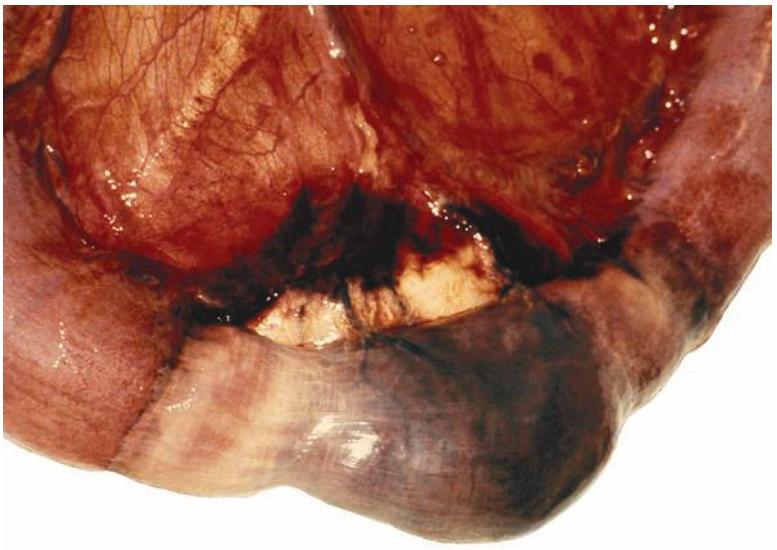
Grade III changes in jejunum strangulated in an inguinal hernia. Note that the changes are grade II in the segment in the surgeon's hand but the black discoloration was attributed to hemorrhage in that portion.

Figure 28-5



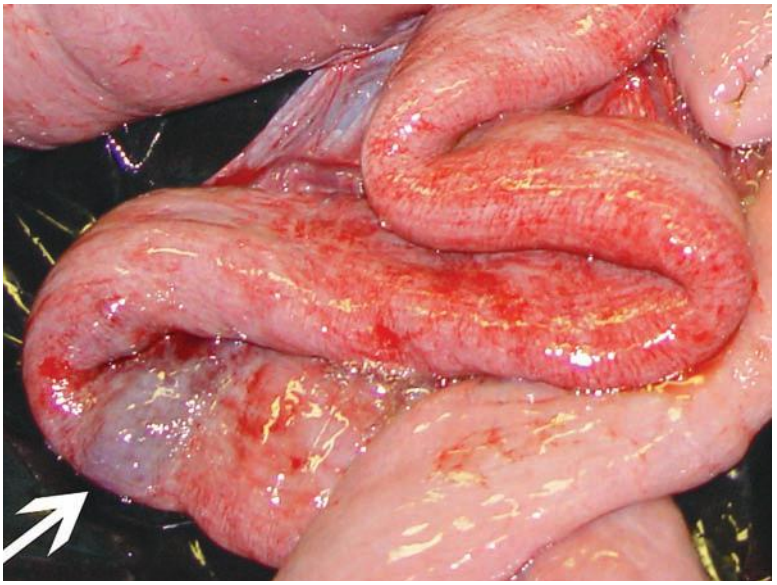
Grade IV changes in bowel that has undergone diffuse dark red and purple discoloration, with marked edema.

Figure 28-6



Grade V lesion in bowel strangulated in an inguinal hernia, with black discoloration, complete circumferential constrictions, and blanching. Compare with Figure 28-4.

Figure 28-7

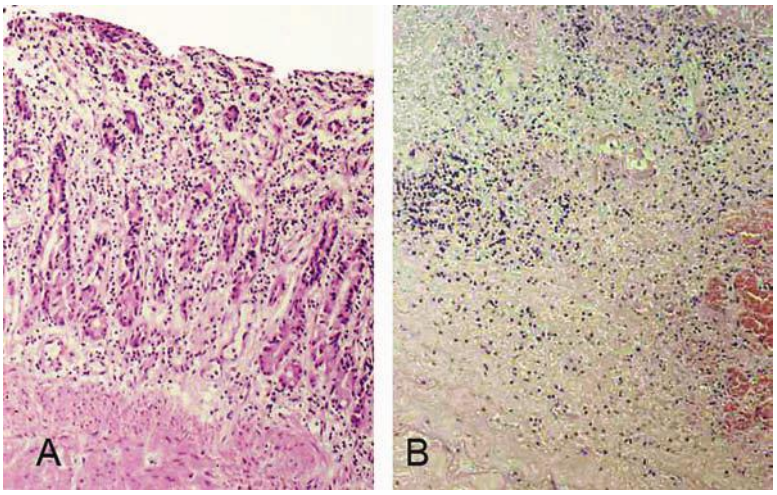


Patch of bluish discoloration (grade IV, arrow) in a jejunal segment that had undergone grade I changes following strangulation and, therefore, was not resected. This was missed at the first surgery but caused severe postoperative obstruction and pain and was resected at this (second) surgery.

The basic premise of this grading system is that changes consistent with early venous strangulation obstruction are consistent with a correct viability score. Such changes include red discoloration and even some black patches or stripes in bowel with a thick and edematous wall (Figures 28-2 to 28-4). Bluish discoloration of the bowel (grade IV) suggests arterial occlusion[4] and a poorer prognosis for survival, especially if the affected area of bowel wall is thin (Figure 28-8). Even a small area of bluish discoloration can cause postoperative obstruction and abdominal pain (Figure 28-7). Because this system is based on observation of subtle color changes in bowel wall, it is highly dependent on lighting conditions and quality of the surgery lights.

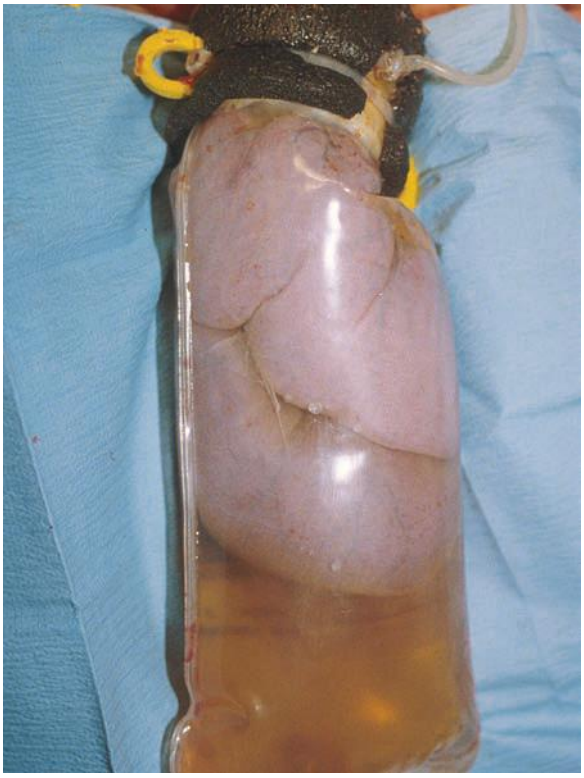
Bowel that becomes ischemic after evisceration tends to progress rapidly through these grades, but the viability seems to decline at a slower rate in these segments. This clinical observation is consistent with the experimental finding that a closed-loop model (Figure 28-9) produces similar mucosal-lesion grades as an open-loop model of strangulation in ponies, but with milder serosal evidence of ischemia[7] (Figure 28-10). This difference can be explained by a more rapid filling of veins and tissue in the open-loop model or in eviscerated bowel because of the lack of opposing pressure on the bowel wall.

Figure 28-8



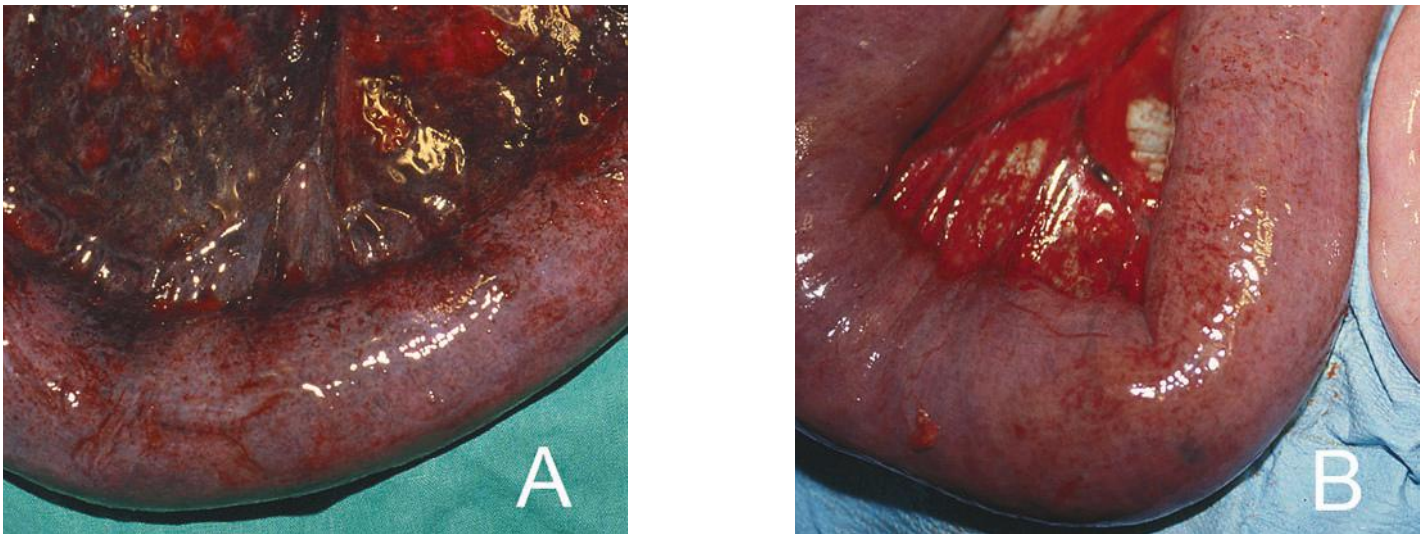
Histologic findings in a segment of jejunum that was removed at surgery because it had undergone grade II changes (A) to grade IV changes (B) following a presumed strangulation that had corrected before surgery. Note that despite loss of villi in grade II (A), crypts are intact and the surface is covered by flattened cuboidal epithelial cells through restitution. The grade IV segment has no recognizable mucosa, and the submucosa contains karyorrhectic debris and vascular thromboses, evidence that it is not viable.

Figure 28-9



A closed-loop strangulation model created by placing strangulated jejunum in a 1-liter IV fluid bag with sufficient physiologic solution to create a peritoneal fluid medium. See reference 13 for more details.

Figure 28-10



Segments of small intestine 15 minutes after release from 3 hours of venous strangulation obstruction created in an open abdomen[5] **(A)** and 15 minutes after release from 6 hours of venous strangulation obstruction in a closed-loop model shown in the Figure 28-9[7] **(B).** Although both segments had similar mucosal grades of injury, the external appearance of A, which is representative of bowel strangulated by evisceration, is worse than that of B, which is representative of an enclosed intraabdominal strangulation.

Fluorescein Fluorescence

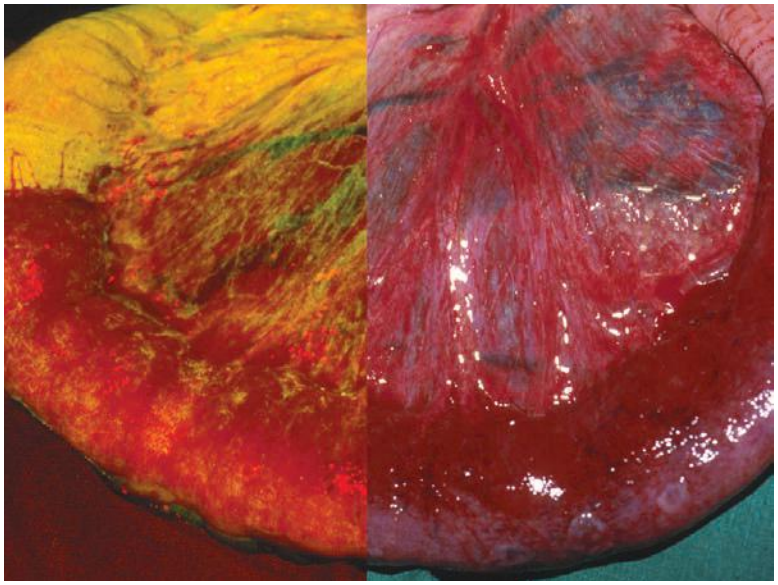
The advantages of fluorescein fluorescence (visual or qualitative fluorescence) in equine small intestine include rapid assessment of large areas of bowel, simplicity of use, safety, and economy (Figure 28-11).[4,8] Fluorescein is administered through the jugular catheter as a 10% solution at a dosage of 15 mg/kg of body weight. A portable UV lamp is used to demonstrate fluorescence in the darkened room, approximately 5 minutes after injection.[4] Unfortunately, interpretation of equivocal fluorescein patterns is subjective and prone to error, and patterns that characterize nonviable intestine in other species are not applicable in the horse.[4,8] In viable intestine that is rendered hemorrhagic and edematous by venous occlusion, intramural hemorrhage shields fluorescein in the tissues from the UV light, and a hypofluorescent or nonfluorescent pattern is produced (Figure 28-12). This accounted for the high false-positive results, low overall accuracy, and low overall specificity for fluorescein in one study of jejunum in ponies.[4] Fortunately, the hyperfluorescent pattern caused by perivascular leakage in nonviable bowel[8,9] seems rare in horses, because this could lead to assignment of viable to nonviable bowel. The concern that nonviable bowel will stain from surface contact with the dye in peritoneal fluid does not appear valid. In conclusion, fluorescein fluorescence offers little improvement over clinical judgment, although a viable fluorescent pattern usually means that the segment can be left in place. Unfortunately, a nonviable fluorescent pattern must be considered inconclusive.[4]

Figure 28-11



Normal pony jejunum illuminated with a Wood's lamp in a darkened room shortly after injection of fluorescein through the jugular vein. This is a normal fluorescent pattern.

Figure 28-12



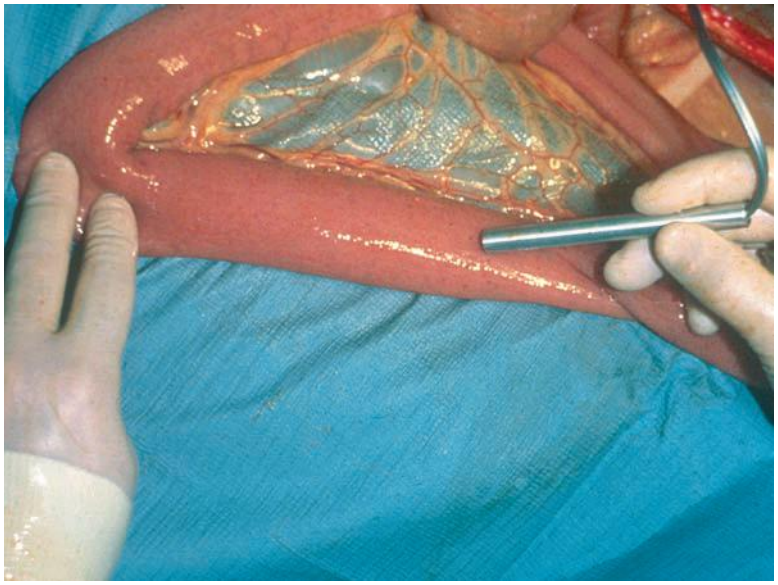
Segment of small intestine 15 minutes after release from 3 hours of venous strangulation obstruction, before (right) and after (left) fluorescein administration. Long-term follow-up confirmed that this segment was viable and did not form adhesions, although it was judged as nonviable based on clinical and fluorescent criteria. Note that the seromuscular hemorrhage interfered with fluorescence on the mesenteric border, so that this is an indeterminate pattern in equine jejunum.

Doppler Flowmeter

The Doppler pencil probe (9 mHz) is calibrated to a Doppler flowmeter, and can be used to detect blood flow at several points in the mesenteric vessels and in the intestinal wall.[4] After the tip of the gas-sterilized probe is coated with sterile, water-soluble gel to enhance contact, it is held at a 45° angle to the tissue surface while it is directed upstream to the direction of blood flow (Figure 28-13). Doppler arterial signals are judged as being present (viable) or absent (nonviable). The Doppler technique is most suitable for identifying small areas of ischemia and for selecting well perfused margins for intestinal anastomosis.[8] Because of this limited range of application, the Doppler probe cannot scan large segments of ischemic bowel adequately and can miss foci of infarction.

In a study of pony jejunum, Doppler ultrasound was superior to fluorescein fluorescence and clinical judgment in predicting the viability of intestinal segments after they were subjected to venous occlusion.[4] However, the Doppler technique has been shown to be inferior to fluorescein fluorescence and to clinical judgment in detecting nonviable segments, regardless of the method of inducing ischemia.[8] The superiority of fluorescein fluorescence has been attributed to its ability to assess microvascular perfusion, which correlates closely with tissue viability, whereas the Doppler device detects blood flow in large vessels.[4,8]

Figure 28-13



Method of applying the Doppler flowprobe to the jejunal wall to detect pulsatile bloodflow. The tip is held at a 45-degree angle and a coating of water soluble lubricant enhances contact. Unlike fluorescein (Figures 28-11 and 28-12), this method can only assess small segments at a time.

Miscellaneous

The perfusion fluorometer (quantitative fluorescence), laser-Doppler flow meter, and tetrazolium analysis of the mucosa, have some potential but are cumbersome and require special equipment.[8,9] Thermography has been evaluated in a preliminary study in pony jejunum, and some criteria were established that could have clinical application.[10] For example, a temperature gradient of less than 0.5 degree between mesenteric and antimesenteric margins and a difference of more than 1.5 degrees between mesenteric border temperatures of ischemic and nonischemic bowel could indicate inadequate reperfusion.[10] In clinical cases, a mean intraluminal hydrostatic pressure of 15 cm of H_2O in small intestine proximal to an obstruction was significantly associated with low survival[11]; however, this would seem to be more useful as an indicator of prognosis than intestinal viability.

Surface oximetry could be applied to viability assessment in equine small intestine.[12] Pulse oximetry has been evaluated in normal equine small and large intestine and could be attractive for clinical use (Figure 28-14) because no equipment calibration is involved and an objective display of information is presented rapidly.[13] The high-intensity ear probe or the flat reflectance sensor (Figure 28-14) can be applied easily and rapidly to intestinal segments. Pulse oximeter oxygen values, pulsatile flow, or the detection of a pulse, alone or in combination, could be used to assess tissue perfusion and intestinal viability. In a study of canine jejunum, ileum, and colon, pulse oximetry and surface oximetry were capable of estimating tissue blood flow, but pulse oximetry was faster and easier to use.[14]

Figure 28-14



Portable handheld monitor suitable for use as a pulse oximeter in detecting bowel viability. The reflectance sensor shown or clip-on sensors can be applied to the serosal surface of the bowel to obtain a rapid recording for blood oxygen saturation (Nonin Medical, Inc, Plymouth, Minn.).

Large Colon and Cecum

In the equine large colon, the term viable refers to ability of the affected segment to recover fully without risk of further mucosal necrosis and death of the horse secondary to endotoxemia and peritonitis. Unlike the small intestine, adhesions are less likely to form in the large colon after a mild to moderate ischemic injury.[15] In the colon, an important consideration is the risk of recurrence of large-colon displacement, particularly in the case of large-colon volvulus.[16] This risk will weigh heavily on the side of resection in horses prone to this condition, even if the horse might survive with the colon left in place after correction.[16] Another important consideration is the risk/benefit of resection of ischemic colon that could allow transmural passage of endotoxin and other bacterial products into the circulation after surgery.[16] The large intestinal disease most likely to present the most difficulty with viability assessment is large-colon volvulus, and the decision to resect is further complicated by poor access to viable margins.

Clinical Judgment

Clinical assessment of viability is considerably more difficult in the large colon than in the small intestine. A segment that appears viable based on serosal appearance can have irreversible mucosal changes and microvascular thromboses. Conversely, a segment with similar or more severe serosal evidence of ischemia can recover if left in place, although these horses usually have signs of endotoxemia for at least 3 days after surgery. A pelvic flexure colotomy can be useful in such cases, as it allows assessment of bleeding from the cut edges. Also, a thin slice of one edge of the enterotomy can be harvested for histologic examination. If the mucosa is dark red and bleeding is brisk, the prognosis is better than if the mucosa is black. However, dark discoloration of the mucosa and failure to bleed do not rule out viability. Visual assessment of motility in the large intestine is not as reliable as in the small intestine because large-intestinal motility normally appears sluggish and the thickened wall may not respond even though it is viable.

Frozen Sections

Evaluation of histologic changes from frozen biopsies has been used to assess the degree of epithelial injury to the equine large colon.[12,17] A full-thickness intestinal biopsy is cooled to –150° to –160°C in 2-methylbutane immersed in liquid nitrogen until the solution almost reaches its freezing point (approximately 5 to 10 minutes) and is processed for immediate evaluation.[12,17] The prediction of viability is based on assessment of hemorrhage and edema in the mucosa and submucosa, the extent of epithelial cell damage, and the interstitium to crypt ratio (normal I:C < 1).[12] Intestine is less likely to survive with more than 50% loss of the crypt epithelium, and an I:C ratio greater than 3.[12] Histologic changes at the pelvic flexure are representative of those at less accessible portions of the colon and at the site of resection and anastomosis, and have been found to be useful in clinical cases of large-colon volvulus.[17]

Surface Oximetry

Combined evaluation of tissue blood flow (surface oximetry or laser Doppler) and histologic injury (frozen tissue sections) has been recommended to assess large-colon ischemia.[12] Surface oximetry is a measure of the partial pressure of oxygen on the tissue surface (PsO_2) and is determined by oxygen content in blood beneath the probe, the diffusion distance from the vessels to the surface, local tissue oxygen consumption, and blood flow.[12] A good outcome is associated with a PsO_2 greater than 20 mm Hg.[12] The disadvantages are that the equipment is expensive, only small areas of tissue can be evaluated, and contact between probe and tissue should be constant. Pulse oximetry can be used to assess oxygen saturation but may not be as sensitive to decreases in local tissue blood flow as surface oximetry.[12]

Fluorescein Fluorescence

A viable pattern in the large intestine could indicate complete recovery, whereas the small intestine with the same pattern could form adhesions.[15] The fiberoptic perfusion fluorometer has the advantage over qualitative fluorescence in that it provides quantitative information and is therefore an objective measure of perfusion.[9] Results with the fiberoptic perfusion fluorometer were inconclusive in one study of experimental ischemia in equine small and large intestine, although it did identify the ventral colon as more susceptible to ischemia than the dorsal colon.[9]

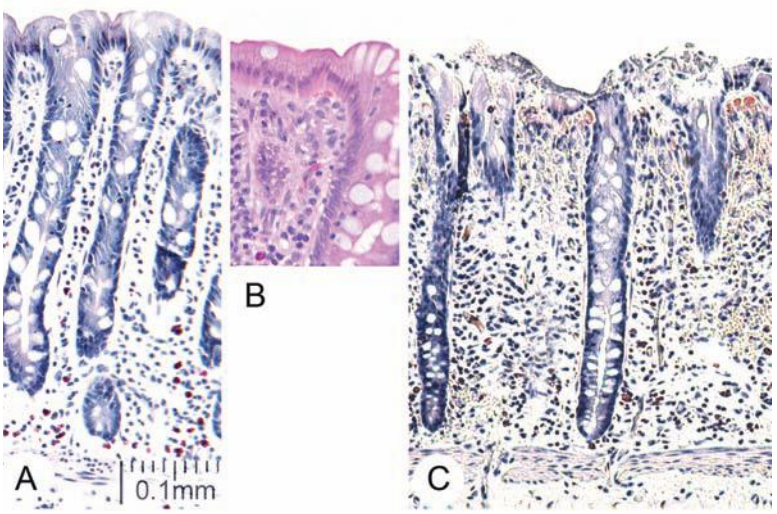
Miscellaneous

Formalin sections from one edge of an enterotomy can be processed for delayed assessment of viability and to help decide the need for further treatment, surgery, or euthanasia, if the horse's clinical condition deteriorates after surgery (Figure 28-15). For example, horses with nonviable colon after correction of large-colon volvulus can remain stable for 3 to 4 days after surgery, and then start to deteriorate from failure of mucosal repair. By that time, the results of a formalin biopsy should be available and could be used to predict the likelihood of mucosal recovery (loss of more than 50% of the crypt epithelium indicates a poor prognosis). In horses with large-colon obstruction, an intraluminal hydrostatic pressure exceeding 38 cm of H_2O had high sensitivity, specificity, and positive and negative predictive values for predicting low survival.[18]

Small Colon

Assessment of small-colon viability has not been studied to the same extent as it has in the large colon and small intestine. The small colon appears to be sensitive to pressure necrosis at the site of a focal impaction, and resection is indicated for segments with black and green discoloration (Figure 28-16). Also, the entire small colon proximal to an obstruction should be examined because it is not unusual for an impaction to move distally and reimpact at several sites, causing scattered areas of necrosis.

Figure 28-15



Histologic changes in equine left dorsal colon subjected to 2 hours of ischemia (C) compared with normal sections (A and B). Sections A and C are stained with Luna's eosinophil stain to show eosinophils and red cells as red and nuclear components as blue. After ischemia (C), the crypts are separated by edema and hemorrhage, and surface epithelial cells are detached, but sufficient crypt cells remain to support recovery. Section B is normal mucosa stained with H & E to demonstrate the intact surface epithelial cells and dark staining microvilli on the apical surface. All sections are 10X.

Figure 28-16



Small colon containing a firm fecalith impaction, with black and green discoloration and mural thinning suggesting pressure necrosis.

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Large-Colon Enterotomy, Resection and Anastomosis

Chapter 29

Joanne Hardy

Large-Colon Enterotomy

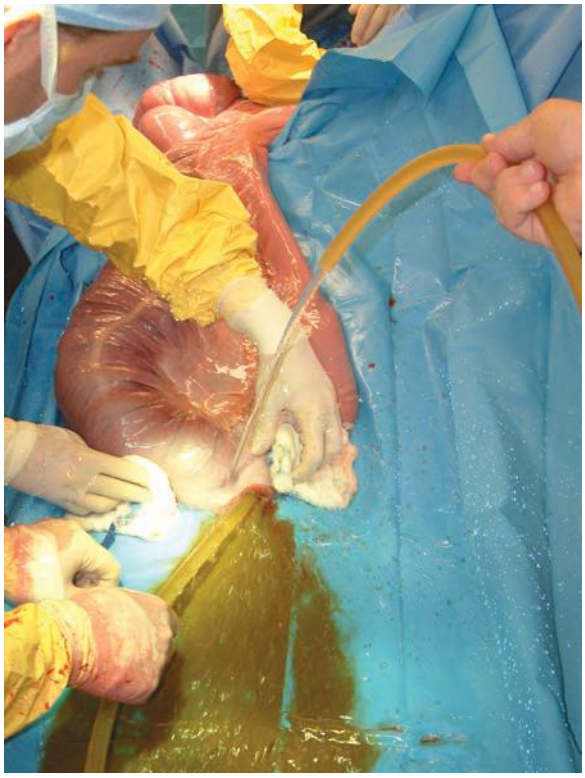
Pelvic flexure enterotomy that allows evacuation of the colonic contents is a commonly performed procedure in horses with abnormalities affecting the large colon. Enterotomy procedures are also performed for removal of foreign bodies (usually in the right dorsal colon), and right ventral colon enterotomy is used to access the cecum in horses with a cecocolic intussusception.

For this procedure, the large colon is exteriorized and placed on a colon tray (Kimzey Metal Products, Woodland, CA) on the left side of the horse or caudally between the horse's hind legs. If a colon tray is not available, the colon is best exteriorized between the horse's hind legs. Some surgeons place the end of the laparotomy drape onto the tray to create a shelf to help support the weight of the colon. The enterotomy drape is then placed on top of the laparotomy drape and secured with towel clamps. The colon tray is angled at about 20° (Figure 29-1). A modified trash can with an ingesta strainer and a liquid outflow hose can be used to collect and evacuate the contents of the colon (Figure 29-2).[1] Alternatively, the end of the tray can be positioned over a disposal system built into the surgery room (Figure 29-3). In anticipation of colonic evacuation, a lavage system should be established. This can be done by using two garden hoses, or one hose with a Y connection. One hose is used for intraluminal lavage and evacuation of the contents, and the other for extraluminal lavage, using warm water (37°C, 98.6°F) or a warm balanced electrolyte solution.[1] If these are not available, stomach tubes, buckets, and pumps can be used.

A full-thickness 8- to 12-cm incision is made on the antimesenteric border of the pelvic flexure.[2] One hose is inserted and gently advanced into the colon, while the other is used to continuously lavage the serosal surface to reduce fecal contamination (Figure 29-1). During the evacuation procedure, it is useful to lift the colon and ensure that the underside is lavaged as well. A sterile assistant helps to feed the hose into the colon and massage its contents. Although a modified colon tray has been described for evacuating the colon, it is not deemed necessary by most surgeons.[3] If colonic evacuation is performed as part of the correction of a large-colon volvulus, an intestinal biopsy can be collected to evaluate the severity of damage at the time of surgery. Closure of pelvic flexure enterotomies is performed using 2-0 absorbable suture material in two layers: a simple continuous seromuscular layer followed by a Lembert or a Cushing pattern.[4] The colon is rinsed with sterile saline or lactated Ringer's solution and replaced in the abdomen.

Enterotomies in the right dorsal or ventral colons are performed after the colon has been draped off from the main surgical field. Enterotomies made in the ventral colon are performed between taenial bands as the fibrous nature of the taeniae preclude successful inversion during suturing. The location of the enterotomy in the dorsal colon is not as critical. Because enterotomies performed at these sites are more likely to bleed post operatively, a full-thickness closure (simple continuous or

Figure 29-1



Exteriorization of the large colon onto a colon tray for evacuation through a pelvic flexure enterotomy.

Connell) is performed on the first layer to achieve better hemostasis.[5] A Lembert or Cushing suture pattern is used as the second layer.

A modified Heineke-Mikulicz technique for pelvic flexure enterotomy closure has been described in two horses having extensive stricture of the large colon.[6] A longitudinal incision was made centered over the stricture and the incision was closed using a transverse closure, effectively increasing the diameter of the colon at that site.

Figure 29-2



Modified trash can used to collect colonic contents during evacuation.

Figure 29-3



Disposal system used to evacuate biological fluids and intestinal contents during large-animal surgery.

Large Colon Resection

Indications

Resection of the large colon is performed for removal of full-thickness mural defects in the large colon. Causes include strangulation, infarction, thromboembolic disease, neoplasia, or scar tissue formation.[6-14]

Techniques

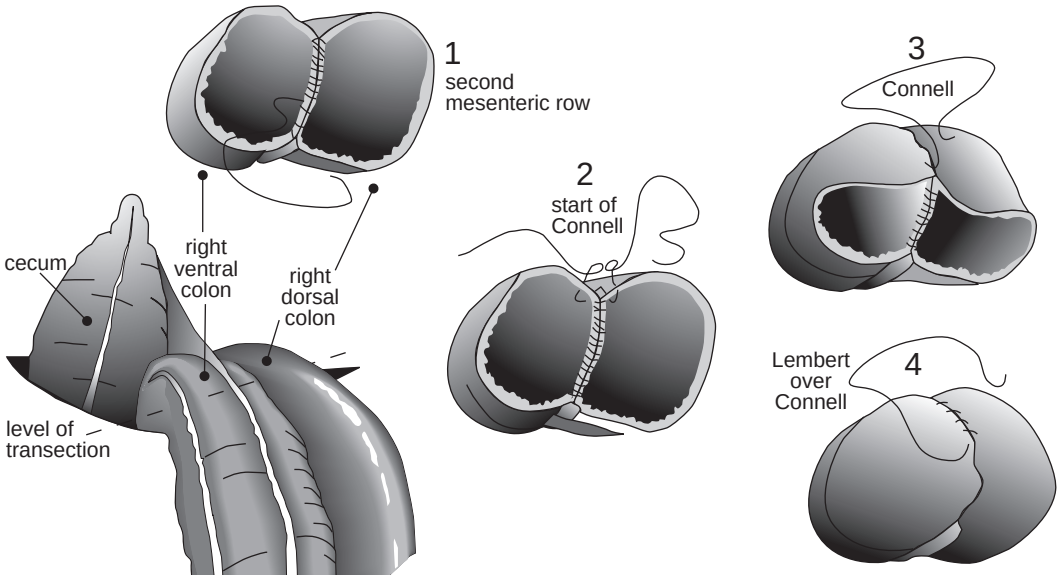
Removal of 50% to 95% of the large colon has been described.[15-20] Techniques for resection of the large colon include resection and end-to-end anastomosis, and resection and side-to-side anastomosis. Because large-colon volvulus of a partially resected colon has been reported, amputation of the entire colon within the limits of the abdominal incision is recommended.

End-to-End Anastomosis

End-to-end procedures are performed for removal of the colon up to 10 to 12 cm from the cecocolic ligament.[21] When resection of the colon closer to or proximal to the cecocolic ligament is required, a side-to-side technique is preferred as the end-to-end technique places too much tension on the anastomosis site. The increased tension places the anastomotis site at increased risk for dehiscence.

For an end-to-end resection, the colon is exteriorized on a colon tray and draped off; the cecum is replaced into the abdomen. All ingesta are massaged into the segment to be removed. If the colon is full, a pelvic flexure enterotomy is performed to evacuate the contents of the colon. Care must be taken to remove all ingesta and water from the right dorsal and ventral colons to minimize contamination during the resection. The site for resection is identified by choosing one that is easily held by the assistant surgeon without tension on the mesentery.[21] The colon is positioned to expose the right colic artery and the colic branch of the ileocolic artery within the mesocolon; the colonic vessels are isolated by blunt finger dissection and double ligated using 1-polyglactin 910. Alternatively, two double rows of staggered staples (TA-90 Premium, US Surgical Corp, Norwalk, CT) are applied across the mesocolon, followed by a third double-staggered row 4-cm distally. The mesocolon is transected between the proximal and distal staple lines. Hemostasis is verified and any bleeding vessels are ligated. The right ventral colon is transected in a line perpendicular to its long axis. The dorsal colon is transected at a 30-degree angle to its long axis, with the antimesenteric border shorter so that the diameters of the colons are similar. In the original description of the procedure, a V-shaped stoma was created between the mesenteric border of the dorsal and ventral colons using an inverting linear anastomotic instrument (GIA Premium 55, US Surgical) reinforced with a double-layer simple continuous pattern. This step was omitted in later descriptions of the procedure.[22] Starting at the mesenteric border, and suturing from the lumen, the colons are apposed with a double row simple continuous pattern using 0 polydioxanone or polyglactin 910 (Figure 29-4). The second layer should be full thickness to achieve hemostasis. Once the mesenteric portion of the anastomosis is completed, suturing is changed to approach it from the serosal side, and the colons are apposed using a double-layer starting with a Connell followed by a Lembert pattern. The colon is lavaged and replaced in the abdomen.

Figure 29-4



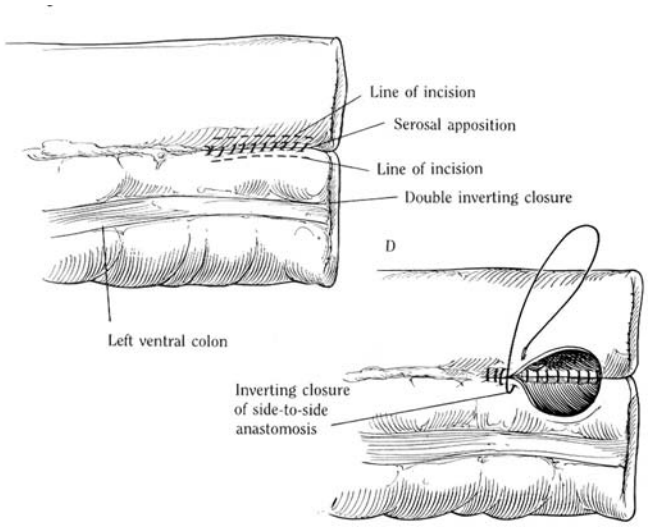
End-to-end resection and anastomosis of the equine large colon.

Side-to-Side Anastomosis

For a side-to-side anastomosis, the site of resection is usually at the level of the cecocolic ligament or oral to it. The colon is exteriorized to the left of the horse on a colon tray, and the colonic vasculature is transected as described above. The stoma is created first, taking advantage of the weight of the colons to facilitate exposure of the anastomotic site. The site for creation of the stoma is identified, taking care to end it just proximal to the level at which the colonic vessels have been ligated, so a blind sac is not formed. A three-tier side-to-side stoma is created; the first layer apposes the colons using #1 polyglactin 910 in a Lembert or Cushing layer for a length of 20 cm (Figure 29-5). A full-thickness incision is made in each colon and a full-thickness simple continuous circumferential closure, interrupted at the 180-degree mark, is made to create the stoma. The upper layer is then apposed using a Cushing or Lembert pattern. Alternatively, the stoma can be created using stapling instrumentation. This may minimize contamination, but may not be possible if the colons are too thick and edematous as a result of the underlying disease process. For an adequately sized stoma, the stapling instrument is fired twice if the ILA-100 or the GIA 90 is used, and three times if the GIA 55 is used; keeping in mind that the staples for the latter have a shorter staple length. Staple lines should be oversewn. Once the staples have been applied, the down layer cannot be approached for oversewing. Therefore, this layer should be done first, before application of the stapling instrument. Once the stoma is created, the colons are resected, starting with the ventral colon, taking care to resect them at the site of colonic vessel ligation. The lumens are closed using a full-thickness simple continuous or Connell pattern, and are oversewn with a Lembert or Cushing pattern. The resected colons are lavaged and replaced in the abdomen. Although resection of the large colon has been reported using stapling instruments, this is usually not possible after correction of large-colon volvulus, as the intestinal edema and congestion do not allow proper closure of the instrument and adequate formation of the staples.

An early method of large-colon resection has been described that uses a luminal approach to create the side-to-side anastomosis, followed by closing the ends of the colons.[18] The technique described for end-to-end resection represents a modification of this technique.

Figure 29-5



Stapled side-to-side resection and anastomosis of the equine large colon.

Colon Bypass Procedures

Successful bypass of the right dorsal colon for the treatment of large-colon volvulus has been described in one horse.[23] In that report, the large colon was judged to be nonviable after reduction of a large-colon volvulus. The right dorsal colon was transected as far distally as possible within the abdomen, using a TA-90 stapling instrument, and the suture line was partially oversewn. The right ventral colon was transected 10 cm from the cecocolic ligament and an end-to-side anastomosis was made between the right ventral colon and the descending colon using a double-layer inverting pattern. Two mild episodes of colic and diarrhea for one week were the reported complications. In a similar fashion, anastomosis of the right ventral colon to the descending colon to bypass a nonfunctional descending colon anastomosis in a miniature pony was reported.[24] A two-layer hand sewn end-to side anastomosis was performed between the right ventral colon and the descending colon. One episode of colic successfully treated with medical therapy was the only postoperative complication encountered in this case.

Complications

Complications arising from large-colon resection performed after large-colon resection are usually a result of the primary disease and include persistent endotoxemia and peritonitis as a result continued bowel devitalization. This is because the site of volvulus is usually at or proximal to the site of resection, such that some portion of compromised large colon cannot be removed. Therefore, it is essential for the surgeon to remove as much of the devitalized colon as possible. In this author's experience this requires a side-to side resection at or proximal to the cecocolic ligament. Even then, a segment of devitalized colon may remain in the abdomen, leading to subsequent complications. Most horses that succumb to endotoxemia and peritonitis do so within 3 to 7 days after the procedure and require considerable intensive care. In contrast, survivors have an improvement in clinical signs within 24 hours after the procedure.

Postoperative pain is common in horses after large-colon resection. This procedure induces clinical signs of pain even in healthy horses. Administration of nonsteroidal anti-inflammatory drugs, lidocaine, and opiates can help alleviate the pain.

Signs of endotoxemia are common after large-colon resection for large-colon volvulus. Signs include fever, tachycardia, injected mucous membranes, dehydration, and hypoproteinemia. Signs of large-colon ileus, manifested by moderate to severe distention, can also occur. Supportive care with fluids, plasma, and treatments designed to counteract the effects of endotoxins are important. Horses should be monitored for signs of postoperative hemorrhage, which is more prevalent with large-colon procedures and occasionally requires a blood transfusion.

Postoperative diarrhea is commonly observed after large-colon resection because of mucosal damage or reduced surface area available for fluid absorption. The diarrhea is usually self-limiting and resolves within a few days if it is not infectious in origin. However, isolation procedures should be followed as dictated by hospital protocol, and infectious diseases should be ruled out.

Horses with successful resection of the large colon usually regain normal fecal consistency in 5 to 7 days. Because of the decreased surface area available for digestion and water absorption, these horses will have increased water and phosphorus requirements, and will require a highly digestible diet.

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Small Intestinal Resection and Anastomosis

Chapter 30

David E. Freeman

Evidence is growing that survival rates after small-intestinal surgery in horses are improving[1-6] compared with rates in earlier reports.[7] The most common causes of death during hospitalization in large retrospective studies of horses with small-intestinal lesions were anastomotic leakage,[7] septic peritonitis,[3,8] postoperative ileus,[6] and shock.[9] Adhesions are reported to account for most long-term deaths,[2,7,8] with a prevalence of 6 to 26% after small-intestinal surgery,[2,5,7,10] although this is apparently a decline.[2,5,7,10] The reason for improvement in outcome lies largely with a trend to earlier referral, so that horses with colic are presented as better candidates for anesthesia and surgery.

The ultimate measure of successful small-intestinal surgery in the horse is early return of intestine to normal function. Minor technical errors are not well tolerated and can trigger events that delay or prevent complete recovery.[2] Therefore, the surgery should be conducted with an organized and planned approach, recognizing that all methods have inherent flaws and that each surgeon should follow a protocol with which he or she is comfortable. This chapter deals with resection and anastomosis from the time that the decision has been made to resect bowel.

Extent of Resection

Although one study suggested that resection of 60% or more of small intestine could lead to malassimilation,[11] a subsequent study demonstrated that resection of 70% of the small intestine of ponies is well tolerated.[12] Because the mural congestion caused by venous strangulation can increase the length of the affected segment of small intestine by as much as 36%,[13] some correction for an increase in length after strangulation is needed to avoid an overly pessimistic estimate of the risk for short-bowel syndrome.[13] It is impossible to establish a correction factor that would apply to different severities of strangulation encountered in clinical cases, and therefore, assessment of the remaining length of small intestine could be a more meaningful predictor of survival. A guideline of 4.5 m (15 feet) as the minimum length of remaining small intestine in an adult horse[5] might prove useful. This approximates what would be left after resection of 75%, according to recent estimates of small-intestinal length in adult horses.[13] Removal of longer segments does not appear to be well tolerated.[2]

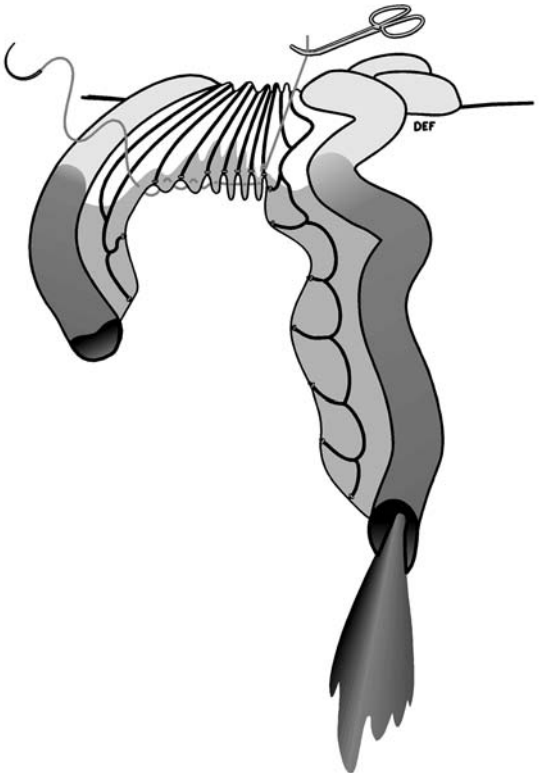
Resection of Mesentery

After the lesion has been corrected, the bowel is arranged in its correct orientation on the left side of the abdominal incision, with the proximal end at the cranial aspect of the abdomen and the distal segment or ileum (if involved) at the caudal aspect. Then, the mesentery is resected and gathered (Figure 30-1) by the following method. For mesenteric resection, a ligature of 3-0 polydioxanone (PDS) is applied to the first mesenteric vascular arcade (artery and vein) in the strangulated bowel, level with the proposed line of mesenteric resection (Figure 30-1). The same ligature is then used to gather the trimmed edge of mesentery as each mesenteric vessel is transected with the Ligate Divide Stapler (LDS). Any major vessel that is bleeding or not securely closed by the stapling instrument should be ligated with 2-0 or 3-0 suture material, and some small mesenteric vessels might require ligation. If in doubt, a second ligation is indicated just proximal to the staple. This method of gathering the mesentery retains any bleeders in view outside the abdomen, avoids a large mesenteric gap that would allow rotation or entrapment of bowel in the mesenteric defect, and allows decompression of the proximal segment. The suture used to gather the mesentery is not tied until after the bowel has been decompressed, because this tie would restrict some degree of mesenteric mobility that is required during decompression.

Decompression

Intraoperative decompression is recommended to reduce the risk of postoperative ileus and prevent the “bent garden hose” effect, which can progress to postoperative volvulus. Also, complete removal of small intestinal contents facilitates abdominal closure. Decompression is accomplished through the strangulated bowel after it has been mobilized far from the surgical field to drain into a container, taking care not to stretch and tear remaining mesenteric attachments (Figure 30-1). As much intestine as possible proximal to the site of transection is manually stripped of its fluid and gas contents, taking care not to traumatize the bowel or mesentery. This amount of intestinal handling does not appear to predispose to adhesions, although carboxymethylcellulose or saline lavage can be applied to lubricate the serosa and facilitate bowel handling. An alternative approach to draining through the strangulated segment is to drain contents into the cecum, but this may involve unnecessary handling of healthy bowel distal to a jejunojejunostomy, and also creates a full cecum that could complicate jejunocecostomy and abdominal closure. If resection is not needed, distended small intestine can be drained into the cecum, and if necessary, the fluid is removed through a typhlotomy. An enterotomy in the small intestine is avoided if possible because it creates another potential site for adhesion formation.

Figure 30-1



A ligature is applied to the first mesenteric vessel in the strangulated bowel and the same ligature is then used to gather the trimmed edge of mesentery as each mesenteric vessel is transected. Decompression is accomplished through the strangulated bowel after it has been mobilized far from the surgical field to drain into a container.

Resection and Anastomosis

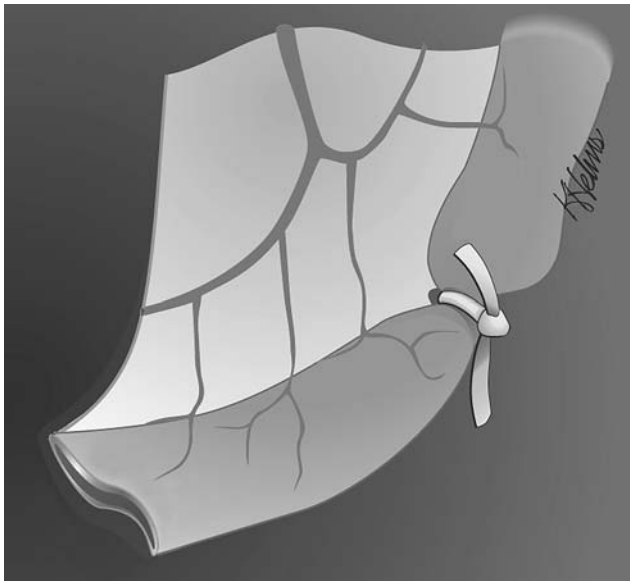
Strangulated bowel is removed along with approximately 30 cm or more of contiguous healthy intestine at each end. Wherever possible, a large arcuate artery (as close as possible to its origin from the major mesenteric artery) is left intact at the edge of the mesenteric defect to supply the anastomosed ends. If the arcuate vessel extends too far from the mesenteric vessel, it might not provide adequate blood flow to the anastomosis. At least 6 cm of mesentery, preferably more, is left beyond the major mesenteric vessels and branches to prevent inadvertent vascular occlusion or puncture during closure of the mesenteric gap.

To prevent leakage into the surgical field, Penrose drains can be applied 15 to 30 cm from each side of the anastomosis site (Figure 30-2), although they are not essential on the distal segment if it is completely empty. This distance is selected to prevent trauma to the critical area of the anastomosis. Penrose drains are preferred over Doyen clamps (Figure 30-3) because they can be less traumatic and allow easier manipulation of the bowel. The mesenteric rents created for Penrose drain placement are closed after removal of the drains. An alternative to Penrose drains are nontraumatic intestinal clamps such as Forgarty clamps, which can be used to manipulate the bowel during the anastomosis.

Bleeding vessels in the transected edges of the intestine can be cauterized or ligated, but this is rarely necessary. Regardless of method chosen for the anastomosis, special care must be taken to appose the mesenteric border first. This area is prone to rapid edema formation that can prevent visual separation of the mesentery from the seromuscular layer so the latter might not be adequately included in the suture. With all handsewn anastomosis patterns, sutures must penetrate deep enough to incorporate the submucosal tissue.

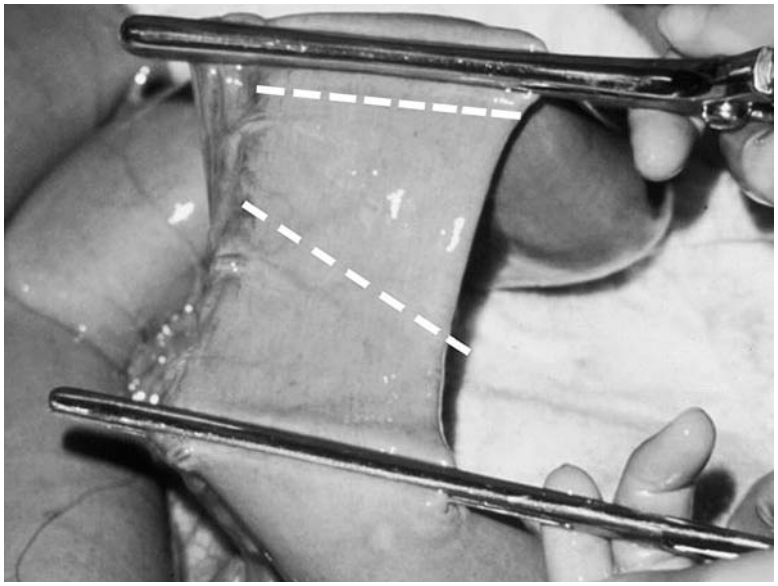
After the anastomosis is complete, the remaining mesenteric defect is closed with 3-0 PDS in a simple continuous pattern (Figure 30-4), taking care to avoid mesenteric vessels or create an accordion effect that could kink the bowel.

Figure 30-2



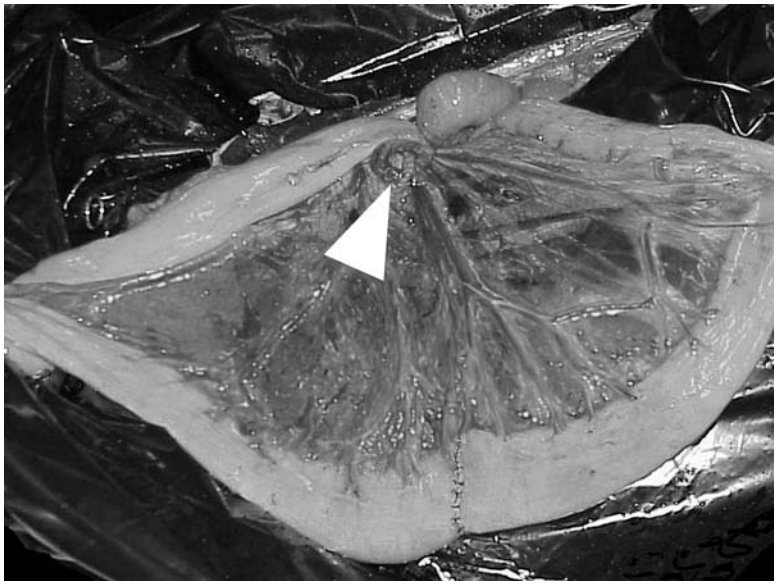
Use of a Penrose drain to occlude the bowel at least 15 to 30 cm from the anastomosis and an angled S-shaped transection that creates a larger stoma. Compare with Figure 30-3.

Figure 30-3



A popular method for using clamps to resect small intestine, with an angled line of transection at 60° to the mesentery (angled broken line). An incision along the edge of the crushing clamp (broken line at top clamp) would provide too small a stoma, unless the crushing clamp is angled.

Figure 30-4



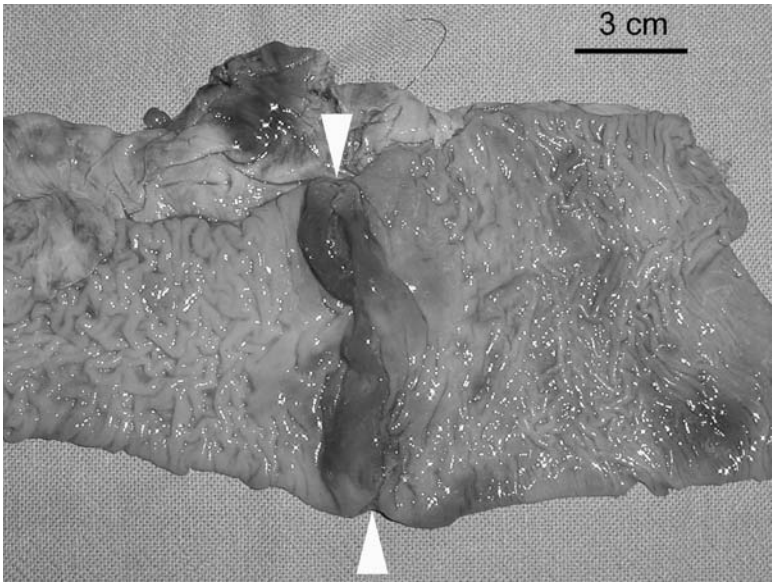
Completed end-to-end anastomosis with an interrupted Lembert pattern, showing that the mesenteric closure did not shorten the mesentery, but allows the anastomosis to fall in line with contiguous bowel. Arrowhead points to the gathered mesenteric stump.

Stoma Size

Regardless of the anastomosis technique used, the size of the stoma can be critical to the success of an end-to-end anastomosis of small intestine in horses. Excessive inversion and stomal constriction must be avoided, and both are usually caused by overzealous attempts to obtain a leakproof seal. If the stoma is too small, it could get critically smaller from edema,[14] (Figure 30-5) and fluid sequestration in the bowel wall could be exacerbated by postoperative fluid therapy.[15] Once the stoma starts to trap solid particles, it can allow water to sieve through, causing dehydration of the trapped material and stomal obstruction. Failure to create a large stoma could also cause low-grade stomal obstruction and postoperative reflux, which could be mistaken for or exacerbate postoperative ileus.

For an end-to-end anastomosis in a 450-kg horse, it should be possible for a surgeon that wears a size 7 1/2 glove to fit at least 3 fingers along the jejunal wall into the anastomosis (Figure 30-6). A two-finger sized stoma is not satisfactory.

Figure 30-5



An end-to-end anastomosis (between arrowheads) removed 24 hours after the first surgery because it became impacted. Bowel was inverted too much and this combined with the obvious mucosal swelling to cause obstruction.

Figure 30-6



Demonstration of a satisfactory stoma size after end-to-end anastomosis with a continuous Lembert pattern. Surgeon is wearing size 7 gloves. (Courtesy of Dr. Anna Rötting.)

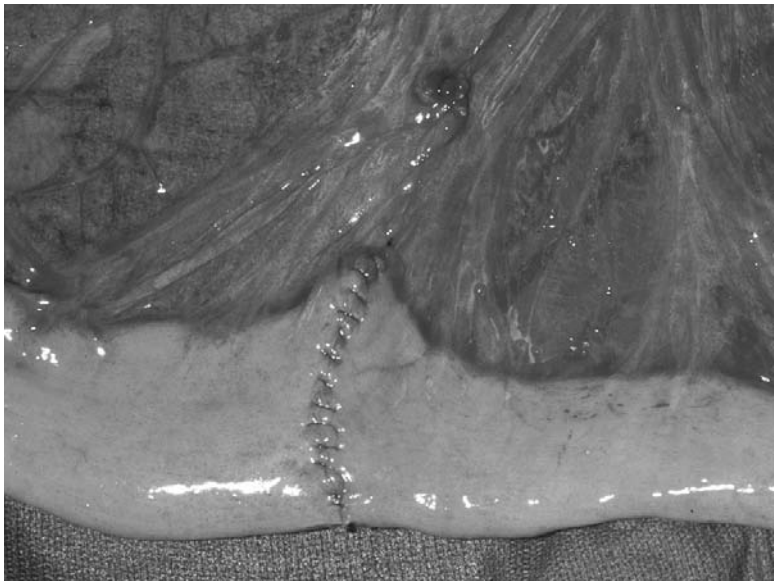
To create a large stoma and to improve antimesenteric blood flow, the angle of transection should be approximately 45 to 60 degrees from the mesenteric attachment. Transecting the bowel by cutting it along the edge of an intestinal clamp will not consistently produce a large enough stoma (Figure 30-3), even if the clamp is angled appropriately. If the angled transection is in a straight line, sharp angles are created at each mesenteric margin that can be difficult to appose (Figure 30-3). This problem can be overcome by using a curved Mayo scissors to produce an S-shaped line of transection that softens the angles by rounding them and distributing them along the anastomosis rather than placing them in one point (Figure 30-2). This technique increases the length of the apposed edges and produces a wide stoma, sometimes with a small diverticulum on the mesenteric border (Figure 30-7) that is inconsequential. Stay sutures placed through the mesenteric and antimesenteric edges of both segments help to align them and to maintain them at similar diameters throughout the anastomosis.

Unlike end-to-end anastomosis, in which stomal size is limited to some extent by the diameter of the bowel ends, such limitation is minimal on stomal size in a side-to-side anastomosis (including functional end-to-end anastomosis). This leads to another error with stoma size that is unique to side-to-side anastomoses.

Side-to-side anastomoses, by necessity, transect the circular muscle fibers responsible for propagation of a food bolus, and a direct relationship exists between stomal size (more fibers cut) and stagnation in the stoma and proximal to it.[16] A side-to-side anastomosis thereby disturbs intestinal motility, accumulates intestinal contents and markers of intestinal transit, and delays gastric emptying.[16] In canine jejunum, 91% of migrating myoelectric complexes can cross an end-to-end anastomosis at 12 weeks after surgery, compared with only 56% at 2 years after a functional end-to-end anastomosis.[17] The functional end-to-end anastomosis alters intraluminal flora compared with a handsewn end-to-end anastomosis, providing further evidence that it imposes some nonphysiologic changes on intestinal function.[17]

The clinical implications of an overly large stoma in a side-to-side anastomosis should be considered by equine surgeons who aim to create a large stoma, even up to 15 cm.[18] The tendency to make an overly large stoma is an attempt to offset the tendencies of jejunocecostomies to swell after surgery and become smaller during short-term[19] and long-term postoperative periods.[20] Unfortunately, a large stoma can become progressively larger with time, and this dilatation has been associated with delayed obstruction after a stapled functional side-to-side anastomosis in dogs[17] and after a hand sewn version of a side-to-side anastomosis in horses[21] and rats.[16]

Figure 30-7



Completed end-to-end anastomosis with a continuous Lembert pattern, showing a wide stoma obtained by an S-shaped transection.

End-to-End Anastomosis

One-layer Interrupted Lembert Pattern

An interrupted Lembert pattern has been used in equine jejunum[2] with size 3-0 polydioxanone (size 4-0 for foal jejunum), bites 6 to 8 mm apart, 6 to 8 mm wide, and passing within less than 1 mm from the cut edge (Figure 30-8). Each suture is tied snugly to the point that the suture indents the tissue, but not enough to strangulate or cut through it.

Experience with the interrupted Lembert pattern[2] suggests that it might be associated with fewer short-term problems than other methods.[4,21] In one study,[2] 15 of 16 horses (94%) with this anastomosis survived short term. No horse required a repeat celiotomy or developed postoperative ileus. The anastomosis was intact and not associated with problems in the only fatality, a horse euthanatized because of laminitis. Compared with continuous patterns, this anastomosis avoids a pursestring effect, it might allow some degree of stomal expansion for a passing bolus, and each individual suture can be tightened sufficiently to achieve hemostasis as needed. The latter benefit cannot be achieved with continuous patterns without constricting the stoma.

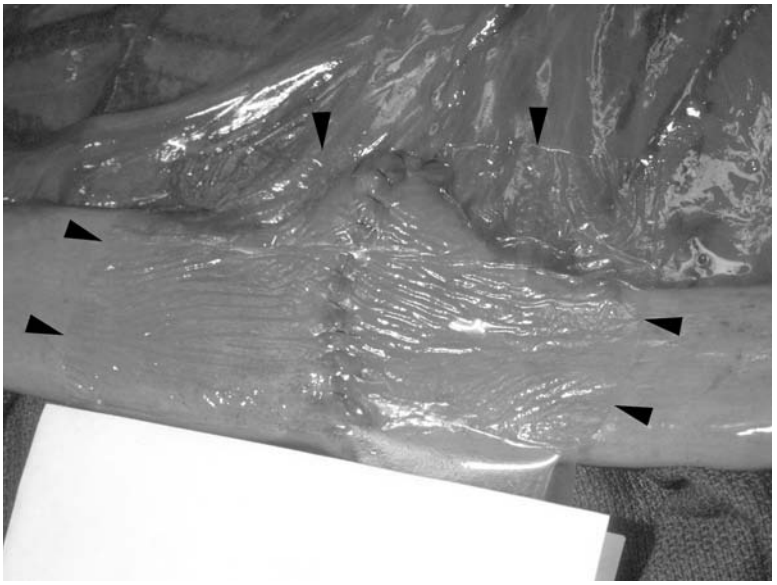
Interrupted patterns have the disadvantages of being slow and tedious and expose a considerable amount of suture material in the knot (Figure 30-8), which could predispose to adhesions.[2] Therefore, the interrupted Lembert pattern might benefit from use of fine suture material, such as size 3-0,[22,23] and from methods that can prevent focal adhesions to anastomoses (Figure 30-9), such as sodium carboxymethylcellulose and a hyaluronate membrane (Seprafilm, Genzyme Corporation, Cambridge, Mass, USA).[24]

Figure 30-8



Close up of a completed end-to-end anastomosis with an interrupted Lembert pattern, showing the large number of knots on the surface, but the satisfactory anatomic continuity of the bowel.

Figure 30-9



Wrapping Seprafilm (Genzyme Corporation) around an anastomosis created with a continuous Lembert pattern. The arrowheads indicate the edges of Seprafilm, which is applied directly from its wrapper, after excess fluid was removed from the bowel wall.

Gambee and Appositional Patterns

The Gambee pattern is a modified interrupted appositional pattern that inverts the mucosal layer, which tends to evert with most appositional patterns.[25] It starts with a full-thickness bite 6 to 8 mm from the cut edge and directed perpendicularly to the incision to emerge through the mucosa only, close to the seromuscular edge. A similar bite but in the opposite sequence is used for the apposing edge. This pattern optimizes stomal diameter, but exposes some raw seromuscular edges, and has the same disadvantages as other interrupted patterns. A tendency to adhesions to exposed suture material has been demonstrated with the Gambee pattern with size 0 suture material[26,27] but not with size 3-0.[22,23] A full-thickness appositional pattern differs from the Gambee because it does not prevent mucosal eversion. An appositional suture in the seromuscular layer only, either as a continuous or interrupted pattern, could overcome this problem. An interrupted crushing pattern has been used in horses, with bites 3 to 5 mm apart and 3 to 4 mm from the edge, and taking care to push the mucosa into the lumen as each suture is tied.[28]

Two-layer Continuous Pattern

A popular method for end-to-end anastomosis of equine small intestine is the Czerny-Lembert pattern.[29] This is a two-layer anastomosis, with a simple continuous pattern for the submucosal/mucosal layer, followed by a continuous Lembert pattern in the seromuscular layer.[29] A popular modification of this is to use a Cushing pattern instead of the Lembert.[26,29] Mucosal and seromuscular rows are interrupted at the mesenteric and antimesenteric margins to prevent a purse-string effect.

Compared with the Lembert pattern, the Cushing pattern is more likely to purse-string the bowel, although it does expose less suture material to serosal surfaces and this could reduce the risk of adhesions. The Lembert pattern exposes more foreign material to the serosa and carries the risk of excessive inversion. The need for separate mucosal closure is questioned because it appears to contribute little in strength, takes additional time, might not improve mucosal apposition, and could cause excessive mucosal hemorrhage during suture application.[30] Two layers of inverting seromuscular patterns, such as combinations of Cushing, Lembert, and Connell patterns, are not necessary and produce a large intraluminal cuff.[23]

One-layer Continuous Pattern

A simple continuous pattern in the mucosal and seromuscular layers, with careful prevention of mucosal protrusion between the apposed seromuscular edges, caused more perianastomotic adhesions and associated stomal distortion and constriction in horse jejunum than a two-layer inverting anastomosis.[24] However, the simple continuous pattern was faster and produced a significantly larger stomal diameter than did the inverting technique. The prevalence of adhesions could be reduced by covering the anastomosis with a bioresorbable membrane of hyaluronate and carboxymethylcellulose.[24] The high risk of adhesion formation with this and other appositional patterns can be attributed to some mucosal exposure to the peritoneal cavity and possibly leakage.[24] A simple continuous pattern has been used successfully in the seromuscular layer for jejunoileostomy[31] and a single layer continuous Lembert pattern can be used for jejunojejunostomy (Figure 30-7).

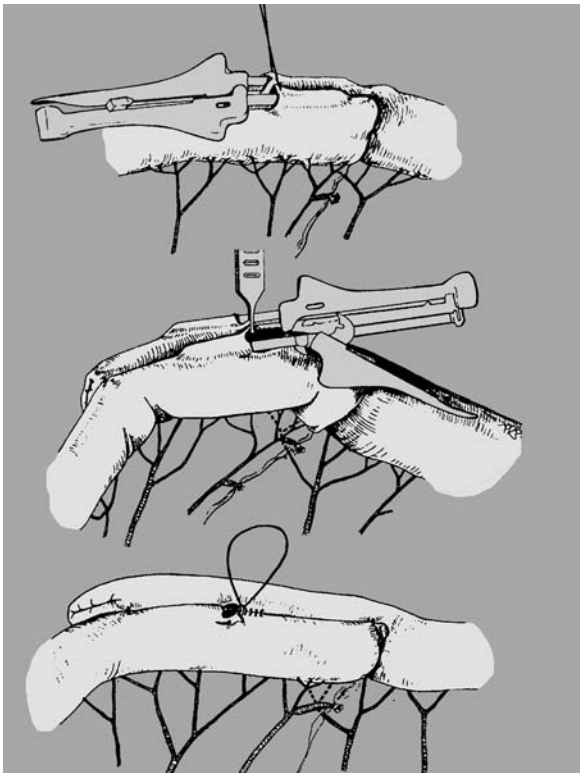
Stapled Jejunojejunostomy

The major advantages claimed for stapling instruments are speed, reduced tissue handling, improved tissue blood flow, minimal contamination, ease of application, production of a stoma of consistent and predictable size, and rapid healing without a potentially dangerous lag period.[29] The disadvantages are that stapling is expensive, requires side-to-side application in adult horses, creates stomal constriction by healing of apposed raw edges at commisures of the stoma, is limited by tissue thickness and occasional staple failure. The 4.8-mm staples (green cartridge) are preferable to the 3.8 mm staples (blue cartridge) for adult equine gastrointestinal surgery.[5] The former close to 2 mm whereas the latter have a closed height of 1.5 mm, which could crush tissues and weaken the closure. However, the 4.8-mm staples might not achieve hemostasis and produce an effective seal in foals.

Side-to-Side Stapled Jejunojejunostomy

The isoperistaltic side-to-side technique involves creating blind stumps of the proximal and distal ends of the jejunum with either a Parker-Kerr technique or stapling instruments (Figure 30-10). These segments are then overlapped and a Gastrointestinal Anastomosis (GIA) instrument is used to create a stoma between them. This places two parallel rows of staggered staples on each side of a stoma cut simultaneously by advancement of the knife blade (Figure 30-10). If the GIA 50 is used, it is placed proximally and then distally through the same stab incisions on the antimesenteric side. If the Multifire GIA 80, the GIA 90 Premium or the ILA100 is used, a single application is sufficient. The two mesenteric edges are sutured to the adjacent mesenteric surfaces at the points of overlap and the anastomosis should be carefully inspected for any defects or evidence of staple failure.

Figure 30-10



Double application of a GIA 50 for a stapled side-to-side jejunojejunostomy after resection and oversew of the jejunal ends. The stab incision is closed and the overlapping mesenteric edges sutured. (From Pascoe JR, Peterson PR. Intestinal healing and methods of anastomosis. Vet Clin North Am Equine Pract 5:309, 1989).

Care must be taken to ensure that the staple lines overlap on the far side of the stab incisions or that any defect on that side is oversewn.[32] A defect is more likely to occur if the stoma is placed midway between the mesenteric and antimesenteric borders because this area is difficult to access for the second application and for inspection.[32] To achieve this, the mesentery of each segment is drawn away from the forks of the instrument so as to roll the antimesenteric edges onto the jaws for more ideal placement; however, antimesenteric placement of the stoma might not be regarded as anatomically correct compared with a stoma closer to the mesentery. If the anastomosis is made with a single application of a stapling instrument, the most likely point of failure is at the stapled end of the anastomosis, not at the end with the handsewn stab incisions.[33] Use of stay sutures at each end of the anastomosis to stabilize the staple rows is recommended to prevent leakage and staple separation. Care must be taken to ensure that the blind ends extend minimally beyond the stoma so that they do not accumulate stagnant contents, impact, dilate, and become ulcerated.[16,34] If all stages of this anastomosis are completed with staples, a minumum of 3 cartridges are required, two TA cartridges and at least one GIA or ILA cartridge, and this increases surgery cost considerably.

Functional End-to-End Stapled Jejunojejunostomy

With the functional end-to-end stapled anastomosis, the bowel ends are lined up in antiperistaltic fashion, the stoma is then created with the GIA instrument through the open ends (open lumen technique), and bowel ends are then closed. Alternatively, the bowel ends can be closed first and the stoma created by inserting the forks of the stapling instrument through stab incisions close to the oversewn ends.[35] The mesentery is then sewn so that part of the mesenteric suture line covers the blind ends of the apposed segments.

As the bowel heals after a functional end-to-end anastomosis, it realigns itself into an end-to-end configuration.[36] Intussusception of a functional end-to-end anastomosis has been described at 2 and 26 days after surgery in two ponies[35] and 8 months after surgery in a horse.[4]

Closed One-stage Functional End-to-End Stapled Jejunojejunostomy

With this technique, the segment to be resected is isolated from healthy bowel with proximal and distal intestinal clamps, and segments to be joined together are apposed in antiperistaltic side-to-side fashion with 2 seromuscular traction sutures, 12 to 14 cm apart.[36] The vessels are ligated and the mesentery incised on the segment identified for removal, and stab incisions are made in the antimesenteric border of the two jejunal segments, 1 cm oral to the traction suture closest to the clamps. Forks of the GIA 90 Premium or the ILA100 are then passed through these stab incisions to form a 10-cm stoma along the

antimesenteric borders of the apposed jejunal segments. A TA-90 linear stapler is applied diagonally across the two segments of jejunum aboral to the stoma. All bowel oral to this instrument, including the stab incisions, is amputated before the stapler is released.[36] Reinforcing sutures are placed at the points of intersection of the anastomotic and linear staple lines and at the oral end of the anastomotic staple line.[36]

This functional end-to-end jejunojejunostomy did not cause adhesions in 18 normal horses in which it was developed, but 3 horses (17%) died from surgical complications.[36] One horse was euthanatized because of persistent postoperative ileus unresponsive to medical treatment, and mild fibrinous peritonitis was the only finding at necropsy 96 hours after surgery.[36] Another horse was euthanatized 6 hours after surgery because of dehiscence of the anastomotic staple line and subsequent severe fibrinous peritonitis.[36] Other nonfatal complications were anastomotic impaction or postoperative ileus in one horse, an impaction proximal to the anastomosis that was not clinically evident in another, and peritonitis in a third horse.[36]

With this anastomosis, mesenteric length is preserved and the mesentery eventually covers the exposed mucosa at the linear staple line.[36] Advantages of this anastomosis over a stapled side-to-side anastomosis are the shorter surgery time and possible savings on cost.[33] There was no difference in bursting strength between this anastomosis and the stapled side-to-side anastomosis.[33] The most likely point of failure in this type of anastomosis is at the oral end of the anastomotic staple line.[33]

Everted Triangulated Stapled Anastomosis

Although a recent study found no difference between an everted triangulated stapled anastomosis and a conventional (unspecified) suture pattern in horses,[37] everted staple lines in horses are prone to severe adhesion formation, luminal stricture, abscessation, separation of the muscularis layer, thinning of the anastomosis, and dilatation of the proximal segment.[38] An inverted triangulated end-to-end anastomosis can be performed in equine jejunum by drawing the two segments to be apposed through an enterotomy so that the mucosal surfaces are presented on the outside of the bowel.[39] Despite the inverted pattern achieved, adhesion formation was comparable to that reported for the everted triangulated stapled anastomosis in horses.[39]

Stapled Versus Handsewn Anastomoses for Jejunojejunostomy

Although short-term survival is similar after stapled and handsewn anastomoses, there are some differences in performance between these techniques (Table 30-1). In one report, horses with a stapled jejunojejunostomy had a poorer outcome than those with jejunoileocecostomy with resection.[3] Because this observation is the reverse of findings of most studies,[2,6,7,40] it raises some concern that staples might be less than ideal for a jejunojejunostomy. Also, stapled anastomoses can have a higher rate of complications such as postoperative ileus, peritonitis, leakage,[18,36,41,42] and anastomotic obstructions[3-5] than reported for handsewn anastomosis.[2] Comparisons with handsewn anastomoses across clinics and surgeons are difficult, however, especially because evidence is abundant that the most commonly used handsewn anastomoses produce different stomal sizes.[23,24,26] However, the stapled side-to-side anastomoses could be predisposed to postoperative ileus[3-5] because they disrupt normal anatomic and physiologic alignment of the bowel, whereas the end-to-end anastomosis preserves it.[16,17]

In equine jejunum, the mobility of small intestine, thickness of intestinal wall, and weight of intestinal contents could subject a staple line to unacceptable amounts of tension. Linear tension probably is more harmful in a stapled than sutured anastomosis, because staples are of small diameter and rigid, and therefore more likely to tear through bowel wall.[43] A supporting suture line is often recommended for this reason.[18] The risk of hemorrhage from a staple line,[42] caused by inadequate compression of small arteries in the B-shaped staple or by a staple lacerating a vessel,[44] is low in horses and is more likely if large intestine is involved.[45]

Although speed has been proposed as an important advantage of staples over handsewn anastomoses,[3,33] this has not been confirmed in experimental,[46] or clinical trials,[4] possibly because any beneficial effect from time saved with an anastomosis might be only a fraction of the total surgery time. Any time benefit might be lost in stapled jejunojejunostomy in horses, because of the number of staple and suture lines needed to close bowel ends, and because of the time involved in performing the anastomosis, in closing the stab incisions, and in suturing two overlapping mesenteric edges (Figure 30-10). Oversewing the staple lines loses the advantages of speed and reduced tissue handling, and the prevalence of adhesions becomes comparable to that with handsewn anastomoses in horses.[46] The reduced peritoneal contamination claimed with staples compared with handsewn anastomoses is probably very slight and has little clinical relevance.

Probably the most important factors with regard to choice of an anastomosis is the amount of training, experience, and comfort level that the surgeon has for the type chosen. Both handsewn and stapled anastomoses have their limitations and each has its proponents, but a major advantage of the staples, when applied correctly, is production of a consistent stoma with minimal bowel handling.

Table 30-1
Results with Jejunojejunal Anastomoses in Horses.

Method of anastomosis (number of horses)	Postoperative ileus (%)	Repeat celiotomy (%)	Discharged (%)	Reference
Stapled (22)	NR	NR	91	Doran et al. 1990[1]
Stapled (12)	NR	45*	79	Vachon et al. 1995[5]
Stapled (27)	16	11	65	Fugaro et al. 2001[3]
Stapled (26)	53	12	88	Semevolos et al. 2002[4]
Handsewn (33)	53	12	88	Semevolos et al. 2002[4]
Handsewn (63)	NR	NR	70	Van der Boom et al. 2001[6]
Handsewn (19)	0	5	89	Freeman et al. 2000[2]

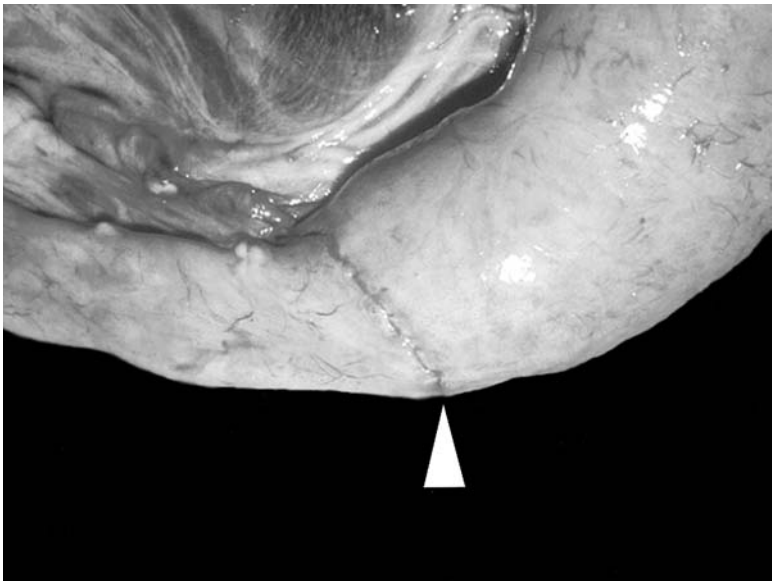
*Report describes 12 repeat celiotomies, but one for enteroliths was excluded in this table because it does not represent an outcome specific for jejunojejunostomy.
NR = not recorded.

Jejunoileostomy

If sufficient healthy ileum is available, jejunoileal anastomosis is an alternative to jejunocecal anastomosis that can be performed more quickly, because fewer steps are required. It also preserves the ileocecal valve, which could be important for integration of small-intestinal and cecal functions.[47,48] This anastomosis functions well,[31] but has a tendency to impact[2,49] (Figure 30-11). One possible explanation for this is that the normal ileum can retain small-intestinal contents that then become more dehydrated than jejunal contents.[49,50] Whereas the thick muscular wall of the ileum can propel this dehydrated material into the cecum, the thin-walled jejunum cannot move it through the anastomosis.[49] Consequently, the jejunum becomes impacted (Figure 30-11). The horse that seems most prone to impaction in this anastomosis is the horse with a large gastric impaction at surgery, which then moves on to obstruct the stoma.[2,34] The vascular problems attributed to the single long ileal artery[20,51] are rare.

The success of jejunoileostomy in one report could be attributed to use of a continuous suture pattern in the seromuscular layer[31] that eliminated inversion obtained with other patterns. Inverting patterns in the ileum can create a more substantial cuff than in jejunum, because the inverted edge of ileum can be thicker and more rigid.

Figure 30-11



Impacted jejunum at site of a jejunoileostomy (arrowhead). (Courtesy of Dr. Lance Bassage.)

Jejunocecal and Ileocecal Anastomoses

Jejunocecal and ileocecal anastomoses can constitute 40% of all small-intestinal anastomoses.[2] Jejunocecostomy has a lower survival rate and more postoperative complications than other types of anastomosis,[2,7,40,52] although long-term outcome is generally comparable.[2] The basic techniques for jejunocecostomy are end-to-side and side-to-side. Proponents of the side-to-side jejunocecostomy believe that it allows for creation of a larger stoma than is possible with the end-to-side technique,[21] and that it is associated with fewer problems related to stomal swelling and obstruction.[19,53] An angled line of transection of the jejunum or ileum, with or without a longitudinal incision on the antimesenteric side ("fishmouth"), can allow construction of a stoma of adequate size with the end-to-side technique. If a side-to-side anastomosis is made too large (>10 cm), it can expand with time, possibly from effects of delayed transit through this type of anastomosis[16,17] and reflux of cecal contents. Progressive dilatation with distention of the jejunum proximal to the anastomosis are features of side-to-side anastomoses.[16,17]

Resection of Ileum

Jejunocecostomy and ileocecostomy have two components, ileal resection and jejunocecostomy. For an ileal resection, the mesentery and small intestine are prepared as for a jejunojejunostomy except that the ileum is transected and oversewn, using either stapling instruments or a Parker-Kerr technique. The goal of the procedure is to remove as much ischemic ileum as possible so that the remaining stump is viable and well sealed. Ileum of questionable viability and even some obviously necrotic ileum can be left in situ, although closure can be difficult, especially if the level of transection is close to the abdominal incision and the edges are friable and edematous. Remaining ischemic ileum can be well tolerated because it is nonfunctional and can intussuscept into the cecum;[54] although stump abscessation and leakage can be fatal complications of this surgery.[7,9] The ileal stump should be short because a long stump could pass through and obstruct the cecocolic orifice.[55,56]

As much cecum should be exteriorized as possible, as well as the large colon if necessary, to empty the abdomen and bring the abdominal incision closer to the ileum. A short stump of ileum can be handsewn, depending on the size of the horse and the depth in the abdomen. Large laparotomy sponges are used to pack off the ileum as an assistant maintains upward traction to maximize ileal exposure (Figure 30-12). An alternative technique is to attach the ileum to a length of stomach tube that can be used to invert it into itself and then into the cecum.[57] Another method requires elevating the ileum with right-angled clamps and then placing interrupted Lembert sutures to force deep inversion of the cut edges.[58]

Figure 30-12



Ileal stump oversewn by a Parker Kerr technique, using the same suture to return over the first row and completed by tying the two ends together (From Freeman DE. Surgery of the small intestine. Vet Clin North Am Equine Pract 13: 261-301, 1997).

If ileal necrosis is extensive, the TA90 can be used for a distal transection in healthy bowel (Figure 30-13) or it can be applied down to the ileocecal orifice, thereby removing the entire ileum and essentially leaving no stump behind (Figure 30-14). Because this has to be done blindly, great care must be taken to include all of the ileum as far as the ileocecal valve in the portion to be removed[40] and to exclude other bowel and mesentery. The 4.8-mm length staples are recommended for this purpose because intraoperative leakage has been reported after application of shorter staples to the ileum.[5] An incision is made in the mesentery dorsal to the ileal artery and continued to the level of ileal transection to create a tract for passage of a loose ligature to that point. A similar incision is made in the ileocecal fold for the same purpose. A ligature of heavy suture material is then placed loosely around the ileum and its remaining mesenteric attachments, and guided down the incisions in

the mesentery and ileocecal fold to the level of ileal transection.[40] There it is tied so that it compresses all mesenteric tissues attached to the distal ileum at the level of transection, including the ileal artery and vein.[40] The ileum is then freed of its mesenteric vasculature up to the level of the abdominal incision, which can leave a length of thrombosed vessels extending proximal to the ligature (Figure 30-14).

Leakage through the staple line is a concern after ileal closure with the TA 90 instrument, but effective closure can be achieved by this method (Figures 30-13 and 30-14). The problem with any technique for distal ileal transection is the difficulty of complete closure of the mesenteric defect in the deep (dorsal) part of the abdomen,[40] which can lead to intestinal strangulation of bowel that migrates through the opening.[6]

Figure 30-13



Stapled ileal stump at 3 days after surgery (reoperation for anastomotic impaction) showing that the stump is well sealed and free of adhesions. (Courtesy of Dr. Allison Stewart.)

Figure 30-14



Ileal transection and TA 90 closure at the level of the ileocecal junction at 7 days after surgery (horse died from colitis). Small black arrowheads indicate the ends of the staple line. The large black arrowhead points to the remaining ileocecal fold. The most distal ligature is indicated by the white arrowhead, and remnants of the ileal mesentery and ileal artery are indicated by the arrow.

Side-To-Side Jejunocecal Anastomosis

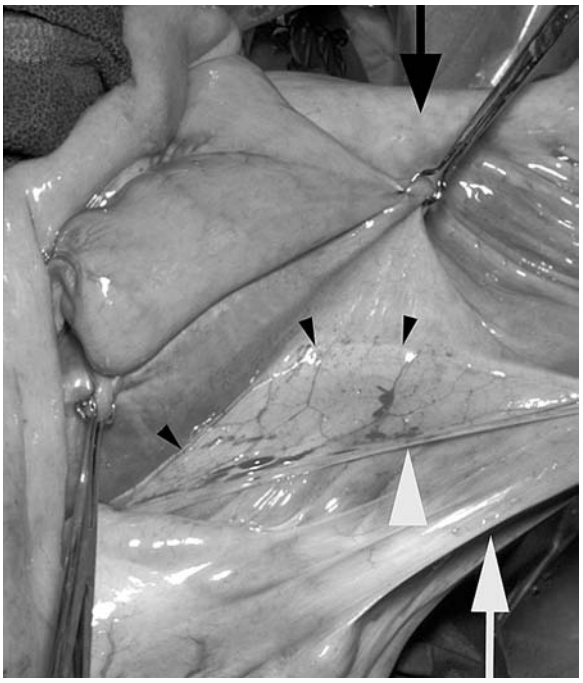
As for a jejunojejunostomy, distended bowel is decompressed through the strangulated segment rather than into the cecum, to reduce leakage of cecal contents into the surgery site during the anastomosis. The stoma should be created as close to the base of the cecum as possible, to reduce the gravitational effects of cecal contents,[58] midway between the dorsal band and the medial band, and with the stoma level with the cecocolic fold (Figure 30-15).

After the small intestine has been drained through the necrotic segment and the resection has been completed, the distal end of jejunum is closed with a Parker Kerr technique. A pouch of the cecum can be clamped off or elevated above cecal contents by applying upward tension on stay sutures or Babcock forceps (Figure 30-15). Approximately 10 to 12 cm of the oversewn end of jejunum is attached to the selected area on the wall of the cecum with interrupted sutures of 3-0 PDS at each end (Figure 30-15). The oversewn end of the jejunum should be directed toward the cecal base, and the anastomosis should be made close to the oversewn end or a stagnant loop will form (Figure 30-15). A handsewn side-to-side method, stapling instruments (Figure 30-16), or the "cutting or sawing thread" technique[20,59,60] can be used to make a 10-cm stoma.

For handsewn techniques, the first row must appose the antimesenteric portion of the jejunum and the cecum approximately 5 to 8 mm closer to the mesentery than the proposed site for the stoma on the antimesenteric edge (Figure 30-15). Failure to do this will place the stoma too close to the mesentery and to the dorsal band of the cecum, and will rotate the jejunum so that it is kinked at the anastomosis. One row of a continuous Cushing pattern is placed on the far side (deepest from the surgeon) of the proposed line for the stoma for 9 to 11 cm, and this is tied at each end. The jejunum and cecum are then incised within 5 mm of each end of that row and 5 mm parallel to it. The next row can be a full-thickness simple continuous pattern that apposes the far edges of the cecum and jejunum inside the Cushing row. This layer can be tied at each end, and must be placed so that each end includes the corners of the stoma to eliminate gaps at these crucial points. Although the edge of the stoma away from the surgeon will invert with this pattern, the near side will require a continuous Lembert or a continuous appositional pattern in the seromuscular layer to invert it. This layer is then oversewn with a continuous Cushing pattern that completes the Cushing row on the far side, but both rows are interrupted at each end of the stoma. The free edge of mesentery is sewn to the cecum, then to the ileocecal fold, ending at the oversewn end of the ileum and the previously gathered mesenteric stump.

If staples are used for the anastomosis, oversewing the entire staple line is optional, and a single Cushing suture at the antimesenteric angle and at the midpoint of each side of the anastomosis can be used to support these critical areas of the staple line. Although one method of staple application involves placement of a suture line to attach the bowel first and then parallel application of the staples along this suture line, it can be difficult to place the stapler accurately with this technique. Therefore, staple application followed by suturing might be easier for most surgeons. A stabilizing suture line between cecum and jejunum proximal to the stoma is optional. Another method is to place a Marshal U suture at the ends of the anastomosis to support it at the points of tension.[61]

Figure 30-15A



Organization of bowel for handsewn side-to-side jejunocecostomy, as described in the text. The stoma is placed parallel to and between the medial (black arrow) and dorsal (black arrowheads) bands of the cecum, and as much of the cecum as possible is exteriorized to place the anastomosis high on the cecal body, almost level with the cecocolic fold (white arrow). The white arrowhead indicates the edge of the ileocecal fold. Note that a pouch of cecum is elevated with Babcock forceps. The next step is a continous suture pattern to appose the jejunum and cecum along the line of contact. It is critical that this suture line is 5 to 8 mm deep to the antimesenteric surface of the jejunum so that the stoma is placed in the desired position.

Figure 30-15B

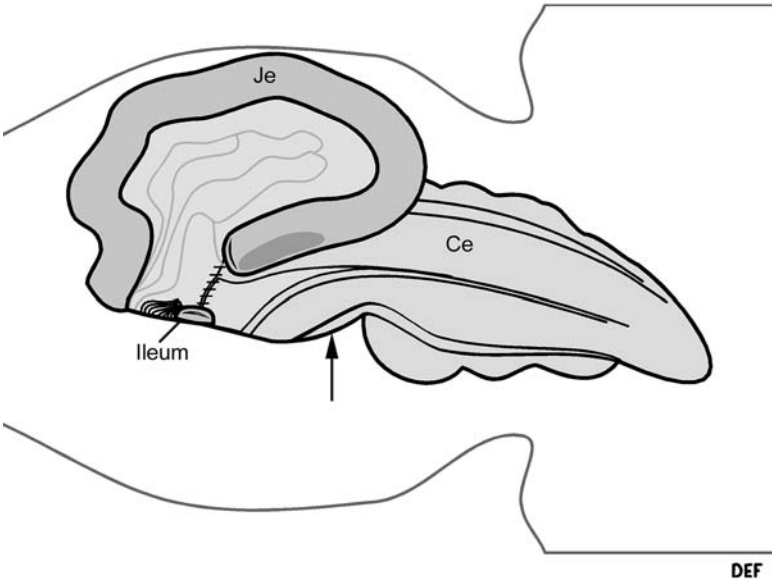
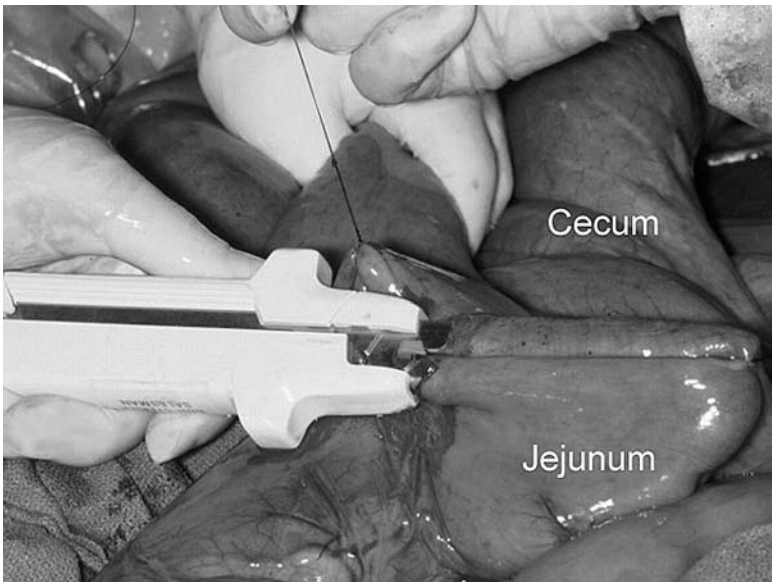


Diagram of a completed side-to-side jejunocecostomy to demonstrate the relationship between cecum and jejunum shown in 30-15A. The shaded area is the stoma. Ce = cecum; Je = jejunum; cecocolic fold (arrow); cranial is to the left.

Figure 30-16



Use of a Proximate Linear Cutter (Ethicon) to create a side-to-side jejunocecostomy, as viewed from the surgeon's perspective on the left side of the horse (cranial is to the right).

End-to-Side Jejunocecal Anastomosis

For an end-to-side jejunocecal anastomosis, the mesenteric and antimesenteric ends of the jejunum are attached to the selected area on the cecum by simple interrupted sutures of 3-0 polydioxanone. A Lembert or Cushing pattern is used to appose the back side of the jejunum to the cecum. An incision is then made in the cecum that corresponds in length with the opening in the jejunum and 5 mm from the suture line. The back edges of this incision (deepest from the surgeon) are apposed with a full-thickness continuous appositional pattern along that side. The same pattern cannot be used in the front edges of this incision (near side or closest to the surgeon) because it will cause mucosal eversion. Instead, either a seromuscular appositional pattern or Lembert pattern is recommended for this side and great care is taken to ensure that the corners are fully incorporated in this line of closure. A Cushing or a continuous Lembert pattern buries this row to complete the anastomosis. All suture lines are interrupted at the mesenteric and antimesenteric corners to prevent a purse-string effect.

The high prevalence of postoperative complications and lower short-term survival rates after jejunocecal anastomosis compared with a jejunojejunostomy[2,7,40,52] could be explained by a number of factors. Unlike jejunojejunostomy, jejunocecostomy creates a sharp transition between intestinal segments of dissimilar functions. The jejunum must overcome intracecal pressure to empty, without the coordinating mechanism of the ileum and the ileocecal valve. In addition, with a jejunocecostomy, all remaining small intestine was subjected to distention that could delay return of function. With removal of a similar length of midjejunum, only a portion of the remaining intestine was subjected to distention, and it remained continuous with intestine that shares its function.

Side-To-Side Jejunocecal/Ileocecal Anastomosis without Ileal Transection

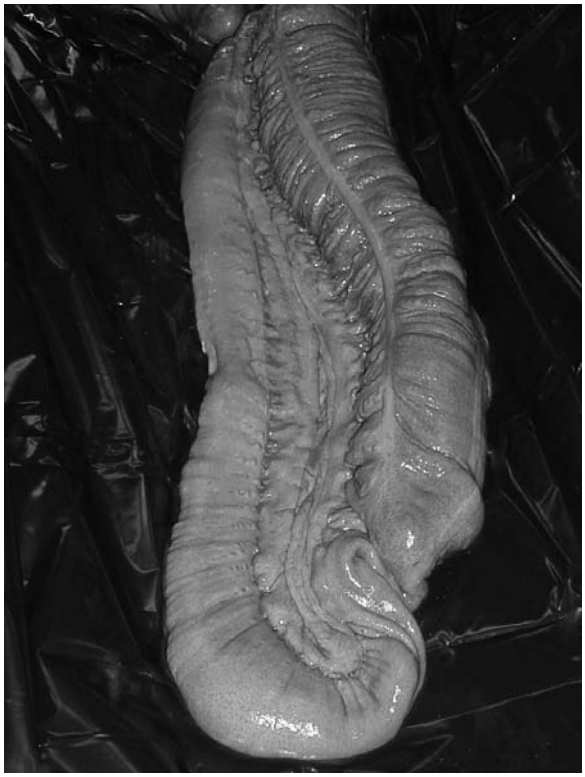
If the ileum is obstructed by a tumor, muscular hypertrophy, or chronic intussusception, an incomplete bypass can be used. In horses with chronic intussusception, all attempts should be made to reduce the intussusception by gentle traction on the ileum and mild digital pressure through the cecal wall on the short stump of intussusceptum. Simultaneous downward pressure on the cecum at the point of invagination should be combined with pressure in the opposite direction on the inverted stump.

A side-to-side handsewn anastomosis is used as described above, except that resection of affected bowel is not necessary. In such cases, the ileum and jejunum are chronically dilated and thick-walled, which makes staple apposition difficult. Because the compensatory hypertrophy in the small bowel at the site of the anastomosis makes the bowel wall rigid and more likely to cut through with a fine suture, a heavy suture material is recommended, such as size 0. The suture pattern on the inner row should be a full-thickness continuous pattern to prevent intraluminal hemorrhage from large submucosal vessels. If a long segment of small intestine is affected by idiopathic muscular hypertrophy, then resection should be considered to prevent creating a long blind loop distal to the stoma. If the bowel proximal to the obstruction (tumor or chronic ileocecal intussusception) is thick-walled and chronically dilated, this should not be resected and will recover with time.

Pelvic Flexure Colotomy

The colon of horses with small-intestinal strangulation is usually tightly contracted around dehydrated contents and, although not truly impacted, this gives the colon a "vacuum packed" appearance (Figure 30-17). Presumably, the degree of preoperative dehydration and contraction of extracellular fluid volume stimulated the renin-angiotensin-aldosterone system and thereby increased colonic absorption of water.[62] Removal of these contents is not essential, but has been associated with a decreased risk of postoperative ileus.[63] Possibly, this procedure could eliminate some downstream resistance and provide a more favorable pressure gradient for emptying of the small intestine into the cecum in horses with ileocecal or jejunocecal anastomoses. With the latter anastomosis, the lack of a jejunocecal sphincter would favor reflux of cecal contents into the small intestine if cecal emptying is impeded by an impacted colon.

Figure 30-17



Typical "vacuum-packed" right ventral colon in a dehydrated horse with a small intestinal lesion. Removal of these dehydrated contents by enterotomy is optional, but might reduce downstream resistance to cecal emptying in horses prone to postoperative ileus, especially after jejunocecostomy.

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Abdominal Closure

Chapter 31

David E. Freeman

Incisional complications have been reported in 40% of horses that have intestinal surgery.[1] They can play a large role in postoperative morbidity and mortality[1-7] and are major causes of nonfatal complications after colic surgery.[8,9] Incisional drainage has been reported in as many as 32% to 36% of horses after intestinal surgery, dehiscence in 3% to 5%, and hernia formation in 6% to 17%. Other complications include swelling,[4-6] local infection,[1,4,6] suture sinuses,[1,4,6] hematoma formation, and peritonitis.[1,4,6] Patient factors associated with incisional complications include age,[1] anemia, chronic illness, dehydration, postoperative leukopenia,[2] hemorrhagic shock,[6] hypoproteinemia, concurrent infection, increased concentrations of fibrinogen in peritoneal fluid,[10] neoplasia, increased intraabdominal pressure, muscle strain, size,[1] postoperative ileus,[11] postoperative mobilization of protein and lipid,[11] increased hematocrit,[12] and nutritional status.[4,7] Surgical factors can include the type of incision,[4,5] type of suture material,[1,4-7,13-15] method of wound closure,[3,5] surgical trauma, length of surgery,[1,12] repeat celiotomy,[11] and difficult anesthetic recovery.[4-7] The most critical factors involved in preventing these complications of abdominal closure are outlined as follows.

Closure of the Peritoneum

The peritoneum can be sutured with a synthetic absorbable suture material of size 2-0 (refer to Table 31-1 for metric equivalents) in a simple continuous pattern.[5] Peritoneal closure is not necessary and has been associated with an increased rate of adhesion formation.[16] Also, the peritoneum is thin and tears easily, even when the falciform ligament is used to appose the edges. However, suturing the peritoneum can exclude bowel from the field during closure of the linea alba, and can retain peritoneal fluid in the abdomen, so that postoperative drainage and incisional swelling are reduced.

Table 31-1

Metric Measures and USP Suture Diameter Equivalents for Synthetic Absorbable and Nonabsorbable Materials.

USP Size	4-0	3-0	2-0	0	1	2	3
Metric measures	1.5	2.0	3.0	3.5	4.0	5.0	6.0

From Freeman DE, Rotting AK, Inoue O. Abdominal closure and complications. Clinical techniques in equine practice. Gastrointestinal series. 1:174-187, 2002.

Linea Alba Closure

Anatomy

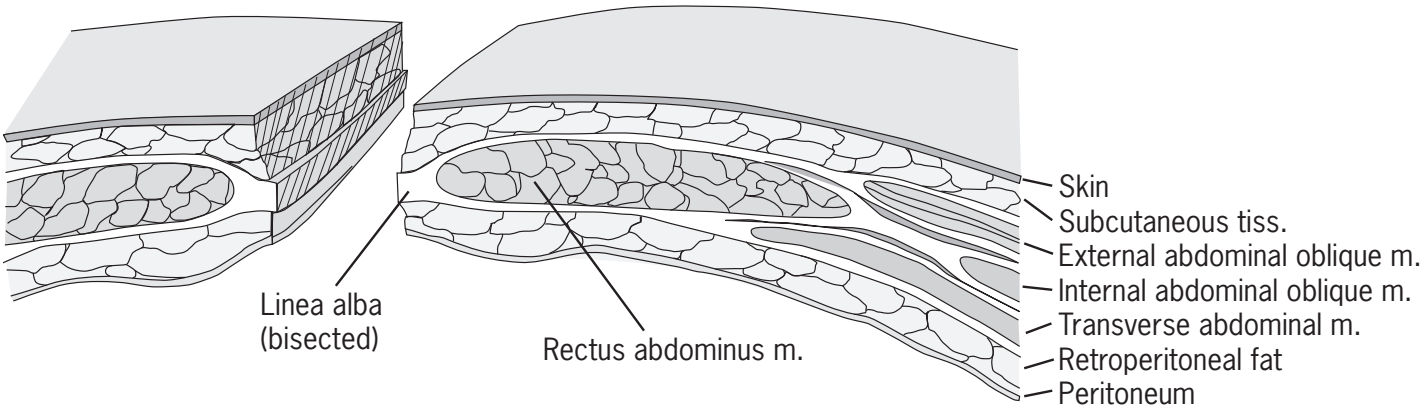
The linea alba is formed by blending of the fascia of the internal and external sheaths on the ventral midline of the abdomen (Figure 31-1). The linea alba is thicker and has greater breaking strength near the umbilicus than in the more cranial parts of the abdomen.[15,17] Fibers of the linea alba run perpendicular to the direction of suture tension and this feature appears to provide for strong closure of the ventral midline incision.[14,15] With a paramedian approach, only the external fascia of the rectus sheath is closed (Figure 31-1). This fascia composes the abdominal tunic and the aponeurosis of the external abdominal oblique, which has fibers interwoven with those of the aponeurosis of the internal abdominal oblique (Figure 31-1). There is no advantage to including the internal sheath (aponeurosis of the transverse abdominal muscle) because its fibers run along the line of suture tension and, therefore, are easily torn. Also, in the dog, inclusion of this layer in closure of paramedian incisions did not provide greater strength of closure than suturing only the external sheath.[18]

Suture Material

The surgeons' preferences will dictate the type of suture used, the method of closure and the number of layers used to close a ventral midline incision. Monofilament or multifilament sutures can be used, and both have advantages and disadvantages. Monofilament suture (polydioxanone and polyglyconate) is generally manufactured by the melt extrusion process that creates an outer core and inner core as the material cools during processing.[14] Therefore, when monofilament suture undergoes rough handling (bending, twisting, crimping), the outer core can be damaged and this decreases the strength of the suture by decreasing its cross-sectional area and by altering its mechanical properties (cross linking of polymers).[14,15] Examples of rough handling are grasping in hemostats or using edges of an instrument to pull up on the suture to tighten a continuous suture line.

Polyglycolic acid or polyglactin-910 are absorbable sutures that have been treated with a lubricant to decrease tissue drag and increase ease of handling, but that have poor knot security.[5] They require at least four to five throws per knot; square knots should be used instead of half hitches to decrease the chances of the knots untying. Rough handling of multifilament suture (polyglactin 910 and polyglycolic acid) can have little effect on its overall strength.[14,15] Multifilament suture does not stretch or elongate as much as monofilament suture, is supple, and has little or no memory, but can harbor bacteria and cause tissue drag. Suture size should be the smallest available to accomplish the task.[14]

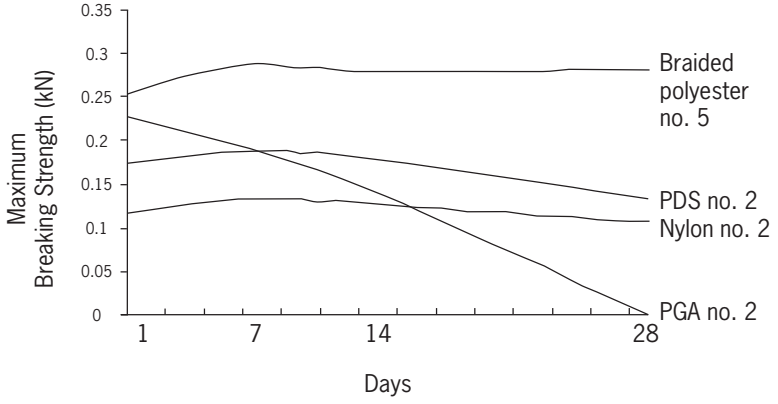
Figure 31-1



Anatomy of equine body wall through ventral median incision. (From Freeman DE, Rotting AK, Inoue O. Abdominal closure and complications. Clinical techniques in equine practice. Gastrointestinal series. 1:174-187, 2002.)

In a study of closure of equine cadaver linea alba, size 5 polyester (nonabsorbable) suture had a greater breaking strength and stiffness than size 2 polyglycolic acid and size 3 polyglactin 910 (both absorbable), followed by size 2 polydioxanone, size 2 polypropylene, and size 1 polyglyconate.[15] Size 2 nylon suture had the lowest breaking strength.[15] In a study on suture material in vitro and after subcutaneous implantation for up to 28 days in horses (Figure 31-2), size 5 braided polyester had the highest maximum breaking strength and polyglycolic acid was significantly stronger than polydioxanone and monofilament nylon.[19] However, polydioxanone had better mechanical performance after 28 days of implantation than did polyglycolic acid.[19] In general, a nonabsorbable material is not recommended because of the risk of suture sinus formation.[20] In addition, currently available absorbable sutures retain their breaking strength for longer than older materials (e.g., chromic gut) and can even prevent herniation in a wound compromised by infection. Therefore, there is no real advantage to using a nonabsorbable material. Suture sinus formation is more likely with multifilament or braided material than with monofilament, largely because the former materials have greater capillarity and are more likely to retain bacteria.[20] However, large monofilament suture, such as polypropylene, has a high memory and, therefore, poor knot security, and requires several throws and a bulky knot.[20] The resulting volume of material, combined with stiffness of this suture, is likely to cause mechanical irritation and lead to suture sinus formation.[20] Unfortunately, no single suture material among those used routinely for closure of the equine linea alba is initially as strong as the normal tissue in which it is placed.[15] In in vitro studies with simple interrupted patterns, the suture materials break before the linea alba tears; the weakest point of the suture is near the knot.[15] Knots are the weakest points of a suture line because they undergo shear stress when loaded, and knot security is inversely proportional to the memory and size of the suture material.[21] At least five to six throws are usually used in equine abdominal closure.

Figure 31-2



Changes in the mechanical properties of suture materials before (day 1) and after in vivo implantation (days 7, 14, and 28) in horses. PDS = polydioxanone; PGA = polyglycolic acid. (From Freeman DE, Rotting AK, Inoue O. Abdominal closure and complications. Clinical techniques in equine practice. Gastrointestinal series. 1:174-187, 2002; and constructed with data from Campbell EJ, Bailey JV. Mechanical properties of suture materials in vitro and after in vivo implantation in horses. Vet Surg 21:355-361, 1992.)

Chromic gut is not recommended for linea alba closure because, in horses and in human beings, it loses strength rapidly and thereby leads to a high rate of dehiscence.[2] Chromic gut is degraded by proteolytic enzymes produced by inflammatory cells. This process is accelerated in an unpredictable fashion by the presence of infection, and the degradation can be complete in 7 days.[5]

Polyglycolic acid or polyglactin-910 sutures degrade by hydrolysis at a rate that is predictable, even in the presence of infection, and these materials induce minimal foreign body reaction.[5] Polyglactin-910 is available in size 3 on a conventional cutting needle. It is the largest absorbable suture material available, an attractive feature when closing linea alba of an adult horse. In a retrospective study in horses, the use of polyglactin-910 sutures had an increased risk of incisional infections when compared with polydioxonone sutures, but the number of incisions closed with polyglactin-910 was small.[10] Presumably, the braided suture entrapped bacteria in its interstices, which favored infection.[10] Incisions in foals, ponies, and American Miniature Horses can be closed with appropriately smaller sized sutures, such as size 1 or 2.

The synthetic nonabsorbable suture materials are very strong and can be coated to improve tissue handling characteristics. Polymerized caprolactam (Vetafil or Braunamid) is a braided multifilament suture ensheathed in polyamide to reduce capillarity.[5] This material was used successfully in clinical cases as a doubled strand after preparation with a coating of bacitracin, neomycin, polymyxin B triple antibiotic ointment, followed by gas sterilization.[22] The polyester sutures consist of Dacron that is uncoated (Mersilene), or coated or impregnated with silicon (Ticron) or polybutylate (Ethibond).[5] The coating substances improve the handling of the suture material but reduce the knot holding ability; therefore, the number of throws per knot should be at least five or six. These suture materials can become a nidus for infection when buried and cause suture abscesses and suture sinuses resulting in recurrent purulent discharge.[5]

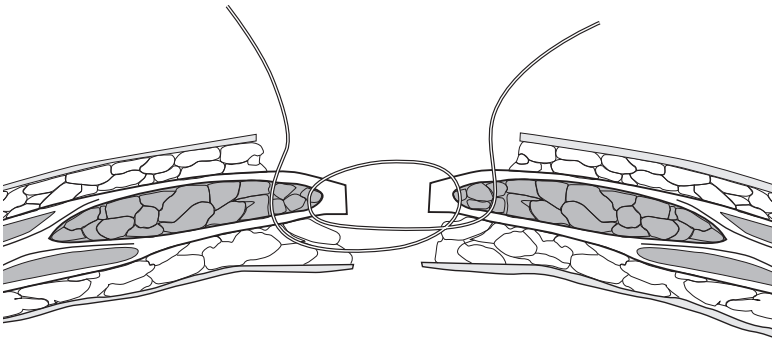
Advantages of monofilament stainless steel suture, such as strength and knot security, would make it suitable for equine linea alba.[23] Simple interrupted or interrupted far-near-near-far sutures can be used and are tied with a square knot that is buried into the external rectus sheath.[23] Because steel does not wick, it is suitable for use in infected areas and for secondary closure of infected incisions;[5,24] however, stainless steel sutures are difficult to handle. Also, metal fatigue can cause the stainless steel sutures to break; it may cause suture sinus tracts many years after original placement of the sutures,[5] and may even cause projection of wire ends through the skin. Suture sinuses necessitate wire removal in approximately 10% of cases.[25]

Suture Patterns

Numerous suture patterns have been used to close the linea alba, including simple continuous,[25,26] simple interrupted, near-far-far-near, far-near-near-far (FNNF; Figure 31-3), cruciate (Figure 31-4), inverted cruciate (figure-of-eight; Figure 31-4), and mattress patterns.[5] A continuous suture pattern allows the biomechanical forces to be more evenly distributed over the entire incision line[27] and is quicker to perform than interrupted patterns.[26,28] In a study on equine cadavers, the simple continuous pattern was significantly stronger than the inverted cruciate pattern,[26] and, in a survival study, there was no difference in clinical appearance, histologic changes, or breaking strength between incisions closed with simple continuous versus simple interrupted patterns.[29] In studies on rats, the continuous suture also had greater wound-bursting pressure than a simple interrupted pattern or a figure-of-eight (inverted cruciate) technique.[27] The continuous pattern also places less suture in the tissues and, therefore, should incite less foreign body reaction and reduce the risk of infection, compared with interrupted patterns. Obviously, breakage of the continuous suture would completely disrupt the closure.

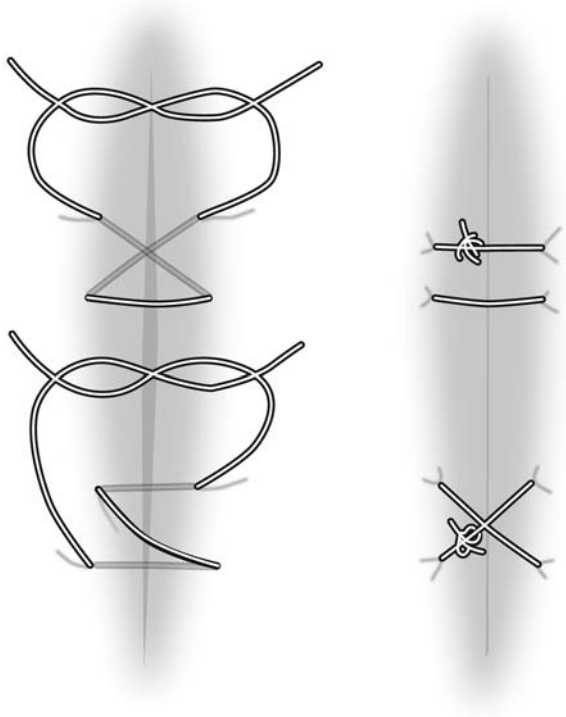
The use of a near-far-far-near pattern to close the linea alba requires more time to place than does a simple continuous suture pattern, but is an excellent pattern where a great deal of tension occurs.[5] In one study, horses closed with the near-far-far-near pattern had a higher rate of purulent incisional drainage.[3] This could be attributed to the increased dead space created by the extent of tissue undermining needed for suture placement,[3] and the greater tissue strangulation and ischemia.

Figure 31-3



Far-near-near-far suture pattern for the linea alba. (From Freeman DE, Rotting AK, Inoue O. Abdominal closure and complications. Clinical techniques in equine practice. Gastrointestinal series. 1:174-187, 2002.)

Figure 31-4



Inverted cruciate, or figure-of-eight (top), and cruciate patterns, placement (left) and on completion (right). The difference is that the crossover point of the sutures is close to the knot in the cruciate pattern, which could stress this vulnerable part of the suture. (From Freeman DE, Rotting AK, Inoue O. Abdominal closure and complications. Clinical techniques in equine practice. Gastrointestinal series. 1:174-187, 2002.)

Techniques and Principles

Good surgical technique, decompression of all distended bowel, and smooth anesthetic recovery can reduce the risk of most complications involving the abdominal incision, although many factors lie outside the surgeon's control. Intraoperative decompression of distended or impacted bowel reduces postoperative strain on a suture line in the linea alba and reduces bowel protrusion into the incision so that closure can be faster. To prevent inadvertent bowel puncture during each bite, the back end of a thumb forceps can be placed under the edge away from the surgeon and be used as a backstop for the needle directed toward it. For the near side, the skin and subcutaneous tissue can be grasped with forceps and elevated to bring the linea edge into view, or the linea itself can be grasped and brought into view. A visceral retainer or "fish" can also be placed to separate bowel from the suture line. Peritoneal fat should not be included in the closure because it interferes with apposition of the linea alba and has no holding strength.

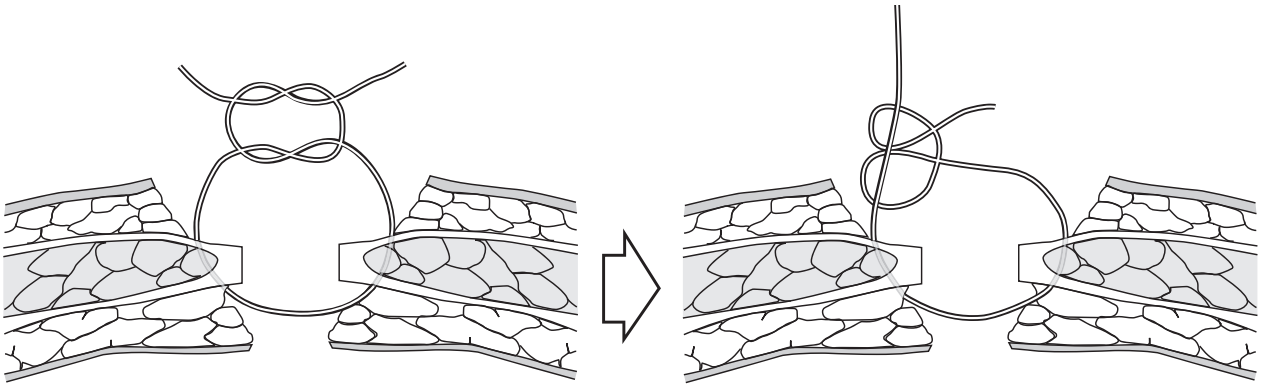
The optimal tissue bite size for linea alba from adult equine cadavers is 15 mm from the edge,[14,15] and sutures are usually placed about that same distance apart. Wider suture bites incorporate the rectus muscle and sheath, increasing the chances for tissue necrosis and tearing. The edges of the incision should be pulled into snug apposition; tissue should not be tied too tightly, because this will strangulate the edges and cause foci of incisional necrosis.[30] Because polyglycolic acid and polyglactin-910 have poor knot security,[5] they require at least five to six throws per knot. In general, knot security is inversely proportional to the memory and size of the suture material.[14,15] Rough handling by pulling up on sutures with instruments or

by clamping knots is more harmful to monofilament than to braided suture, because the outer core of monofilament suture can be damaged and this decreases its cross-sectional area.[14,15] However, clamping the first throw of a square knot made with nylon does not alter load-to-yield and actually increases structural stiffness.[21]

The method of knotting influences the structural properties of suture materials and could be detrimental in knots tied under tension, especially those placed with a surgeon's knot or a sliding half-hitch.[21] The equine linea alba poses a challenge to knot security, because the edges are under some tension and closure requires the use of large synthetic absorbable materials that have poor knot security. One technique to improve knot security is to use one and a half surgeon's knots on the first throw followed by a surgeon's knot on the second, and then a succession of single throws.[31] Square knots should be used instead of half hitches to decrease the chances of the knots untying. Another technique is to place a surgeon's knot and then pull the knot into the subcutaneous tissue as it is being tightened so that it binds in this tissue and cannot slip as the second throw is placed. The author prefers to start with a sliding half hitch that is guided loosely down to the tissue surface and then is tightened to produce a secure purchase before subsequent throws are placed (Figure 31-5).[31] Subsequent throws should be square knots to reduce slippage of the sliding half hitch.

The author prefers to end continuous patterns in the linea alba by having surgeons situated on opposite sides of the horse starting at each end of the incision and meeting in the middle to tie the long ends of the sutures together.[31] Other alternatives are to tie the end to a loop formed from the second to last bite, or to place a simple interrupted suture at the end of the incision and tie the end of the continuous pattern to it.[31] If the incision is so long that several continuous strands are required, the new strand can be started and tied and the previous strand can be tied to its short end.[31]

Figure 31-5



Method of converting a square knot to a sliding half hitch by pulling up on one end of the square knot. (From Freeman DE, Rotting AK, Inoue O. Abdominal closure and complications. Clinical techniques in equine practice. Gastrointestinal series. 1:174-187, 2002.)

Subcutaneous Closure and Skin

The subcutaneous or subcuticular tissues can be closed with a simple continuous pattern in a horizontal mattress fashion, with a small size (2-0 or 3-0) synthetic absorbable material. This closure eliminates dead space, protects sutures in the linea alba and supports skin apposition. The author does not close the subcutaneous tissues in the belief that subcutaneous suture adds foreign material to the wound, serves as a nidus for infection,[32] and retains the infection in the body wall and deeper sutures. This concern is justified by studies in human patients and in laboratory animals that demonstrated greater wound induration and increased infection rates with subcutaneous sutures.[27] In one study on feline linea alba, the lack of a subcutaneous closure reduced incisional inflammation but caused microscopic evidence of seroma formation.[33] In a similar feline study, subcutaneous sutures increased early incisional swelling compared with no subcutaneous suture and did not seem to be essential to healing of the abdominal incision.[34] Without subcutaneous sutures in horses, drainage of an infected incision is easily established, and healing does not seem to be adversely affected based on subjective assessment in clinical cases. One study suggested that a 2-layer closure (i.e., linea alba and skin) results in more incisional edema but less drainage than a 3-layer closure.[35]

The skin can be closed with a variety of materials and patterns with staples, synthetic nonabsorbable or synthetic absorbable material. Staples have the advantage of being quick and easy to use but, like nonabsorbable suture materials, they must be removed. Staple removal can be painful and difficult, even with a special staple remover. The skin can be closed with polyglycolic acid size 2-0 or 3-0 in a simple continuous pattern, so these sutures do not need to be removed, a distinct advantage with a ventral median incision and in horses that are difficult to handle. Despite concerns about leaving sutures in for this duration, there do not seem to be any adverse effects on wound healing and this suture material is usually gone in 3 to 5 weeks. Polydioxanone is not recommended for skin as it takes weeks to months to disappear.

Incisional Dressing

A water-impervious self-adhesive plastic drape (Steri Drape – 3M) may be beneficial in reducing the risks of incisional contamination from dirt and debris in the recovery stall.[6] While the horse is on the surgery table, one or more dry dressings (Telfa pads) are applied to the incision, and the surrounding skin is then sprayed with a medical grade adhesive (Medical Adhesive, Hollister Inc, Libertyville, IL, USA). This improves adhesion of the plastic drape to skin, and the drape (Figure 31-6) can be removed after the horse is able to stand in the recovery stall.[6] Alternatively, a roll of towel or gauze can be applied to the wound and secured in place with temporary horizontal mattress sutures placed in the skin along the edge of the material.[36] Care must be taken with this technique, because the mattress pattern can distract the edges of the skin incision if the suture is tightened sufficiently to draw the skin upward along each horizontal bite.

Figure 31-6



An iodophor-impregnated plastic drape applied to secure dressing to the skin closure for protection against soilage in the recovery stall. This can be removed shortly after recovery from anesthesia.

Recovery Stall

In the horse, the intact linea alba undergoes maximum peak stress, peak strain, and change in strain during anesthetic recovery.[37] Recovery stall conditions, therefore, can contribute considerably to the development of incisional complications. The recovery stall floor should be as clean and dry as possible to prevent awkward falls that stress the incisional closure, and to reduce contamination of the incision when the horse lies in sternal recumbency. Adhesive drapes over the incision during recovery can protect against contamination from the floor of the stall and from sweat and dirt from the horse's body.[38] A tail rope or deep padded foam under the body might help to provide a smooth recovery.

Abdominal Bandages

Abdominal bandages are used according to the surgeon's preference. They can be composed of Army-Navy bandage or similar material retained with brown gauze and Elastikon adhesive bandage material or with commercially available bandages (Figure 31-7) that can be laundered and reused (Equus Therapeutics, Afton, VA or DePuy Inc, Warsaw, IN). Bandages probably provide little support to the abdominal wound and have been shown to exert no significant effect on in vivo strain in the intact linea alba in horses.[37] However, in a preliminary investigation, a belly band did reduce the number and severity of complications in the abdominal incision.[39] Bandages can protect the wound from contamination and trauma, reduce edema,[4-6] and retain prolapsed bowel.[31] They are expensive and require frequent changing. One study has suggested decreased abdominal wound morbidity when abdominal bandages are applied daily. The abdominal bandage can be especially useful to protect the incision in a nursing mare from contamination by the foal and to protect an incision in the horse that has developed laminitis or postanesthetic myopathy and tends to lie down. Abdominal bandages can become a source of contamination, especially if they are wet and remain in place too long.[4,6] Male horses tend to urinate on and in the abdominal bandage.[4] A wet abdominal wrap should be changed every 12 to 24 hours or sooner if is soaked.

Figure 31-7



Commercially available abdominal bandage (Equus Therapeutics, Afton, VA).

Postoperative Care

The goals of most procedures after colic surgery are to facilitate early return of normal gastrointestinal function and to prevent complications related to the gastrointestinal tract. Indirectly, these measures also protect the abdominal incision and facilitate its healing. Postoperative pain should be managed as the individual case dictates, but those horses that are refractory to analgesics and gastric decompression may warrant a second celiotomy. Anything that stresses the repair, such as rectal examinations or any physical activity, should be avoided after surgery.[37]

Potassium penicillin and gentamicin sulfate should be administed IV at 30 minutes or more before induction of anesthesia,[38] although they do not seem to provide adequate prophylaxis against incisional infection. Duration of antibiotic administration after abdominal surgery varies from 1 to 14 days, depending on lesions and the necessary surgical procedures.[8] Procaine penicillin is not recommended because a procaine reaction can cause manic physical activity that will disrupt an abdominal incision. Postoperative rest is critical, such as 2 weeks in a stall, followed by an additional 2 weeks in a stall with handwalking exercise, and 4 weeks in a small paddock before work resumes, provided that incisional healing has been uncomplicated. This program is justified by the finding that incised and sutured linea alba in horses has a tensile strength at 8 weeks comparable to that of nonincised linea alba.[17]

Healing of the Equine Linea Alba

The cranial portion of the equine linea alba may be at higher risk for dehiscence,[25] possibly related to a combination of a thinner linea alba and an abdominal shape that increases visceral load in the cranial abdomen.[17] This is supported by evidence that greater forces are required to disrupt caudal portions of intact linea alba of horses compared with cranial portions.[17] In healing incisions in the horse, location along the linea alba is not significantly related to tensile strength, and the thickness of the healing linea alba is inversely proportional to its breaking strength.[17] This can be attributed to edema and granulation tissue that thicken the tissue equally in the cranial and caudal portions, but do not provide strength.

In a study on healing and tissue strength in equine linea alba, tensile strength of the healing linea alba was significantly less than nonincised linea alba at 2 weeks after surgery.[17] Important changes at this stage are increased tissue thickness from edema and granulation tissue and lack of new collagen formation. The incision is weak at this time and probably derives most of its strength from the sutures.[17]

At 4 weeks after surgery, tensile strength increases significantly compared with that at 2 weeks, most likely from increases in the number and maturation of new collagen fibers.[17] Because the mean tensile strength at 4 weeks is considerably less than at 8 and 16 weeks, and because of immature collagen in the 4-week tissues, an incision may not be stable at 4 weeks. Edema and granulation tissue persist at this time, making the 4-week tissues significantly thicker than nonincised linea alba.[17]

At 8 and 16 weeks after celiotomy, the strength of the equine linea alba is not statistically different from nonincised linea alba.[17] By 8 weeks, the healing linea alba is thinner because edema is reduced and scar tissue is remodeling.[17] Tensile strength is statistically similar to nonincised linea alba, possibly reflecting collagen maturation and less granulation tissue. At 16 and 24 weeks, the healing linea alba becomes progressively thinner and stronger, and at 24 weeks, it is significantly stronger than nonincised linea alba, possibly as a result of scar tissue formation.[17] Tissue thickness exceeds that of nonincised linea alba at 24 weeks.[17]

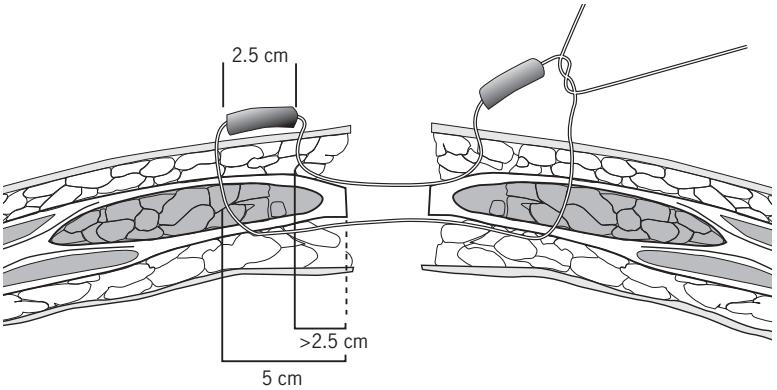
The aforementioned study used a single-cycle load with continuous distraction, which differs from the clinical situation in which strains are cyclic and may be abrupt.[17] Based on the observations of collagen maturation at 8 weeks and a tensile strength comparable to nonincised linea alba at 8 weeks, returning horses to controlled exercise at 60 days postoperatively is justified.[17]

Peritoneal healing can resolve defects in 6 to 8 days by a combination of fibroplasia and connective tissue repair in subperitoneal tissues.[40] Mesothelial cells on the margin of the wound transform into fibroblasts that lay down new connective tissue, and fibroblasts that line up on the surface transform into a new mesothelial membrane.[40]

Special Circumstances

In large breed horses (>700 kg), mares in advanced pregnancy, or horses that have undergone a second exploratory operation through a recent incision, the risk of postoperative dehiscence in the recovery stall appears to be considerable. In these cases, 3 to 5 retention sutures can be placed to give additional support to the ventral median incision during recovery and the immediate postoperative period (Figure 31-8).[31] These are vertical mattress sutures with doubled #2 nylon placed through polypropylene bolsters (see secondary closure further on). The far bites are placed through all layers at least 5 cm from the edge, and close bites are placed 2.5 cm from the skin edge and only through the skin and subcutaneous tissues. These sutures are placed at 8- to 10-cm intervals along the incision, and should be inserted using a large curved needle immediately ahead of the continuous pattern in the linea. In this way, deep insertion of the needle can be guided and the risk of inadvertent penetration of an existing suture strand or bowel is avoided. Because these sutures can induce incisional infection, they should be removed in less than 7 days, unless integrity of the incision is suspect. It is not necessary to reinforce continuous suture patterns with interrupted patterns in most horses, and this procedure also carries the risk of suture laceration or bowel puncture if placed after the continuous pattern has passed through that section of body wall.
A repeat celiotomy is required in 14.7% to 28% of horses that have colic surgery, mostly after correction of small-intestinal lesions.[41] In a study of small-intestinal surgeries in one clinic, infection of the abdominal incision was recorded in 7.4% of horses that had one surgery and in 56% that had more than one surgery through the same ventral median approach.[41] This is similar to the overall infection rate of 28% reported after colic surgery, but with a 67% wound complication rate after a repeat celiotomy.[42] Incisional infection after repeat celiotomies is probably caused by transfer of bacteria from the raw edges and diminished resistance in the friable and edematous linea alba. A separate paramedian approach could be used instead, although there is concern that the second incision parallel to the first could create an ischemic section of body wall between the two incisions. If the same ventral median incision is used, it could be closed with a simple continuous suture pattern using size 3 polyglactin[910], bolstered with vertical mattress sutures of doubled size 2 nylon placed through 2.5-cm segments of plastic or hard rubber tubing. Another alternative is to use secondary closure, especially if the surgeon is concerned about viability and integrity of the incision edges.[24]

Figure 31-8



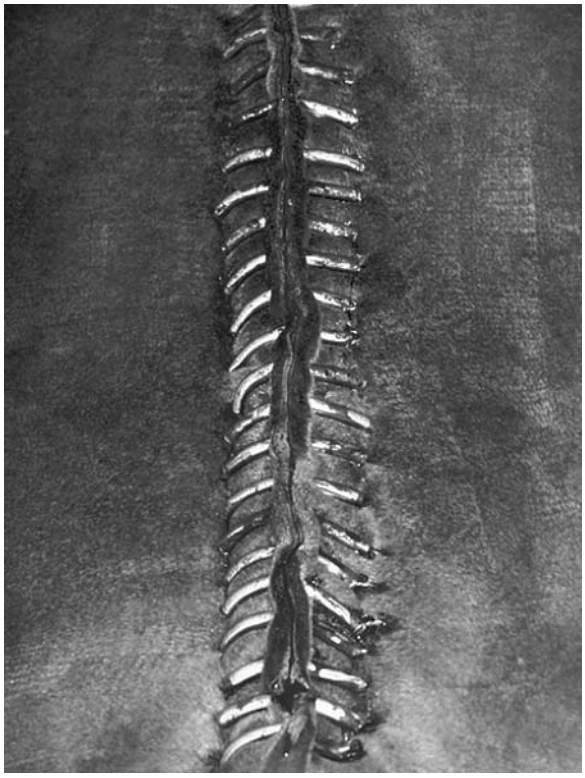
Method of suture placement for a secondary closure. (From Freeman DE, Rotting AK, Inoue O. Abdominal closure and complications. Clinical techniques in equine practice. Gastrointestinal series. 1:174-187, 2002.)

Secondary Closure

Secondary closure of the linea alba can be used to repair infected abdominal wounds with impending dehiscence, dehisced wounds, or to correct infected hernias.[24] All existing suture is removed and the tissue edges debrided by sharp dissection and abrasion with a saline-soaked sponge. Retention sutures of 18-gauge stainless steel wire are preplaced in a vertical mattress fashion with a large cutting needle or by threading the wire through a 14-gauge needle so that each suture spans a bite 5 cm from the skin edge through the full thickness of the body wall (excluding retroperitoneal fat) and then passed through skin and subcutis at 2 to 2.5 cm from the skin edge (Figures 31-8 and 31-9). To protect the skin, the wire is passed through hard and thick-walled plastic or rubber tubing (stomach tube or thick suction tube) cut to a length of 2.5 cm, and the suture knot is placed at the end of the tubing furthest from the incision (Figure 31-10), where it can be subsequently located for removal. Silicone rubber or fine plastic tubing should not be used, because these will allow premature recession of the wire into the skin and rapid loss of tension. The retention sutures are spaced 2.5 cm apart and then the ends are twisted down securely to produce eversion of skin and subcutis for ventral drainage (Figure 31-10). A commercially available wire tightener that is used in aviation construction provides the most secure and consistent twist on the wire ends. It is essential that, as the wires are tightened, all the slack is taken out of the deep component so it cannot form a loop to ensnare small intestine. Once the twist is secure, the wire is cut to leave 1 to 1.5 cm of the twist, which is then coiled so the sharp ends turn into the tubing.

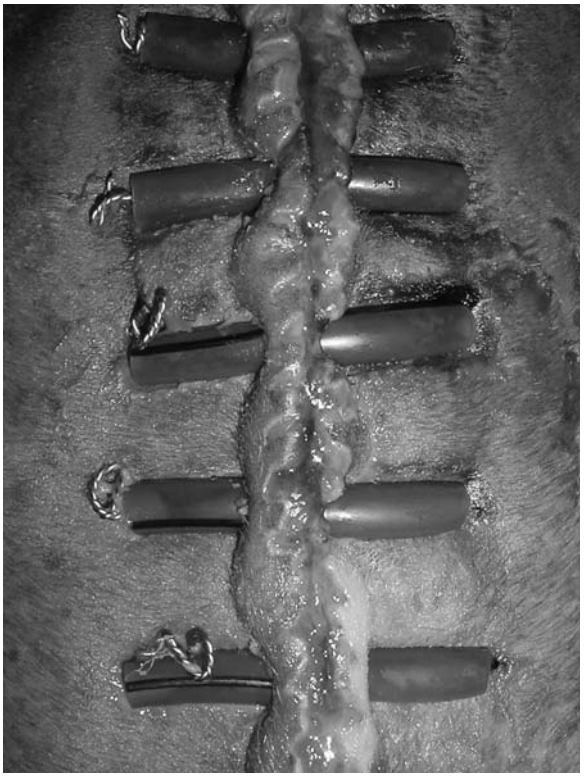
The sutures and bolsters should be removed in approximately 3 to 5 weeks, by which time most sutures are loose and no longer effective. Removal can be staged so that some sutures that appear functional are left in place as long as possible. Ultrasound can aid in the location of bolsters as some can become embedded in granulation tissue and may not be visible. The tissue reaction around the tubing usually resolves after its removal and following local wound care.[24] Although this procedure exposes infected tissue to the abdominal cavity, peritonitis does not ensue.

Figure 31-9



Secondary closure with wire and thick-walled tubing for bolsters in a draft horse that had incisional dehiscence 5 days after surgery for a displaced colon. Sutures are spaced 2.5 cm apart.

Figure 31-10



Closer view of a secondary closure with wire and thick-walled plastic tubing. Note eversion of skin and subcutis and method for securing the wire ends by twisting. Sutures are spaced 2.5 cm apart.

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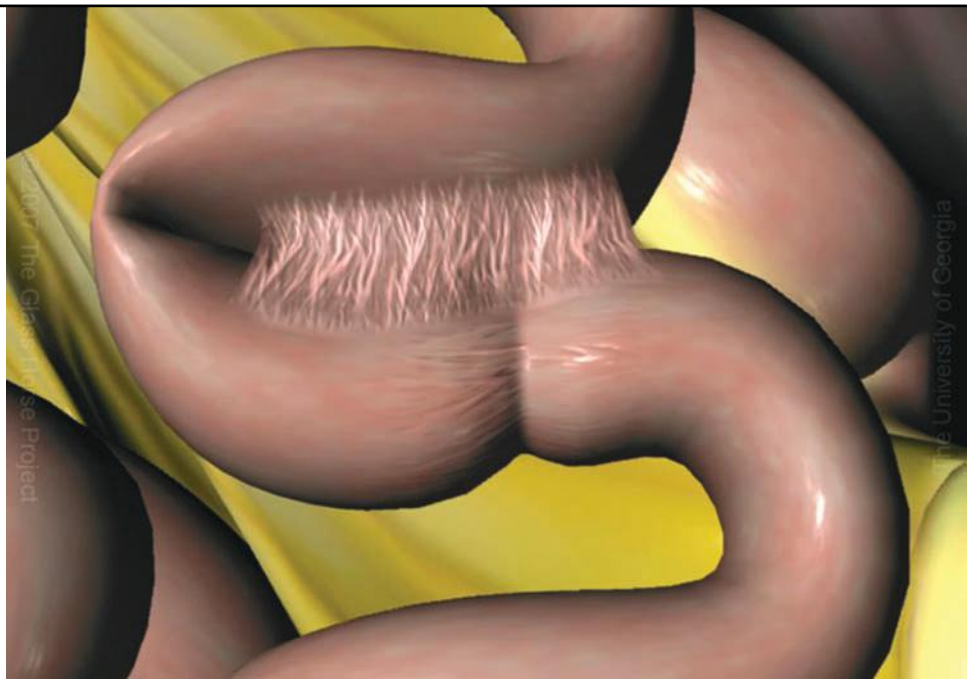
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Intensive Care and Postoperative Care

Part 10



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Monitoring Treatment for Abdominal Disease

Chapter 32

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Thomas J. Divers

Monitoring treatment is an essential part of the overall management of horses affected by a wide variety of abdominal conditions. Careful monitoring of gastrointestinal function is important so that the response to therapy can be assessed, and any derangements or deteriorations of gastrointestinal function can be identified and supportive therapy instituted rapidly. The critically ill patient may develop abnormalities and dysfunction of many organ systems in addition to the system affected by the primary disease. The result can be multiorgan dysfunction, and ultimately multiorgan failure, which is invariably fatal. It is important, therefore, that monitoring allow assessment of the function of all major organ systems and not just gastrointestinal function. This monitoring includes repeated physical examinations, monitoring of temperature, pulse and respiratory rates, and assessment of clinical pathologic data.

Frequency of Examinations

The frequency of examinations is dependant on the condition of the horse and the underlying lesions. Thus, seriously ill horses need continuous supervision and frequent (at least hourly) re-examinations, whereas less critically ill horses require less frequent re-examinations. Suggested protocols for the monitoring of horses with different gastrointestinal diseases are summarized in Table 32-1. It should be recognised, however, that these are guidelines only, and the precise monitoring protocol must be tailored to the individual needs of the patient.

Physical Examinations

Horses receiving intravenous fluid therapy (which includes most horses with significant bowel damage such as strangulating and ischemic lesions, colitis/enteritis, etc.) should be examined hourly, and their hydration status evaluated by measuring PCV and total protein (TP) concentration at least every 6 hours. Horses with less serious gastrointestinal diseases are generally examined every 3 to 4 hours until the condition has stabilzsed or is improving. Keeping a flow chart to record the different physical examination values as well as noting treatments and fluid therapy can help to identify trends in the patient's condition and is recommended for critical care (Table 32-2).

These examinations should include assessments of the following:

- Degree of pain
- Cardiovascular status (heart rate, mucous membrane colour, capillary refill time, etc.)
- Rectal temperature
- Respiratory rate
- Gastrointestinal function (fecal production, intestinal sounds)
- Appetite
- Urine production
- Assessment of the feet for evidence of laminitis (pain, warmth, increased digital pulses)
- Assessment of intravenous catheter sites for evidence of thrombophlebitis (heat, swelling, pain, distention of the vein)
- Assessment of the wound in horses that have undergone surgery
- Abdominal shape and "pings"

Pain

Analgesic therapy is considered necessary in all horses in the immediate postoperative period. Postoperative pain may originate from peritoneal inflammation, the abdominal incision, or intestinal distention or ischemia. Pain relief should be provided without impeding gastrointestinal motility or masking any deterioration of the horse's condition that might require another type of treatment (e.g., re-laparotomy). Flunixin meglumine is the most commonly administered analgesic drug for the first 24 hours after surgery, being effective in controlling pain as well as combating some of the effects of endotoxemia. Thereafter, analgesic drugs are used as necessary. "Low-dose" flunixin meglumine (0.25 to 0.5 mg/kg) is commonly used for several days after colic surgery. This dose has been shown to counteract the cardiovascular effects of endotoxemia,[1] and is less likely to mask a clinical deterioration in the horse's condition. Most horses show an immediate cessation of abdominal pain after colic surgery. However, a small number may demonstrate bouts of low-grade pain within the first few days after surgery, and if there is no improvement after gastric decompression, these horses may require further analgesic therapy. Recurrence of significant signs of colic within 24 to 48 hours of surgery is not usual, and may be an indication to consider an early re-laparotomy. Horses with postoperative ileus may also demonstrate pain because of gastrointestinal distention. This pain usually abates after nasogastric intubation and gastric decompression. A full description of the different analgesic drugs is given elsewhere (see Chapter 16).

Lidocaine (lignocaine) is administered intravenously by some clinicians as a treatment for postoperative ilieus.[2] Lidocaine is also effective in treating visceral pain, and has synergistic effects with other analgesic drugs. Its use allows the dose of other analgesics to be reduced (see Chapter 7).

Table 32-1

Guidelines for Monitoring Intensive Treatment of Horses with Gastrointestinal Diseases*

Condition	Common complications	Frequency of physical examinations	Check Gastric Reflux	PCV/TP	Full hematology	Electrolytes and urea/creatinine
Postoperative simple obstruction of small intestine	Ileus	every 1 hour while on I.V. fluids	every 4 hours or if painful or if increase in heart rate	every 6 hours until no gastric reflux	every 24 hours	every 12 hours until no reflux
Postoperative simple obstruction of large intestine	Diarrhea	every 3-4 hours	Not routinely necessary	every 24 hours	every 24 hours or if febrile or diarrheic	every 24 hours
Postoperative strangulating obstruction of small intestine	Ileus Endotoxemia Adhesions Thrombophlebitis Laminitis	every 1 hour while on I.V. fluids	every 4 hours or if painful or if increase in heart rate	every 6 hours until no gastric reflux	every 24 hours	every 12 hours until no reflux
Postoperative strangulating obstruction of large intestine	Endotoxemia Hypoproteinemia Diarrhea Laminitis	every 1 hour while on I.V. fluids	Not routinely necessary unless evidence of ileus	every 6 hours	every 24 hours or if febrile or diarrheic	every 12 hours
Postoperative simple obstruction of small colon	Small colon impaction Diarrhea	every 3-4 hours	Not routinely necessary	every 24 hours	every 24 hours or if febrile or diarrheic	every 24 hours
Postoperative strangulating obstruction of small colon	Endotoxemia Adhesions	every 1 hour while on I.V. fluids	every 4 hours or if painful or if increase in heart rate	every 6 hours	every 24 hours	every 12 hours
Small colon impaction	Small colon impaction Diarrhea Salmonellosis	every 3-4 hours	Not routinely necessary	every 24 hours	every 24 hours or if febrile or diarrheic	every 24 hours
Large intestinal impaction	Diarrhea	every 3-4 hours	Not routinely necessary	every 24 hours	every 24 hours	every 24 hours
Anterior enteritis	Ileus Laminitis Renal failure	every 1 hour while on I.V. fluids	every 4 hours or if painful or if increase in heart rate	every 6 hours until no gastric reflux	every 24 hours	every 12 hours until no reflux
Acute colitis	Endotoxemia Laminitis Thrombophlebitis Acute renal failure	every 1 hour while on I.V. fluids	Not routinely necessary	every 6 hours	every 24 hours	every 12 hours

*Other monitoring, e.g., Blood pressure, CVP, abdominal pressure etc. may be required in some cases.

Table 32-2

An example of an Intensive Care Flow Sheet, which can be used to record vital signs and administration of treatments over 12 hours. The sheet can be double sided to collect information over 24 hours. This type of sheet helps to identify trends in the horse's response to help identify complications.

Intensive Care Flow Sheet

Date:_____ Case Number:_____ Owner:_____ Horse Name:_____

Time AM/PM	1:00	2:00	3:00	4:00	5:00	6:00	7:00	8:00	9:00	10:00	11:00	12:00
Attitude												
Appetite												
Temperature												
Heart rate												
Respiratory rate												
Mucous membrane color/Refill												
Intestinal motility												
Digital pulse												
Feces/Urine												
PCV/ TP												
Urine S.G.												
Gastric reflux volume												
Fluid therapy rate												
Total fluids administered												
Medications												
Initials												

Cardiovascular status

Monitoring of the patient's cardiovascular status (based on physical examinations coupled with clinical pathologic monitoring) is important to identify ongoing fluid and electrolyte losses and acid-base disturbances. These examinations are used to determine and monitor the type and rate of intravenous fluid therapy. Deteriorating cardiovascular status despite adequate fluid therapy may suggest on-going intestinal damage, ileus, or "third space" fluid loss, and may, in some circumstances and in combination with other signs, be an indication to consider an early re-laparotomy.

Horses are usually mildly to moderately tachycardic (heart rate 50 to 70 bpm) for the first 12 to 24 hours after colic surgery;[3] but heart rate usually decreases rapidly to normal values thereafter. Severe or prolonged tachycardia (more than 80 to 90 bpm for longer than 24 hours) generally indicates a poor prognosis. The mucous membranes may be initially bright red after surgery, but should improve during the first 24 hours. The mucous membranes should be moist and the capillary refill time should be less than 2 seconds in an adequately hydrated horse. Additional monitoring of the cardiovascular system could include central venous pressure (CVP), arterial pressure, and blood lactate concentration.

Fever

Postoperative fever is common within the first 24 hours of surgery, but usually resolves thereafter. A persistent fever is abnormal, and could indicate the development of peritonitis, ischemic intestine, impending colitis, septic thrombophlebitis, wound infection, or pneumonia. Fever may also occur as a result of endotoxemia. Horses with persistent fevers should be thoroughly examined to determine the cause of the fever.

Septic peritonitis is an uncommon complication of colic surgery. Clinical signs include depression, fever, low-grade abdominal pain, anorexia, and ileus. These signs are not unique for peritonitis, and can occur in horses with other gastrointestinal problems, including enterocolitis, endotoxemia, and ileus. Recognition of these signs in the postoperative period, therefore, should initiate a full clinical and laboratory evaluation so that the precise cause can be identified. Septic peritonitis in the postoperative period may develop as a result of devitalized intestine or leakage from a previous anastomosis, and surgical exploration may be necessary. Abdominal ultrasonography may be helpful in establishing a diagnosis of septic peritonitis. Peritoneal effusion and thickening of the intestinal walls (>0.2 cm) are characteristic of peritonitis. Peritoneal fluid changes are expected in all horses after abdominal surgery, and persist for at least 7 days.[4] Such changes include increased total nucleated cell counts and increased total protein concentrations; these features cannot, therefore, be used to diagnose septic peritonitis in the postoperative situation. The diagnosis should be based on the cytologic appearance of peritoneal fluid, including the identification of toxic and degenerate neutrophils, and intra- or extracellular bacteria. Serum-to-peritoneal-fluid glucose concentration differences of more than 50 mg/dL (>2.8 mmol/L), peritoneal fluid pH of less than 7.3, glucose concentration less than 30 mg/dL (<1.7 mmol/L) and fibrinogen concentration greater than 200 mg/dL (>2g/L) are indicative of septic peritonitis.[5]

Respiratory Rate

The respiratory rate is variable in horses after colic surgery. Increased respiratory rate may indicate pain (including abdominal pain and laminitis), acidosis, or secondary respiratory tract complications (such as pleuropneumonia).

Gastrointestinal Function

Gastrointestinal function is assessed by monitoring bowel sounds and fecal production. In many horses after colic surgery, gastrointestinal sounds are reduced initially, but return during the first 24 hours. In most cases, the return of normal gastrointestinal function is accompanied by resolution of abdominal pain, normalization of the cardiovascular status, cessation of gastric reflux, and return of normal defecation patterns. Prolonged absence of gastrointestinal sounds in combination with signs of abdominal pain, and possibly evidence of abdominal distention are poor prognostic signs. A normal 500-kg horse passes approximately 5 to 7 piles of feces per day (depending on the type and amount of food, and the time since surgery). Any sudden change in the amount of feces being produced, or the nature of the feces (e.g.,development of soft feces or diarrhea) may indicate a deterioration of gastrointestinal function. Horses affected by small-intestinal diseases are at particular risk for developing postoperative ileus, whereas diarrhea is more commonly seen in horses with large intestinal lesions.

Adynamic ileus is defined as a functional obstruction of aboral transit of gastrointestinal contents, and is an important problem in horses after colic surgery. Adynamic ileus can also occur in horses with other, nonsurgical, diseases of the gastrointestinal tract, including enteritis, colitis, and peritonitis. Although ileus occurs most commonly in horses after surgery involving the small intestine, it can also occur after surgery for other lesions, such as large-colon volvulus.[6] Postoperative

ileus is serious, and is associated with 40% of postoperative deaths in horses with abdominal crisis. The disruption of the normal propulsive motility results in sequestration of fluid and ingesta in the segment of the intestinal tract that is dysfunctional and in the intestine orad to this area. This process occurs most commonly in the small intestine and stomach, but can also occur in the large intestine, especially with severe damage to the large intestinal wall associated with colonic volvulus and colitis, resulting in severe endotoxemia. The signs of ileus relate to the accumulation of gas and fluid within the gastrointestinal tract. Affected horses become depressed, anorexic, and show signs of increasing abdominal pain. Borborygmi are reduced or absent, and abdominal distention may be present. The sequestration of fluid within the intestinal tract results in deterioration of cardiovascular function, with an increasing heart rate, discolored mucous membranes and prolonged capillary refill time. PCV and TP increase as a result of hemoconcentration. All of these signs should alert the clinician to the possibility of the development of postoperative ileus. Nasogastric intubation and gastric decompression should be performed every 2 to 4 hours if more than 2 liters of nasogastric reflux are retrieved with the nasogastric tube. As the amount of reflux decreases, the frequency of nasogastric intubation can be reduced. In most horses, the volume of gastric reflux gradually decreases as normal gastrointestinal motility returns. In some horses, however, an initial reduction in the volume of reflux is followed by a sudden increase in reflux that is then followed by a decrease again.[7]

Information about gastrointestinal function can also be gained by repeated diagnostic ultrasound examinations. Transabdominal ultrasound can be used to monitor distention, wall thickness, and contractility of the intestines, as well as the volume of peritoneal fluid. Small intestine is normally identified in the caudoventral and cranioventral abdomen. In the normal horse, small intestinal loops measure 1.8 ± 0.8 cm in diameter, with a wall thickness of 0.16 ± 0.05 cm, and contract 6 to 15 times per minute.[7] The position, degree of distention, and contents of the stomach can also be assessed by abdominal ultrasonography. This examination should be performed before nasogastric intubation because the latter may introduce air into the stomach that alters its position and causes distention. In the normal horse, the stomach can be viewed in the left cranial abdomen, between the 9th and 12th ribs.[8] The gastric wall is thick (0.75 cm) and a bright gas echo is usually seen within the lumen of the stomach. If the stomach is identified beyond the 12th intercostal space or if it is distended by fluid contents, then gastric decompression should be performed.

Motility problems affecting the cecum or large colon can arise after strangulating obstructions (such as colonic volvulus) or secondary to colonic impaction. Gas distention of the cecum and large colon is diagnosed by auscultation and percussion of the abdomen, and rectal palpation. Abdominal ultrasound examinations are less helpful than with small intestinal distention. If the horse is in pain as a result of large-bowel tympany, then percutaneous decompression may be attempted if a gas cap can be identified in the paralumbar fossa (usually on the right side). After clipping and aseptic preparation of the skin in the paralumbar fossa, a bleb of local anaesthetic solution is injected subcutaneously. A 14-gauge intravenous catheter is then advanced through the skin and body wall, and into the gas-distended viscus (see Chapter 16). Once the gas has been removed, the catheter is withdrawn (3 to 5 mL of antibiotic solution, such as gentamicin, or sterile saline should be injected as the catheter is withdrawn). This procedure carries a risk of inducing septic peritonitis or abdominal wall abscess, and should only be performed if deemed essential.

Monitoring gastrointestinal function is important in helping to determine when feeding can be safely resumed after surgery. In horses affected by ileus, feeding can usually be resumed safely when the horse has become pain-free with normal cardiovascular parameters and has not refluxed for 12 hours. In most cases, water is offered first, followed by small amounts of wet hay or grass. In horses with large-intestinal disorders and in those with small-intestinal disease not complicated by ileus, food can generally be offered by 8 hours after surgery. Some clinicians advocate even earlier feeding in the belief that food is the most effective stimulator for normal gastrointestinal motility and function. However, feeding is best delayed in horses after surgery for large-colon volvulus until evidence exists of mucosal integrity.

Gastrointestinal function must be carefully monitored in horses after treatment for intestinal impactions (including ileal, cecal, large-colon, and small-colon impactions) as horses with these diseases are at risk of reimpaction after the reintroduction of food. Colonic impaction may also occur in horses recovering from other gastrointestinal problems when feeding is reintroduced or when intravenous fluids are discontinued. These impactions frequently are easily resolved by administering water, electrolytes, and mineral oil by nasogastric tube. The horse can also be stimulated to drink more by giving sodium chloride or potassium chloride (30 to 60 grams) orally. Cecal impactions are less common, but often are more serious than large-colon impactions. Development of such impactions may occur in any horse after general anaesthesia and surgery. Use of α-2 adrenergic drugs may also disrupt normal cecal motility patterns and predispose to impaction.[9] Clinical signs of cecal impaction include reduced fecal production, decreased appetite, depression, and mild abdominal pain. These signs may be particularly mild if the horse is being treated with nonsteroidal anti-inflammatory drugs. The diagnosis is confirmed by rectal

palpation, when a large, firm viscus is palpated from the middle to the right side of the abdomen, with a taut ventral cecal band. The most dorsal part of the impacted cecal base cannot be felt because it is attached to the dorsal body wall and out of reach. Monitoring the size and consistency of the cecal impaction is important because cecal rupture can occur if the condition does not resolve. Treatment of affected horses with oral and intravenous fluid therapy, laxatives, and prokinetic drugs is often successful; however, if the impaction fails to resolve with this treatment, or if the clinical signs worsen, then surgical treatment should be considered (see Chapter 37).[9]

All horses undergoing intensive therapy for gastrointestinal disease are at risk of developing diarrhea. Specific risk factors include antimicrobial drug administration, gastrointestinal surgery, anorexia, ileus, oral fluid and laxative therapy, and being housed in the intensive care unit.[10] Important infectious agents associated with diarrhea in horses with abdominal disease include *Salmonella* spp, *Clostridium difficile*, and *Clostridium perfringens*. Identification of these agents is important in view of the possibility of spread to other susceptible horses in the hospital. All horses that develop diarrhea should be managed with elevated awareness of possible infectious colitis, and those with associated pyrexia and neutropenia should be isolated pending microbiologic testing. Noninfectious causes of diarrhea, including resolution of pelvic flexure impaction, can be difficult to differentiate from the early stages of infectious causes. Since more than 40% of horses with gastrointestinal disease test positive for *Salmonella* species based on polymerase chain reaction testing,[11] routine daily fecal cultures (for a minimum of 5 days) is recommended for all horses in the intensive care unit.[7] Routine infection control measures (e.g.,use of disposable shoe covers, gowns, and gloves for each stall, regular disinfection of equipment and facilities, and individual equipment for each horse) should be used to limit the spread of infectious agents before they become clinically apparent.

Horses undergoing intensive therapy are also at risk of developing gastric ulceration. Risk factors include starvation, nonsteroidal anti-inflammatory drug therapy, hypovolemia, and stress. Clinical signs of gastric ulceration may include inappetence, depression, mild abdominal pain, bruxism, and ptyalism. These signs are not pathognomonic for gastric ulceration, and can be seen with many other gastrointestinal diseases. The diagnosis is achieved by gastroscopy. This technique and the treatment of gastric ulcers are described in Chapters 5 and 15.

Urine Production

A normal 500-kg horse will produce approximately 6 liters of urine per day. If the horse is receiving replacement fluids intravenously, the urine output is expected to be higher. Decreased or absent urine production should be immediately investigated. Potential causes include hypovolemia, “third space” fluid loss, and acute renal failure. Urine specific gravity should also be evaluated. Increases in urine concentration indicate dehydration or poor renal perfusion even when fluid is being administered intravenously.

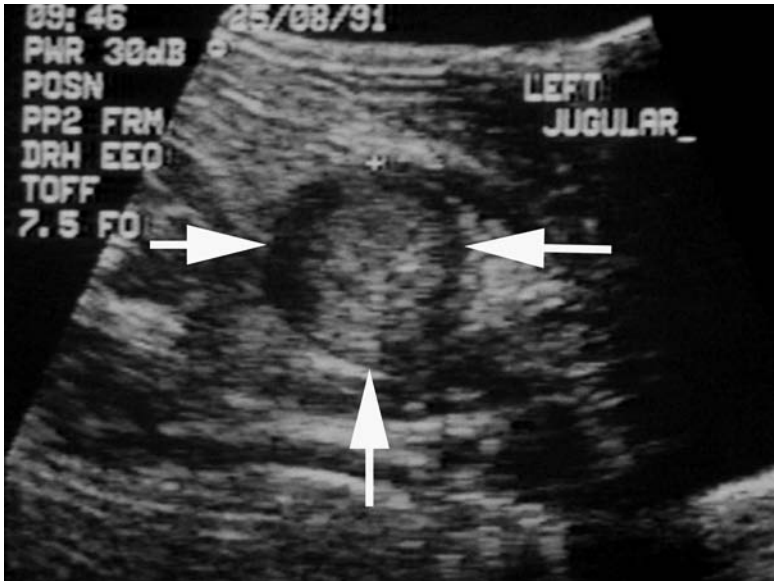
Laminitis

Laminitis is a potential complication for all horses with intestinal disease, especially those with concomitant endotoxemia. Horses that have had significant bowel wall damage should be carefully monitored for signs of laminitis. Because many of the treatments for laminitis are most effective when used as prophylactic therapies, some clinicians advocate their use on horses at particular risk of laminitis rather than waiting for the development of clinical signs.[6] Such therapies include sole and frog supports, acepromazine, topical nitroglycerine vasodilator creams, and maintaining foot temperature at 4 degrees centigrade. Treatments for endotoxemia should also be used to try to prevent laminitis (see Chapter 44).

Thrombophlebitis

Horses with endotoxemia, diarrhea, fever, and generalized debility are predisposed to thrombophlebitis, particularly if catheterization is prolonged.[12,13] The catheter site should be regularly checked for evidence of heat, swelling, pain, or drainage. Use of ultrasound is helpful in detecting thrombus formation as well as gas within thrombi resulting from bacterial gas production (Figure 32-1).

Figure 32-1



Sonogram of jugular venous thrombosis (arrows) at the site of previous jugular vein catheter placement. The vein is obstructed by the thrombus and patency can be monitored with sequential ultrasound examinations.

Monitoring Clinical Pathology Parameters

Regular monitoring of certain clinical pathology parameters is necessary to assess both cardiovascular and renal function and to identify electrolyte and acid-base derangements. Monitoring should include the following:

- Packed cell volume (PCV) and total plasma protein concentration (TP); if synthetic colloid therapy is used, measurement of plasma osmolality can be helpful in directing fluid therapy
- Urea and creatinine concentrations
- Sodium, potassium, chloride, calcium, and magnesium concentrations
- Acid-base status and blood gas analyses

Fluid Balance

Most horses affected by serious gastrointestinal disease develop varying degrees of hypovolemia and dehydration. Careful monitoring of PCV and TP is essential (along with other measurements of hydration and circulatory status) during intensive therapy (see Chapter 17). The rate of fluid administration may require modification depending on the results of this monitoring. In most cases, reasonable indicators of successful cardiovascular support include maintaining the heart rate at less than 80 bpm, PCV less than 50%, and TP greater than 4.5 g/dL (45 g/L).[6]

Continued fluid losses occur in horses with ileus (becauseof loss in gastric reflux and sequestration into the intestine) and horses with diarrhea. In addition, "third space" loss of fluid can occur as a result of endotoxemia. In these horses, increased capillary permeability results in loss of fluid and protein into the interstitium. As a result, it can be difficult to maintain the plasma volume despite fluid therapy because of decreased plasma oncotic pressure (due to plasma protein loss) and fluid sequestration in the tissues. The PCV may continue to increase and the TP continue to decrease despite fluid therapy. In most cases, maintaining the PCV at less than 50% and the TP greater than 4.5 g/dL (45 g/L) is adequate to sustain effective cardiac output. These parameters should be measured every 6 hours in critically ill horses, and the rate of fluid administration altered accordingly. If the TP decreases to less than 4.1 g/dL (41 g/L) (corresponding to a decrease in plasma oncotic pressure to less than 12 mm Hg),[14] colloid administration is likely to be beneficial in order to increase plasma oncotic pressure and allow continued fluid administration without causing severe edema. Commonly available colloids for use in horses include equine plasma, 25% human albumin, dextrans, and hydroxyethyl starch (see Chapter 17). Plasma has several advantages over synthetic colloids in that it not only provides oncotic support (through albumin), but it also provides coagulation factors and antithrombin III. Frozen plasma should be thawed slowly at 37°C, and then administered immediately. It should be administered slowly using an in-line filter. The volume of plasma to be administered can be estimated from the following formula:

$$\text{Volume} = (PP_g - PP_r)\,(0.05\ BW) / PP_d$$

where PP_g is the goal plasma protein concentration,
PP_r is the plasma protein concentration of the recipient,
and PP_d is the plasma protein concentration of the donor.

Although this may underestimate the actual end measurement, in most cases, a volume of 4 mL/kg is a standard initial treatment.

When synthetic colloids are administered, a colloid osmometer should be used, if available, to monitor the therapy. The objective is to maintain the plasma oncotic pressure above 12 mm Hg. If an osmometer is unavailable, clinical parameters such as a decrease in edema and PCV can be used to assess the efficacy of therapy. Dextran-40 (molecular weight 40,000) and Dextran-70 (molecular weight 70,000) are available as 6% solutions, and are generally administered at rates of 4 mL/kg over 15 to 20 minutes. Solutions containing hydroxyethyl starch are available as either hetastarch or pentastarch. Pentastarch is more rapidly degraded than hetastarch (half-life 2.5 hours compared with 25 hours).[15] Hetastarch infusion (10 mL/kg) to clinically normal ponies has been shown to significantly increase plasma colloid oncotic pressure for 120 hours.[16] Hetastarch exerts a dose-dependent effect on hemostasis, which may be significant at doses exceeding 20 mL/kg. Recently, 25% human albumin has been safely given to horses, and this product has the highest oncotic value of available colloids.

Renal Function

Horses with abdominal disease may develop acute renal failure as a result of vasomotor nephropathy, which arises as a result of sepsis, systemic inflammatory response syndrome, and/or hypotension.[17] The renal disease occurs as a result of intravascular depletion, coagulopathies, poor vasomotor tone, and capillary leak syndrome, all of which affect renal perfusion and intrarenal vasoconstrictor-vasodilator forces.[18] Monitoring renal function by urine production and serum concentrations of urea, creatinine, and electrolytes is important to identify early stages of acute renal failure. Increasing the intravenous fluid administration rate will frequently be successful in restoring normal renal function if such changes are identified early. Urinalysis should be performed in horses with persistently high creatinine concentrations. If the horse has increased creatinine concentrations with oliguria or anuria, diuretic therapy (furosemide 1 to 2 mg/kg every 2 hours, or dopamine 3 to 7 μg/kg/min) can be instituted in hope of improving urine production. If aminoglycosides are being administered, the measurement of peak and trough levels can help insure that adequate yet nontoxic amounts are being administered.

Electrolyte Balance

Electrolyte abnormalities, especially hypocalcemia, hypokalemia, and hypomagnesemia can develop in postoperative patients.[6] If possible, it is more informative to monitor the ionized calcium concentration rather than total calcium concentration. Total calcium concentration can be affected by a variety of other factors, and, therefore, can be misleading. For example, total calcium concentration is usually low if the total plasma protein concentration is low, but the ionized calcium may be normal. Alternatively, total calcium concentration may be normal yet ionized calcium may be abnormally low if the horse is alkalotic. Hypocalcemia may develop as a result of lack of dietary calcium intake, diuresis, endotoxemia, and acid-base disorders. Calcium is essential for intestinal motility, and hypocalcemia may contribute to ileus. Low serum ionized calcium concentrations are common in horses after colic surgery, and such horses will benefit from having calcium added to the intravenous fluids (50 to 100 mL of 23% calcium gluconate added to every 5 liters of fluid).[19,20] However, excessive or rapid calcium administration should be avoided as this may exacerbate cellular death associated with reperfusion injury.

Hypokalemia is common in horses after colic surgery and horses with diarrhea. Hypokalemia can develop as a result of lack of dietary potassium intake, diuresis, and gastrointestinal loss. Horses with metabolic acidosis can become hyperkalemic as a result of the exchange of intracellular hydrogen and potassium ions. Excessive potassium excretion may occur after correction of acidosis. Most of the total body potassium is intracellular, and therefore measurement of serum potassium concentration may be misleading. Provided renal function is adequate, routine potassium supplementation is recommended in horses with reduced or lack of intake and continued fluid therapy for more than 24 hours. Potassium can be safely supplemented at a rate of 20 to 40 mEq of KCl per liter of fluids. Supplementation should not exceed 0.5 mEq/kg/hour to avoid development of hyperkalemia.

Hypomagnesemia has been documented in horses with a variety of gastrointestinal diseases, and appears to be particularly prevalent in horses affected by ileus. Low serum magnesium concentrations can cause depression, ileus, poor appetite, and tachydysrhythmias. Magnesium supplementation can be achieved by administering magnesium sulphate at a rate of 5 mg/kg/hour. Rates as high as 25 g can be administered in 30 minutes. Daily oral supplementation of magnesium oxide, which has less of a laxative effect than magnesium sulfate, should be given at a maintainance dose of 20 to 30 mg/kg/day, usually in a divided dose. (Personal communication, Harold McKenzie, Leesburg, VA, 2005.)

Acid-base Balance

Acid-base disturbances are most commonly the result of hypovolemic shock resulting in lactic acidosis. Correction of acid-base balance is generally achieved by correction of the hypovolemia and circulatory support; however, bicarbonate therapy may be beneficial in severely acidotic horses (pH less than 7.2, blood bicarbonate less than 15 mEq/L, or base excess greater than 10 mEq/L). The bicarbonate deficit can be calculated from the following formula:

Bicarbonate deficit (mEq) = Base deficit x 0.3 x Body weight (kg)

Half of the calculated bicarbonate requirement should be administered intravenously over 1 hour, and the remainder administered over 12 to 24 hours. Acidosis is also common in horses affected by colitis resulting from bicarbonate loss in the intestine, and these horses can also benefit from bicarbonate supplementation once the anion gap and/or high blood lactate are corrected. Horses continually receiving 0.9% or greater saline solutions as the predominant crystalloid therapy may become acidotic from the disproportionately high chloride concentration in these fluids.

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Postoperative Complications

Chapter 33

Christopher J. Proudman

Postoperative Colic

At various times in the postoperative period, horses that have undergone colic surgery may show recurrence of abdominal pain. This is particularly disheartening for the surgical team who were expecting a comfortable, pain-free horse. In a study of 341 horses undergoing colic surgery,[1] 32% of horses suffered one or more episodes of postoperative colic (Figure 33-1). Although the proportion of horses affected is high, only 5% of horses suffered 3 or more episodes. Most colic episodes occurred in the first year postoperatively, and many in the first 50 days after surgery (Figure 33-2). Horses that have undergone colic surgery have an incidence of colic of 0.55 episodes/horse year at risk, which is approximately 5 times higher than the prevalence reported for the general horse population.[1]

The time of occurrence relative to colic surgery gives some clues to the possible etiology of postoperative colic:

Colic within 48 hours of surgery:

- Persistent ischemic bowel, e.g., ileal stump
- Continued ischemia/reperfusion injury of colon
- Leakage at an enterotomy or anastomosis site
- Postoperative ileus (POI)
- Idiopathic/unknown.
- Recurrent displacement

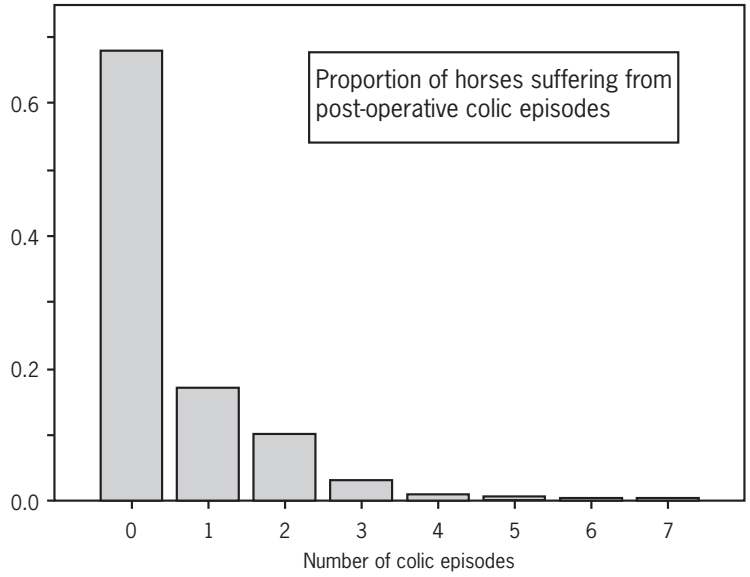
Colic within 2 to 7 days of surgery:

- Obstruction at an anastomosis (e.g., hematoma, impacted ingesta)
- "Delayed adaptation" at an anastomosis
- Peritonitis
- Postoperative ileus
- Large-colon impaction
- Gastric ulcers

Colic at least 7 days after surgery:

- Adhesions
- Recurrence of previous problem, e.g., colon displacement, small-intestinal entrapment.

Figure 33-1

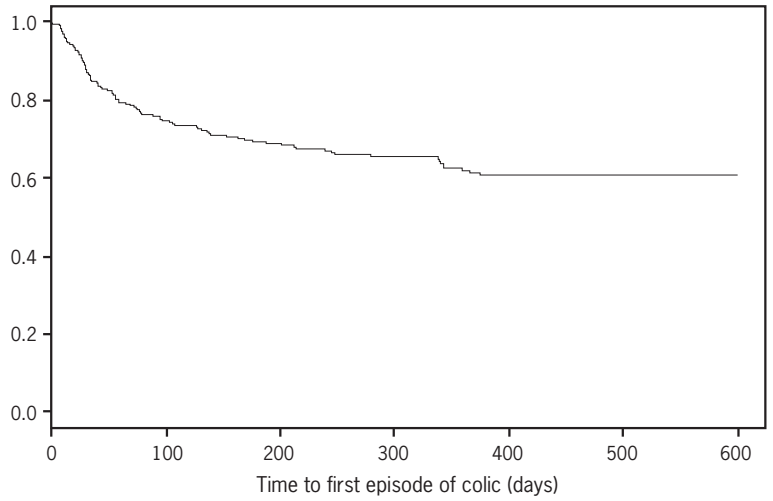


Proportion of 341 postoperative colic cases that suffered one or more colic episodes.[1]

Differentiation of these various causes can be difficult. As with a primary episode of colic, the key decision is whether surgery is necessary to correct the underlying problem. This decision is made by considering the results of repeated evaluations to ascertain trends in clinical parameters and by considering the list of differential diagnoses shown above (see Chapter 15).

Cardiovascular parameters will deteriorate in the presence of ongoing endotoxemia arising from ischemic bowel or anastomotic leakage. Under intensive care conditions, this may be apparent as increased fluid requirement rather than increases in PCV or heart rate. Rectal examination and/or ultrasound evaluation of the abdomen will reveal the presence of distended small intestine consistent with intestinal obstruction or postoperative ileus. A helpful distinction between the two is that ileus is commonly associated with dullness and depression. Obstruction of the small intestine at an anastomosis site is more likely to result in colic pain that increases with time.

Figure 33-2



Cumulative probability of not developing postoperative colic amongst 341 horses surviving colic surgery.[1]

"Delayed adaptation" to an anastomosis occurs most often 48 to 72 hours postoperatively as feed is being reintroduced to the horse. Transient colic episodes may be observed after feeding and these may be of sufficient duration to cause small-intestinal distention. The precise cause of these episodes, which respond well to administration of analgesic or spasmolytic agents, is unknown, but the author suspects that the condition is associated with delayed adaptation of electrical conduction across the new anastomosis site or inflammation of the previously distended small intestine. Some research has been conducted in horses and dogs that supports this hypothesis.[2,3]

Treatment of colic in the postoperative patient depends on the likely cause. Some horses require a second surgical operation in order to repair a leaking anastomosis or to revise an anastomosis that has become obstructed. However, many postoperative colic episodes, and particularly those occurring within the first 48 hours after surgery, respond well to medical therapy. In the absence of clear indications for surgery, administration of analgesic and spasmolytic agents (e.g., hyoscine and dipyrone) is usually sufficient to resolve the episode. Increasing pain or deterioration of cardiovascular parameters indicates the failure of medical therapy.

Postoperative Ileus (POI)

This condition, characterized clinically by the absence of intestinal sounds and progressive distention of the small intestine and stomach, is due to the failure of coordinated small-intestinal motility. In the author's hospital, the condition affects 10% of surgical colic cases,[1] a prevalence similar to that reported in other studies,[4,5] with 30% of affected horses dying or requiring euthanasia as a result of the condition. A related study concluded that horses with an increased PCV prior to surgery and horses suffering from strangulation of small intestine by a pedunculated lipoma were at increased risk of developing POI (see Chapter 4).[6]

All horses that have undergone small-intestinal surgery should be monitored for POI until they are successfully returned to a normal diet. Monitoring should take the form of clinical examinations every 2 to 4 hours for the first 48 hours postoperatively, with particular attention paid to intestinal sounds, cardiovascular parameters (membrane color, heart rate, and PCV), and passage of feces. It is not uncommon for horses to have good intestinal sounds on auscultation of the abdomen within a few hours of surgery. Clinicians should be aware that POI often develops subsequent to this time. Median time to onset of POI was 24 hours postoperatively in the author's study. Although clinical definitions of POI have varied among published studies, a useful diagnostic criterion is the reflux of more than 2 liters of gastric fluid on at least 2 consecutive occasions within 24 hours, by nasogastric intubation.[6] This is usually accompanied by increases in heart rate and PCV and by reduced intestinal sounds.

Treatment of POI has two major components: nursing care and the use of prokinetic agents. The relative importance of each is a matter of clinical preference. To date, little scientific evidence exists to aid clinicians in the management of these cases, and no studies unequivocally document the clinical efficacy of prokinetic agents.

Nursing Care

Horses with compromised intestinal motility should not be fed or offered water to drink. This means that the animal's fluid requirements must be supplied by intravenous fluid therapy. Isotonic fluids should be administered to meet maintenance requirements and to replace ongoing losses associated with gastric reflux. Monitoring PCV every 4 hours is a good indicator of the success of fluid therapy. If intravenous fluid therapy is needed for more than 24 hours, serum electrolyte concentrations should be monitored (see Chapter 17). Monitoring of urine specific gravity may provide evidence of systemic dehydration in the presence of relatively normal PCV and plasma protein concentration. POI results in a physiologic obstruction of the small intestine, allowing fluid secretions of the proximal intestine to cause small-intestinal distention and, eventually, distention of the stomach. Failure to recognize gastric distention (often associated with a depressed horse starting to show signs of overt colic) can result in gastric rupture and death of the horse. To prevent this, nasogastric decompression of the stomach is recommended every 2 to 4 hours. The volume of reflux obtained over a defined time period can be a useful indicator of the success, or otherwise, of therapy. Horses with ileus are usually dull and depressed. They appear to benefit from frequent short walks out of the stable, grooming, and other nursing attention.

Prokinetic Therapy

In addition to the nursing interventions that have been described, prokinetic agents may be used to stimulate intestinal motility in the affected segment of bowel (usually proximal small intestine (see Chapters 4 and 16). Several studies provide a pharmacologic rationale for using metaclopramide, an adrenergic and dopaminergic antagonist, for the treatment of POI.[7,8] More recent research suggests that the prokinetic action of metaclopramide may be a result of its action as a $5HT_4$ agonist.[9] Use of this drug as an intravenous infusion at a dose rate of 0.04 mg/kg/hour has proved safe in many hospitals. Higher dose rates have been associated with neurologic signs (box-walking, head pressing, excitement). Such signs rapidly abate once the infusion of metaclopramide is discontinued.

The local anesthetic lidocaine (lignocaine) can be administered as a prokinetic agent; however, the mechanism of action of this drug has yet to be determined.[10] Lidocaine is administered intravenously as a loading bolus of 1.3 mg/kg given in polyionic fluids over 15 minutes, followed by a maintenance infusion of 0.05 mg/kg/minute. Studies suggest that this protocol is safe and there is some indication of efficacy,[11,12] but more rigorous evaluation has yet to be reported. Lidocaine appears to decrease pain and bowel inflammation, which can also help resolve POI.

Cisapride and erythromycin have also been used to stimulate intestinal motility in POI patients. Preliminary studies with cisapride suggested that it may be highly effective as a prokinetic agent, however, the intravenous form of cisapride is no longer available.[13,14] Erythromycin is known to stimulate motilin receptors in the intestinal tract and has been reported to decrease gastric solid phase emptying time;[15] however, other studies have shown variable effects of erythromycin on intestinal motility,[16] and the drug is reported to be ineffective in the treatment of POI in people.[17]

Jugular Thrombosis and Thrombophlebitis

Catheterization of the jugular vein is a common procedure in the management of both medical and surgical colic cases. Prolonged catheterization with repeated use of the catheter for medications and fluid therapy can lead to thrombosis, with or without associated infection. In one study of postoperative complications, the prevalence of jugular thrombosis was reported as 10% of horses recovering from colic surgery.[1] Risk of thrombophlebitis is increased by catheter type, inappropriate site preparation, poor catheter care, endotoxemia (18x), salmonellosis (68x), hypoproteinemia (5x), large-intestinal disease, and in horses receiving antidiarrheal drugs or antiulcer drugs compared with those not receiving those treatments (31x).[18,19]

The jugular veins of horses are most commonly affected as they are most frequently used, but any catheterized vein is susceptible to thrombus formation. The clinical signs of unilateral jugular thrombosis are "cording" of the affected vein (Figure 33-3) and prominence of facial veins on the affected side. If thrombosis is bilateral, swelling of the muzzle and face may occur (Figure 33-4), accompanied by swelling of the nasal mucosa, causing respiratory obstruction and, in extreme cases, neurologic signs resulting from cerebral edema. Thrombosis that is associated with bacterial infection causes hot, painful swelling in the jugular region, and abscesses that may eventually rupture through the skin. Fever, depression, and an unwillingness to move the neck are other hallmarks of jugular thrombophlebitis. Ultrasonographic imaging of jugular veins is helpful in the early detection of thrombosis.[20] It can also be useful in localizing abscesses and in following the progress of recanalization after thrombosis.

Treatment of thrombosis is symptomatic. It is important to remove the catheter from the affected vein at the first indication of thrombus formation. At this time, the catheter tip may be cultured for bacterial contamination. Some clinicians feel it is helpful to apply hot packs to the affected area several times daily to stimulate blood flow. The topical use of DMSO has also been advocated, although no evidence supports the efficacy of either treatment. If infection is suspected or confirmed by

Figure 33-3



A "corded" jugular vein at the site of intravenous catheterization.

bacterial culture, appropriate antibiotic therapy should be used. Fortunately, the majority of unilateral thrombi resolve and the affected veins recanalize, although this may take weeks to months. After removal of a catheter from a thrombosed jugular vein, it is important not to compromise the contralateral vein by placing a catheter in it. Horses can function effectively with one patent jugular vein, but bilateral thrombosis is life-threatening. Alternative veins (lateral thoracic, cephalic) should be used if a venous catheter is still necessary.

There was a widespread belief that jugular thrombosis in postoperative colic patients was caused by the use of irritant anaesthetic agents, and by glycerol guaiacolate ether in particular.[21,22] It has become apparent, however,that endotoxemia, characterized by increased heart rate and PCV, is probably a major risk factor.[6,18,23] This is consistent with clinical and in vitro studies that report a hypercoagulable state in endotoxemic colic cases.[24,25] The risk of jugular thrombosis is most effectively decreased by the early referral of surgical colic cases, before the horses become severely endotoxemic. Once surgery has been performed, the risk of jugular thrombosis is minimized by maintaining a "long-stay," polyurethane catheter in the vein for the minimum period necessary and with careful attention to hygiene. All catheters should be removed at the earliest opportunity.

Figure 33-4



Muzzle edema and edema of the nasal mucosa necessitating nasal intubation as a result of bilateral jugular thrombosis.

Incisional Infection

Infection of the laparotomy wound is a common complication of colic surgery. Reports of the prevalence of postoperative wound infection range from 7.4% to 37%. In the author's hospital, wound suppuration was recorded in 16% of horses that recovered from colic surgery.[6] This complication causes discomfort to the patient, prolonged hospitalization, and therefore, increased cost to the client. Wound suppuration also increases the risk for the development of an incisional hernia.

Infection of the subcutaneous tissues adjacent to a laparotomy incision usually becomes apparent at 3 to 5 days postoperatively. The wound may not be draining at this stage but the presence of a large plaque of edema on the ventral abdomen and extending cranially under the chest is an indicator of infection. Subsequently, pus is likely to break out through the suture line and drain for a period of several days to weeks (Figure 33-5). During the early stage of infection, before drainage has been established, the horse may become dull and show signs of somatic pain upon palpation of the incision. Administration of phenylbutazone may alleviate the discomfort associated with a nondraining infection.

Figure 33-5

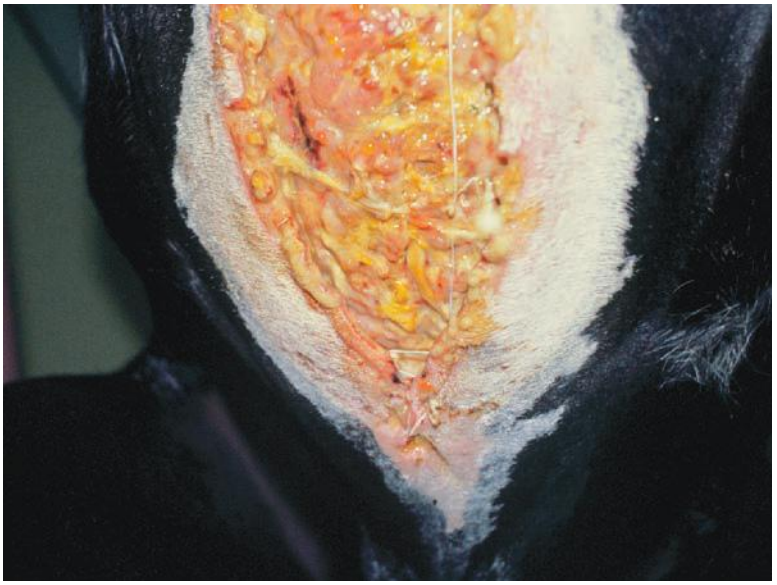


Purulent discharge from a ventral midline laparotomy incision.

Incisional infections can be managed effectively by promoting drainage of purulent material from the subcutaneous space. This is achieved by daily bathing of the wound, removing crusted exudates, and massaging the surrounding area toward the wound opening to encourage drainage. As drainage decreases, granulation tissue will fill the subcutaneous defect and the draining sinus tract will contract and close. Occasionally, horses with extensive subcutaneous accumulation of pus suffer complete breakdown of the sutured skin edges (Figure 33-6). As long as the linea alba closure remains intact, these wounds can heal by second intention although the underlying abdominal wall will be weakened and at risk of stretching, with subsequent hernia development. It is extremely unusual for subcutaneous infection to migrate dorsally into the peritoneal cavity.

Several studies have attempted to identify risk factors associated with postoperative incisional infection. One study identified an increased risk associated with performing an enterotomy or resection;[26] others found no such association.[6,27,28] No evidence has been found to support the use of one perioperative antibiotic regimen over another. Surgical technique employed for closure of the abdominal incision has been implicated in altering the risk of postoperative infection. The near-far-far-near suture pattern was significantly associated with an increased prevalence of infection in one study,[27] and some evidence suggests that using a subcutaneous suture may potentiate infection.[29,30] The benefit of stent bandages and abdominal bandaging remain unsubstantiated; the choice is left to individual clinicians. Until evidence is presented to suggest the most effective preventative interventions, surgeons must rely on meticulous preoperative skin preparation, careful draping of the surgical site, and good surgical technique to minimize the risk of postoperative wound infection.

Figure 33-6



Ventral view of a laparotomy wound that has undergone complete breakdown. Note white permanent suture material originating from caudal part of the wound.

Incisional Hernia Formation

Published reports suggest that between 6% and 16% of horses undergoing colic surgery will develop incisional herniation.[1,27,31] Hernia formation at the incision site can be detected by visual observation of a defect in the abdominal wall and by palpation of the edges of a hernial ring. Some hernias are single, others constitute two or more discrete hernial rings in a stretched, thinned area of abdominal wall. The significance of the hernia is dependent on its size and the intended use of the horse. Small hernias, with minimal distortion of the profile of the abdominal wall are well tolerated and need not be repaired, especially in horses undertaking only light exercise. Large hernias are cosmetically unacceptable and are at risk of ulceration and dehiscence (Figure 33-7). These should be repaired.

The appropriate management of horses with incisional hernias is important to the success of subsequent surgical repair. Once the hernia is recognized, the horse should be confined to a stable to minimize further increase in the size of the hernia. Large hernias may benefit from bandage support and protection to prevent ulceration of the skin prior to corrective surgery. It is recommended that hernia repair be delayed for 4 to 6 months after colic surgery to allow the abdominal wall to heal and collagen to mature along the edge of the hernia. This is important to maximize the suture-holding capacity of the tissue. Incisional hernias may be repaired by 2 different methods: suture repair and mesh implant repair.

Figure 33-7



Large incisional hernia in a postoperative colic case.

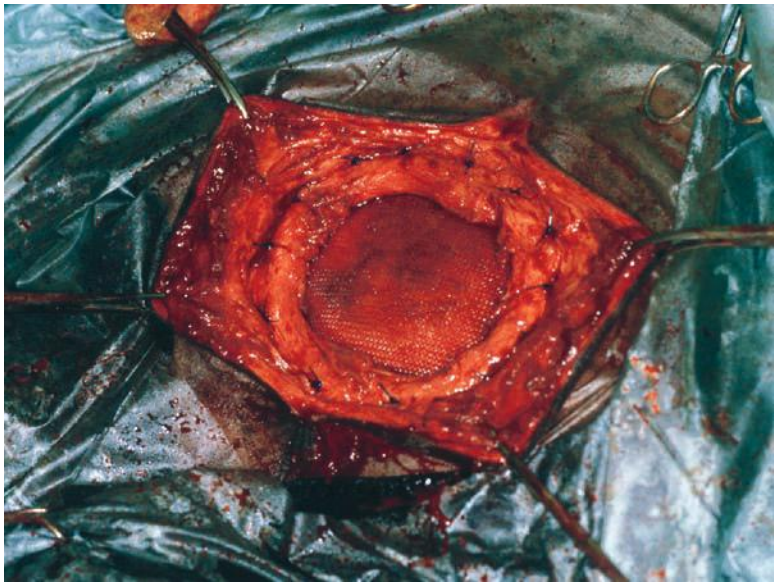
Suture Repair

The use of a continuous or interrupted suture pattern of absorbable suture material (e.g., 5 metric polyglactin 910) is advocated by some surgeons for herniorrhaphy.[32] This can be achieved by closed repair, wherein the peritoneal lining of the hernia is dissected away from the hernial ring and pushed into the abdominal cavity, and the healthy abdominal wall sutured over the top. Alternatively, an open repair can be performed wherein the hernial sac is removed, allowing exploration of the abdomen and its contents (see Chapter 31).

Mesh Implant Repair

This technique involves the implantation of a woven, polypropylene mesh into the abdominal wall. The mesh is intended provide a "scaffold" over which fibroblasts can proliferate and collagen deposition can occur. The technique for mesh repair involves dissection of the hernial ring and creation of a "shelf" between the abdominal wall and the hernial sac where the mesh can be inserted (Figure 33-8). The mesh is secured in place with multiple Mayo mattress sutures of polypropylene. Dead space can be considerable if repairing a large hernia, so it is advisable to close subcutaneous tissues as thoroughly as possible. Postoperative problems include seroma formation and drainage. Mesh repair of incisional hernias has been the technique of choice in the author's hospital for many years, even for relatively small hernias. One perceived advantage over suture repair is greater postoperative comfort as the abdominal defect is not being closed under tension. Infection of the mesh prosthesis is the chief reason for mesh rejection and failure of the repair.

Figure 33-8



Polypropylene mesh repair of an incisional hernia. Mayo mattress sutures are used to anchor the mesh onto the abdominal wall.

Adhesions

The presence of adhesions after abdominal surgery can often be determined only at post-mortem examination or, more commonly, after the horse has been admitted to the hospital for surgical treatment of a subsequent colic episode. Several studies have reported the prevalence of adhesions in horses (Table 33-1).[4,5,28,33-36] Differences in protocols, in population under investigation, and in reporting of results makes comparisons among studies difficult.

Adhesions result from alterations in peritoneal fibrinolytic activity (see Chapter 7). In normal horses, fibrin deposited at the time of surgery is lysed during the postoperative period. This homeostatic mechanism fails to operate in some animals, leading to maturation of fibrin clots that may cause adhesion of adjacent intestine or between intestine and body wall. Horses with adhesions that cause partial obstruction of intestine commonly begin to show signs of colic at 5 to 7 days postoperatively (Figure 33-9). Adhesions that do not cause intestinal obstruction may occasionally cause problems later in the horse's life by acting as a focus for strangulation of intestine. Many peritoneal adhesions are likely asymptomatic. Common sites for adhesion formation are between cecum and the ventral body wall and between loops of small intestine. Although the diagnosis of post-surgical adhesions is hampered by the infrequent opportunities to examine the abdomen of postoperative equine patients, the occurrence of repeated colic episodes may be associated with the presence of adhesions. Diagnosis, therefore, is confirmed by laparoscopy or laparotomy.

Table 33-1

Reported Prevalence of Postoperative Abdominal Adhesions in Horses.

Authors	Year	Study Population	Prevalence of Adhesions
Ducharme et al.[35]	1983	All surgical colics.	1.5%
McCarthy & Hutchins[36]	1988	All surgical colics.	5%
Baxter et al.[33]	1989	Mature horses, small intestinal surgery.	22%
McDonald et al.[5]	1989	Mature horses, small intestinal surgery.	26%
Phillips & Walmsley[28]	1993	All surgical colics.	14%
Cable et al.[34]	1997	Foals, all colic surgey.	33%
Freeman et al.[4]	2000	All horses, small intestinal surgery.	6% confirmed, possibly 13%*

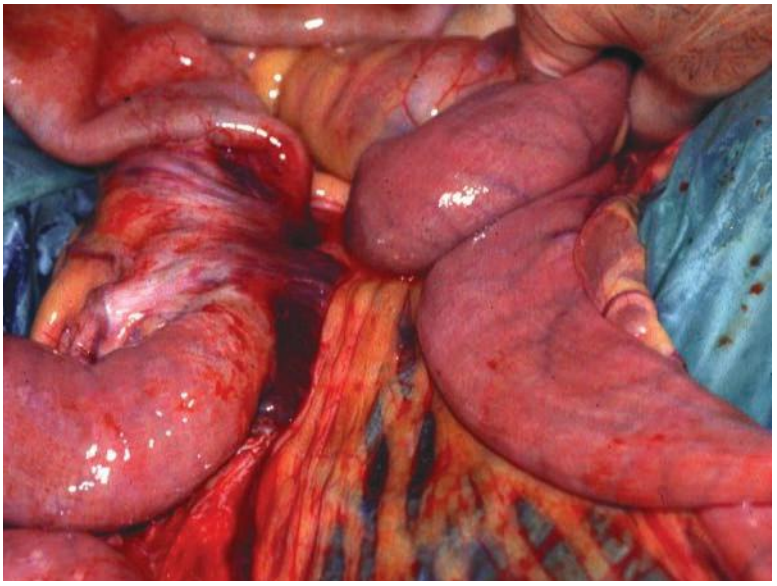
*Adhesions confirmed at post-mortem exam in 6%, a total of 13% of horses had problems possibly attributable to adhesions but no post-mortem exam.

In the author's hospital, 32% of postoperative colic cases suffered one or more episode of postoperative colic,[1] and 18% of all postoperative deaths were "colic related," i.e., the horse underwent euthanasia because of colic but no post-mortem examination was conducted. It is likely that a proportion of these colic episodes were related to adhesions. The Bolshoi study of 4,279 colic cases seen at North American University equine hospitals recorded a prevalence of 5% of cases caused by adhesions, with 45% case fatality.[37] A case-control study conducted in Texas in the 1990s involving 821 first-opinion colic cases, identified a strong association between previous colic surgery and the risk of colic (odds ratio 5.3, 95% C.I.2.5 – 11.0)[38] One possible explanation for this association is the presence of abdominal adhesions.

Good surgical technique is the equine surgeon's primary approach to prevent postoperative adhesions. Minimizing serosal trauma is achieved by careful handling of intestine and the prevention of desiccation of the intestine with sterile lavage fluid. Lessons learned from human surgery suggest that starch-powdered gloves should never be worn during equine surgery, and resection of as much ischemic tissue as possible removes any focus for adhesion formation from the peritoneum. The careful removal of fibrin clots and coagulated blood from peritoneal surfaces is thought to be helpful prior to closure of the abdomen.

Mechanical and liquid barriers to prevent adhesion formation have been used by some surgeons. In particular, hyaluronic acid – carboxymethylcellulose preparations (Seprafilm and Sepracoat, Genzyme, USA) and carboxymethylcellulose solutions have been used by some equine surgeons (see Chapter 7). Critical evaluation of the efficacy of these preparations is limited to experimental studies on small numbers of horses,[39,40] making it difficult to justify their use. A new treatment for adhesions is 4% icodextrin solution (Adept, Shire Pharmaceuticals, UK). This product is marketed as a hydroflotation solution, causing mechanical separation of serosal surfaces by the persistence of fluid in the peritoneal cavity. To date, experience of its use in horses is limited, but in the author's hospital it has been used in the abdominal cavity in a few colic cases. Three liters of 4% icodextrin can be infused into a horse's abdomen at the end of colic surgery while the surgeon is closing the laparotomy wound. The safety and efficacy of this product in horses has yet to be evaluated.

Figure 33-9



Band of adhesion tissue causing partial obstruction of jejunum.

Laminitis

This is an uncommon complication of colic surgery. In hospitals in the UK, just 1% of postoperative cases have been reported to suffer from this complication.[1,28] Horses that are endotoxemic (i.e., those suffering from strangulating and ischemic lesions) are at greatest risk of developing laminitis. For this reason, postoperative patients should be monitored for the development of increased digital pulses and foot pain. The early recognition of the condition allows the early institution of appropriate palliative measures. The pathophysiology, diagnosis, and treatment of this condition are discussed in Chapter 44).

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Specific Diseases

Part 11



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Diseases of the Stomach

Chapter 34

Michael J. Murray

Gastric Ulcer Syndromes

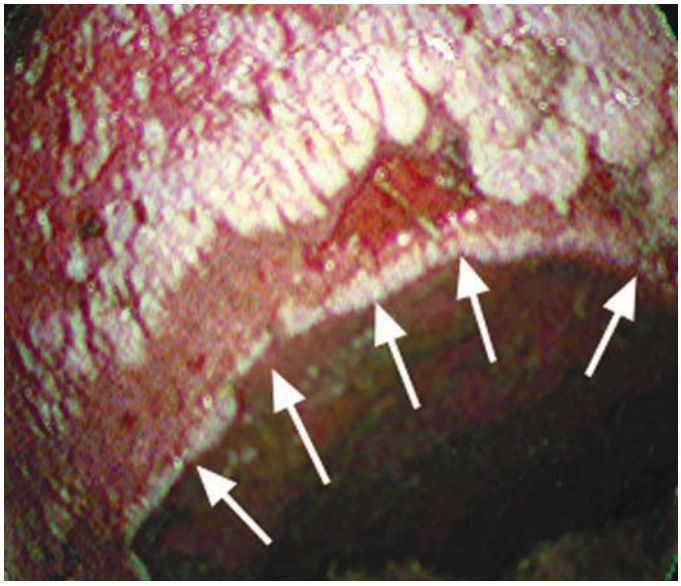
Horses with gastric ulcers can present with an array of clinical and subclinical signs that reflect varying degrees of discomfort. These signs can be as vague and nonspecific as behavioral changes, reduction of feed intake, or signs of colic. When colic is the presenting sign or is in the animal's history, it is important to perform a complete physical examination and rule out other causes of colic, even if gastric ulcers are diagnosed by endoscopy.

In foals, colic signs can be mild to severe.[1] Many different disorders can cause pronounced signs of abdominal pain in foals, and often these cannot be differentiated without a thorough evaluation, including passing a nasogastric tube, radiography, ultrasonography, CBC, chemistry profile, and abdominal fluid analysis (see Chapters 15 and 22). In many foals, gastric ulcers occur secondary to enteritis, and these foals often present with fever and an increased peripheral WBC count. Whereas the enteritis may be the cause of fever and lethargy, the ulcers are often the cause of the presenting signs of abdominal discomfort. Nasogastric intubation may recover dark brown fluid, which is indicative of bleeding ulcers. Unfortunately, signs of colic that are caused by ulcers are often only apparent when ulcers are severe (Figure 34-1) or severe complications have occurred, such as pyloric/duodenal stenosis (Figures 34-2 and 34-3), esophagitis (Figure 34-4), megaesophagus, or gastric perforation.

In adult horses, gastric ulcers can both cause colic and result from other disorders that cause colic.[2] In horses in which ulcers are a primary cause of colic, discomfort is usually mild to moderate, and episodes of colic are often frequent and recurrent. In rare cases, ulcers may cause such severe pain that exploratory surgery is performed. The author sometimes has associated ulcers with recurrent episodes of gaseous distention of the large intestine. This may be a visceral sympathetic response to gastric pain.

Often, gastric ulcers develop secondary to another intestinal problem, and these ulcers become evident when the horse has persistent mild to moderate abdominal discomfort or impaired appetite after the primary intestinal problem has been resolved. In other instances, ulcers may contribute to abdominal discomfort but are not the primary problem. Signs of colic may even abate when the horse is treated for ulcers, but acute colic recurs as a result of the primary problem.

Figure 34-1



Severe ulceration of the squamous mucosa adjacent to the margo plicatus in a foal with pyloric stricture (Figure 34-2). The severe ulceration results from impeded gastric outflow and elevation of the normal level of acidic gastric fluid, continuously exposing the squamous mucosa to acid injury.

Diagnosis

Gastroscopic examination is currently the only method for accurately diagnosing gastric ulcers. Other methods are under investigation, but they have not been validated. Abnormalities in a CBC or in clinical chemistry analytes do not indicate gastric ulceration as a primary problem. The presence of any such abnormalities should alert the clinician to another disorder, which may be the primary problem. A thorough gastroscopic examination should include evaluation of the antrum and pyloric regions of the stomach. Such examinations require a 3-meter-long endoscope in adult horses. In one report,[3] ulcers were present in the antrum/pylorus of horses with colic that had normal-appearing squamous mucosa. Failure to identify these ulcers would have resulted in a misdiagnosis. Endoscopic examination of the proximal duodenum to the level of the major duodenal ampulla is possible in many horses, although in horses with colic, examination of this portion of the intestine usually has not been of diagnostic value.

Figure 34-2



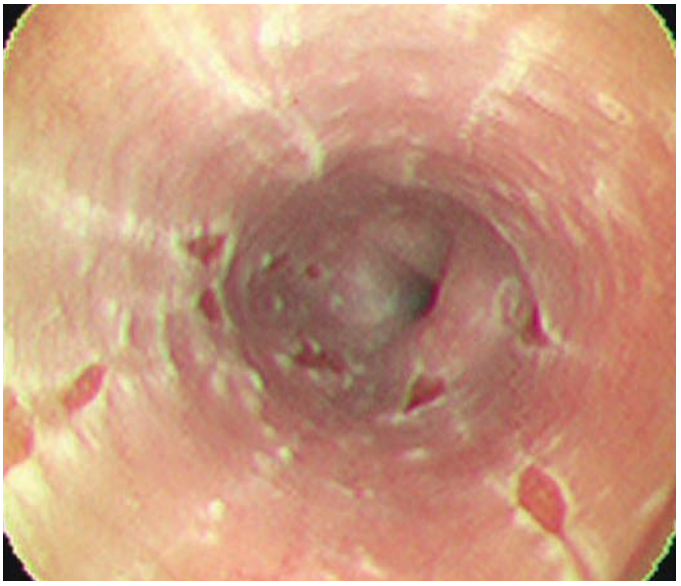
Pyloric stricture in a 2 month-old foal that had intermittent diarrhea and colic for several weeks. The foal had responded with improved clinical signs when intermittently treated for 5 to 7 days, and relapsed when treatment was stopped.

Figure 34-3



Endoscopic biopsy forceps is passed through a stricture in the duodenum, orad to the major duodenal papilla, in a 10 month-old weanling. The diameter of the lumen was approximately 2 mm at the stricture.

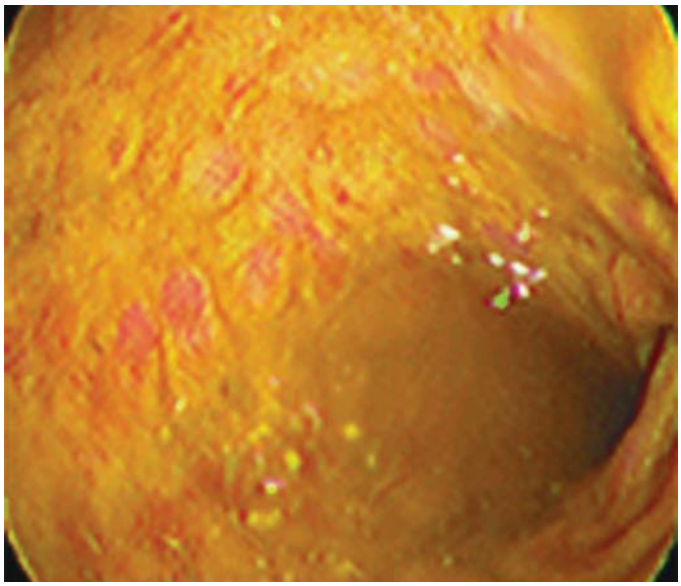
Figure 34-4



Erosions in the esophagus of the foal with pyloric stricture. Reflux of gastric contents can occur secondary to pyloric or duodenal stricture, and in chronic cases esophageal dilation (megaesophagus) can develop.

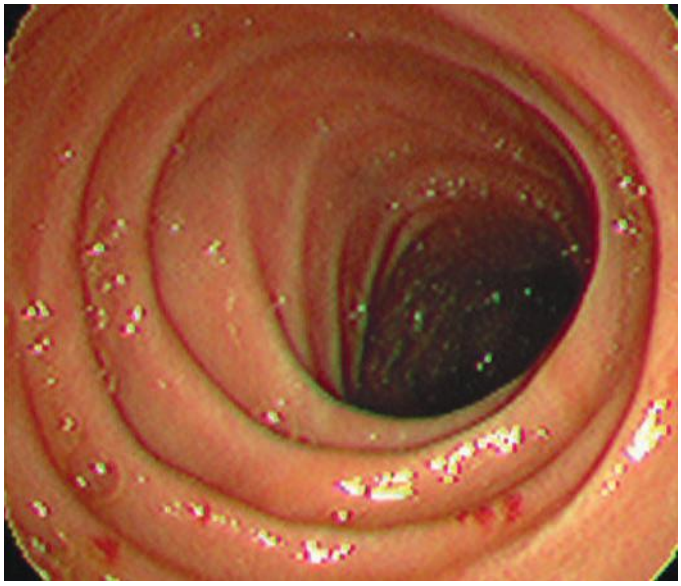
In foals, severe gastric ulceration can accompany duodenitis and enteritis (Figure 34-5). Consequently, endoscopic examination of the duodenum should be attempted. In foals 4 to 7 months old, the author has occasionally been able to pass the endoscope the length of the descending duodenum (Figure 34-6), and in some cases this confirmed a diagnosis of enteritis. The reason for successful passage of the endoscope into the descending duodenum in foals of this age range is not known, and may reflect optimal anatomic size and configuration for the procedure. If duodenoscopy is not possible, ultrasonography and contrast radiography should be done if enteritis, duodenal ulceration, or duodenal stricture is suspected. The initial portion of the duodenum is best radiographed within 2 minutes after administering a barium suspension, because rapid filling of the proximal duodenum with barium highlights this portion of the duodenum where ulcers and strictures often occur.

Figure 34-5



Fibrinous duodenitis in a 3 month-old foal that presented with acute fever, abdominal discomfort, and diarrhea. The foal also had severe gastric ulcers, presumably as a result of delayed gastric emptying. Several foals on the farm became similarly ill within a few days, implying an infectious cause of the duodenitis.

Figure 34-6



Endoscopic view of the descending duodenum in a 6 month-old foal. The endoscope could be advanced several centimeters aborad to the major duodenal papilla.

Treatment

In all animals with clinical signs due to gastric ulceration, reduction of gastric acidity is a primary objective. In some cases, medications that enhance mucosal integrity or stimulate gastric emptying may be effective. Few treatments have been critically evaluated for gastric ulcers in horses, and currently only products containing the histamine type-2 receptor antagonist ranitidine (Australia) and the H^+,K^+-ATPase inhibitor omeprazole (worldwide) have been approved by governmental regulatory bodies for the treatment of gastric ulcers in horses. Other medications have been advocated, but evidence of their effectiveness is lacking.

Suppression of gastric acidity does not stimulate ulcer healing but is permissive to ulcer healing. Mechanisms of healing are initiated with the onset of mucosal injury, and removal of the acid allows healing to proceed unimpeded. When considering using acid-suppressive therapy in foals or adult horses, one must recognize that the horse is a continuous secretor of

hydrochloric acid,[4] and unlike human beings, does not have a diurnal pattern to gastric acidity.[5] Therefore, effective treatment requires prolonged reduction of gastric acidity. The mechanism of action of an acid-suppressive agent and the dose administered will affect the potency and duration of acid suppression. Additionally, the bioavailability of orally administered drugs is generally poor, varies considerably from horse to horse, and may be affected by the animal's age. Consequently, deviating from recommended dosages often results in treatment failure. In such cases, low doses of an acid-suppressive agent that appear to result in improved clinical signs may not result in ulcer healing. In fact, sometimes this has resulted in permanent damage to the stomach or fatal consequences.

Antacids

In humans, antacids are used primarily to control symptoms of dyspepsia (heartburn, upset stomach) and these agents are not considered primary therapy for the treatment of ulcer disease. Antacids reduce gastric acidity by neutralizing existing acid. Most antacids are based on a combination of aluminum and magnesium hydroxides or calcium carbonate. Antacids can effectively reduce gastric acidity in horses, but only briefly.[6,7] Liquid antacid products must be given both in large volumes (240 mL) and frequently (6 to 12 times daily) to be effective in promoting ulcer healing. Feed additives that contain antacids are popularly considered to be helpful in controlling gastric ulcers in horses, but no supportive data exist. Also, an acid-neutralizing effect is most desirable when the stomach is empty, not when it is full, because gastric pH is naturally high when horses ingest feed.[5]

Histamine Type-2 Receptor Antagonists

The histamine type-2 receptor antagonists (H_2 antagonists) inhibit hydrochloric acid secretion by competing with histamine for receptor sites on the parietal cell.[8] Histamine is the most potent stimulus for hydrochloric acid secretion and, because occupation of the receptor site is by competitive inhibition, the greater the concentration of H_2 antagonist at the receptor site, the greater and more prolonged the degree of suppression of hydrochloric acid secretion. The H_2 antagonists registered for use in humans are cimetidine, ranitidine, famotidine, and nizatidine, and all are available in generic formulations. Injectable formulations of cimetidine and ranitidine are also available.

In horses, ranitidine inhibits gastric acid secretion,[4] increases gastric pH,[5,6,9] and has been associated with ulcer healing in a retrospective report.[10] The most effective dose for increasing gastric pH was 6.6 mg/kg, and increased gastric pH was best sustained when ranitidine was given at 8-hour intervals.[6] Intravenous (2.0 mg/kg) and oral (6.6 mg/kg) administration of ranitidine increased mean gastric pH for 5 to 8 hours in young foals.[9] Individual horses have different dose-response profiles (based on bioavailability of the drug), and as the dosage of ranitidine is decreased, the percent of horses that fail to respond to the drug increases.[6] In some horses, reducing the dose to less than 6.6 mg/kg results in no increase in gastric pH.

Orally administered cimetidine has been shown to increase equine gastric pH,[11] but in other studies cimetidine was not effective in promoting ulcer healing in horses given up to 20 mg/kg 3 times daily.[12,13] The effect of intravenous administration of cimetidine on gastric pH in horses has not been reported, although pharmacokinetic data would support its use.[14] The author's clinical experience of using cimetidine intravenously at a dose rate of 6.6 mg/kg every 6 to 8 hours has been consistently positive, with ulcer healing progressing at a rate consistent with excellent suppression of gastric acidity.

H^+,K^+-ATPase Inhibitors

The H^+,K^+-ATPase inhibitors, also referred to as proton pump inhibitors, interact specifically with parietal cell H^+,K^+-ATPase because of their chemical structures and the uniquely highly acidic environment of the secretory domain of the parietal cell H^+,K^+-ATPase. Omeprazole is the only H^+,K^+-ATPase inhibitor approved for use in horses. The magnitude of inhibition of acid secretion is dose-dependent, so that at higher doses more catalytic sites are blocked, and omeprazole can inhibit acid secretion by up to 99% for 24 hours or longer.[15] Proton pump inhibitors are highly unstable within the acidic environment of the stomach and lose their activity prior to absorption in the small intestine unless protected from acid. The approved paste formulation of omeprazole developed for horses (GastroGard, Merial Limited, Duluth, GA) protects the molecule through the stomach. The bioavailability of omeprazole is lower from the paste formulation than from the enteric-coated granules used in human beings, but bioavailability was enhanced when the paste product was given to horses from which feed was withheld.[15] The dosage of omeprazole (GastroGard) for treatment of ulcers is 4.0 mg/kg once daily,which has been shown to be highly effective in treating gastric ulcers in foals and adult horses.[16,17] It was reported that gastric ulcers were prevented in 80% of racing horses administered a reduced dose of 1 mg omeprazole/kg for 28 days;[18] this dose has been approved by the FDA for prevention of gastric ulcers in horses.

Drugs Acting on Gastric Motility

Ulcers are sometimes the result of accumulation of acid due to delayed gastric emptying. This may result from generalized intestinal ileus, enteritis, or pyloric/duodenal obstruction. Obstruction of the pylorus or duodenum can occur in foals as a

result of chronic ulceration, and the author has observed this condition in several adult horses. Often, the pyloric stenosis is irreversible because of severe scar tissue formation, but in some instances, prolonged treatment with acid suppression and prokinetic drugs may result in substantial recovery.

The cholinergic agonist bethanechol has been used to stimulate gastric emptying in foals and horses with duodenitis, pyloric stenosis, and pyloric ulceration. Bethanechol also has been used to facilitate gastroduodenoscopy in foals and adult horses. Clinically, bethanechol is given subcutaneously, at a dose rate of 0.02 mg/kg, or orally, at 0.35 mg/kg, every 8 hours. Cholinergic-mediated side effects are not noted at these doses unless the drug is given intravenously. Bethanechol has been given to some horses chronically (weeks to months) without apparent adverse effects.

Metoclopramide has been used effectively in humans to improve gastric emptying and in foals with suspected gastric emptying disorders. Metoclopramide has the potential to cause severe excitation in foals and adult horses because of its ability to cross the blood-brain barrier and its inhibitory effects on dopamine receptors. Therefore, the challenge is to administer a dose that effectively stimulates propulsive motility while avoiding adverse effects. Foals have been given doses ranging from 0.1 mg/kg to 0.25 mg/kg, at 6- to 8-hour intervals. In one report, metoclopramide, given to horses as a slow infusion at a dose rate of 0.125 mg/kg, increased gastric emptying in a low-dose endotoxin model.[19] Bethanechol appears to be preferable to metoclopramide because it produces limited side effects.

Treatment Recommendations for Horses with Colic as the Presenting Clinical Sign

Because gastric ulcers can be both the cause of colic and the result of conditions that cause colic, effective treatment of gastric ulcers is often an important part of the treatment or aftercare of horses with colic. In horses with colic, treatment should consist of medications given at dosages that are recognized to be effective in reducing gastric acidity and promoting ulcer healing. In horses in which gastric emptying and small-intestinal function are thought to be normal, the approved omeprazole paste product should be used according to the label (4 mg omeprazole/kg, once daily). In horses with acute colic and in horses with gastric or small-intestine motility concerns, cimetidine (6.6 mg/kg, every 6 hours) should be administered intravenously. Once the horse can utilize oral medications, the omeprazole paste should be given, with cimetidine continued for 24 hours after omeprazole treatment is begun. A formulation of omeprazole for intravenous injection is available in many countries (not in the U.S.), although this product is registered only for human use and is expensive. A suggested dose is 0.5 mg omeprazole/kg, once daily, IV. Depending on the condition of the foal or horse, a prokinetic drug (bethanechol or metoclopramide) may be indicated to facilitate gastric emptying and the delivery of orally administered medication.

Gastric Impaction

Gastric impaction can occur as a primary condition, but often it is diagnosed at surgery as a finding secondary to other disorders in the intestinal tract. Gastric impaction can be a serious condition, because untreated cases can proceed to rupture. In some horses predisposing causes may exist, such as ulceration or fibrosis at the pylorus, whereas in other horses, gastric impaction may occur spontaneously. Management practices that may contribute to gastric impaction include feed stuffs that can become desiccated in the stomach (beet pulp, bran, straw, wheat, and barley), dental disorders affecting mastication of feeds, and feeding a horse that has signs of colic. This latter scenario occurs when the primary signs of colic have subsided but the initiating problem persists, and gastric emptying is impaired along with generalized intestinal motility impairment.

Gastric impaction may be suspected during an examination for colic if it is difficult to pass a nasogastric tube into the stomach, which can occur with an impacted or dilated stomach. If the horse has not eaten for several hours, yet poorly macerated or digested feed material is recovered from the nasogastric tube, a gastric impaction may be suspected. On rectal examination, the spleen may be displaced caudally and medially because of gastric distension, but this finding is not specific for gastric impaction or dilation.

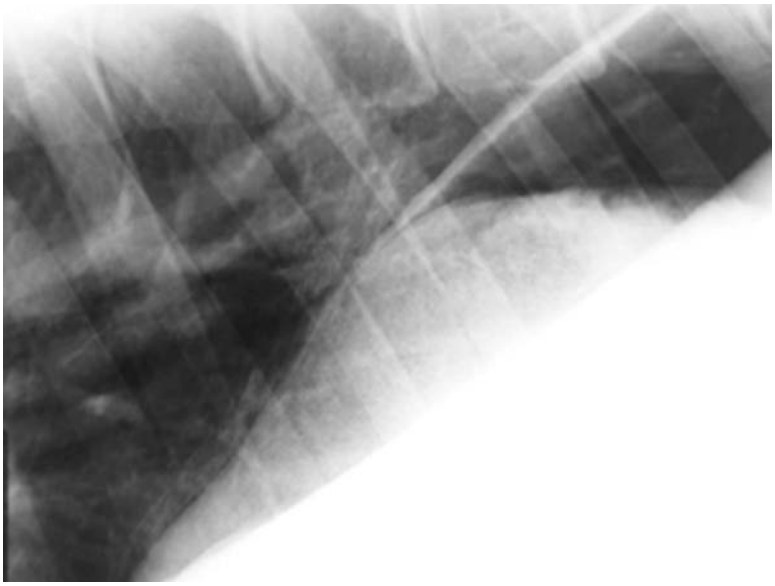
Endoscopy is often of little help in making the diagnosis, because simply identifying a stomach full of ingesta is not diagnostic for an impaction, and it is difficult to assess distention by endoscopy. Radiography may be useful in some cases, in which the impacted stomach will be noted to displace the diaphragm cranially (Figure 34-7).

Medical treatment of affected horses can include gastric lavage to remove as much ingested material as possible. This may need to be done repeatedly. Instillation of 100 to 200 mL of 8% dioctyl sodium sulfosuccinate (DSS) may facilitate hydration of desiccated ingesta. Treatment with analgesics and intravenous fluids should also be given, as needed, although intravenous fluid administration is unlikely to increase the hydration of desiccated gastric contents. We have treated horses with gastric impactions that were diagnosed at surgery with bethanechol, 0.02 mg/kg, SQ, every 8 hours, with no adverse

effects. Gastric motility stimulants should be avoided if the extent of the impaction is not known, because of a possibility of inducing gastric rupture.

Surgical treatment can include direct infusion of balanced polyionic fluids into the impaction through the stomach wall. The stomach is massaged to break down the impaction and facilitate movement of fluid into the ingesta. Alternatively, fluid may be infused via a nasogastric tube, followed by massage of the stomach. Postoperatively, the horse should be held off feed for 48 to 72 hours. A gastroscopic examination is indicated, both to document resolution of the impaction and to determine whether there is an underlying disorder in the stomach.

Figure 34-7



Radiograph of the caudal thorax of an adult horse with a gastric impaction. The impaction is apparent because of the contrast with the radiopaque gas cap in the stomach.

Gastric Dilation

Dilation of the stomach with fluid or gas usually results from obstruction of the small intestine, but primary gastric dilation can occur if a horse eats highly fermentable material, generating a large volume of gas. This is dissimilar to frothy bloat in ruminants, in which a stable gas/fluid froth develops in the rumen as a result of plant/rumen microbial interactions. It is possible for fluid to spontaneously reflux from the stomach into the esophagus, but with distention, the gastroesophageal junction is distorted such that it is tightly closed. This promotes progressive gastric distention as fluid continues to move into the stomach from the duodenum or as gas is generated within the stomach.

The clinical signs associated with gastric dilation are the same as for gastric impaction, although the onset may be more acute and the signs more severe. Affected horses are often tachypneic because of compression of the thorax by the distended stomach. Diagnosis of primary gastric dilation can be presumed if passage of a nasogastric tube releases a large volume of gas, which resolves the colic episode. If a large volume of fluid is retrieved, gastric dilation may have been temporarily resolved, but the underlying cause of enterogastric reflux will need to be determined.

Treatment is removal of excessive fluid or gas via a nasogastric tube, or at surgery via needle aspiration. An underlying reason for the gastric dilation should be determined and appropriately treated. Because the cause of gastric dilation in horses is dissimilar to frothy bloat in ruminants, treatments designed for this condition are not indicated for gastric dilation in horses. Also, products designed to treat "stomach gas" in humans, such as simethecone, are not indicated for horses with gastric distension.

Neoplasia

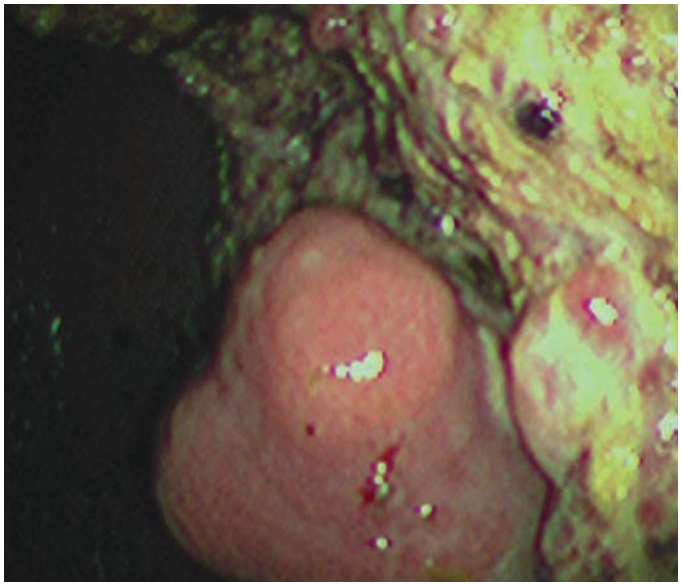
Squamous cell carcinoma is the only primary gastric neoplasia reported in horses. Squamous cell carcinoma affects the esophageal and gastric squamous mucosa, and by the time the disease is recognized, treatment is rarely possible. In some horses, tumors remain localized within the stomach, whereas in other horses tumors may extend through the stomach wall and spread to other abdominal viscera or metastasize to other locations in the body.

Typical signs associated with, but not diagnostic for, gastric squamous cell carcinoma include chronic weight loss, poor appetite, abdominal discomfort, and lethargy. Ascites or edema may occur in some cases. If the esophagus is involved,

dysphagia or ptyalism will be the predominant sign. Involvement of the stomach with squamous cell carcinoma at the cardia may also result in dysphagia, while involvement at other sites in the stomach may result in signs of obstruction to outflow (colic) and/or weight loss. In some horses, tachypnea will be a prominent sign, either because of metastasis to the thorax or pressure on the diaphragm from an enlarged tumor.

Endoscopy is the best means for diagnosis (Figure 34-8), but other potentially useful diagnostic techniques include radiography of the caudal thorax (displacement of the diaphragm cranially or soft-tissue density overlying gastric gas cap), cytologic evaluation of gastric lavage fluid, peritoneal fluid cytology, and ultrasonography.

Figure 34-8



Endoscopic view a gastric squamous cell carcinoma in an aged horse.

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Liver Diseases in Foals

Chapter 35

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Thomas J. Divers

Portosystemic Shunts

Portosystemic shunts are anomalies of the portosystemic circulation that allow direct communication between the portal circulation and a systemic vein such as the vena cava.[1] The shunting vessel(s) circumvents portal blood from entering the hepatic circulation and being cleared of toxic metabolites by the liver. Portosystemic shunts are classified as congenital or acquired, intrahepatic or extrahepatic, single or multiple.

Intrahepatic shunts represent a failure of the ductus venosus to close normally 2 to 3 days after birth. Congenital extrahepatic shunts most commonly originate from the portal vein, but may also originate from the left gastric vein, splenic vein, cranial or caudal mesenteric vein, or gastroduodenal vein, and typically empty into the caudal vena cava or azygous vein. There are few reports of congenital extrahepatic shunts in foals.[2,3]

Pathophysiology

Portosystemic shunts divert portal blood away from the liver, thereby allowing noxious substances, such as ammonia, mercaptans, short-chain fatty acids, and false neurotransmitters that are normally cleared by the liver, to remain in the systemic circulation, resulting in hepatic encephalopathy. The shunting of portal blood away from the liver also results in liver atrophy.

Clinical Signs

Portosystemic shunts have been reported in foals between 2 weeks and 11 months of age.[2-5] The presenting history and clinical signs may include failure to thrive and intermittent signs of hepatic encephalopathy, such as disorientation, seizure, stupor, head pressing, circling, apparent cortical blindness, and coma.

Diagnosis

Foals with portosystemic shunts usually have normal hematocrit and total protein values, but poikilocytosis may be noted on evaluation of red blood cell morphology. Serum biochemistry values are typically within normal limits, with the possible exceptions of increased total bilirubin concentrations and hypoglycemia. Blood ammonia and total serum bile acid concentrations are increased.

Positive-contrast portography remains the diagnostic technique of choice for shunt confirmation and location. The surgical approach for access to the portal circulation may be made through either a ventral midline celiotomy or a right flank incision. If shunt ligation is to be performed during the same anesthetic procedure as the contrast portogram, then a right flank approach is recommended as this is the preferred approach for shunt ligation. A catheter is advanced within the cranial mesenteric vein and an iodinated contrast agent is injected, followed immediately by radiography. If a shunt cannot be identified by positive-contrast portography, a liver biopsy should be obtained to look for hepatic dysplasia or microvascular shunting. The hepatic histologic abnormalities observed in hepatic dysplasia are similar to and possibly indistinguishable from those observed in animals with portosystemic shunts. Hepatic scintigraphy is useful for shunt confirmation, but provides no information on shunt location and, therefore, is also a less rewarding technique than positive-contrast portography. Abdominal ultrasonography may identify a portosystemic shunt; however, a positive-contrast portogram should still be performed preoperatively to confirm the ultrasonographic findings.

Treatment

Surgical ligation is the only effective treatment. Medical management of the hepatic encephalopathy must be carried out before anesthesia and surgery are attempted. The preferred surgical approach for portosystemic shunt ligation is a large right paracostal incision with an 18th rib resection.[5] After the shunt is located, a catheter is placed in a jejunal vessel to facilitate measuring portal pressures during shunt ligation. The shunt is ligated with nonabsorbable suture, while the portal pressure is monitored and abdominal viscera are observed for signs of cyanosis and congestion. Cellophane banding instead of suture ligation for shunt attenuation may be considered so that progressive and partial closure of the shunt vessel is possible. Surgical mortality in foals with congenital portosystemic shunts is high; only one successful case of portosystemic shunt ligation has been reported in the literature.

Tyzzer's Disease

Tyzzer's disease is an acute, fulminant bacterial hepatitis caused by *Bacillus piliformis*, a gram-negative filamentous bacterium.[6-12] The disease has been reported in foals from 7 to 92 days of age. Tyzzer's disease usually occurs sporadically, but has been reported in outbreaks, and is endemic in certain geographic locations. The disease is not contagious. The route of infection is thought to be oral intake of feces or soil. Soil is contaminated by infected individuals or possibly by rodents.

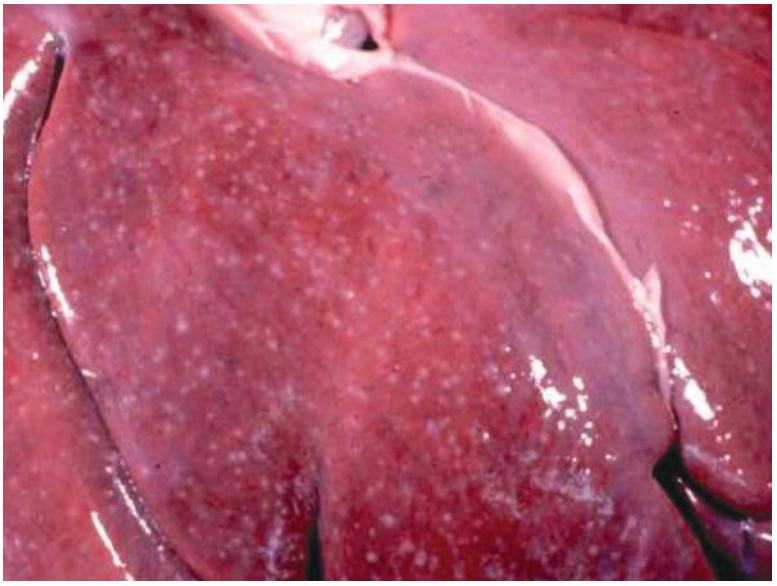
Clinical Signs

The onset of clinical signs is usually peracute. Signs include sudden death, depression, weakness, tachypnea, tachycardia, anorexia, coma/stupor, blindness, seizures, hyper- or hypothermia, icterus, injected mucous membranes, petechiation, abdominal pain, diarrhea, and discolored urine. Tyzzer's disease should be a primary differential diagnosis for a foal that is suddenly found dead. Physical examination identifies variable signs of sepsis and cardiovascular shock. Icterus of mucous membranes is variable, as the acute nature of the disease may not have resulted in a significant hyperbilirubinemia. Petechiation and high fevers may be present. Abdominal pain and/or hemorrhagic enterocolitis can be associated with this disease. The abdominal pain is likely to be secondary to colitis or acute swelling of the liver capsule. Myocarditis is an occasional post-mortem finding in foals with this disease.

Diagnosis

The diagnosis is based on the age of the foal, clinical signs, and laboratory findings, which include severe metabolic acidosis, hypoglycemia, and increases in serum concentrations of direct and indirect bilirubin, hepatic enzymes [amino aspartine transferase (AST), sorbital dehydrogenase (SDH), and gamma glutamyl transferase (GGT)], and bile acids. Additional frequent findings are a degenerative left shift on the leukogram and a thrombocytopenia. Liver biopsy is rarely performed because the clinical signs and laboratory findings are so characteristic of Tyzzer's disease that a biopsy is not required for a diagnosis.

Figure 35-1



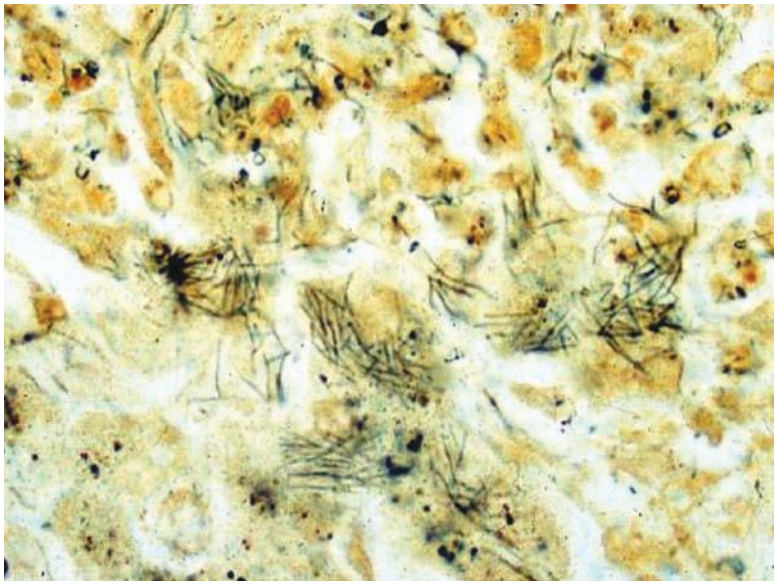
Tyzzers disease. Gross post-mortem appearance. White spots scattered over the surface and throughout the liver.

Because of the frequent occurrence of thrombocytopenia, a biopsy may be contraindicated. Blood cultures should be performed, but are rarely diagnostic. Gross necropsy identifies typical white spots in the hepatic parenchyma (Figure 35-1). Histopathology confirms a diagnosis of Tyzzer's disease. Warthin Starry stains identify filamentous bacteria in affected tissue (Figure 35-2). Routine bacterial culture techniques are unrewarding.

Treatment

Successful treatment of a definitively diagnosed case of Tyzzer's disease has rarely been reported in the literature.[6] Emergency therapy with appropriate crystalloid fluids, dextrose, and bicarbonate-replacement therapy varies depending on the cardiovascular status and interference of the disease process with intermediary metabolism. Fluid therapy may be followed by vasopressor therapy if needed to improve blood pressure and urine production. Flunixin meglumine should be administered to decrease fever and to inhibit the production of inflammatory prostanoids. If the metabolic acidosis does not improve and pH remains at less than 7.25 after fluid therapy, sodium bicarbonate should be administered. If the foal is demonstrating obvious signs of hepatoencephalopathy, mannitol can be administered. Routine therapy for septic shock should be provided. The lack of antibiotic-sensitivity testing necessitates a choice of broad spectrum antimicrobial therapy. High doses of intravenous preparations of penicillin in combination with an aminoglycoside or other broad spectrum antimicrobials are appropriate choices.

Figure 35-2



Tyzzers disease. Filamentous bacteria in the liver stained by Warthin Starry.

Equine Herpes Virus 1 Hepatitis

History and Clinical Signs

Mares that become infected with EHV1 late in gestation may abort in the third trimester or deliver a stillborn foal. Sometimes, infected mares will deliver a live foal that is jaundiced and weak at birth. Alternatively, the foal may appear normal at birth but subsequently develop icterus, respiratory distress, and rarely, diarrhea within the first 5 days of life.[13,14] Secondary bacterial septicemia is common.

Diagnosis and Differential Diagnosis

Icterus is a common finding in any septic foal, so any and all causes of septicemia, especially if concurrent evidence exists of pulmonary dysfunction, should be considered in EHV1-infected foals. This should include all common bacterial agents, in addition to equine viral arteritis, which may mimic EHV1 infection in the neonatal foal. Foals infected with EHV1 commonly have concurrent bacteremia as a result of immunosuppression.

The diagnosis should be suspected if there is known activity of EHV1 abortion and/or respiratory disease on the farm and a neonatal foal develops the clinical signs listed above. Liver enzymes may or may not be increased more than occurs in foals with bacterial sepsis, so blood chemistry profiles will not always be helpful.[14] Foals with EHV1 are usually neutropenic and lymphopenic, but these hematologic findings may also be seen with acute bacteremia. Confirmation of the disease is usually achieved at necropsy by finding severe diffuse pneumonia, icterus, and hepatic necrosis with viral inclusion bodies. *Actinobacillus,* which is also a common cause of sepsis and acute death in neonatal foals, can cause a similarly abnormal appearing liver, but foals infected with that organism often have multifocal necrosis of the kidney and lack the diffuse pneumonia that characterizes EHV1 infection.

Treatment

Treatments are usually unsuccessful if there is multiorgan involvement and severe neutropenia, but some foals can survive. Interferon and acyclovir may be helpful in the treatment of affected foals, but proper dosages and bioavailability in the foal are not known. Affected foals may also be administered granulocyte-stimulating factor, but most EHV1-infected foals seem to have a poor response (no increase in neutrophils). Antibiotics, oxygen, fluids, and supportive care also are indicated.

Liver Failure in Foals after Neonatal Isoerythrolysis

History

Foals can develop liver failure after a prolonged or refractory course of neonatal isoerythrolysis that required 2 or more transfusions. The etiology of this liver failure is unknown, but may be a result of chronic hypoxia to the liver and/or iron toxicity associated with multiple transfusions or, more likely, a cholangiopathy associated with the neonatal isoerythrolysis and/or its treatment.

Clinical Signs and Diagnosis

After prolonged but eventually successful treatment for neonatal isoerythrolysis, affected foals develop lethargy and may be noticeably jaundiced, or may not grow as well as other foals of the same age. A blood chemistry profile confirms hepatic failure with increases in serum concentrations of bile acids, direct bilirubin, and liver enzymes. Ultrasound findings of the liver and histologic examination of biopsy specimens are both abnormal, with the ultrasound examination revealing increased echogenicity and irregular appearance. Most often, evidence of hepatopathy with both regeneration and fibrosis is found on histologic examination of tissue samples.

Treatment

No proven treatment exists for this poorly understood liver problem. Drugs that may decrease inflammation and/or oxidative injury in the liver and promote bile flow would be recommended. These include pentoxyfilline, 8.5 mg/kg P.O. once daily, S-adenosylmethionine, 0.5 g P.O. once daily, and supplemental vitamin E and selenium.

Umbilical Vein Abscess affecting the Liver

Foals, particularly those with inadequate colostral antibody absorption, are predisposed to infection of the umbilical structures. Often, the umbilical vein may be infected and enlarged (>1 cm), extending from the urachal area into the liver. A variety of organisms, including gram-negative enteric bacteria, gram-positive cocci, and occasionally, anaerobic bacteria, may be cultured from the abscessed vein.

Clinical signs

Affected foals are usually between 3 and 14 days of age when the diagnosis is made. Foals are febrile, depressed, and may be lame from infectious arthritis or have signs of pneumonia. The umbilical area may or may not appear to be abnormal.[15] Complete blood counts and biochemistry evaluation reveal leukopenia or leukocytosis, frequently accompanied by a left shift. Other markers of inflammation (low serum iron, high fibrinogen) are usually present as expected, but serum concentrations of liver enzymes are usually within normal limits.

Diagnosis

The diagnosis is based on signalment and clinical signs, and ultrasound examination of the umbilical structures.[16,17] Occasionally, if the foal can remain relaxed in lateral recumbency, the umbilical vein can be palpated through the abdominal wall.

Treatment

If the vein is only marginally enlarged, and a positive blood culture is present such that the bacterial pathogen can be identified, then antibiotic therapy may be all that is required. If the vein is more enlarged and the abnormality extends into the liver, surgery is recommended. The vein is either removed as close to the liver as possible and the stump ligated or cauterized, or the distal part of the vein is removed and the remaining vein (running into the liver) is marsupialized to allow drainage. Plasma is usually administered to all affected foals. Unless there is severe organ dysfunction (pneumonia), or infectious arthritis, the prognosis with appropriate therapy is good. Marsupialization of the umbilical vein requires significant aftercare.

Portal Vein Thrombosis

This is rare in foals and occurs secondary to another illness. The thrombosis may be septic, e.g., with *Rhodococcus equi* infection, or occur secondary to enteritis, generalized sepsis, and coagulopathy.

Clinical Signs

The signs attributed to portal vein thrombosis include depression, presumably because of hepatic shunting of gut-derived proteins, and diarrhea if the thrombotic occlusion is acute and complete. The diarrhea is likely a result of increased mesenteric venous pressures. If the thrombosis is septic, persistent fever would be expected.

Diagnosis

The diagnosis is unlikely to be made antemortem unless there is an increase in hepatic-derived enzymes and the thrombus can be identified ultrasonographically.

Treatment
Usually, the thrombosed portal vein is identified at necropsy. Consequently, there is little experience with treatment of affected foals. One foal with nearly 90% occlusion of the portal vein was treated with macrolides and rifampin. Anticoagulant therapy such as aspirin and/or pentoxyfilline might be of benefit.

Hyperammonemia of Morgan Foals
Although not well documented, this condition is presumed to occur as a result of an inherited abnormality in hepatic ammonia metabolism.[18]

Signalment and Clinical Signs
Affected Morgan foals are usually 4 to 7 months of age and have an acute onset of signs caused by cerebral dysfunction. These signs include blindness, head pressing, circling, and seizures. In some cases, hemoglobinuria (red discoloration of the urine) is present.

Diagnosis
The diagnosis is based on signalment and clinical signs in addition to measurement of blood ammonia. Blood ammonia concentrations are often high (300-600 μmol/L).

Treatment
Although the disease has been uniformly fatal, some affected foals improve for several days only to have a second onset of severe neurologic signs. Treatments could include mannitol (0.5-1.0 mg/kg) and neomycin (4-8 mg/kg P.O. every 8 hours), in addition to intravenous administration of crystalloids supplemented with potassium chloride.

Bile Duct Obstruction
Equines have two biliary openings into the duodenum, the major and minor biliary papillae. Both drain into the proximal duodenum in close proximity. Foals with gastroduodenal ulceration may develop strictures of the duodenum associated with healing of duodenal ulcers. If the stricture is at the site of the biliary opening, obstruction of the bile flow may occur. If the stricture is distal to the opening, ingesta may reflux into the bile ducts. The clinical signs are similar with stricture at either site, but the prognosis differs.

History and Clinical Signs
A history often exists of a previous illness, e.g., diarrhea, from which the foal seemingly recovered. Either during the primary illness or soon thereafter, the foal begins to show clinical signs of prolonged gastric outflow, ptyalism, colic, bruxism, and decreased nursing.[19] If biliary obstruction is present, the foal may be mildly icteric.

Diagnosis
The history and clinical signs are characteristic of delayed gastric emptying because of ulceration. Endoscopy reveals esophageal ulcers and gastric ulceration.[20] The stomach may contain a large amount of milk that must be removed to complete the endoscopic examination. If a duodenal stricture is present and radiographs are taken prior to endoscopy, an enlarged stomach with an obvious fluid line can be seen. If the stomach is obviously enlarged, a barium study should be performed to help determine the severity of the duodenal obstruction. If the duodenal obstruction is nearly complete and distal to the biliary opening, barium may be seen in the bile ducts, but little or no barium leaving the stomach 30 minutes after administration.

Treatment
Medical treatment of affected foals should include intravenous administration of H_2 blockers (e.g., ranitidine 1.5 mg/kg every 8 hours), sucralfate and antiacidase misoprostil (dose and frequency depending on the degree of gastric dysfunction), and bethanechol (0.025 mg/kg SQ every 4 hours). If the history, clinical signs, and endoscopic and radiographic findings suggest chronic obstruction, medical therapy is unlikely to be curative.

Toxic Hepatopathy

Although several drugs administered to foals, e.g., NSAIDs, rifampin, antifungal drugs, inhalants, herbal products, anti-ulcer medication, etc., have been associated with temporary increases in serum concentrations of liver enzymes, only iron has been documented to cause toxic hepatic failure.[21,22] The iron-induced hepatic failure in foals only occurs when iron is administered prior to colostrum.

Clinical Signs

Typically, 3- to 5-day-old foals with iron-induced acute liver failure have an acute onset of hepatoencephalopathy (coma, blindness, seizure, etc.) that is almost uniformly fatal.

Diagnosis

The diagnosis is based on history (iron administration prior to colostrum), clinical signs and laboratory findings of hepatic disease and dysfunction.

Treatment

Intensive supportive care with crystalloids, dextrose, branch-chain amino acids, and "gut sterilization" with neomycin has been attempted, but has rarely been successful. Products containing iron should not be given to foals in the first days of life.

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Diseases of the Small Intestine

Chapter 36

David E. Freeman

Up to 64% of all colic cases in adult horses and in foals involve the small intestine.[1-5] The majority of small-intestinal colic cases (58% to 85%) are caused by strangulating lesions, compared with nonstrangulating obstructions (simple and functional),[2-4,6,7] and 41% to 46% involve the ileum.[7-9] The most common small-intestinal lesions in most reports are strangulation by lipoma, entrapment in the epiploic foramen, and small-intestinal volvulus, each accounting for more than 22% of all small-intestinal lesions.[2-4,9-20]

Strangulating Obstruction

Pedunculated Lipoma

Pedunculated lipoma is one of the most common causes of small-intestinal strangulation in horses,[2-4,9-13,15,16,19] with a reported prevalence of up to 41% of surgical lesions of the small intestine.[8] A pedunculated lipoma is a benign, smooth, fat tumor that is suspended by a mesenteric pedicle of variable length that wraps around intestine and its mesentery (Figure 36-1). It can be a solitary tumor or several can exist in the same horse, with 90% involving the small intestine.[13] Mesenteric lipomas can cause simple, recurrent obstruction, but this is uncommon.[10,21]

Figure 36-1



A pedunculated lipoma strangulating a segment of small intestine.

Intestinal strangulation by a mesenteric lipoma is a disease of old horses with a mean age of 14 to 19.2 years at diagnosis; horses under 10 years are rarely affected.[10,11,13,19,22] Ponies, Arabians, American Saddlebreds, and Quarter Horses have been reported to be at a higher risk, whereas Thoroughbreds are at a lower risk for this disease.[22,23] Affected horses tend to be heavier than the average in the hospital population,[13] but not all are overweight.[10] Geldings seem to be at a significantly higher risk for this lesion.[10,13,22]

Clinical signs are not always suggestive of a strangulating lesion, and many affected horses might not show signs of pain at the referral institution.[10] Consequently, in horses with a large volume of reflux, this disease can be confused with duodenitis-proximal jejunitis. On ultrasonography of horses with strangulating lipomas, intestinal distention is identified more often in the caudal ventral abdomen, middle ventral abdomen, and ventral right paralumbar fossa than in other regions.[24]

At surgery, the lipoma can be found wrapped in the jejunal mesentery. Blind resection of the pedicle is necessary if the involved intestine is difficult to exteriorize, but this carries the risk of causing a mesenteric rent and mesenteric bleeding.[25] Incidental lipomas with distinct pedicles should be removed by ligation of the stalk and transection. A significant association between postoperative ileus and strangulation by lipoma has been reported[26] and short term survival rates for this strangulation range from 48%[22] to 78.6%.[10]

Entrapment in the Epiploic Foramen

The epiploic foramen, or foramen of Winslow, is an approximately 4 cm wide entry into the vestibule of the omental bursa (Figure 36-2).[23] The visceral surface of the base of the caudate process of the liver forms the craniodorsal boundary of the epiploic foramen, the portal vein contributes to the cranioventral border, and the gastropancreatic fold forms the ventral border.[23] Uncommon versions of entrapment in the epiploic foramen (EFE) include simultaneous strangulation of 2 loops of small intestine, strangulation of the cecum by the entrapped small intestine,[27] simultaneous incarceration of the cecum and jejunum, a Littré's hernia (entrapment of a Meckel's diverticulum),[17] a parietal (or Richter's) hernia,[28,29] and impaction in the incarcerated segment.[30] Although EFE can be from right to left,[31] left to right entrapment (Figure 36-2) is far more common (97 to 100% of cases).[17,20,32] The ileum is involved in as many as 72% of cases, either alone or usually with the jejunum.[17,20,32,33] The longer the duration of colic, the more likely for the ileum to become involved.[17]

Figure 36-2



Epiploic foramen entrapment of jejunum from left to right. The epiploic foramen is viewed from the right side with the duodenum in the foreground, the liver reflected dorsally, and with the cranial abdomen to the right. (From Freeman DE: Surgery of the small intestine. Vet Clin North Am Equine Pract 13:261, 1997, with permission.)

Horses of all ages can be affected, including foals[34,35] and horses under 3 years;[11,17,20,23,31,36,37] most affected horses are under 11 years old.[11,17,23] The age predisposition to EFE that was once demonstrated in a total of 6 horses[37] was not confirmed in other studies,[11,17,23] especially when compared with strangulation by lipoma, which is truly a disease of older horses.[11] Some studies reported that Thoroughbreds, Thoroughbred crosses, and males are at a higher risk for this disease.[17,20,31,32,38] In the United Kingdom (U.K.), 74% of cases occur between November and March, mainly in January, suggesting that stabling predisposes to this disease.[32] According to data from one U.S. and one U.K. university hospital, up to 68% of horses with EFE were crib-biters before surgery compared with 10.4% or fewer in the control groups, and this association was significant.[39]

Clinical signs and findings can be confusing: 38% of horses with EFE did not show signs of abdominal pain at the referral hospital in one study, and in 52% of those horses, no gastric reflux was obtained.[20] The signs of abdominal pain were sufficiently mild in one horse to delay referral for 2.5 days.[40] Traction on the ventral band of the cecum is reported to induce a painful reaction in horses with the ileum incarcerated in the epiploic foramen,[27] but this could not be confirmed in another report.[36]

In horses with EFE, ultrasonography could accurately detect small-intestinal distention in 94% to 100% of horses, compared with 74% to 78% for palpation per rectum.[14,20] With this lesion, distended or edematous small intestine is identified more often on transabdominal ultrasonography in the ventral right paralumbar fossa, caudal ventral abdomen, and middle right paralumbar fossa.[24]

In most cases, surgical correction of EFE is accomplished by careful traction in a horizontal direction combined with pushing of the strangulated bowel in the same direction.[41] Careful milking of fluid into the empty and collapsed distal segment can decompress the strangulated bowel, or nonstrangulated bowel can be drawn into the foramen so distention of the strangulated segment can be reduced by spreading its contents into the nonstrangulated bowel.[20] Bowel should not be drawn upward to the abdominal incision[41] as this line of traction could tear the portal vein and cause fatal hemorrhage.[20,31,42] (Procedures for management of irreducible entrapments are described in Chapter 27, Surgical Techniques).

The short term survival rate after completed surgery for EFE varies from 18% to 88%.[2,14,15,17,20,32,36,37] In a recent study on long-term survival after colic surgery, EFE was the only categorical variable associated with decreased survival,[43] and horses with this lesion were more than four times as likely to undergo a second exploratory surgery as horses with other conditions causing colic.[26] Complications unique to this lesion are fatal hypoglycemia, thrombosis of the portal vein, ischemic necrosis in the liver,[44] and rupture of the portal vein.[20,31,42]

Volvulus

Volvulus is typically a 360-degree rotation[45] of long segments of small intestine into distinct spirals around the mesenteric axis. It can develop as a primary lesion or secondary to an acquired inguinal hernia,[27,46,47] a mesodiverticular band,[48] a Meckel's diverticulum,[49] strangulation in mesenteric rents,[48] distention from any cause, and fixation by vitelloumbilical bands[50] and adhesions.[51] Volvulus can affect a horse of any age, but represents the most common indication for intestinal surgery in foals.[5,34]

Volvulus nodosus is a less common form of small-intestinal volvulus. It is caused by a 360° torsion of the ileum and jejunum so they form a mesenteric pouch in which prestenotic jejunum becomes entrapped.[52,53] Distention of the entrapped bowel draws the ileum into the mesenteric pouch to form a tight loop that knots the entrapment.[53] Volvulus nodosus can account for 27% of small-intestinal lesions that require surgery in foals,[34] occurring typically in foals 2 to 7 months of age.[53]

Clinical signs of volvulus are typical of acute small-intestinal strangulating obstruction, and distended, occasionally thick walled small intestine can be palpated per rectum in 69% of horses.[45] Pain can be intermediate to severe in 74% of horses.[45] Correction of volvulus nodosus can be difficult,[52] but can be accomplished by massaging the contents of the entrapped loop into the proximal segment, thereby allowing the bowel to be pulled through the ring formed by the ileum.[53] If the bowel involved in a volvulus nodosus is necrotic, time can be saved by resecting the entire lesion without reduction.[53] In a recent study of 115 horses with small intestinal volvulus, survival to discharge for horses that recovered from anesthesia was 80%.[54] Compared with survivors, nonsurvivors had higher heart rates, longer capillary refill time, greater hemoconcentration, and more exudation of cells and protein into peritoneal fluid at admission.[54]

Intussusception

Suspected predisposing factors for small-intestinal intussusceptions (Figure 36-3) in horses are enteritis, heavy ascarid burden, infection with *Anoplocephala perfoliata*, mesenteric arteritis, and abrupt dietary changes.[55,56] A transverse enterotomy,[57] functional side to side anastomosis,[58,59] end-to-end anastomosis,[60] and pedunculated mucosal mass (Figure 36-3C), such as a papilloma, leiomyoma, cryptococcal granuloma, granuloma of unknown cause, and carcinoid, can form the leading edge of a jejunojejunal intussusception in horses.[56,61-63]

Ileocecal intussusception (Figure 36-4) constituted 74% of all small-intestinal intussusceptions in one report;[19] 27% of ileocecal intussusceptions cause chronic, recurrent colic.[64] Intussusceptions of long segments cause signs of severe small-intestinal obstruction.[56,63,64] Short ileocecal intussusceptions cause colic that is mild, intermittent, and usually postprandial, and also cause reduced appetite and fecal output, fever, weight los, and failure to thrive.[64,65] Ileoileal intussusceptions usually form a short, doughnut like lesion that causes recurrent colic.[56,66-68] In a jejunojejunal intussusception, tension on the mesentery of the intussusceptum forms a corkscrew configuration in the bowel (Figure 36-3A), and short-to-long segments (up to 10 m) can be involved.[62,63] However, short jejunojejunal intussusceptions can cause recurrent colic.[63,68] With chronic intussusceptions, the repeated bouts of obstruction cause compensatory changes in much of the proximal jejunum, such as marked jejunal dilatation, even when empty, thickening of the muscular wall, and ecchymosis on the antimesenteric surface.[64,65]

The female predisposition once demonstrated in a study of 7 horses with this disease[38] was not evident in other studies,[55,56,64-66] but Thoroughbred horses[66] and ponies appear to be at risk.[56] Although regarded mainly as a disease of foals, intussusceptions have been reported over a wide age range up to 24 years.[56,63,64] Ileocecal and ileoileal intussusceptions, both of which are more likely to cause recurrent mild to moderate colic, are more common in horses 3 years of age and younger.[55,56,64-68]

Rectal examination may reveal distended loops of small intestine, and the intussusception can be palpated as a firm, painful, tubular structure in some horses.[56,63] Ileocecal intussusceptions were palpated in the right dorsal quadrant of the abdomen in 31% to 50% of horses in 2 reports.[56,64] During a painful episode, the hypertrophied small intestine proximal to the obstruction can be palpated per rectum as large diameter, moderately distended, thick-walled loops.[64] On transabdominal ultrasonography, a cross sectional view of a jejunojejunal or ileocecal intussusception can be seen as concentric rings with a "bull's eye" appearance (see Chapter 15, figure 15-51).[58,69] Because the strangulated intussusceptum is partly or totally sequestered within the intussuscipiens, peritoneal fluid may not reflect changes consistent with strangulation.[63,64]

Figure 36-3A



Figure 36-3B

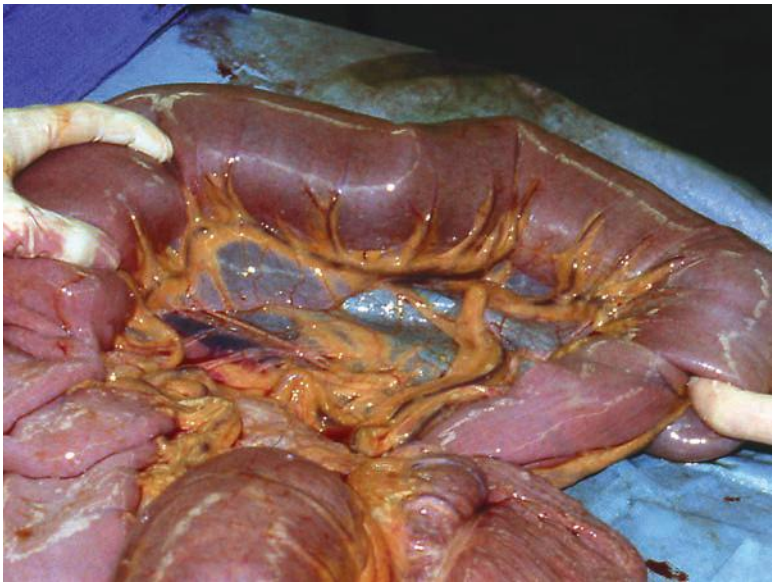
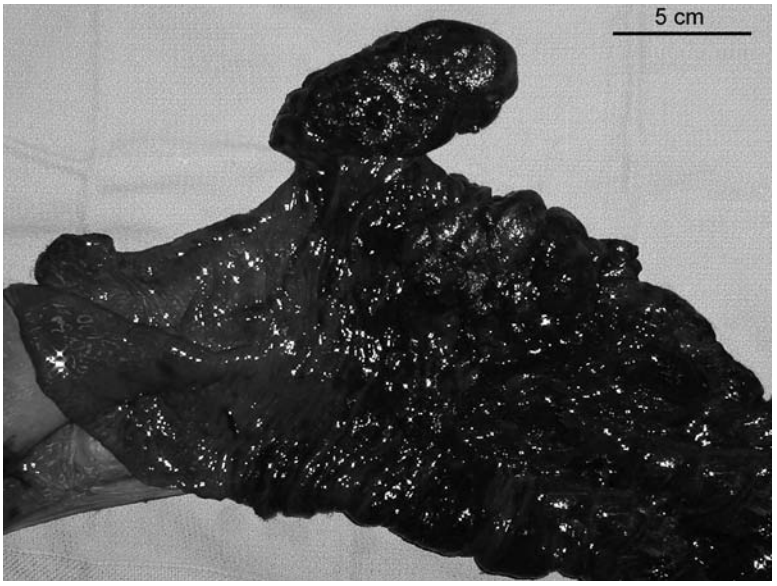


Figure 36-3C



A.) Jejunal intussusception in an adult horse, showing the tightly spiraled coils produced by the intussusceptum drawing the mesentery into the intussusception. Arrowhead points to the leading edge, which was a mucosal polyp (see Figure 36-3C). **B.)** Jejunal intussusception demonstrating the inversion of the nondistended intestine into the intussuscepiens. **C.)** Opened intussusception (same lesion as in Figure 36-3A) showing a mucosal polyp that formed the leading edge of the intussusceptum.

Figure 36-4



Intraoperative view of an ileocecal intussusception in a weanling. Exposure was enhanced because of the small size of the horse. (From Freeman DE. Surgery of the small intestine. Vet Clin North Am Equine Pract 13:261, 1997, with permission.)

Chronic intussusceptions of short segments of ileum (approximately 10 cm long) are not strangulated, but can be difficult to reduce because of chronic folding of the intestinal wall at the leading point of the intussusception.[64,66] Horses with ileocecal or ileoileal intussusceptions have been treated successfully by reduction only[66,67] and by reduction and myotomy.[66,70] Incomplete bypass by ileocecostomy, with or without reduction, can be used for chronic ileocecal intussusceptions,[64,65,71] and short-term results are excellent.[64] A handsewn technique is preferable to stapling instruments because the ileal wall is so thick, and the hypertrophied jejunum should recover over time. Rare long-term complications include stomal impaction,[56,64] stomal constriction, ileal hypertrophy, and rupture.[72]

In acute ileocecal intussusception, the intussuscepted ileum and jejunum can be too edematous and hemorrhagic to reduce, and bypass by a jejunocecostomy without reduction can cause postoperative hemorrhage.[64] Jejunojejunal intussusception is reduced by slow traction on the intussusceptum and gentle massage of the distal end of the intussuscipiens.[62] If it is nonreducible, the entire intussusception can be removed by resection only,[63] although this can make ligation of mesenteric vessels difficult.[56] (Procedures for management of irreducible intussusceptions are described in Chapter 27, Surgical Techniques). Because *A. perfoliata* may be involved in the pathogenesis of intussusceptions in horses, affected horses and pasture mates should be treated with pyrantel pamoate or praziquantel.[55,73]

Prognosis is favorable for all intussusceptions.[12,63,64] Some horses can have a protracted recovery after surgery for chronic ileocecal intussusception, with slow weight gain and episodes of mild colic.[64]

Mesenteric Rents

Mesenteric rents can be primary lesions, congenital defects, secondary to mesodiverticular bands, or secondary to an old anastomosis but situated remote from it.[20,74] Tears in the ileal and duodenal mesentery have been reported, but the jejunal mesentery is involved in most cases.[74,75] Tears can also develop in multiple sites. Horses of a wide age range appear to be prone to developing mesenteric rents, although postpartum mares are more likely to be affected (Figure 36-5A).[74,76] Mesenteric tears can cause segmental ischemic necrosis of the related segment of jejunum in postpartum mares or can strangulate a more distant portion of small intestine.[75]

Surgical treatment can be complicated by an inability to correct the strangulation (Figure 36-5B), by strangulation of long intestinal segments, by hemorrhage from the affected mesentery, and by failure to close the entire mesenteric defect.[74] Closure of the defect can be difficult or impossible through a ventral midline approach (Figure 36-5A),[77] so elective laparoscopic closure should be attempted as a standing procedure shortly after the ventral median celiotomy is performed.[77] Because access to the tear can be difficult, both sides of the abdomen might have to be examined to locate it.[77]

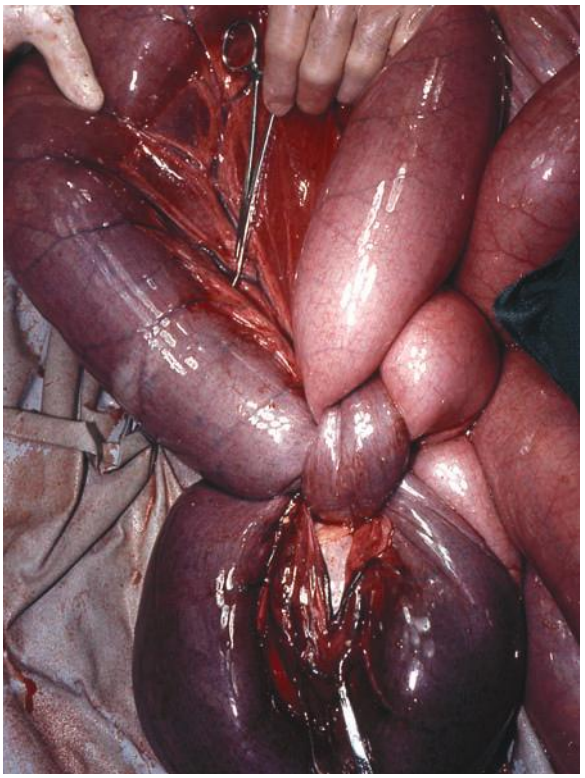
Inguinal Hernia

An indirect inguinal hernia is caused by small intestine passing through the vaginal ring into the vaginal tunic, and is the most common form of inguinal hernia in horses (Figure 36-6). Bilateral cases are rare.[78,79] In a direct inguinal hernia, jejunum and,

Figure 36-5A



Figure 36-5B



Mesenteric rent in a postpartum mare. The arrows demonstrate the extent of the rent, which had strangulated jejunum but could not be closed from a ventral median approach. Mare died from a recovery stall accident.

occasionally, the testicle escape through a rent in the peritoneum and transverse fascia to lie in the subcutaneous space of the scrotum and prepuce (Figure 36-6).[80-82] Direct hernia is more common in foals than in adults.[80-84] Direct and indirect inguinal hernias are rare in geldings.[83,85-87]

In adult horses, indirect inguinal hernias involve short segments of small intestine (median of 15 cm), whereas direct hernias can involve greater lengths of intestine.[88] Indirect inguinal hernias in adult horses are usually acquired and nonreducible, whereas congenital inguinal or scrotal hernias in foals involve long segments and are reducible; in the latter, the intestine remains viable. This difference can be attributed to the relatively shorter, wider, and more direct configuration of the foal's inguinal canal and vaginal tunic. Because of the size of the external inguinal ring, it does not play a critical role in the development of an inguinal hernia. The vaginal ring is the first structure to be traversed as a hernia develops (Figure 36-6). Although a hernia must start by entry through the vaginal ring,[27] the intestine is actually strangled 2 to 3 cm further distally in adults by a ring formed by merging of the internal spermatic fascia into loose connective tissue.[89] Ileum, alone or with jejunum, is involved in approximately half of adult inguinal hernias,[46,84,88] and the risk of ileal involvement might increase with increased duration.[27]

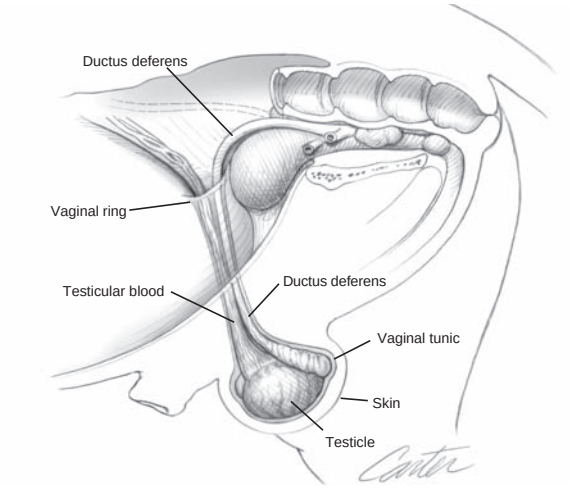
Although many breeds can be affected,[79,87] a higher incidence of inguinal/scrotal hernia has been reported in Standardbreds,[38,87] Tennessee Walking Horses, and American Saddlebreds.[46] In acquired inguinal hernias, almost all age groups over 1 year are at risk.[23,87] Predisposing factors are not always recognized,[79] but include recent strenuous exercise, recent breeding,[46,87] or trauma.[46]

Congenital scrotal hernias are noted shortly after birth and usually resolve spontaneously within 3 to 6 months. Direct or ruptured inguinal hernias in foals are evident within 48 hours after birth and cause intermittent colic, depression, severe scrotal and preputial swelling, and edema, with skin excoriation and tearing caused by abrasion against the inside of the thigh.[80,81] These are not reducible and are treated as surgical emergencies, although strangulation of intestine occurs rarely.[81]

Acquired inguinal hernias in adult horses cause mild to severe colic.[79] The strangulated intestine compresses the testicular vessels and causes the testicle to become swollen, firm, and cold. Rectal examination will reveal small intestine entering the vaginal ring and distention of the small intestine. Ultrasonography can facilitate early diagnosis and is especially useful if rectal palpation is impossible.[46]

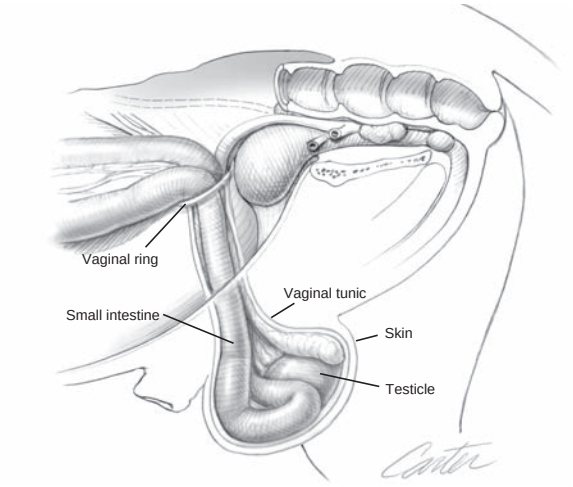
With congenital hernias in foals, surgical correction is indicated if the hernia does not resolve spontaneously, if the owner is concerned because of an apparent increase in size of the hernia, or if the vaginal tunic ruptures. In the early stages, a direct hernia in an adult horse can correct spontaneously after the anesthetized horse is placed in dorsal recumbency[84] or it can be treated by external compression with the horse anesthetized. If these methods fail, surgical correction can be performed through an inguinal approach, combined with a ventral median incision to facilitate resection. (Procedures for management of inguinal hernias are described in Chapter 27, Surgical Techniques). A survival rate of up to 76% has been reported for horses with acquired inguinal hernia.[79,84,87]

Figure 36-6A



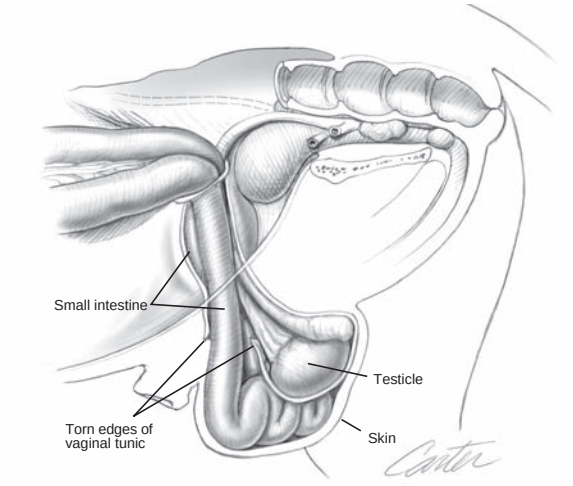
Normal inguinal structures in a horse that are relevant to formation of an inguinal hernia. Note the vaginal ring is the point of entry from the abdomen to the vaginal tunic.

Figure 36-6B



Indirect inguinal hernia.

Figure 36-6C

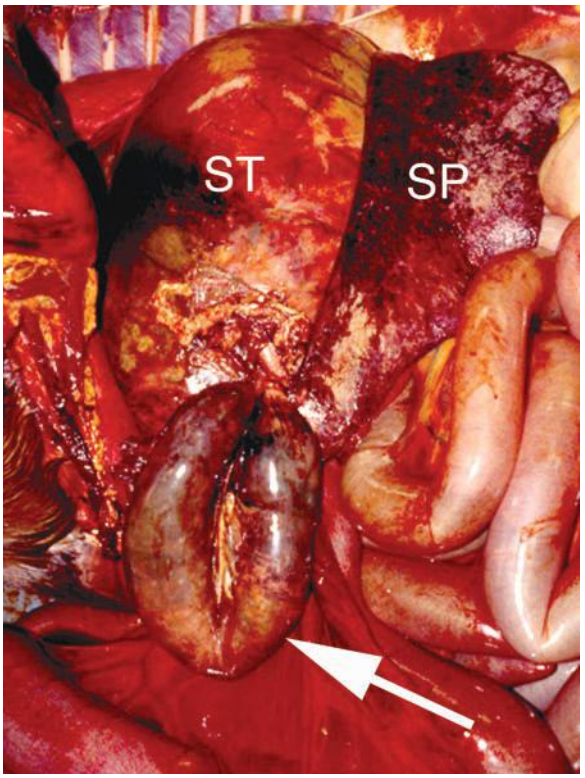


Direct inguinal hernia. The difference between this and Figure 36-8B is that the tunic has ruptured to allow bowel to escape into a subcutaneous position. (From Bartmann C-P, Glitz F, v Oppen T, et al. Diagnosis and surgical management of colic in the foal. Clin Tech Equine Prac 1:125, 2003 with permission.)

Incarceration through the Gastrosplenic Ligament

The gastrosplenic ligament is a broad but delicate attachment between the greater curvature of the stomach and the hilus of the spleen.[90] Small intestine passes from caudal to cranial through acute tears in this ligament to place the strangulated loop lateral to the stomach and craniolateral to the spleen (Figure 36-7).[90] At surgery, the strangulation is easily corrected by traction, and enlarging the rent does not cause problems or predispose to recurrence. If the most ventral edge of the strangulating ring is accessible, it can be transected between two ligatures to disrupt its continuity.[91]

Figure 36-7



Necropsy specimen of incarceration in the gastrosplenic ligament. A segment of small intestine (arrow) is strangulated after moving through a defect in the ligament from medial to lateral between the stomach (ST) and the spleen (SP).

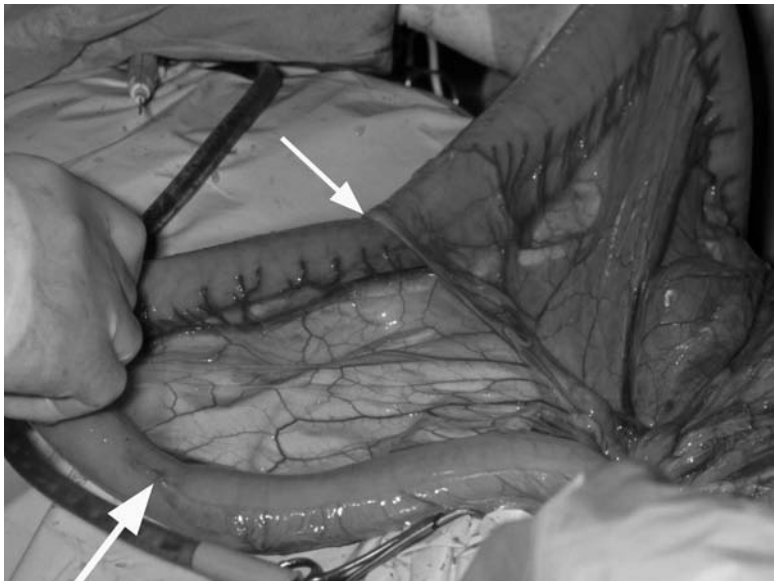
Vitelline Anomalies

Failure of a vitelline artery and associated mesentery to atrophy during early embryonic development forms a mesodiverticular band.[48] The band is usually present in the distal jejunum, approximately 1.5 m from the ileocecal junction (Figure 36-8). It extends from one side of the mesentery, usually the left, to the antimesenteric surface of the small intestine to form a triangular space (Figure 36-9). Small intestine can become entrapped in that space; it then stretches or tears adjacent mesentery, and becomes strangulated in the resulting mesenteric rent.[48] Although a mesodiverticular band is a congenital anomaly, obstruction can be delayed for many years and often bands are incidental findings at necropsy or at surgery for other reasons.[48]

The omphalomesenteric (vitelline) duct, which provides a communication between the yolk sac and early embryonic gut, can persist to form a Meckel's diverticulum (Figure 36-10). This is evident as a blind tubular extension from the antimesenteric surface of the distal jejunum, approximately 120 cm from the ileocecal junction.[92,93] The diverticulum can be up to 35 cm long and 5 to 10 cm in diameter.[93] Occasionally, a fibrous band will persist from the apex of a Meckel's diverticulum to the umbilicus to form a vitelloumbilical band, which can create an axis for small-intestinal volvulus.[50]

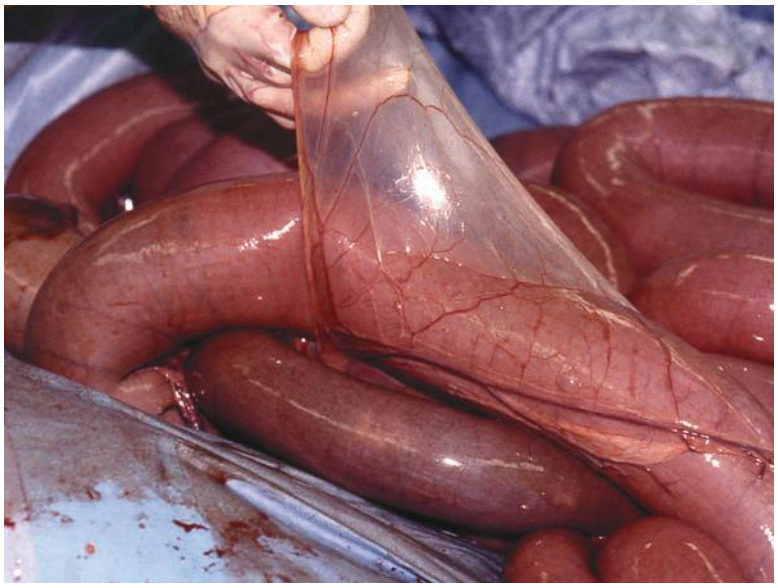
Meckel's diverticulum can cause colic by strangulating small intestine,[92,94,95] forming an axis for volvulus nodosus,[49] becoming strangulated in an umbilical hernia (Littré's hernia),[96] or becoming impacted[94] to the point of necrosis and rupture.[93] Although Meckel's diverticulum is a congenital anomaly, it can cause colic in horses of a wide age range.[92-95] In a review of 15,000 necropsies, Meckel's diverticulum caused the death of all 5 horses (0.03%) in which it occurred.[93]

Figure 36-8



Mesodiverticular band (upper arrow) that was an incidental finding in a yearling, located at the typical distance from the end of the ileocecal fold (lower arrow).

Figure 36-9



Mesodiverticular band that was an incidental finding in a segment of intestine examined for other reasons, showing the entry into the blind pouch (arrow) formed between the mesenteric fold of the band and the adjacent jejunal mesentery. Strangulation seems to be preceded by entry of bowel into this pouch.

Figure 36-10

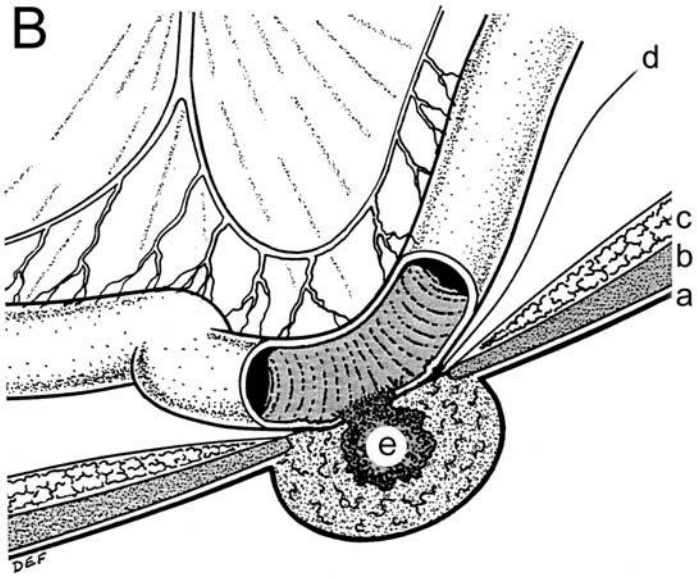


Meckel's diverticulum that had strangulated contiguous jejunum. Arrow points to the single vessel supplying the diverticulum. (Courtesy of Dr. John Madison.)

Strangulated Umbilical Hernia

Strangulation of a loop of small intestine in an umbilical hernia is rare, and can develop in two ways. The strangulated loop of intestine can rupture through the hernial sac and dissect subcutaneously in a caudal direction to cause an inguinal enlargement.[97] More commonly, a parietal, or Richter's, hernia develops, in which only a portion of the antimesenteric wall of the ileum is incarcerated and the lumen is not compromised (Figure 36-11).[97,98] This causes the umbilical hernia to become nonreducible, swollen, firm, edematous, and painful to palpation. Ultrasonography can be used to evaluate the hernia and its contents.[99] Colic can develop in horses with a parietal hernia,[97,98] but a more common progression is umbilical abscessation (Figure 36-11), which can lead to rupture of the hernia and formation of an enterocutaneous fistula (Figure 36-11C).[97,98] Surgical correction of these lesions is accomplished by digital guidance of en bloc removal through a 10 to 15 cm celiotomy cranial to the ring, followed by resection and anastomosis, if necessary.[97,98] The prognosis for survival is good.[97,98]

Figure 36-11A



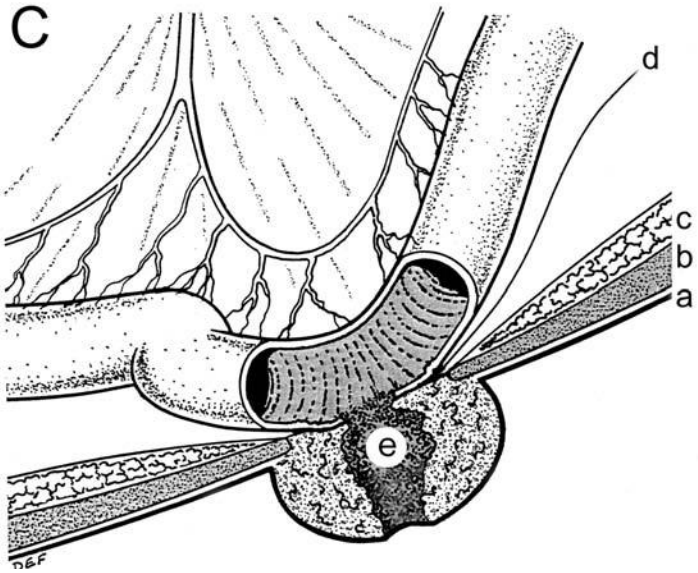
Richter's hernia showing the antimesenteric segment of small intestine entrapped and swollen in the hernial sac, which contains fluid (e), without compromise of the intestinal lumen. Relevant anatomy is skin (a), body wall (b), retroperitoneal fat and peritoneum (c), and ileocecal fold (d). (From Freeman DE, Orsini JA, Harrison IW, et al. Complications of umbilical hernias in horses: 13 cases (1972–1986). J Am Vet Med Assoc 192:804, 1988, with permission.)

Figure 36-11B



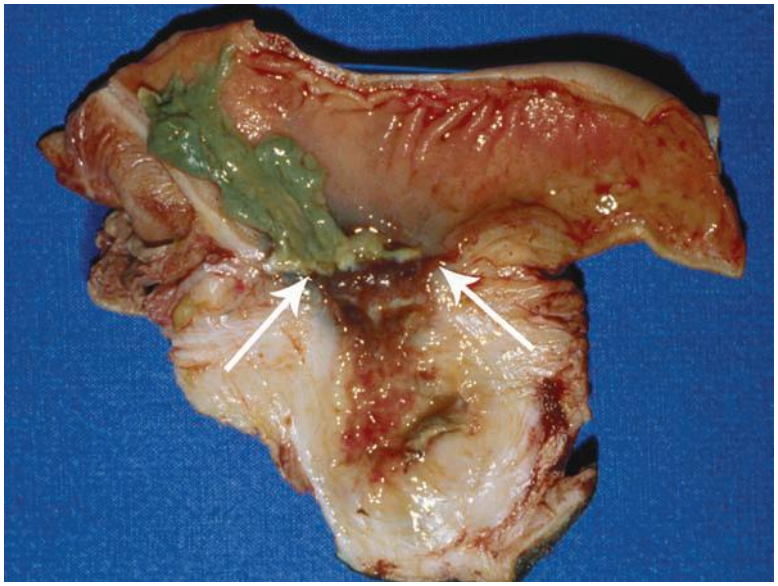
Ileum that has a focal infarct in the side of the wall because of entrapment in a Richter's hernia.

Figure 36-11C



Richter's hernia with progression to an umbilical fistula secondary to erosion of the abscess through the body wall. The resulting continuity with the lumen allows intestinal contents to drain through the fistula, which produces dehydration and electrolyte imbalances.

Figure 36-11D



Richter's hernia. a. Infarction of the side of the ileum from incarceration in an imbilical hernia. b. Longitudinal section of a Richter's hernia showing communication between the abscess cavity and intestinal lumen (between arrows), as illustrated in Figure 36-11A.

Diaphragmatic Hernias

Small-intestinal strangulation in diaphragmatic defects has been reported as the cause of death in foals from 7 hours to 8 days after birth.[100,101] A congenital diaphragmatic defect or a diaphragmatic tear inflicted by a rib fracture, usually at or close to the costochondral junction of ribs 3 to 8, are likely causes of diaphragmatic hernia in foals.[100,101] The presence of omental adhesions to a callus on fractured ribs on the thoracic side of the defect is suggestive of previous trauma,[102,103] possibly at birth. The most common causes of diaphragmatic hernia in adult horses are trauma, parturition, particularly dystocias, and recent strenuous activity.[104] Although several abdominal organs can enter the diaphragmatic defect, small intestine is the most commonly reported.[105] Large defects are more likely to cause dyspnea from pulmonary compression by intrathoracic displacement of the colon, but do not incarcerate bowel and cause colic.[104,106] There does not appear to be an age, breed, or gender predisposition to this disease.

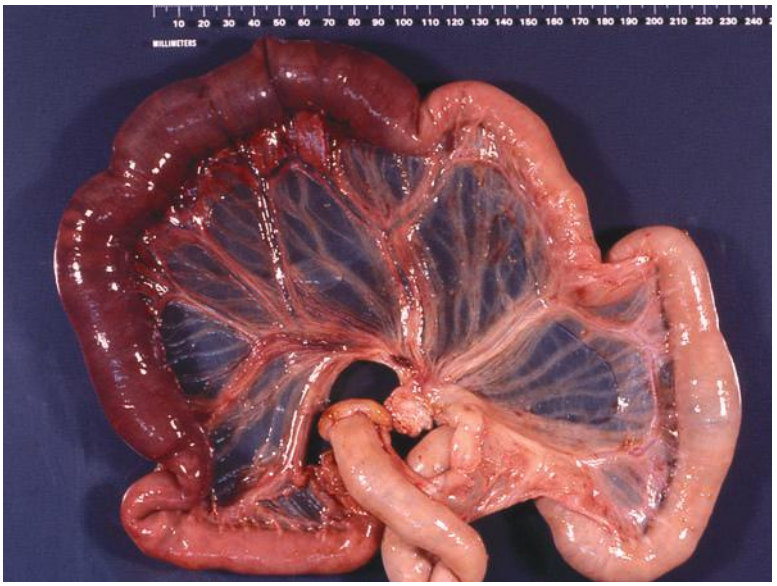
Increased intraabdominal sounds can be detected on auscultation in some horses,[107] but are not easily distinguished from intestinal sounds heard in normal horses. Both radiography and ultrasonography allow preoperative diagnosis (see Chapter 6),[108-112] but ultrasonography might be superior, especially for small tears with little visceral involvement or when pleural effusion obscures the ventral portion of the diaphragm.[108]

Miscellaneous Strangulating/Ischemic Diseases

Small intestine can become strangulated in mesenteric ligamentous bands, in a uterine torsion,[113] through rents in the mesometrium,[19,114] gastrohepatic ligament,[2] small-colon mesentery,[2,27] lateral ligament of the urinary bladder,[115] cecocolic fold,[4,19,27,116] and large-colon mesentery,[19] by components of the spermatic cord,[117] and by omental adhesions.[3] Small intestine eviscerated through a lacerated vaginal fornix, a defect in the bladder and urethra,[118] or a castration wound[33] can become strangulated. Entrapment of small intestine within the nephrosplenic space has been reported in two horses, and the affected bowel did not require resection.[119] Mesenteric hematomas of unknown cause and in locations that are difficult to access can cause colic and ischemic necrosis of affected intestine.[120] A parietal hernia of the duodenum into the epiploic foramen[28] and duodenal torsion have been reported,[121] but are rare.

Adhesions after any intraabdominal procedure can form an axis around which attached small intestine can form a volvulus, or they can form fibrous bands through which small intestine can become strangulated.[51,122] Nonstrangulating infarction and necrotizing enterocolitis in the small intestine (Figure 36-12) are rare and have a poor prognosis.[99,123] Abdominal radiographs in foals with enterocolitis can demonstrate gas separating layers of the bowel wall, linear strips or "bubbles" of gas in the intestinal wall, and gas distention of the affected segment.[58]

Figure 36-12



Necrotizing enteritis in a foal at necropsy.

Nonstrangualting Obstruction

Ileal Impaction

Impaction of the ileum is usually a primary condition but can occur secondary to other conditions affecting the ileum. The impaction forms a doughy to solid, tubular mass of variable length that extends proximally from the ileocecal junction (Figure 36-13).[124-128] In the United States, most cases occur in the southeast, probably related to the feeding of coastal Bermuda grass hay.[128] Ileal impaction also occurs in parts of the United States and in Europe where coastal Bermuda grass hay is not fed.[2,9] The disease appears to be more common in the United States from June through November, especially in the fall,[124,126] although this was not confirmed in one study.[129] The risk of ileal impaction was not reduced by combining coastal Bermuda hay with other hay; it appeared to be increased by recent introduction or feeding of poor quality hay, and appeared to be lowered by feeding a pelleted concentrate feed in addition to hay.[129] A wide age range of horses is affected,[124,125] including newborn[130] and older foals;[5] mares and Arabian horses were significantly overrepresented in one study.[127]

Studies from the United Kingdom and from North Carolina suggest that tapeworm infection could predispose horses to ileal impaction.[129,131] Orbatid mites are the intermediate hosts for tapeworms, and their preference for humid regions could contribute to the geographic predisposition for this disease in horses in the southeastern section of the United States.[131] The severity of mucosal damage and edema caused by tapeworms at the ileocecal junction is proportional to the number of parasites present and could predispose to obstruction at that site.[131]

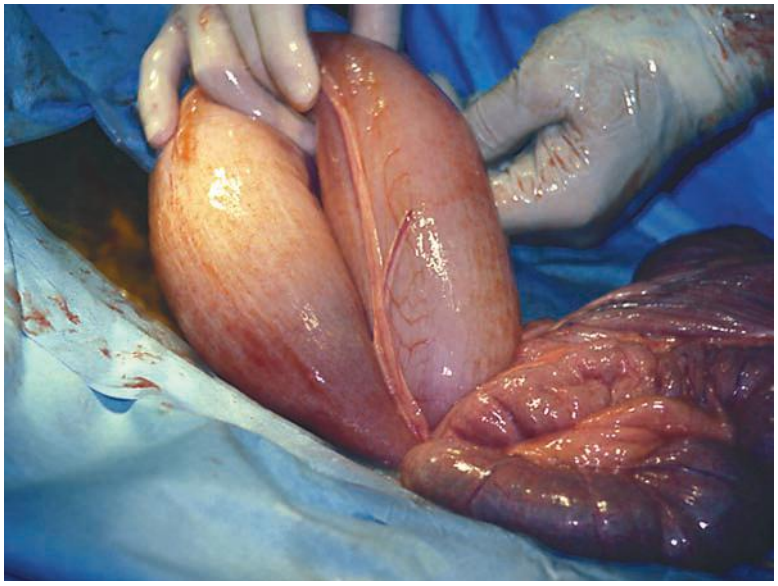
Spasmodic contraction of the bowel around the impaction could explain the early presence of signs consistent with abdominal pain, but pain becomes more severe and constant as distention of the jejunum becomes more pronounced.[128] The impacted

ileum is more easily palpated early in the disease course, before small-intestinal distention becomes severe, but small-intestinal distention is generally a consistent finding on rectal examination.[124,125,128] Gastric reflux can be obtained in most affected horses, depending on the duration of obstruction.[124,126,127] Distinction between horses with ileal impaction, small-intestinal strangulating obstruction, and proximal enteritis can be difficult.

Medical treatment can be successful early in the disease, when the impaction can be felt per rectum.[125,128] Medical treatment consists of intravenous fluids at 5 L every 2 hours, and flunixin meglumine at 0.5 mg/kg 3 or 4 times daily.[128] Mineral oil should be administered when gastric reflux has ceased. If surgery is required, the impaction is broken down by gentle manual massage, aided by mixture with fluid from the proximal bowel or by intraluminal infusion of saline.[126] Dioctyl sodium sulfosuccinate has been included in the infusion, but is irritating to mucosal surfaces. Enterotomy is contraindicated, except in rare instances, and jejunocecostomy[127] is not recommended in the absence of a predisposing lesion or severe changes in the muscle wall.[126,128,129]

The prognosis is favorable,[125,126] although ileus, gastric rupture, laminitis, mucosal necrosis, and perforation of the ileum are complications of delayed treatment.[124] Reimpactions are rare.[132] Because of the potential role of tapeworms in this disease,[129,131] pyrantel pamoate at 6.6 mg/kg to 13.2 mg/kg and dewormer combinations with praziquantel should be administered to affected horses and pasture mates.

Figure 36-13



Intraoperative demonstration of ileal impaction with coastal Bermuda grass hay.

Muscular Hypertrophy of the Ileum

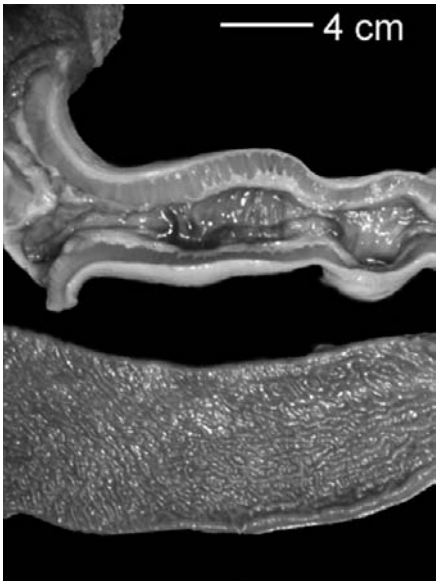
Muscular hypertrophy of the ileum causes recurrent colic but can also cause ileal impaction. The condition is considered idiopathic.[133] Both the circular and longitudinal layers are increased in thickness[133,134] and the lumen is markedly reduced (Figure 36-14). The affected segment is usually 1 m long, diverticula are common (Figures 36-14 and 36-15), and full thickness rupture can occur.[72,133-135] The jejunum immediately proximal to the affected ileum can undergo compensatory hypertrophy in longstanding cases, but with an increase in lumen diameter.[134]

Muscular hypertrophy of the ileum has been reported in foals,[135] but it is most common in mature horses (more than 5 years old).[8,133,134,136,137] There does not appear to be a breed predilection.[134] Most horses present with a history of recurrent, low grade colic of variable duration, up to 2.4 years in 1 horse,[134] with or without anorexia, and weight loss. The involved segment can be palpated per rectum in some horses.[134] Bypass of the affected segment by side to side ileocecostomy or jejunocecostomy, with or without transection or removal of part of the ileum, is usually successful.[8]

Ascarid Impactions

Intestinal stages of *Parascaris equorum* can cause small-intestinal obstruction (Figure 36-16), intussusception, abscessation, and rupture in foals, weanlings, and horses up to 24 months.[138] Affected foals usually appear unthrifty. Impaction usually follows shortly after anthelmintic treatment, but can arise without this history.[139] Ultrasonographic examination can demonstrate ascarids in the small intestine.[140] Emerging resistance in *Parascaris equorum* to ivermectin[141] could increase the risk of this disease for foals and young horses.

Figure 36-14



Ileal muscular hypertrophy with affected ileum and ileocecal junction (top) opened to demonstrate the thick wall of the ileum, the antimesenteric diverticula, and the narrow lumen compared with normal proximal bowel (bottom).

Figure 36-15



Ileal muscular hypertrophy at surgery, showing the thick tubular wall of the affected ileum, the numerous diverticula on the antimesenteric wall, and the compensatory thickening in bowel proximal to the affected segment. (Courtesy of Dr. Gary Baxter.)

Figure 36-16



Ascarid impaction in the jejunum, with ascarids evident through the intestinal wall, mixed with dry jejunal contents. These were removed successfully by enterotomy. (From Bartmann C-P, Glitz F, v Oppen T, et al. Diagnosis and surgical management of colic in the foal. Clin Tech Equine Pract 1:125, 2003 with permission.)

Animals with ascarid impactions that can be resolved at surgery by manual dispersal or by typhlotomy appear to have the best prognosis, possibly because they have mild small-intestinal damage.[142] Enterotomy is required in more severe cases, and resection is indicated if the bowel is devitalized.[5,139] Not all the worms can be removed at surgery, regardless of the method used, and anthelmintic treatment after surgery is recommended.[142] Postoperative mortality was 92% in one report,[139] with focal necrotizing enteritis, peritonitis, abscess formation, and adhesions causing most deaths.[142] A poor prognosis after surgery could be attributed to undetected ascarid-induced damage in the intestinal wall, release of toxins from the ascarids, release of antigenic proteins after organophosphate-induced rupture of the cuticle, preexisting debilitation, low-grade liver disease, low-grade pneumonia, and failure to remove all worms at surgery.[142]

Ascarid impaction can be prevented by a proper deworming program, careful environmental management, and routine fecal egg counts to assess anthelmintic efficacy. Foals should be dewormed at 6-week intervals from 6 weeks of age to 6 months.[142] Heavily parasitized foals at high risk of impaction should be given mineral oil with the anthelmintic.[142] Some recommend an anthelmintic capable of rapid kill or complete paralysis to prevent impaction as worms undergo agonal contortion (piperazine, organophosphates), and others recommend a slower kill that would allow gradual elimination in small groups (fenbendazole, ivermectin, or pyrantel pamoate).[142] Fenbendazole at 10 mg/kg PO should be used if ivermectin resistance develops.[141]

Neoplasia

Lymphosarcoma (Figure 36-17), adenocarcinoma, ganglioneuroma, intestinal carcinoid, leiomyosarcoma, and leiomyoma have been reported as rare causes of small-intestinal obstruction in the horse.[12,25,143-148] Presenting signs vary from a single bout of acute colic to repeated bouts of mild colic. Surgical removal of a discrete, focal, and accessible tumor is often successful,[143,145-147] but lymphosarcoma is generally a multiorgan disease with a grave prognosis.[144]

Figure 36-17



Lymphosarcoma in the jejunal wall of a 22-year-old mule. (Courtesy of Dr. Gary Baxter.)

Duodenal Ulceration and Stricture

Duodenal ulceration and stricture can develop in foals, particularly those treated with phenylbutazone or subjected to stress of surgery, transportation, or illnesses.[149] Foals younger than 4 months of age are at greatest risk, although duodenal obstruction has been reported in yearlings and in an adult horse.[99,149-151] Duodenal obstruction can cause reflux of duodenal contents into the bile and pancreatic ducts, inducing diffuse cholangiolitis, perilobar hepatitis, and pancreatitis, with acute erosive and fibrinous inflammation of the large ducts.[149]

Clinical signs of duodenal ulcers and obstruction include depression, weakness, anorexia, teeth grinding (odontoprisis), salivation, gastric reflux, fever, diarrhea, and colic.[99] Abdominal pain may be worse after nursing. Rupture of duodenal ulcers causes peritonitis.[149]

Diagnostic findings on plain radiographs include aspiration pneumonia, dilated fluid filled esophagus, and gastric distention.[99] Gas may be evident in the hepatic duct.[99] Endoscopy is more sensitive and specific than radiography in diagnosing gastric

and duodenal lesions,[58,99] although ultrasonography could be used to demonstrate any abnormalities in duodenal peristalsis, wall thickness, and lumen size.[152,153] Contrast radiography will demonstrate delayed gastric emptying, and barium in dilated bile ducts is indicative of cholangitis or cholangiohepatitis.[99]

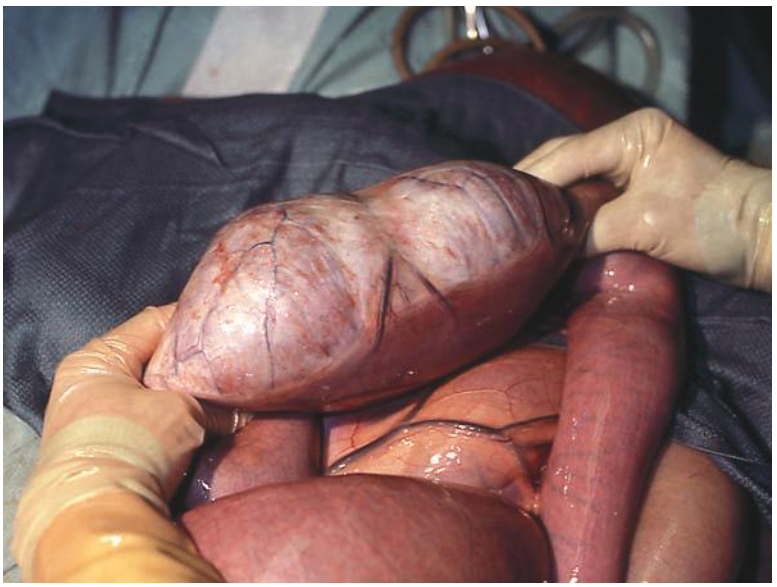
Surgical bypass of the obstruction[99,151] should be followed by medical treatment of gastric ulcers.[99] (Procedures for duodenal bypass are described in Chapter 27, Surgical Techniques). Contrast radiographs are recommended 24 hours after surgery to confirm successful bypass of the obstruction.

Miscellaneous Simple Obstructions

Duodenal obstruction in horses can cause severe pain, voluminous gastric reflux, and, in some horses,[128] spontaneous gastric reflux through the nostrils.[154] Impactions of the duodenum and jejunum are rare, and causes include impacted feed material,[128,155,156] compressed cracked corn,[157] trichophytobezoar,[158] compacted wood fragments,[159] persimmon fruit,[160,161] molasses-based stable treats,[154] baling twine,[162] and a cholelith.[163] Ripening of persimmon during fall and winter in the southeastern region of the United States apparently makes this fruit palatable to animals,[161] and water-soluble tannins in the fruit form a solid phytobezoar when exposed to gastric acid.[160] Gastric impaction with persimmon can be diagnosed by gastroscopy.[160] Idiopathic muscular hypertrophy and aganglionosis of the proximal duodenum have been reported in 3 horses.[121] The latter appears to be a disease of old horses (>12 years) and is characterized by distention of the duodenum to 25 cm in diameter, starting 20 cm from the pylorus and ending in a contracted segment immediately proximal to the caudal duodenal flexure.[121] The contracted segment had aganglionosis, and the distended proximal segment had a thick wall.[121] Hypertrophy of the pylorus can cause gastric dilatation with accompanying gastric reflux and has been corrected by pyloromyotomy and gastrojejunostomy. Pylorus hypertrophy is rare with no known cause and no reports of the prognosis.

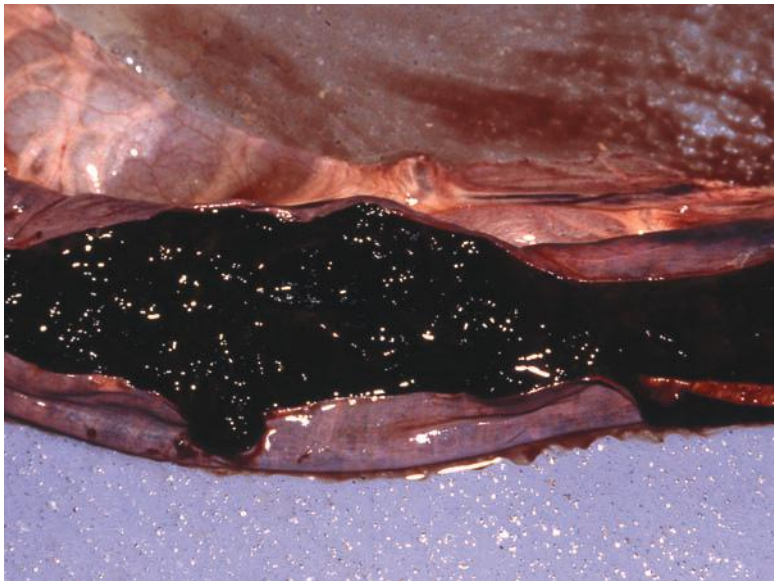
Diffuse or localized peritonitis and localized intestinal necrosis can follow small intestinal perforation by wire,[164,165] a porcupine quill,[166] ulcers,[167] and unidentified materials.[164,168] Localized lesions can be resected.[164,165] Congenital segmental aplasia of jejunal lymphatics in foals or tearing of postsurgical mesenteric adhesions and other intestinal lesions may cause chyloperitoneum and colic.[169-171] Resection of involved intestine can be satisfactory,[170] but mild cases can respond to nonsurgical treatment. An ileal diverticulum (Figure 36-18),[172,173] other rare forms of intestinal malformation,[174] and congenital jejunal duplications have been described as causes of recurrent small-intestinal obstruction in horses.[175] Extraluminal causes of simple obstruction include intraabdominal abscesses,[3] intramural hematoma (Figure 36-19),[176] and adhesions (see Chapter 7).[121]

Figure 36-18



Ileal diverticulum that became impacted and caused obstruction of the ileum.

Figure 36-19



Intramural hematoma that caused obstruction of the jejunum by extraluminal compression.

Inflammatory and Infiltrative Diseases

Duodenitis-Proximal Jejunitis

Duodenitis-proximal jejunitis (DPJ), or gastroduodenitis jejunitis, hemorrhagic fibrinonecrotic duodenitis, proximal jejunitis, proximal enteritis, and anterior enteritis, causes inflammation of the proximal small intestine, fluid accumulation in the stomach and small intestine, and endotoxemia.[177] The cause is unknown. Clinical signs vary in severity, and age, breed, and gender predispositions have not been established.[177] Most affected horses are over 1.5 years of age,[177] although the condition has been reported to occur in nursing foals. The prevalence of the disease has been reported as 3% to 22% of all small intestinal colics.[2,4,19,178] Prevalence in California is lower than in other parts of the United States and Europe, and the disease appears to be more severe in the southeastern United States[179] than in the northeast.[177]

The clinical hallmark of DPJ is reflux of a large volume of fluid through a nasogastric tube (usually more than 48 L in the first 24 hours) in a horse that has signs of mild to severe pain initially, and then depression and less pain.[180] In contrast to horses with strangulating lesions, horses with DPJ can have a fever, leukocytosis, a greater volume of gastric reflux, and considerable improvement in overall attitude and a reduction in heart rate after gastric decompression.[177,179] On palpation per rectum and ultrasound examination, the degree of small intestinal distention is variable, but usually is less than with a strangulating lesion. Peritoneal fluid from horses with proximal enteritis is rarely serosanguinous, and has a smaller increase in nucleated cell count compared with that in strangulating obstruction.[177,179] Total protein concentration in peritoneal fluid is variable but can exceed that seen with strangulating obstruction.[177,179]

Most horses with DPJ have tachycardia, prerenal azotemia, dehydration, hypotension, and electrolyte abnormalities. Horses with DPJ can have a higher activities of serum gamma-glutamyltransferase (GGT), aspartate aminotransferase (AST), and alkaline phosphatase (ALP) than horses with strangulating obstruction.[181] The greater risk of hepatic injury in horses with DPJ can be attributed to ascending infection from the common bile duct, absorption of endotoxin or inflammatory mediators from the portal circulation, or hepatic hypoxia caused by systemic inflammation and endotoxemic shock.[181]

Treatment of horses with DPJ involves frequent gastric decompression, correction of disturbances in water and electrolyte homeostasis, and restoration of normal intestinal function. Food and water are denied until the condition has resolved. Calcium and potassium deficits can develop in horses with intestinal injury and decreased food intake, and must be corrected. Fluid rate and type are largely determined by clinical and laboratory evidence of hydration status and electrolyte balance.

Flunixin meglumine can attenuate the hemodynamic responses to endotoxin, reduce endotoxin-induced increases in plasma thromboxane and prostaglandins,[182] and block the effects of endotoxin on intestinal motility. Pentoxifylline, a methylxanthine derivative, can also reduce endotoxin-induced production of cytokines and thromboxane in horses.[182] Anti-endotoxin antibodies (J5 *E. coli* or Re *Salmonella mutants*) and polymyxin B can be used to bind and remove circulating endotoxin.[182] Potential for nephrotoxic side effects should be considered before polymyxin B is administered to dehydrated horses.

Antibiotic use in DPJ is controversial, but metronidazole (2 g IV then 1 g IV, b.i.d.) and procaine penicillin (4.5 g IM, b.i.d.) have been used based on a high rate of positive cultures of gastrointestinal contents for *Clostridium perfringens*.[183] Treatment with prokinetic drugs can be used to improve gastric emptying and small-intestinal motility, although the response is variable. Prophylaxis against laminitis is important, and should include confinement in a sand stall or on deep wood shavings and application of frog support.

Surgery is performed in approximately 6% of horses with DPJ and may be required to make sure a strangulating lesion is not present.[177,180] The proximal small intestine has characteristic petechial and ecchymotic hemorrhage with slight mural thickening (Figure 36-20). Although the prognosis was reported to be decreased in the southwestern United States, survival does not appear to be affected or possibly improved by surgery.[180,183,184] Advantages of prompt surgical treatment are early return of normal circulation and peristalsis to the affected intestine and definitive diagnosis if a physical cause of obstruction cannot be ruled out.[183] However, all forms of DPJ might not respond favorably to this treatment, and the inactivity imposed by surgery could be a disadvantage.[183] Also, horses with DPJ that undergo surgery are at risk for obstructive adhesions.

Reported survival rates for horses with DPJ range from 25%[146] to 94%,[177,180] and recurrence is rare.[184] Anion gap, abdominal fluid total protein concentration, and volume of gastric reflux in the first 24 hours were significantly associated with death by univariate analysis.[180] Laminitis is a life-threatening complication of DPJ, and the risk is greater in horses with hemorrhagic reflux at the time of admission.[185] The considerable cost of continued medical treatment can necessitate euthanasia in protracted cases.

Figure 36-20



Small intestine identified at surgery with duodenitis-proximal jejunitis with characteristic hemorrhage and discoloration.

Equine Proliferative Enteropathy

Equine proliferative enteropathy (see Chapter 20) caused by *Lawsonia intracellulari* infection in the small intestine results in weight loss, colic, hypoproteinemia, and diarrhea in weanling foals.[186,187] Although treatment with erythromycin alone or in combination with rifampin is effective,[186] surgical bypass[187] or resection of the affected segment can be curative. Antemortem diagnosis is difficult, although serology appears promising, and the disease can attain epidemic proportions under intense management conditions.[186]

Enteric Pythiosis

Pythiosis caused by *Pythium insidiosum* is a granulomatous disease, typically of skin and subcutis, that is most commonly diagnosed in the Gulf Coast states, but also in the midwestern region of the United States.[188] *Pythium insidiosum* granuloma can cause jejunal obstruction, and clinical signs are weight loss and mild, intermittent abdominal pain.[188] Reported cases have been amenable to resection,[188,189] which can be an effective treatment.[189]

Intestinal Fibrosis

Intestinal fibrosis has been reported as a cause of weight loss and colic in horses in a small geographic distribution in Colorado,[190] but the disease appears to be more widespread and the signs more variable than originally reported.[191] This

disease causes extensive thickening of the intestinal wall, mainly in the submucosa, involving most or all of the jejunum and ileum, and with multifocal petechial hemorrhages on the serosa in some horses.[190] The thick-walled small intestine can be palpated per rectum.[190] Resection could be an effective treatment, but the extent of involvement can be too extensive to allow normal postoperative absorption of nutrients to occur.[190]

Intestinal Infiltrative Diseases (see Chapter 10)

Eosinophilic gastroenteritis is a well known but poorly understood cause of colic, diarrhea, and weight loss in horses.[138] Peritoneal fluid total protein concentration can be increased and eosinophils are present in peritoneal fluid in affected horses.[138] In one series of cases, weight loss was not a feature, but affected horses had colic from jejunal obstruction with a red intramural mass or a circumferential plaque of fibroplasia and infiltration on the antimesenteric surface.[138] The seasonal distribution of the cases corresponded to the grazing period, suggesting a dietary association.[138] Although treatment by complete or wedge resection was successful because of the focal nature of the lesions,[138] a multifocal form of eosinophilic enteritis also has been described.[192]

A similar cause of acute or chronic colic is characterized by small, focal to multifocal, well demarcated areas of intestinal thickening and fibrosis that form constrictive mural bands in the jejunum and other parts of the intestinal tract.[193] These are free of mucosal ulceration and granulomatous response, but have histologic evidence of lymphocytic, plasmacytic, and eosinophilic infiltration of all layers, and most lesions are associated with the vasculature.[193] Treatment with surgical resection or medical treatment with corticosteroids can be effective.[193]

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Diseases of the Cecum

Chapter 37

James N. Moore
Joanne Hardy

Based on studies of horses presented to university referral centers for evaluation of abdominal pain, approximately 4% of these horses had diseases that primarily affected the cecum.[1] In another study of horses undergoing exploratory celiotomy for gastrointestinal disease, approximately 4% of the conditions had primary involvement of the cecum.[2] However, results of the former study indicate that the survival rate for horses presented with pain owing to diseases of the cecum is less than 50%. Thus, although diseases of the cecum that result in abdominal pain are encountered less commonly than diseases affecting some other portions of the horse's gastrointestinal tract, diseases of the cecum should be regarded as being important by equine practitioners. The most common diseases of the cecum encountered in clinical practice are cecal tympany, cecal impaction and cecocecal/cecocolic intussusception. The purpose of this chapter is to review the important clinical aspects regarding these and other diseases that affect the cecum, their identification, methods of treatment, and prognosis for survival. Specific attention will be given to complications associated with diseases affecting the cecum.

Cecal Tympany

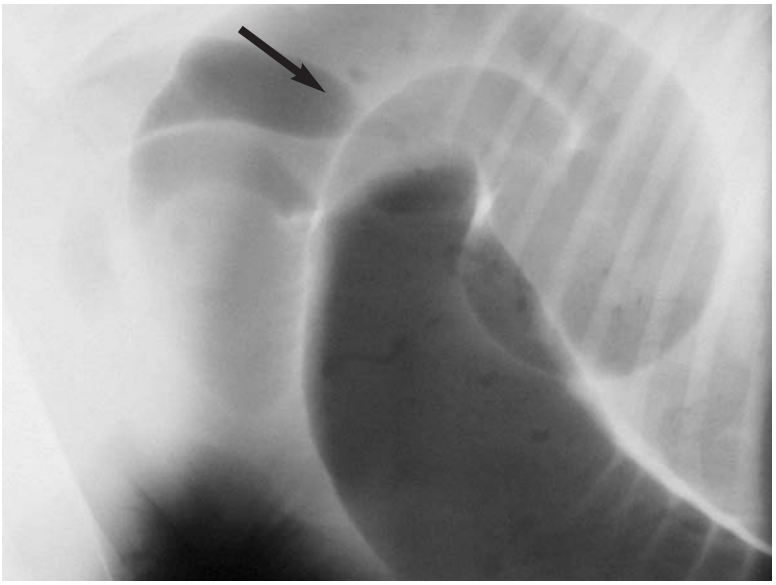
Prevalence, Etiology and Risk Factors

Distention of the cecum with gas occurs commonly in horses with conditions affecting the large colon, most notably colonic displacements, colon volvulus, or obstruction of the small colon. Less often, cecal tympany occurs as a primary disease, presumably because of rapid fermentation of lush pasture grasses or an abrupt change in diet.[1] In either situation, distention of the cecum causes or contributes to pain.

Clinical Findings

The most obvious clinical findings are distention of the barrel of the abdomen, taut paralumbar fossae, pain, tachycardia, and tachypnea. Simultaneous auscultation and percussion of the abdomen in the right paralumbar region will reveal a high-pitched pinging sound, characteristic of a severely distended viscus (Figure 37-1). The rectal examination will reveal a taut ventral cecal band, which courses diagonally from the right dorsal to the left ventral abdomen, and nonindentable distension of the cecum (see Chapter 6).

Figure 37-1



Abdominal radiograph of a horse with cecal tympany. The needle for percutaneous decompression is placed in the right paralumbar fossa in the base of the cecum (arrow).

Treatment

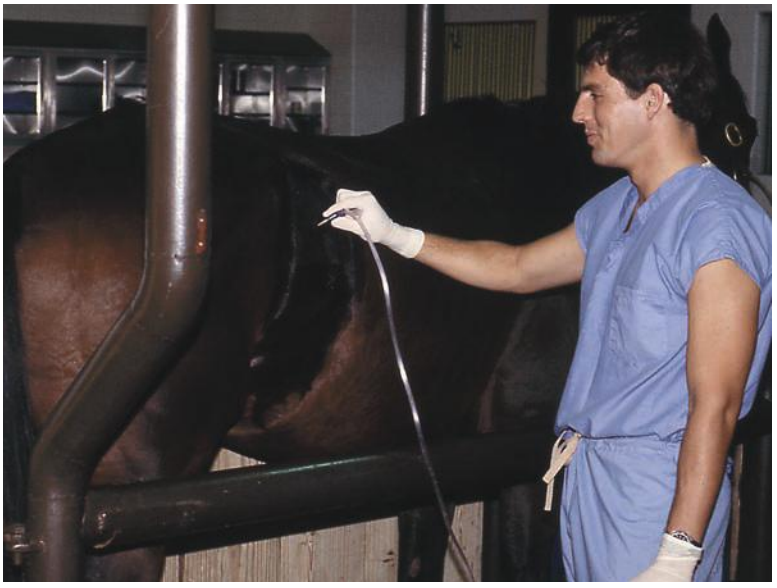
Treatment of primary cecal tympany includes removal of the gas. This can be achieved by surgically preparing a site in the right paralumbar region, desensitizing it with local anesthetic, and inserting a 14- to 16-gauge 12.7 cm intravenous catheter into the base of the cecum. The hub of the catheter is connected to a suction device and the gas is evacuated (Figure 37-2); this procedure can be facilitated by applying pressure to the cecal base *per rectum*. After the gas has been removed, the catheter is flushed with physiologic saline solution or a broad-spectrum antibiotic during removal of the catheter to reduce the likelihood of cellulitis along the needle track in the body wall. If cecal tympany has developed secondary to other conditions, there is no need to use this procedure, as correction of the underlying problem will resolve the tympany.

Figure 37-2A



During percutaneous cecal decompression, a catheter or needle is directed perpendicular to the skin midway between the last rib and the ventral border of the tuber coxae.

Figure 37-2B



Gas can be removed rapidly by applying suction to the needle.

Prognosis and Complications

The prognosis for survival from primary or secondary cecal tympany is good, depending on the severity of the underlying condition. Although peritonitis can result after trocharization of the cecum to remove the excess gas, in the majority of cases the colic is resolved and the horse appears normal. The total protein concentration and number of neutrophils in the peritoneal fluid will be increased, but these findings must be considered in light of the horse's clinical appearance and demeanor.

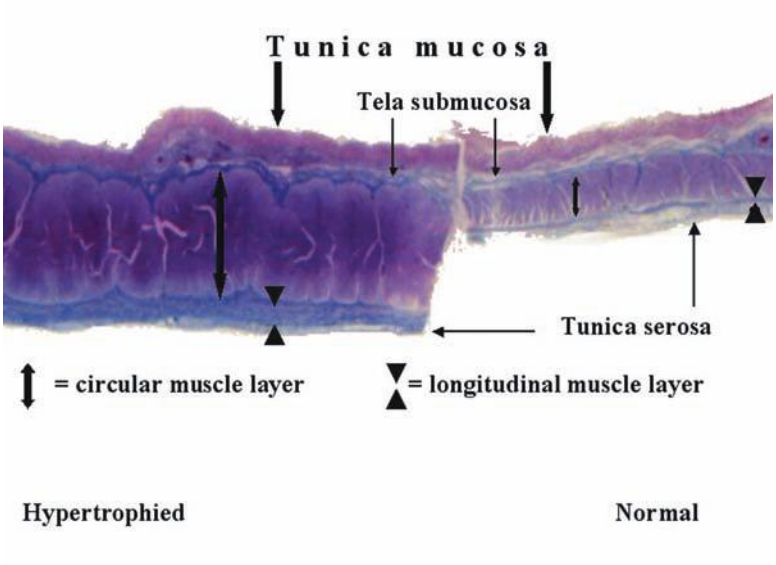
Cecal Impaction

Prevalence, Etiology and Risk Factors

Cecal impactions in horses appear to be of two types: those in which the ingesta in the cecum is hard and dehydrated, and those in which the contents are hydrated but the cecum fails to evacuate them in a normal fashion.[1] Historically, the first type of cecal impaction has been associated with ingestion of coarse feed, inadequate mastication (because of poor teeth), or insufficient water supply or reduced intake of water. More recently, the condition has been associated with hospitalization, general anesthesia, and other diseases requiring prolonged treatment with nonsteroidal anti-inflammatory drugs.[3-5] The underlying reason for the second form of cecal impaction remains unknown, although it has been speculated that cecal muscular activity is abnormal in affected horses. A form of this disease characterized by hypertrophy of the circular muscle layer in the cecal base and mechanical obstruction of the cecocolic orifice has been identified in horses in Germany (Figure 37-3).[6] Risk factors that have been associated with cecal impaction include insufficient water intake, coarse feed, hospitalization and administration of nonsteroidal anti-inflammatory drugs, and infestation with *Anaplocephala perfoliata*.[7]

Classically, cecal impactions have been reported to occur more commonly in middle-aged horses (8 – 11 years), although cecal impactions in younger hospitalized horses have also been reported.[1,3,5] The results of one clinical case study suggested that Arabians, Appaloosas, and Morgans are predisposed to the condition.[4] Cecal impactions have been associated more with abrupt rupture than are impactions involving other parts of the intestinal tract. Consequently, the fecal output of any horse being treated for other abnormalities should be assessed on a routine basis.

Figure 37-3



Photomicrograph of cecal wall hypertrophy from a horse with recurrent impaction compared with a cecal wall from a normal horse. (Courtesy of Gerald Schusser)

Clinical Findings

Most horses with dehydrated ingesta in the cecum exhibit mild intermittent colic signs and have minimal systemic deterioration unless the impaction has a prolonged course. The heart rate usually is only slightly increased, intestinal sounds usually can be heard and may be associated with signs of pain, presumably as intestinal muscles work against the obstruction. The diagnosis can be made upon rectal examination; the impacted cecum is relatively easy to identify as the mass is situated in the right paralumbar region. The cecum can be identified by palpating the taut ventral cecal band and the fat and blood vessels overlying the medial cecal band.[1,3,5]

In contrast, clinical signs in horses with hydrated cecal contents (a clinical syndrome also called cecal dysfunction) are more variable, ranging from those consistent with mild to those consistent with severe abdominal pain. The first signs include mild pain, which is easily controlled with analgesics; signs consistent with severe pain are present only when cecal distention is excessive. Gas distention of the cecum occurs more commonly in horses with the latter condition; the horse's heart rate may be normal or increased. Early in the disease, peritoneal fluid values are within normal limits; however, the total protein concentration may increase as the course becomes prolonged. Horses with this type of cecal distention are likely to experience acute rupture unless the distension is relieved.

Treatment

Some controversy exists regarding the best method of treatment of horses with cecal impaction, as the prevalence of spontaneous cecal rupture in horses with cecal impaction has been reported to be as high as 50%.[8] Medical treatment of horses with cecal impaction generally involves the administration of analgesics as necessary (e.g., nonsteroidal anti-inflammatory drugs), large volumes of balanced intravenous fluids, and intragastric administration of mineral oil, dioctyl sodium sulfosuccinate (DSS), magnesium sulfate, water, or magnesium sulfate. Feed should be restricted until the impaction is relieved. Many veterinarians consider aggressive fluid therapy to be the mainstay of treatment of these impactions. Balanced electrolyte solutions are administered either IV or via nasogastric tube, and often require administration of more than 50 liters of fluid daily to a 450-kg horse until the impaction is resolved. The results of recent studies with enteral fluid therapy in horses indicate that this is at least as effective as IV fluid therapy in hydrating colonic contents.[9,10] In one clinical case study, 89% of horses that survived longer than 24 hours after the diagnosis was made responded positively to aggressive medical therapy.[3]

With the obvious concern about the propensity for an impacted cecum to rupture, other clinicians support surgical intervention in such cases. Surgical intervention for treatment of cecal impactions requires general anesthesia and a ventral midline

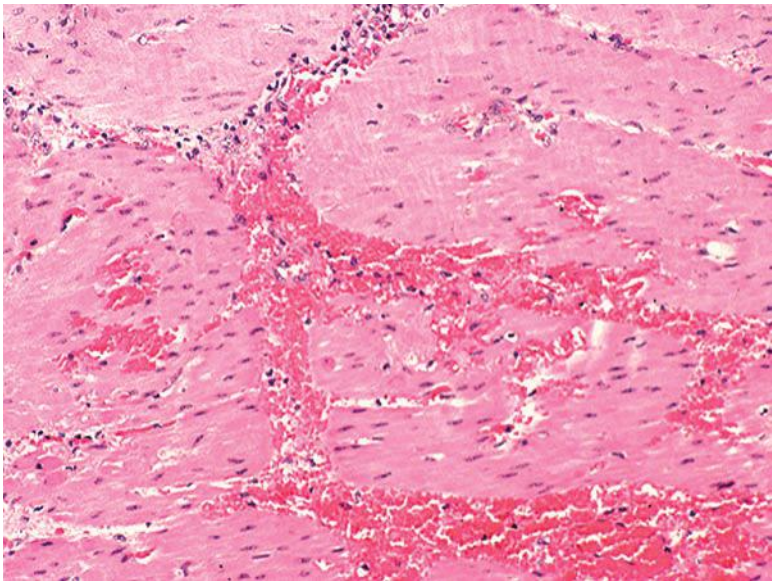
celiotomy. The affected portion of the cecum is exteriorized carefully and packed off from the celiotomy site. A typhlotomy is then performed and the contents of the cecum are removed. Contamination of the tissue can be minimized by coating the serosal surface of the cecum with sterile carboxymethylcellulose. Some controversy exists regarding the need for procedures other than typhlotomy. Because simple evacuation of the impacted material has been reported to be followed by recurrence of the impaction, some surgeons elected either to anastomose the cecum and colon, enlarge the cecocolic orifice, or bypass the cecum altogether. With massive distention, the cecum can be susceptible to ischemia and reperfusion injury. When the cecal wall is thickened and discolored (Figure 37-4), motility dysfunction should be expected after surgery. Consequently, the surgeon should consider performing a bypass procedure to prevent recurrence of the impaction.

Figure 37-4A



Cecal impaction (dysfunction) causing discoloration, and wall thickening from massive cecal distention in a horse.

Figure 37-4B

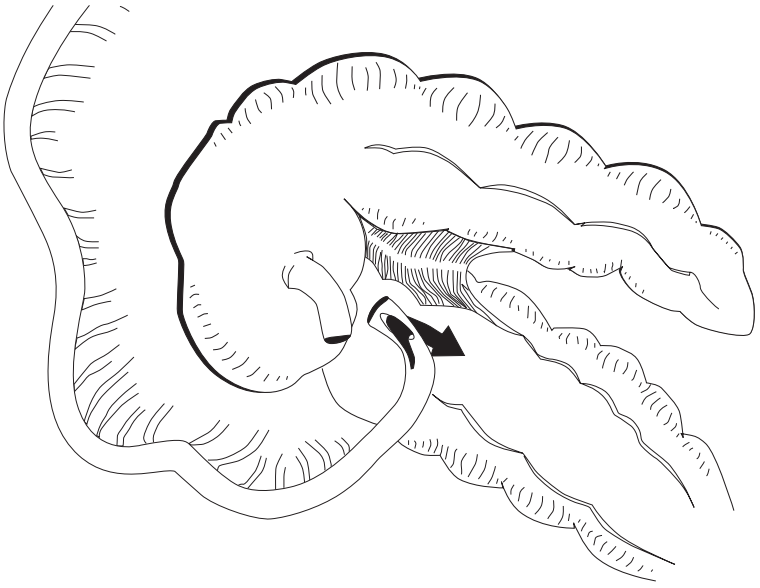


Photomicrograph of the cecal wall which has been injured by ischemia and vascular leakage. The cecum with this type of injury will be more prone to ileus and re-impaction if a bypass procedure is not performed during surgery.

The first of these approaches involves creating a cecocolostomy between the dorsal surface of the cecum and the right ventral colon. Based on the results of one clinical study in which this technique was used, however, 40% of the horses treated in this fashion had recurrent abdominal pain associated with distention of the cecum or colon.[11] As a result of these findings, techniques were developed to bypass the cecum by jejunocolostomy or ileocolostomy (Figure 37-5).[12] The results of a clinical case study involving 9 horses treated in this manner suggest that evacuation and bypass of the cecum is effectve.[13] In one report summarizing treatment by typhlotomy of 10 horses with cecal impaction owing to dysfunction, all horses survived a mean of 43 months after surgery without recurrence of the impaction. The authors of that report recommended that anthelmintics directed against *Anaplocephala perfoliata* and strongyle larvae should be administered postoperatively.[7]

Chronic recurrent impaction of the cecum can be a particularly frustrating condition. In a clinical study summarizing the response to surgical enlargement of the cecocolic orifice along the lesser curvature of the cecal base, affected horses responded positively unless the horse had pre-existing hypertrophy of the cecal musculature. The authors recommend that those horses should be treated with ileocolostomy.[6]

Figure 37-5



Schematic drawing of an ileocolostomy to by-pass the cecum viewed from the ventral abdomen.

Prognosis and Complications

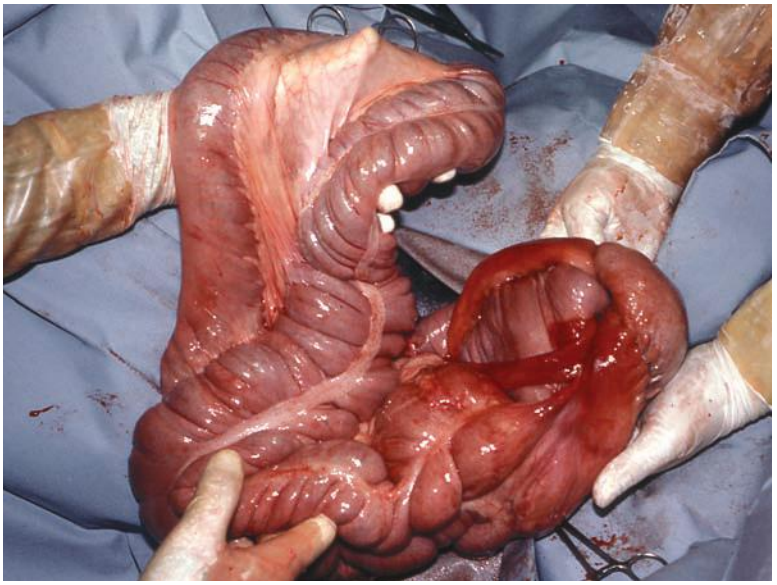
Because of the propensity of the cecum impacted with hydrated ingesta to rupture, the prognosis for survival is guarded-to-good with aggressive therapy. Taking into account the reported high rate of cecal rupture in horses that develop the condition during hospitalization for treatment of other diseases, the overall survival rate associated with cecal impactions is approximately 50% to 55%.

Cecocecal and Cecocolic Intussusception

Prevalence, Etiology, and Risk Factors

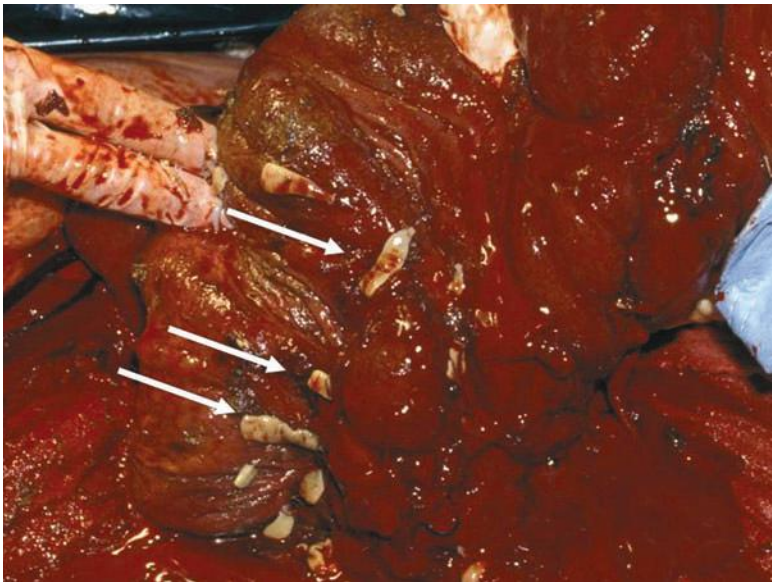
Cecocecal and cecocolic intussusception are uncommon causes of colic in horses and are most prevalent in young horses (Figure 37-6). A prevalence of 1.48% was reported in one study;[14] the condition affected 3 of 106 horses examined for chronic colic,[15] and 1 of 151 horses with conditions requiring surgical intervention for colic.[2] The underlying cause for the development of either cecocecal or cecocolic intussusception is not known, but the conditions are thought to be associated with altered cecal motility. Some common associations include parasite infestation by tapeworms (*Anaplocephala perfoliata*) (Figure 37-7)[14,16,17] or cyathostomes,[18] cecal wall abscessation associated with *Strongylus vulgaris*[19] or *Eimeria leukarti*,[20] deworming with organophosphate compounds,[21] parasympathetic drug administration, and typhlocolitis, particularly salmonellosis. Young horses between 2 and 3 years of age appear to be at greatest risk for developing these conditions, with more than 60% of affected horses in a retrospective study of 30 cases being less than or equal to 3 years of age.[16]

Figure 37-6



Intraoperative photo of the cecocecal intussusception with invagination of the cecal apex into the body of the cecum.

Figure 37-7



Intraoperative photo of a cecocolic intussusception. A right ventral colon enterotomy was perfomed and the intussuscepted cecum is exteriorized through the enterotomy. Two tapeworms are seen on the exposed cecal mucosa (arrows).

Clinical Findings

In cecocecal intussusception, signs of mild chronic colic, scant feces, intermittent fever, and weight loss, or severe unrelenting abdominal pain can be observed.[22] In cecocolic intussusception, where the invaginated cecum is located in the lumen of the right ventral colon, signs of acute colic predominate. Variable abnormalities may be identified during the physical examination and abdominocentesis, depending on the severity and duration of the intussusception. Rectal palpation will usually reveal a firm mass at the cecal base. A pre-surgical diagnosis can be made by ultrasound examination of the right abdominal quadrant using either the transabdominal or transrectal approach.[23] Although peritoneal fluid samples obtained from horses with the chronic form of the disease tended to have higher total protein values and WBC counts than horses with the acute form of the disease in one retrospective study, the differences were not significant.[16]

Treatment

Surgical correction is indicated in all cases. A ventral midline approach is commonly used (see Chapter 26). An alternative approach for cecocecal intussusception uses the right flank (17th or 18th rib resection) or paracostal incision to provide better access to the cecal base and body. In horses in which the cecal apex has inverted into the cecal base, it may be possible to reduce the intussusception manually. An attempt at manual reduction of the intussusception is made by inserting the hand into the intussusception and attempting to reduce it by gentle traction. In some cases this procedure may take as long as 30 minutes. If successfully reduced, the cecum is examined for evidence of devitalization and, if indicated, a partial

typhlectomy is performed to resect the affected involved portion of the cecum. In cases of irreducible cecocolic intussusception, two options are available to restore continuity of the gastrointestinal tract: right ventral colon enterotomy and partial amputation of the intussuscepted cecum within the right ventral colon; and complete cecal bypass by ileocolostomy.[14,16,23-26] For the first procedure, the large colon is exteriorized, preferably on a colon tray, and draped off. A sterile plastic drape is sutured circumferentially onto the colon at the site of the proposed enterotomy, in order to minimize contamination (Figure 37-8).[24] A right ventral colon enterotomy is performed between the lateral and medial free bands of the ventral colon. The intussuscepted cecum is exteriorized through the enterotomy. Reduction can be attempted then, but usually is not successful. Large overlapping mattress sutures are placed across the invaginated cecum and a section of the cecum is amputated. It is not necessary to remove all of the affected cecum; amputation of the most accessible portion is sufficient to allow reduction of the intussusception. The right dorsal ventral-colon enterotomy is then closed using a double-layer inverting pattern, with the first layer being full-thickness. The intussusception can then be reduced and the rest of the devitalized cecum amputated. The prognosis for horses with a reducible intussusception is excellent, even if a typhlectomy must be performed.[16]

Figure 37-8A

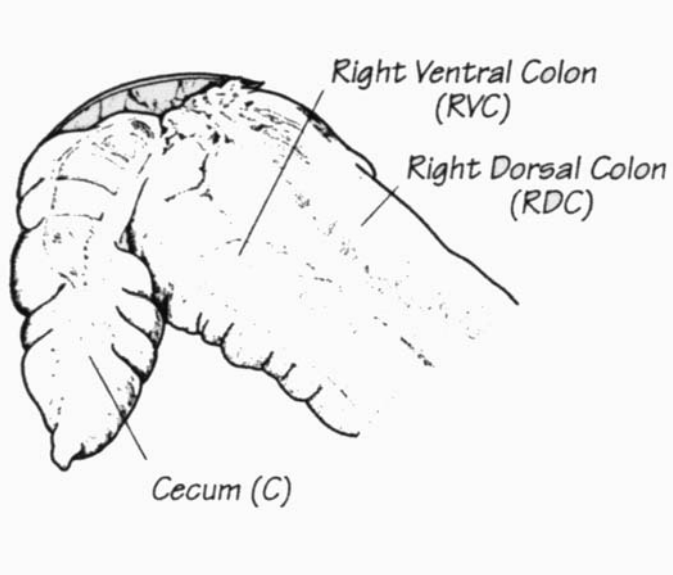


Figure 37-8B

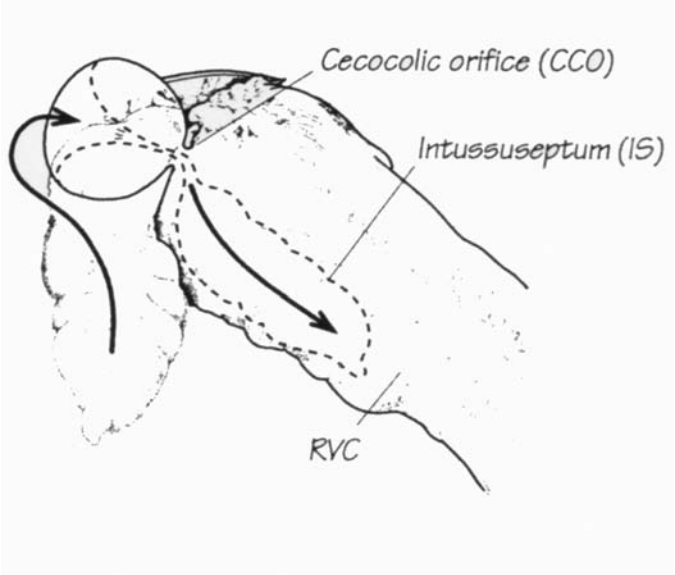


Figure 37-8C

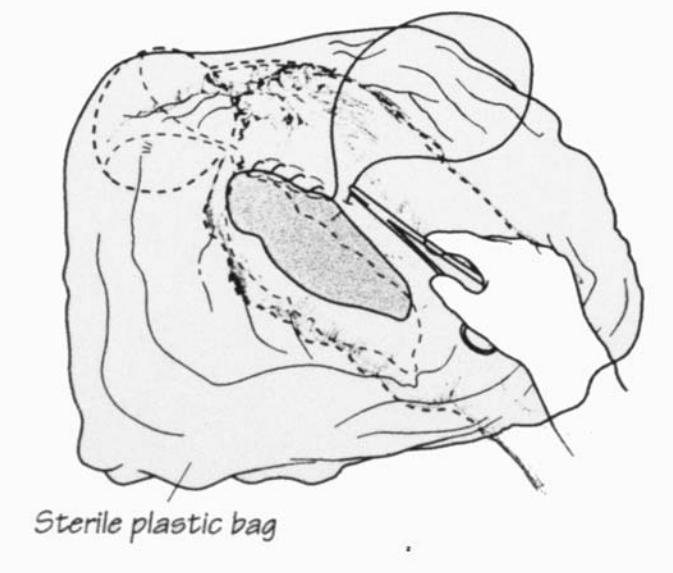


Figure 37-8D

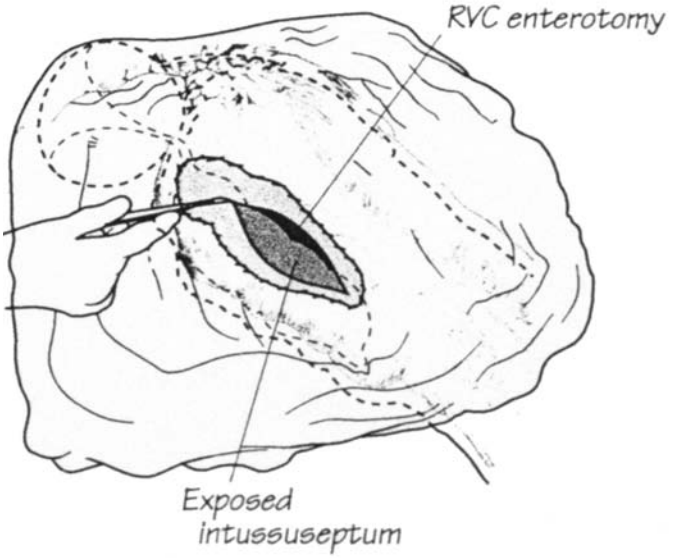


Figure 37-8E

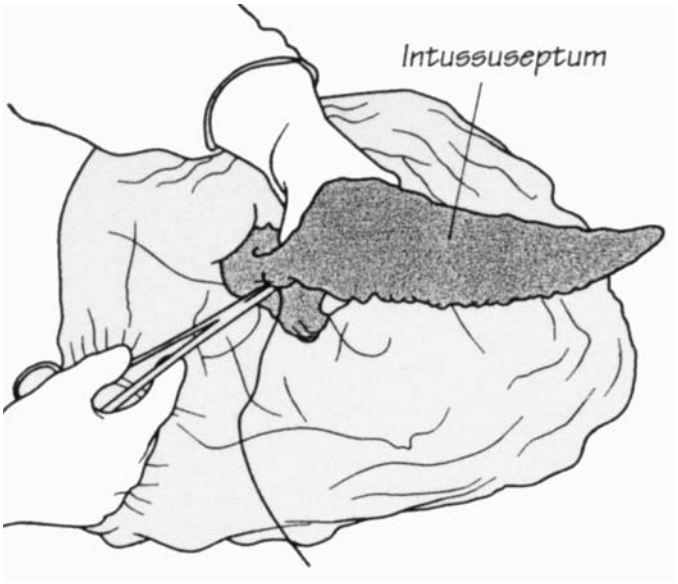


Figure 37-8F

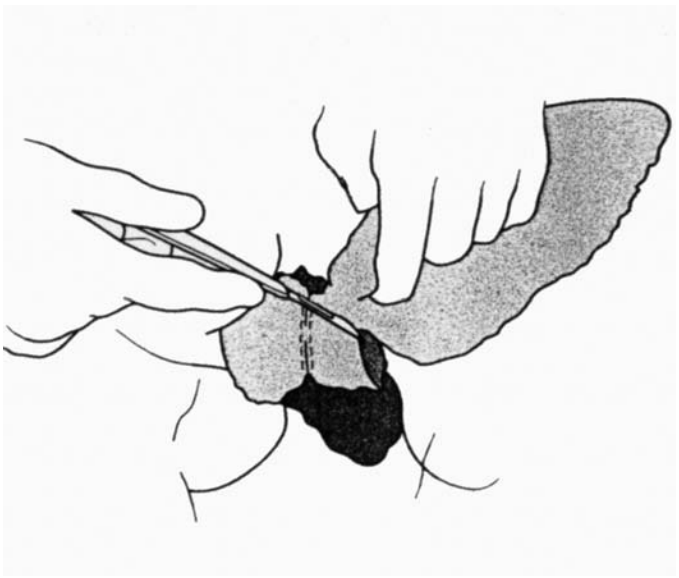


Figure 37-8G

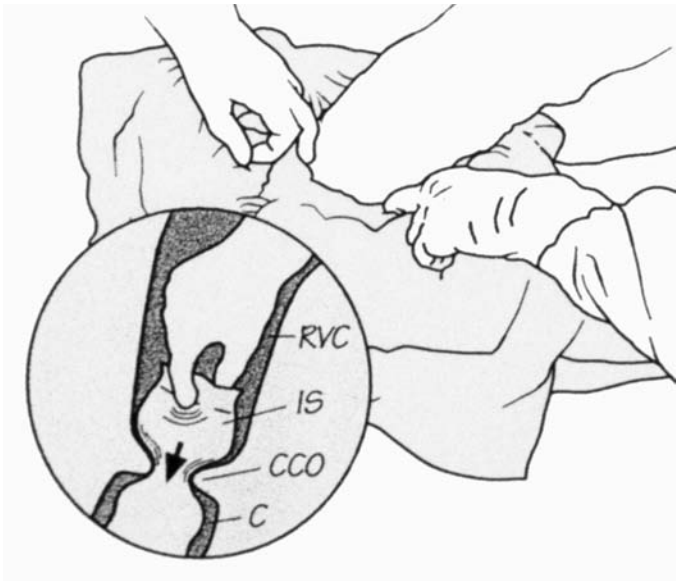


Figure 37-8H



Cecum intussuscepted into the right ventral colon through the cecocolic orifice. **A.)** The normal anatomy of the cecum in relation to the right ventral colon. **B.)** The dashed line represents the outline of the invaginated cecum. **C.)** A window is made in the base of a sterile pastic bag that is sutured to the seromuscular layer of the right ventral colon before colotomy to help contain contamination. **D.)** Right ventral colotomy exposing cecal intussusectum. **E.)** Occluding mattress sutures are placed in the inverted cecum to facilitate removal of as much cecum as possible, thus enabling reduction of remaining invaginated tissue. **F.)** Amputating the intussusceptum through the right ventral colon. **G.)** Careful manual reduction and repositioning of remaining invaginated cecum through the cecocolic orifice. Secure closure of the cecal stump is critical to prevent abdominal cavity contamination. **H.)** A second typhlectomy is performed to ensure only viable tissue remains. (From Hubert JD, Hardy J, Holcombe SJ, et al. Cecal amputation within the right ventral colon for surgical treatment of nonreducible cecocolic intussusception in 8 horses. Vet Surg 29:317-325, 2000.)

Prognosis and Complications

The long-term prognosis for survival is variable, with reported rates ranging from 27% to 100%.[5,7] Although the outcomes of the colostomy and partial typhlectomy procedure were associated with poor results in early reports, more recent studies have reported good to excellent results with this procedure, with 6 of 6 horses and 7 of 8 horses surviving long term.[16,24] Postoperative complications included ileus, peritonitis, incisional infection, and colic.[16,24,25]

As an alternative for management of irreducible cecocolic intussusception, a jejunocolostomy or ileocolostomy can be performed; the intussuscepted cecum is left in place. In the reported cases, the intussuscepted cecum was not oversewn. Early reports of this procedure were associated with a poor outcome, with 2 of 2 horses euthanized because of peritonitis. Subsequent reports were associated with a better outcome, with 4 of 6 horses surviving long term.[23] In the latter report and another, horses were reported to have several postoperative complications including colic and peritonitis.[23,26] Whether the

colic episodes were caused by the procedure or by the fact that the intussuscepted cecum was left within the colon is unknown. It is the author's experience that horses affected with irreducible cecocolic intussusception treated with colostomy and partial typhlectomy have a better postoperative course than horses treated by ileocolostomy.

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Specific Diseases of the Large Colon

Chapter 38

Joanne Hardy

Large-Colon Tympany

Prevalence, Etiology, Risk Factors

Large-colon tympany (gas colic, spasmodic colic) is the most common reported cause of colic in horses.[1-3] This condition is thought to result from excessive gas fermentation in the colon, resulting in distention and pain. In one study evaluating risk factors for simple colonic obstruction and distention colic in horses (including large-colon impaction), the following factors were associated with an increased risk for this type of colic:[4] crib-biting or windsucking, increasing number of hours spent in a stable, recent change in regular exercise program, absence of administration of ivermectin or moxidectin anthelmintic in the previous 12 months, and a history of travel in the previous 24 hours. An association between tapeworm infestation and spasmodic colic has been demonstrated.[5] Horses fed a hay and grain diet containing a large amount of soluble carbohydrates and less fiber had decreased water content in ingesta and increased gas, which predispose to gas colic.[6] Although large-colon tympany can be self-limiting, it is thought to precede large-colon displacements; therefore, identification of risk factors in affected horses may help to decrease the risk of future occurrences and the development of displacements.

Clinical Findings

Horses examined for large-colon tympany are in acute pain and may show signs of visible external abdominal distention. Although these horses are in pain they are minimally compromised, and clinico-pathologic parameters, including results of abdominocentesis, remain within normal reference ranges. The challenge for the clinician is to differentiate this type of colic from other, more serious causes of abdominal pain. The differentials for gas colic resulting in large-colon distention include large-colon displacement, large-colon volvulus (torsion), ileus (impending colitis), and aboral obstruction (transverse or small-colon obstruction). Rectal palpation will reveal moderate to severe gas distention of the large colon. Treatment includes administration of analgesics and withholding feed. If the response to medication is favorable, and if the diagnosis is correct, the horse will remain comfortable. Lack of response to analgesics may indicate a more serious problem. If response to treatment is unsatisfactory, early referral is recommended, considering that large-colon volvulus is part of a differential diagnosis for this condition.

Large Colon Impaction

Prevalence, Etiology, Risk Factors

The most critical functions of the equine large colon are storage, microbial digestion, and fluid reabsorption. In a 24-hour period, the large intestine must recover a volume of water approximately equivalent to the extracellular fluid of the horse (approximately 20% to 30% of body weight or 90 to 135 liters for a 454-kg horse).[7] The storage function of the large colon allows time for microbial digestion and absorption of volatile fatty acids, the horse's main source of energy (see Chapter 2).[8] The principal mechanism for delay in transit is the retropulsive activity initiated in a pacemaker region near the pelvic flexure (approximately 30 cm aboral to the termination of the medial and lateral free taenia of the left ventral colon).[9,10] The coordinated contractions originating at the pelvic flexure pacemaker promote physical separation of small, well digested particles, which are propelled aborally, from more coarse particles, which are propelled orally for further digestion (see Chapter 2).[11] This may explain the role of poor quality feed in the development of large-colon impaction.

Large-colon impaction is the second most common reported cause of colic in horses, and is the most frequent type of simple obstruction.[2,12] This condition represents up to 13.4% of colics examined at referral centers.[13,14] Risk factors identified in one studywere listed earlier.[4] Additional factors identified in that study include history of previous colic, recent (less than 4 weeks) lameness, and increasing time since last dental care.[4] In another study, 79 of 147 horses (53.7%) had a change in routine in the 2 weeks prior to development of a large-colon impaction, and 17 of 147 (11.5%) developed the impaction while hospitalized for a reason other than gastrointestinal disease.[14] Decreased water intake and parasites are factors also mentioned, although not well documented as being involved in the development of this condition. Diets high in grain content may predispose to colonic impactions, as grain feeding is associated with an internal fluid flux and subsequent dehydration of ingesta, setting the stage for impaction.[15] Right-colon dry-matter content was higher when grain was part of a free choice hay diet.[16] In another study, water consumption was 40% greater in ponies offered warm drinking water under cold weather conditions.[17] Hospitalization and general anesthesia have been suggested as risk factors for the development of impaction colic.[14,18] In one study, 37 of 85 horses (43.6%) developed postoperative reduced fecal output; of these, 10 horses (12%) developed signs of colic. Of 9 horses that had rectal examinations performed in that study, 2 had pelvic flexure impactions. Additionally, administration of phenylbutazone decreased the risk of reduced fecal output in that study.[18] In contrast, the results of in vitro studies suggest that nonsteroidal anti-inflammatory drugs have a negative effect on large-colon intestinal smooth muscle motility.[19,20] The benefits of nonsteroidal anti-inflammatory drug administration for pain control is still a matter of debate, considering the negative effects on intestinal health.[18,21] Amitraz, an acaricide, has been used to induce experimental large-colon impaction in

horses.[22] Topical spraying of amitraz was associated with systemic illness and impaction colic in 3 horses.[23] Amitraz, atropine, glycopyrrolate, and morphine significantly prolonged intestinal transit time in horses.[24] Atropine (0.044 mg/kg and 0.176 mg/kg, IV) resulted in decreased intestinal motility and decreased appetite for 2 to 7.5 hours after injection; signs of abdominal pain were observed in 3 of 10 ponies after administration.[25] Topical ocular administration of 1 mg of atropine hourly resulted in decreased intestinal motility (as assessed by auscultation) for 2 to 18 hours after administration, and signs of abdominal pain were observed in 4 of 6 horses.[26] Subconjunctival administration of 3 mg of atropine resulted in decreased intestinal sounds in 3 of 6 horses, and signs of abdominal pain in 1 horse.[26] Lowering the luminal temperature to 20°C (room temperature) over a 100-cm length of colon cranial and caudal to the pelvic flexure for 2 hours significantly decreased conduction velocity, and amplitude and duration of pressure peaks in the intestinal wall. This finding has direct relevance to surgery of the large colon, in which the colon may be exteriorized from the abdomen for prolonged periods and luminal lavage is performed. Minimizing the time of exteriorization and using warm water for luminal lavage may facilitate the return of normal colon function. The role of intestinal parasites on pelvic flexure motility has been evaluated. In one study, arteritis of the cranial mesenteric artery induced by inoculation of *Strongylus vulgaris* larvae resulted in reduced relative colonic blood flow; but did not cause altered motility patterns.[10] In another study, increased motility patterns were observed in the cecum and colon at intermittent intervals for several days after infection.[27] Horses with chronic (>24 hours) obstructions of the large colon or with previous obstruction had decreased neuron density in the pelvic flexure, which may predispose to future obstructions.[28]

Clinical Findings

Megacolon with myenteric hypoganglionosis has been described in a 6-month old foal with severe large-colon impaction and colic.[29] Recurrent impactions of the large colon were diagnosed in a mare with eosinophilic enterocolitis.[30] In that mare, diarrhea, hypoproteinemia and weight loss characteristic of the disease were not present, and the intestine appeared grossly normal at surgery and at post-mortem examination. These cases support the use of intraoperative intestinal biopsies as part of the diagnostic evaluation of horses with unexplained recurrent large-colon impaction.

Large-colon impactions usually affect horses greater than 1 year of age, although miniature horses may be predisposed to impactions as foals. Historically, horses presented to referral centers with large-colon impactions have colic of greater than 24 hours duration.[14]

The most common location for large-colon impaction is the pelvic flexure, followed by the right dorsal colon and transverse colon. On physical examination, horses typically show mild to moderate abdominal pain, decreased or absent intestinal sounds, decreased or absent fecal production, and occasionally, mild to moderate abdominal distention.[14] Nasogastric reflux is rarely present. Rectal palpation is diagnostic in horses with impaction of the pelvic flexure; however, impactions of the right dorsal and transverse colon can be difficult to palpate in adult horses. When a large - colon impaction is suspected on the basis of rectal palpation, it is essential to differentiate that from a large-colon displacement with secondary right dorsal colon impaction.[31] Prolonged treatment of a horse with a large-colon displacement with fluids and cathartics could result in pre- or intraoperative colonic rupture. In a large-colon displacement, the right dorsal colon can become severely impacted; in these cases, the examiner's hand follows the impacted colon to the right and lateral to the cecum. This is in contrast to a pelvic flexure impaction in which the pelvic flexure can readily be identified. Another important difference in large-colon impaction is the palpation of dehydrated fecal contents in the large colon as a result of a small-intestinal obstruction. In contrast to large-colon impaction, the taenia and haustra of the ventral colon in horses with small-intestinal obstruction become more prominent and distinguishable.[31]

Laboratory data typically observed in horses with large-colon impaction reflect mild to moderate dehydration, a normal leukogram, and normal electrolytes and blood gas analysis. The results of abdominocentesis should be within normal range. Deteriorating cardiovascular status or peritoneal fluid changes are an indication of bowel degeneration.[14]

Treatment

Medical treatment of large-colon impaction includes fluid therapy, analgesics, cathartics, and withholding of feed until the impaction is resolved. Intravenous replacement fluids are reserved for horses with impactions of long-standing (>24 hours) duration, when dehydration is documented, or when nasogastric reflux is present, precluding the use of enteral fluid therapy. Balanced electrolyte solutions are administered at twice the maintenance rate, or 120 ml/kg/day, both to restore circulating blood volume and to allow secretion of fluid into the large colon in response to cathartics. Overhydration in combination with an oral cathartic such as magnesium sulfate is thought to promote rehydration of ingesta.[32,33] Systemic rehydration should be performed before cathartics are administered.

Enteral fluid therapy can complement and even supplement treatment with intravenous replacement fluids. Advantages of enteral fluid therapy include administration of fluid directly into the gastrointestinal tract, stimulation of colonic motility through the gastrocolic reflex, decreased expense, and decreased need for precise adjustment of fluid composition.[33] Enteral fluids can be administered by intermittent nasogastric intubation or by placement of an indwelling feeding tube (18 French equine enteral feeding tube, Mila International, Florence, KY), allowing continuous fluid administration. An isotonic electrolyte solution can be made by mixing 5.27 g of NaCl, 0.37 g of KCl, and 3.78 g of $NaHCO_3$ per liter of tap water.[33] This solution results in electrolyte concentration of 135 mEq/L of Na; 95 mEq/L of Cl; 5 mEq/L of K; and 45 mEq/L of HCO_3, with a measured osmolality of approximately 255 mOsm/L, representing a balanced slightly hypotonic electrolyte solution compared with plasma.[33] Plasma concentrations of electrolytes remain within normal range with administration of this solution compared with the marked hypernatremia and hyperchloremia observed when 0.9% saline is administered enterally.[34] Although normal horses can tolerate up to 10 liters hourly via repeated nasogastric intubation,[34] it is usually not possible to administer more than 5 liters every 2 hours to horses with impactions; horses with impactions develop gastric reflux when more fluid is administered. Therefore, intermittent intubation allows administration of approximately 60 liters of fluids per day. When continuous enteral fluids are given, a greater rate of administration is tolerated, and horses can be given between 4 and 10 liters per hour. At the higher rate of 10 liters per hour, mild signs of abdominal pain were observed in normal horses,[33] and in horses with large-colon impaction, a rate of 5 liters per hour is better tolerated. For enteral fluid therapy, fluids used can be water, or water containing electrolytes. In one study, hydration of right dorsal colon ingesta was significantly increased after enteral fluid therapy compared with that after intravenous fluid therapy combined with enteral administration of magnesium sulfate.[33]

Cathartics are useful to increase the amount of water in the large colon or promote transit of ingesta. Mineral oil is a mixture of aliphatic hydrocarbons derived from petrolatum that is indigestible and absorbed to a limited extent. It is an intestinal lubricant that can also serve as a marker of intestinal transit. Administration of 5 to 10 ml/kg is usually recommended, and oil should be evident in the feces 12 to 24 hours after administration. Unformed feces were apparent 18 to 24 hours after its administration in normal horses.[35] Administration of mineral oil to normal horses decreased glucose absorption and decreased intestinal transit time.[36,37] Chronic usage can result in a foreign body reaction in the intestinal mucosa.[38] Careful administration is necessary, as inadvertent administration into the lung results in lipid pneumonitis, which is severe and often fatal.[39,40] Mineral oil is easily confused with propylene glycol, used in the treatment of ketosis in cattle; inadvertent administration of propylene glycol was the cause of death in a horse.[41]

Dioctyl sodium sulfosuccinate is an anionic surface-active agent that by lowering surface tension may facilitate penetration of the fecal mass by water and fats. Effects on motility and secretion are also attributed to this product. The recommended dose range is 16.5 mg/kg to 66 mg/kg, and the maximal recommended dose is 0.2 g/kg; death due to circulatory shock can occur at doses of 1g/kg.[42] In one study in normal horses, toxic signs were observed at a dosage of 50 mg/kg.[32] It is important to correctly label the product to avoid overdosing. Its advantage is that it requires a low volume of administration; however, its low margin of safety and lack of efficacy at low dosage make its use questionable. Concurrent absorption with mineral oil can result in emulsification and subsequent systemic absorption of oil. The significance of this is unknown, but because of this, many references discourage the use of the combination.

Osmotic or saline cathartics have been used to increase colonic water content. Sodium sulfate is the most effective product to increase colonic water content, whereas magnesium sulfate, while it did not increase colon water content, did increase small-colon water content.[16,32] Sodium sulfate can create an electrolyte imbalance; therefore, horses should be monitored if it is administered more than once. Because of their potential to shift water into the colons, these products should be used after systemic rehydration. Recommended dosages are 0.5 g/kg to 1 g/kg. Absorption of magnesium resulting in signs of toxicity was reported in 2 horses that had received a combination of dioctyl sodium sulfosuccinate and magnesium sulfate.[43]

Raw linseed oil produced from flaxseed was a commonly used laxative for the treatment of impactions. The addition of metallic salts to make boiled or pure boiled oil enhances its properties as a wood preservative and is highly toxic. Only raw linseed oil should be used. Administration of 2.5 mL/kg to normal horses resulted in watery diarrhea, anorexia, mild signs of colic, and neutropenia.[35] Although raw linseed oil has greater laxative effects than mineral oil, the toxic effects of raw linseed oil may preclude its use, particularly in horses with compromised intestinal mucosa.[35]

Polyethylene glycol 3350 is an effective osmotic laxative that is used in humans for the treatment of constipation or for colonic cleansing.[44,45] This product has not been evaluated rigorously in horses, although this author has used it successfully to treat horses with large-colon impactions. The cost of this product is much greater than the previously mentioned cathartics. Castor oil has been used to induce experimental colitis in ponies.[46] Its use for the treatment of impaction colic is not recommended.

Analgesics are indicated as part of the management of large-colon impaction. Nonsteroidal anti-inflammatory drugs are commonly used. Use of low-dose flunixin meglumine can help control pain without affecting large-colon motility. In the course of treatment of severe impactions, some horses may require intermittent dosing with xylazine to relieve intestinal spasm.[47] Alternatively, a constant rate infusion of lidocaine can be used to modulate pain (see Chapter 7).

Most horses respond well to medical therapy. In one study, 24 of 147 horses required surgery.[14] Indications for surgery included uncontrollable pain, deteriorating cardiovascular status, or peritoneal fluid changes indicating bowel compromise. Of the horses that went to surgery, 5 were euthanized following tearing of the colon during exteriorization.[14] Surgical management of large-colon impaction involves evacuation of the colon by pelvic flexure enterotomy.

Complications

Complications of surgery include intraoperative rupture of the colon, postoperative diarrhea, incisional drainage, and rarely, septic peritonitis.[14]

Prognosis

The prognosis for large-colon impaction is excellent, and the majority of horses will respond to medical therapy. The prognosis is better for horses treated medically than surgically. In one study, long-term outcome for horses treated medically was 95.1%, compared with 57.8% for horses treated surgically.[14] The most common complication was jugular vein thrombophlebitis, so catheter sites should be monitored carefully. In the management of these horses, it is important to avoid risk factors that predispose to impactions as horses with impactions are at higher risk for re-impaction. A small number of horses will require permanent dietary modifications to avoid re-impaction.

Sand Impaction

Prevalence, Etiology, Risk Factors

Accumulation of sand in the equine large colon can result in variable signs including colic, diarrhea, weight loss, and poor performance. Sand should be considered in the evaluation of chronic diarrhea in foals and adult horses.[48,49] Risk factors for sand impaction include insufficient roughage in the diet, access to sand, and mineral composition of the soil. Sand impaction has been diagnosed in horses that were exposed to sand 3 to 8 weeks before examination.[50] Higher incidences of sand colic are reported in California, Florida, Michigan, and coastal regions. Although most horses with sand impaction are older than 1 year,[50] sand accumulation has been documented in foals;[51,52] miniature horses may also be predisposed to sand impaction, because of environmental and management practices.

Clinical Signs

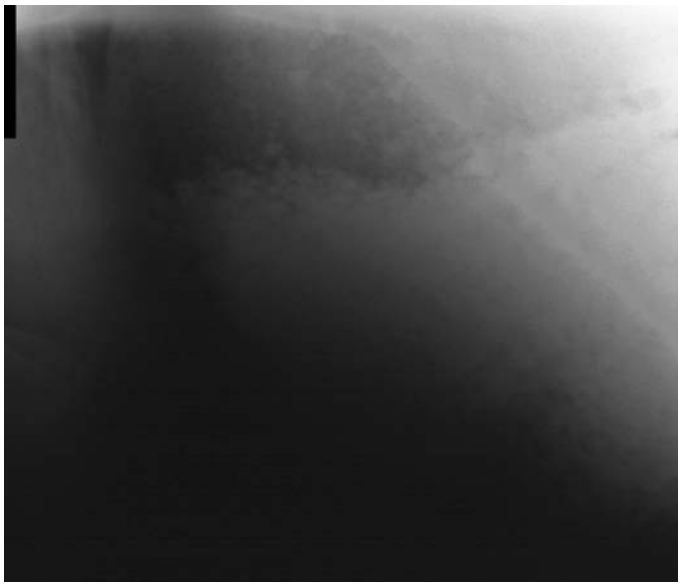
Horses with sand impaction manifest signs similar to those in horses with large-colon impaction, unless a concurrent large-colon displacement or volvulus is present. Large-colon displacements or volvulus were identified in 10 of 40 (25%) and 26 of 48 (54%) of horses with sand impaction, respectively.[50,51] Clinical signs commonly reported in horses with sand impactions include mild to moderate abdominal pain, reduced fecal production, and decreased intestinal sounds. The sound of moving sand may be heard when the ventral abdomen is ausculted caudal to the xiphoid. Signs can be present for several weeks. Horses with sand impactions often are responsive to analgesics. Cardiovascular status should be normal unless dehydration or intestinal devitalization has occurred. Occasionally, horses with sand impaction may show signs of endotoxemia, presumably as a result of mucosal or intestinal damage associated with the weight and abrasiveness of the sand.[52]

Diagnosis

Diagnostic procedures that are used to detect the presence of sand include sand observed in the feces, sand obtained or palpated during abdominocentesis, abdominal auscultation, rectal palpation of a sand-filled viscus, abdominal radiography, and abdominal ultrasound.[51-53] In one study, 23 of 40 horses (58%) were diagnosed with intestinal sand before surgery by one or more methods.[51] Fecal sedimentation is performed by adding water to a handful of manure, which is allowed to sediment in a rectal sleeve or a bucket of water. The presence of sand on sedimentation, however, may be incidental, and horses with sand impaction may not have sand in their feces at the time of examination. The appearance of sand in the feces during treatment is considered a sign of clearance of the sand.[52] Results of abdominocentesis are often normal or show an increased total protein. Abdominocentesis is not diagnostic for sand colic, but rather indicates the degree of intestinal compromise. However, the weight of the colon makes it easy to perform an unintentional enterocentesis during the procedure, and sand can be palpated with the tip of the needle or cannula.[50] In one study, 13 of 23 horses in which sand

impaction was correctly diagnosed before surgery, had the condition identified by the presence of sand obtained or palpated during abdominocentesis.[51] Abdominal auscultation for the detection of sand is performed on the ventral abdomen, with emphasis on the area caudal to the xiphoid process.[54] The sound produced has been described as similar to that produced by sand in a partially filled paper bag and slowly rotated.[54] The intensity of sound is loudest with larger accumulations of coarse as opposed to fine sand.[54] In an experimental study of sand impaction in horses, all horses had at some point auscultable sounds of sand, but in most cases after several doses of sand, and after several repeated 5 minute periods of auscultation.[54] Rectal palpation of horses with sand impaction most commonly reveals distention of the cecum and/or large colon. The impaction is seldom palpated on rectal examination. If coarse sand is present, it may be palpated through the intestinal mucosa. Abdominal radiography provides the best method to evaluate the amount of sand accumulation, and provides a tool for monitoring disappearance of sand with treatment (Figure 38-1).[52] Imaging of the cranioventral abdomen is the most useful projection.[52] Abdominal ultrasound can be used in an attempt to diagnose sand impaction, but is best used in combination with abdominal radiography to monitor clearance of the sand.[53] Ultrasonographic evidence of sand accumulation is more subjective, and includes close and increased contact of the large colon with the ventral body wall, decreased or absent intestinal motility, and hyperechoic acoustic shadowing. In one study, results obtained with radiography and ultrasonography were similar in only 50% of cases.[53] Because ultrasonography is more readily performed and can be easily repeated, it is thought to be a useful tool for monitoring once a diagnosis has been made; although repeated radiographs may be indicated when ultrasonographic results are equivocal.[53]

Figure 38-1



Lateral projection of the ventral abdomen of a horse showing impaction of the ventral colon with coarse sand.

Treatment

Medical treatment of horses with sand impaction includes removing the horse's access to sand, rehydration by intravenous and or oral methods, and the use of laxatives. Mineral oil is usually not effective, as it will pass around the sand. Magnesium sulfate and/or psyllium are used to promote evacuation of sand. In one study, psyllium failed to increase evacuation of sand in an experimentally induced model of sand impaction.[55] However the number of horses in that study was small, and the model may not reflect naturally occurring disease. In a clinical study,[52] horses that were refractory to treatment were responsive to administration of magnesium sulfate and mineral oil.[52] Monitoring of the resolution of the impaction can be performed using abdominal radiography or ultrasonography.[52,53]

Horses with sand impaction can develop abnormal motility patterns and subsequent large-colon displacement. These horses experience more pain and develop gas distention of the large colon. Surgical intervention is indicated when a displacement is suspected or diagnosed, when abdominal pain is uncontrolled, when cardiovascular parameters deteriorate, or when there is evidence of intestinal devitalization.[50,51] Standing flank laparotomy does not allow sufficient access to the large colon for evacuation of sand, and injection of the impaction was not successful in providing relief. Therefore, a surgical approach through a ventral midline is recommended. At surgery, the sand is evacuated through a pelvic flexure enterotomy (Figure 38-2).

The most common location for accumulation of sand is the right dorsal colon, but any location, from the ileocecal junction to the small colon, is possible, and multiple impaction sites are commonly encountered. Care must be exercised during exteriorization

of the large colon, as the weight of the sand predisposes the colon to rupture. To facilitate exteriorization, the horse may be tilted toward the left side of the abdomen. Only the minimum length of large colon necessary to safely perform a colotomy should be exteriorized; as the colon is evacuated, more of its length can be carefully exteriorized from the abdomen.

Figure 38-2



Intraoperative illustration of evacuation of gravel through a pelvic flexure enterotomy in a horse.

Complications

Results of surgical treatment of horses with sand impaction include good long-term survival. The most common complication is postoperative diarrhea, but this complication is commonly reported after surgical evacuation of the large colon for any reason. Other complications include peritonitis associated with intestinal devitalization from pressure necrosis.

Prevention

Prevention of sand impaction includes provision of adequate roughage, feeding off the ground, and provision of additional roughage when pastures are insufficient. The use of different formulations of psyllium (pellets or flakes) has been advocated at different dosage regimens (once a day for 3 weeks, then 1 week off, to twice a day for 2 weeks, then 1 week off), but the efficacy of these different dosage regimens in preventing further sand accumulation has not been documented. There is concern that long-term use of psyllium results in alteration in colonic microflora with subsequent bacterial digestion of the psyllium and decreased efficacy;[55] this is the rationale behind interrupted administration of psyllium.

Enterolithiasis

Prevalence, Etiology, Risk Factors

Obstruction of the large or small colon by enteroliths is a well documented cause of intestinal obstruction in horses. Risk factors associated with development of enteroliths include: geographic location, with California and Florida having high prevalence for this cause of colic; breed predisposition, such as Arabians and Arabian crosses, Morgans, American Saddlebreds, donkeys and miniature horses; feeding alfalfa hay; and less than 50% of time spent outdoors.[56,57] Stallions appear to be at a lower risk for developing this condition; however, other as yet unidentified factors may explain why horses fed the same diet in the same geographic area do not develop enteroliths.

Enteroliths are composed of stuvite crystals and magnesium ammonium phosphate, and often form around a nidus such as a stone or metal object (Figure 38-3). Horses with enteroliths have a significantly higher colon pH, more colonic dry matter, and higher mineral content in the colon ingesta; they more often have a diet consisting of alfalfa hay diet, and are in areas with hard water with higher concentrations of magnesium than horses not having enteroliths.[49,58]

Enterolithiasis can result in acute severe luminal obstruction or can cause intermittent mild signs of colic, depending on the location of the enterolith. Those in the large colon are usually localized in the right dorsal colon and cause mild signs of intestinal discomfort. Once the enteroliths migrate into the transverse or small colon, signs of acute luminal obstruction develop, with progressive abdominal distention. Although this condition causes a colonic simple obstruction, transmural

pressure necrosis can occur. Critical attention to results of the abdominocentesis can help determine such occurrence. An increase in total protein concentration above the normal range and an increase in white blood cell count can alert the clinician of such an occurrence.

Figure 38-3A

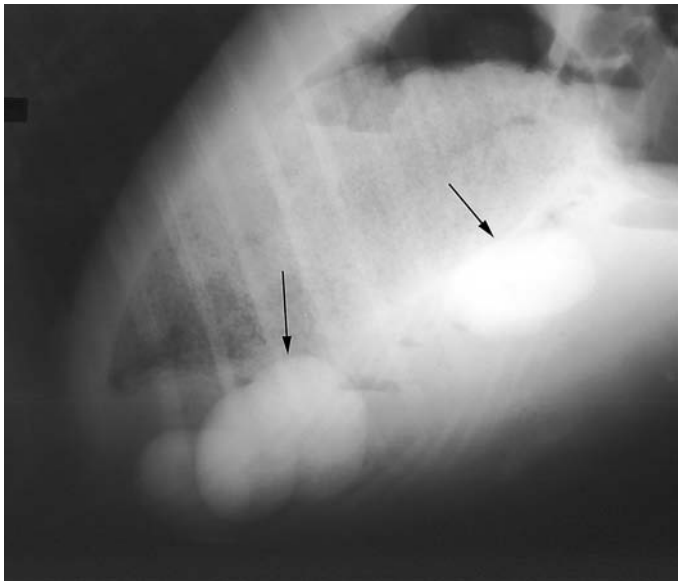
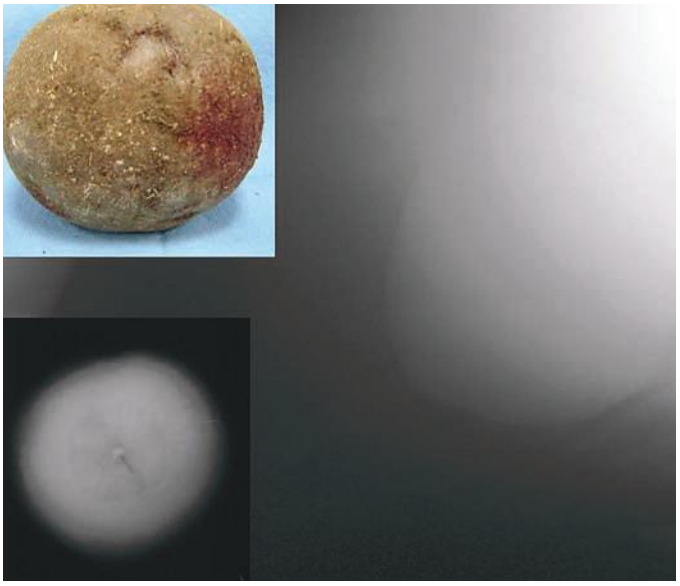


Figure 38-3B



A.) Lateral projection of the abdomen of a miniature horse with several enteroliths in the dorsal colon and small colon. **B.)** Lateral projection of the abdomen of a horse with a large enterolith in the right dorsal colon.

Clinical Signs

Parameters of the physical examination also vary, depending on the location of the enterolith and whether intestinal devitalization has occurred. Results of rectal palpation can be normal or may reveal large-colon distention. The enterolith rarely can be palpated. Results of the abdominocentesis are often normal, although increased total protein concentration is an early sign of intestinal devitalization. Radiographs are a useful diagnostic method for the detection of enteroliths, although the sensitivity and specificity vary depending on the location of the enterolith and the prevalence of the disease in the hospital population (Figure 38-3).[59] In one study performed in a high-prevalence area for enteroliths,[59] the sensitivity of radiographic diagnosis of enterolithiasis was 84.3% for those located in the large colon, compared with 50.0% for those located in the small colon. The mean overall positive predictive value for radiographs was 96.4% and the negative predictive value was 67.5%.[59]

Treatment

Surgical removal of enteroliths is indicated. If the enterolith is located in the large colon, the large colon is evacuated via a pelvic flexure enterotomy. A second enterotomy may be required in the right dorsal colon if the enterolith is too large to be evacuated through the pelvic flexure enterotomy. If the enterolith is lodged in the transverse colon, retrograde flushing by enema can facilitate its movement back into the dorsal colon. If the enterolith is in the small colon, it is removed by a small-colon enterotomy. A partial-thickness enterotomy can facilitate movement of the enterolith to a more accessible portion of the small colon.[60] If pressure necrosis of the intestinal wall at the site of the obstruction is significant, a resection may be required.

Prognosis

The prognosis for horses with enterolithiasis is usually excellent. However, necrosis of the intestine in an area that cannot be exteriorized such as the transverse colon is associated with a grave prognosis. In one study, bypass of the transverse colon by end-to-side anastomosis of the ventral colon to the small colon was successful in a miniature horse with intestinal necrosis resulting from obstruction of the transverse colon by a fecalith. The reccurrence rate of enteroliths is unknown, but dietary modifications, such as avoidance of alfala hay, are usually recommended.

Large-Colon Displacement

The equine large colon, because of its lack of mesenteric attachment to the body wall, is freely mobile and prone to displacement. In addition, normal longitudinal shortening of the left colon promoted by contractions of the longitudinal muscle layers move the pelvic flexure toward the diaphragm, followed by backward movement toward the pelvis during relaxation;

alterations in this motility pattern, initiated at the pelvic flexure pacemaker, could result in displacements and volvulus.[11] Large colon displacements have been classified into left dorsal displacement of the large colon, also referred to as nephrosplenic or renosplenic entrapment; right dorsal displacement of the large colon; and retroflexion of the large colon. The large colon can adopt a location intermediate to these displacements, such that the exact displacement can be difficult to describe.

Entrapment in the Renosplenic Space

Prevalence, Etiology, Risk Factors

Renosplenic entrapment (also termed nephrosplenic entrapment or left dorsal displacement of the large colon) is a form of non-strangulating large colon displacement in the horse, where the left dorsal and ventral colons migrate lateral to the spleen in a dorsal direction until they are entrapped in the renosplenic space. This condition has been reported in horses of all ages, as early as 9 months.[61] Although one report mentions the increased prevalence in male horses, others have not substantiated that finding.[61-63] No reports of this condition exist in miniature horses and pony breeds. It is theorized that excessive gas formation within the left colon, perhaps in association with abnormal motility, causes the left colons to displace lateral to the spleen and dorsally into the renosplenic space; alternatively, the colon may displace during rolling episodes.[3,64-66] The pelvic flexure has also been identified in the space between the spleen and stomach and entrapped in horses with adhesion of the spleen to the abdominal wall, suggesting movement of the colon along the cranial edge of the spleen to the renosplenic space. In most cases, there is also ventro-medial rotation of the left colons, such that the left dorsal colon is rotated ventral to the left ventral colon. The weight of the colon causes the spleen to displace medially and ventrally and to become congested. Because of impaired flow of ingesta over time, with duration there is also concurrent impaction of the left dorsal colon. With continued gas formation, the sternal and diaphragmatic flexures can migrate cranial and dorsal to the stomach between the stomach and the left liver lobe,[67,68] a displacement classified as type II in one publication.[68] Renosplenic entrapment is a nonstrangulating lesion of the large colon; however, when duration of the condition exceeds 24 hours, colonic congestion and edema can develop and mural damage can occur.[64] Obstruction to gastric outflow occurs because of pressure of the colon on the duodenum, or tension on the mesentery. Entrapment of the small colon or small intestine in the renosplenic space have been described, but these conditions are rare.[69,70]

Clinical Signs

Horses with renosplenic entrapment show variable degrees of pain depending on the location of the colon, the amount of gas distention, and the presence of secondary gastric distention. Location of the colon lateral to the spleen is associated with minimal to no discomfort, and the colon is found in this location in the resolving stages of the displacement. Entrapment of the colons within the renosplenic space with the spleen in a relatively normal position is a very painful condition. Affected horses will crouch, want to go down, and often lean to the left. When the spleen is pushed away from the body wall and displaced ventrally, effectively opening the renosplenic space, there is less pressure on the colon and horses show only mild signs of abdominal pain.

Diagnosis

The diagnosis of renosplenic entrapment is based on the presence of abdominal pain, which can be mild to severe depending on the location of the colon and the degree of gas distention. Cardiovascular parameters are relatively normal, consistent with a simple obstruction. The CBC and chemistry values should be normal or consistent with mild dehydration. A low PCV in the presence of dehydration has been reported as an indication of red blood cell sequestration in the spleen. The results of abdominocentesis should be within normal range. Collection of splenic blood (characterized by a PCV higher than peripheral blood) is supportive of a diagnosis of renosplenic entrapment, and was obtained in 25% of horses with this condition at admission.[62] Horses with increased WBC counts in peritoneal fluid were more likely to have a long-standing condition and to be treated surgically.[62] Nasogastric reflux is commonly obtained in horses with renosplenic entrapment as a result of pressure on the duodenum or increased mesenteric tension. Up to 43% of horses with renosplenic entrapment were reported to have nasogastric reflux.[61] In one study, resistance to nasogastric intubation was encountered in horses with displacement of the sternal and diaphragmatic flexures dorsal to the stomach.[68]

Ultrasound examination of the abdomen can serve as an adjunct to the diagnosis of renosplenic entrapment and was diagnostic in 88% (36/41) horses with renosplenic entrapment.[71] A 2.5 mHz or 3.5 MHz ultrasound probe is positioned over the 15th to 17th intercostal space in a direction parallel to the ground and the spleen is imaged. In the normal horse, the left kidney is imaged deep to the spleen. In horses with renosplenic entrapment, the presence of gas-filled colon dorsal to the spleen precludes imaging the kidney. Ventral displacement of the dorsal aspect of the spleen is also consistent with renosplenic entrapment. If the left dorsal and ventral colons are displaced lateral to the spleen, then imaging of the spleen is obscured as well. It is important to direct the probe in a horizontal direction; if the probe is angled in a dorso-ventral

direction, the kidney can occasionally still be imaged, giving a false-negative diagnosis. It is important to realize that the inability to image the left kidney is only supportive of a renosplenic entrapment and should be used in conjunction with rectal palpation findings. Nonspecific large-colon distention or the normal presence of small colon in the renosplenic space can impair imaging of the left kidney.[72] In addition, if the colon is fluid-filled, imaging of the left kidney is still possible, but the entrapped bowel is also seen.[71]

Rectal palpation remains the mainstay of diagnosis of renosplenic entrapment. On palpation, the left colons will most often be gas–distended, and the ventral colon will be dorsal to the left dorsal colon; the left dorsal colon will often be impacted. It is important for arriving at a correct diagnosis to follow the colons into the renosplenic space as in other conditions ranging from gas colic to large colon volvulus, the colon can assume a dorsal position within the abdomen, leading to a false diagnosis of renosplenic entrapment.[73] This could be disastrous if nonsurgical management is attempted and the horse has a large colon volvulus. In three studies, left dorsal displacement of the large colon was correctly identified by rectal palpation in 61.2%, 68.7%, and 72% of cases,[61-63] although an early study reported a much lower rate of correct identification of only 18%.[68] Results of rectal palpation can be impaired by patient size or temperament, or in the presence of severe distention.

Thorough physical examination, rectal palpation, and abdominal ultrasound should be performed in horses diagnosed with renosplenic entrapment because a small number of animals will have a lesion involving another segment of the gastrointestinal tract; gastric rupture, small intestinal volvulus, ileal impaction, large-colon displacement, large-colon volvulus, cecal torsion, and small-colon obstruction have been documented in association with renosplenic entrapment.[61-63,71,74]

Treatment

Once a diagnosis of renosplenic entrapment has been made and the clinician is confident that no other abnormalities are present, options for treatment should be considered. These include medical therapy with intravenous replacement fluids and withholding of feed; exercise with or without the use of a vasopressor agent; rolling under general anesthesia with or without the use of vasopressor agents; standing flank laparotomy; and ventral midline celiotomy.

Medical therapy and nonsurgical management by rolling are described elsewhere in this text (see Chapter 21). If nonsurgical manipulations are unsuccessful or if findings are questionable, surgical intervention is indicated. Standing flank laparotomy or ventral midline celiotomies are therapeutic options.

Standing flank laparotomy allows correction of a renosplenic entrapment, providing the diagnosis is correct. The advantages of the standing flank approach include avoidance of general anesthesia, direct access to the problem, access to the renosplenic space for closure as an option for prevention of recurrence, and more rapid return to use of the horse. The major disadvantage, as is the case for nonsurgical manipulation, is if an incorrect diagnosis was made, precluding correction by this approach.

The horse is restrained in stocks with the tail bandaged and tied to avoid contamination of the incision. Sedation with xylazine with or without butorphanol is sufficient for most horses. Depending on the anticipated disease process (see below) a left- or right-sided approach is decided on. After standard preparation of the surgical site, local anesthesia is performed. This can be accomplished with a paravertebral block,[75] an inverted L-block, or a line block, taking care to add local anesthesia for placement of towel clamps. In the author's experience, the paravertebral block often requires additional local block in the distal aspect of the planned incision. Draping is routine, with the addition of a drape folded to form a pocket to support the exteriorized bowel. The standard surgical approach for a flank laparotomy is midway between the last rib and the cranial aspect of the tuber coxa, starting approximately 2 cm above the palpable internal oblique muscle. In the standing horse, the modified grid is the preferred approach, as the muscles will help keep the intestines in the abdomen during the surgery. In the modified grid, the external oblique muscle is incised but the internal oblique and transverse abdominal muscles are bluntly separated by finger traction. Additional topical application of anesthetic may be required before perforating the peritoneum. Once the abdomen is entered, the spleen and large colon are located. In the author's experience, it is easier to push the spleen down and under the large colon than it is to lift the large colon over the spleen. Once the colon is lateral to the spleen, it is gently pushed into the ventral abdomen. Closure is routinely performed.

A ventral midline celiotomy is recommended for correction of renosplenic entrapment if nonsurgical management is unsuccessful or if there are clinical or clinico-pathologic findings that indicate either the loss of intestinal integrity or the presence of another lesion. This approach is also used when a presurgical diagnosis is not possible because of the small size of the patient, which precludes rectal palpation, or excessive large-colon distention. The advantages of the ventral midline celiotomy are that it ensures correction of the abnormality, particularly in cases in which the colons are dorsal and cranial to

the stomach, and that it allows correction of other undiagnosed problems. The disadvantages of this approach include the need for general anesthesia, longer postoperative recovery, and increased cost. A routine ventral midline approach is performed, although to facilitate access to the renosplenic space the horse may be shifted temporarily from dorsal recumbency slightly to its right side. In the situation of excessive splenic congestion or excessive weight of the colon, phenylephrine may be administered to reduce splenic size and facilitate correction. The base of the spleen is grasped and the spleen is lifted and pushed medial to the colon, thus freeing the colon from the renosplenic space. The colon is then cradled over the forearm and lifted out of the abdomen. In some cases, because of tension of the colon, the colon cannot be lifted from the renosplenic space. Retraction of the colon cranially toward the stomach will release tension and allow the colon to be pulled lateral to the spleen. Although feed has often accumulated in the dorsal colon, evacuation is usually not necessary as the feed redistributes when the displacement is corrected. The colon is assessed for signs of devitalization. Rarely, a large-colon resection will have to be performed.

Prognosis

The reported recurrence rates of renosplenic entrapment are 7.5% to 8.5%.[61,62] Considering this relatively low risk, surgical intervention procedures for prevention of recurrence are not recommended after a first incidence. However, feeding and management practices should be carefully reviewed to minimize the risk of gas formation in the large colon and subsequent displacement. A clinical study of renosplenic entrapment in Germany reported a recurrence rate of 21% in horses with signs of colic.[76]

Prevention

Procedures that have been advocated for prevention of recurrence of left dorsal displacement of the large colon include: closure of the renosplenic space; large-colon colopexy; and large-colon resection. The reader is referred to other sections for discussions of large-colon resection and colopexy procedures.

Closure of the renosplenic space will not prevent migration of the large colon lateral to the spleen, or the occurrence of other forms of large-colon displacement. The procedure can be done through a flank laparotomy or though a minimally invasive laparoscopic approach.[77,78] The flank approach is performed in the standing or laterally recumbent horse. The abdomen is entered either through a modified grid or laparotomy approach. The spleen and renosplenic ligament are identified, and the renosplenic space is verified to be free of intestine. Cruciate sutures are then placed between the ligament and the tip of the spleen, using a nonabsorbable suture such as 2-polypropylene in a cruciate pattern. Approximately 6 to 12 stitches are pre-placed and then tied. The abdomen is closed in a routine fashion. Alternatively, laparoscopic ablation of the renosplenic space can be performed in the standing horse,[77] and has been reported successfully in 5 experimental animals. The procedure is performed through 3 laparoscopic portals and using polyglactin 910 suture material in a simple continuous pattern. There are a few reports regarding the long-term efficacy of this procedure,[77,78] with the most recent ones collectively involving more than 50 horses with renosplenic entrapment.[76,79] The results reported in these studies are encouraging, although it is important to note that closure of the renosplenic space does not prevent the development of other colonic displacements.[79]

Right Dorsal Displacement of the Large Colon

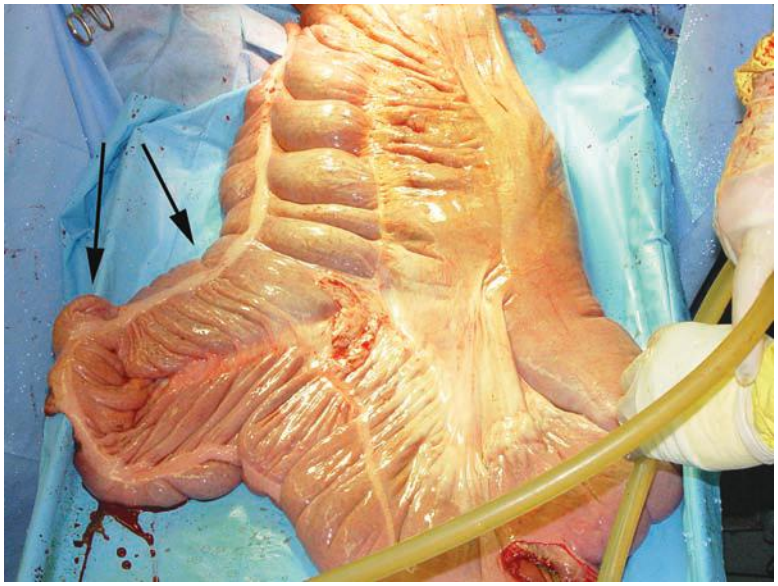
Etiology

This type of displacement is thought to be initiated by retropulsive movement of the pelvic flexure, with subsequent migration of the left colon cranially, and then to the right abdominal quadrant, until the right ventral and dorsal colons are located between the cecum and the body wall. The colon can also rotate on its long axis, resulting in variable degrees of venous congestion.

Clinical Signs

The location of the colon at the time of examination is related to the clinical signs. When the colon is displaced cranially, all parameters are usually within normal limits, and abdominal pain is mild and intermittent. Horses with this condition may be comfortable when held off feed, with their abdominal pain recurring when feed is re-introduced. These horses continue to pass small amounts of manure. On palpation per rectum, no abdominal distention is felt, but the examiner is unable to locate the pelvic flexure. As the colon continues to migrate in a clockwise direction, the flow of ingesta is impaired and a secondary impaction of the right dorsal colon can develop. Gas distention also becomes more significant as does the associated abdominal pain. When a dorsal colon impaction develops, it is important not to mistake this for a pelvic flexure impaction, as continued medical treatment may result in rupture of the colon. This condition can be differentiated from a pelvic flexure impaction by the fact that the palpable colon travels cranially to the right, and that the pelvic flexure cannot be identified. In right dorsal displacements, the cecum can be enlarged and fluid filled.

Figure 38-4



Photograph of a congenital malformation (arrows) of the ventral colon in an 8 month old filly that had suffered several colic episodes. Large colon resection and anastomosis resolved the problem.

Horses with right dorsal colon displacements present with mild to moderate abdominal pain. Depending on the degree of displacement, rectal palpation will reveal absence of the pelvic flexure, presence of large colon lateral to the cecum, large-colon distention, and right dorsal colon impaction. Nasogastric reflux may be present if there is large-colon distention. Laboratory findings are usually unremarkable, although a significant number of horses present with an increased serum concentration of gammaglutamyl transferase (GGT), probably related to partial obstruction of the bile duct or duodenum.

When horses are presented early, with normal parameters, mild abdominal pain, and minimal to moderate large-colon distention, medical therapy may be attempted. Intravenous fluids are administered and the horse is monitored for resolution of the distention and relocation of the large colon.

Treatment

In horses in which the pain is severe, or that have significant large-colon distention or a severe secondary impaction, surgical intervention is recommended. Although in some specific circumstances the author has successfully corrected right dorsal colonic displacements via a standing flank laparotomy, a ventral midline celiotomy is preferred because of the ease of exposure and correction.

At surgery, the pelvic flexure is identified, the large colon is exteriorized, and the displacement is corrected. In cases where a severe large-colon impaction coexists, the large colon is exteriorized at the pelvic flexure but an attempt to correct the displacement is not made until the large colon has been evacuated, to avoid rupture during colonic manipulations. Although one report exists of successful treatment of a horse following intraoperative rupture during surgery,[80] most cases in which contamination has occurred within the abdomen are fatal.

Prognosis

The prognosis for correction of large–colon displacement is excellent. Recurrence is possible, and the author has treated horses with large-colon displacement recurring within 48 hours of the first procedure. In the author's opinion, it is important to not completely evacuate the large colon during surgery, but to leave some ingesta in the colon. The author also returns these horses to feed within 8 hours of surgery, again to try and maintain ingesta in the large colon.

Nonstrangulating Volvulus of the Large Colon

Nonstrangulating volvulus of the large colon is identified when the colon is rotated from 90 to 270 degrees on its long axis, a step that precedes the 360-degree large-colon volvulus.

Clinical Signs

Horses with this type of displacement have a clinical presentation similar to those associated with other simple large-colon displacements: minimal cardiovascular compromise, mild to moderate abdominal pain, normal findings on abdominocentesis, and mild to moderate large-colon distention identified on rectal palpation. As in other displacements, medical management

may be attempted. Horses that remain in pain or that have worsening of abdominal distention are candidates for surgical intervention. At surgery, the colon is replaced in its normal position.

Prevention

As in all forms of large-colon displacements or volvulus, prevention of recurrence should be considered. Colopexy and large-colon resection are two procedures that are performed in an attempt to prevent recurrence. Usually these procedures are not recommended on a first-time occurrence, but should be discussed with owners of horses that have two or more displacements.

Other Simple Obstructions of the Large Colon

Congenital malformation of the large colon was reported as a cause of recurrent colic in a horse, and has been identified by the author in several horses (Figure 38-4).[81] Resection and anastomosis of the colon orad to the malformation successfully resolved the problem.

Fibrosis and stricture of the large colon caused by focal fibrosis at the pelvic flexure was identified in three horses and corrected by transverse closure of a pelvic flexure enterotomy made at the site of the fibrosis.[82]

Pelvic flexure adhesions resulting in impaction were reported in a filly with peritonitis. Laparoscopic adhesiolysis was successfully performed to allow return of ingesta transit.[83]

A massive duplication cyst of the ascending colon was reported in a 27-year-old mare with a history of recurrent colic and a pendulous abdomen. The cyst was successfully removed and the mare made an uneventful recovery.[84]

Defects in the mesentery of the large colon (Figure 38-5), observed by the author, allow displacement or torsion of the colon upon itself, as it is no longer confined by the mesentery. Closing the defects with sutures corrects the problem.

Figure 38-5



Large colon of a horse with a mesenteric defect in the large-colon mesentery, which resulted in a partial large-colon volvulus.

Large-Colon Torsion/Volvulus

Prevalence, Etiology, Risk Factors

Large-colon volvulus is one of the most painful and devastating gastrointestinal problems in the horse. Successful management depends on rapid referral and prompt surgical intervention. Without intervention, death occurs in a matter of hours.

The prevalence of large-colon volvulus is increased in areas having a high concentration of brood mares. Risk factors include recent parturition, recent dietary changes, and recent access to a lush pasture.

Clinical Signs

The history of horses with large-colon volvulus can vary depending on the rapidity and completeness of the development of a complete volvulus. Some horses present with a history of chronic (> 24 hours) colic, that suddenly worsens to intractable pain; others present with an acute onset of uncontrollable pain. Initially, despite the severe pain, horses will maintain normal cardiovascular parameters, and findings of rectal palpation can be unremarkable. As time elapses, these horses will develop progressive large-colon distention and accompanying progressive cardiovascular collapse. In mares, the color of the vaginal mucosa changes and reflects the degree of compromise of the large colon (Figure 38-6). If untreated, horses with large-colon volvulus die of hypovolemic shock caused by abdominal compartment syndrome associated with the severe distention, by pooling of blood in the strangulated large colon, and by poor pulmonary expansion because of severe distention.

Figure 38-6A

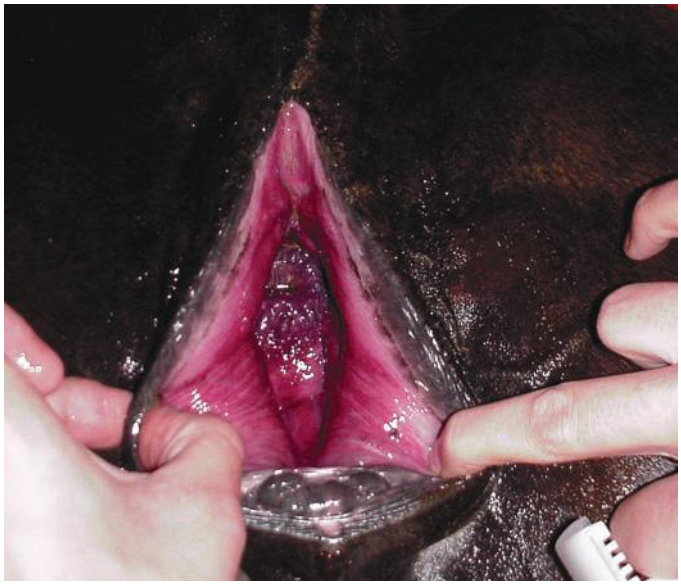


Figure 38-6B



A.) Pre-operative appearance of the vaginal mucosa in a mare with large-colon volvulus. **B.)** Appearance of the large colon in the same mare at surgery.

Treatment

The treatment of large-colon volvulus is surgical. However, during preparation for surgery, resuscitative measures should be initiated to increase circulating blood volume and decrease abdominal pressure. Fluid therapy, including administration of hypertonic saline, colloids, and crystalloids should be initiated. Percutaneous large-colon decompression to relieve abdominal distention can improve lung expansion and venous return, and can help support the horse during induction of anesthesia, until the colon can be exteriorized and decompressed.

In preparation for surgery, the horse can be tilted to one side to facilitate exteriorization of the colon and remove pressure on the caudal vena cava. Intravenous administration of lidocaine can be used to decrease the concentration of inhalant agents (see Chapter 9). A long ventral midline incision is performed to help in exteriorizating the colon. Lengthening the incision cranial is preferred to facilitate exposure of the colonic base.

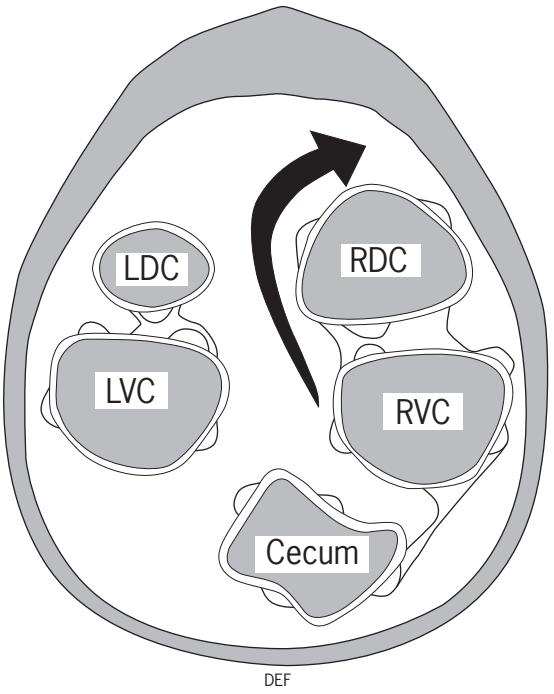
The direction of the volvulus is best described in relationship to the position of the ventral colon to obviate the need for describing the observer position. Therefore, a dorsomedial volvulus indicates rotation of the right ventral colon medially and dorsally or in a clockwise direction if viewed from the caudal aspect of the horse (Figure 38-7).[85] Most often the colon twists in a dorsomedial direction, and the location of the volvulus is at or proximal to the cecocolic ligament. Occasionally, a volvulus involving the sternal and diaphragmatic flexures is encountered. Volvulus of 270-degrees to 720-degrees have been described.[86] Correction of the volvulus can be difficult, particularly if the colon is full and/or edematous; this places the colon, particularly the right dorsal colon, at risk for rupture during surgical manipulation.

Initially the ascending colon is exteriorized; if the colon is full or edematous and friable, a pelvic flexure enterotomy is performed to empty the colon before attempting further manipulation. To correct the most common direction of the volvulus, the surgeon, situated on the left side of the horse, places both hands in the abdomen around the base of the colons, and gently manipulates the colon in a clockwise direction. To determine the correct direction to rotate the colon, the surgeon's hand follows the right ventral colon toward the cecocolic ligament. The direction of the hand in following the direction of

twisting of the colon is the direction the colon is rotated to resolve the volvulus. The surgical assistant can facilitate manipulation by rotating the exteriorized portion of the colon in the same direction. Gas translocation and return of serosal color are indications that the colon is manipulated correctly. Once a 360-degree rotation has been achieved, the surgeon must then ascertain that the volvulus is corrected and that another rotation of the colon is not needed. This is accomplished by examining the normal position of the cecum and exposure and normal position of the cecocolic ligament (see Chapter 26), and ensuring by palpation that the mesenteric attachment of the right dorsal colon to the dorsal body wall is straight.

Once the colon has been returned to its normal position, the surgeon must determine the viability of the colon; this may indicate the need for euthanasia; recovery of the horse without further intervention; colopexy for prevention of recurrence; or large-colon resection. It is essential to involve the owner in the decision-making process, particularly if the colon is compromised, as the cost of further intervention or postoperative care can be significant. The surgeon must also understand that if the colon is not resected and the horse is recovered from anesthesia, it is unlikely that a second laparotomy will be an option. By the time clinical signs indicate that a second laparotomy with large-colon resection is needed, the horse's condition will often have deteriorated to the point at which chances of survival following a resection are poor.

Figure 38-7



Large-colon volvulus depicting the terminology for describing the direction of the volvulus.

Prognosis

Several factors are useful to help the surgeon reach a decision. Of critical importance is the horse's systemic condition both preoperatively and intraoperatively. A PCV above 50% which increases during surgery and is associated with a decreasing total plasma protein concentration, is indicative of a poor prognosis for survival. Inabilities to maintain mean arterial blood pressure despite the use of pressor agents, persistent hypoxemia, and persistent tachycardia during surgery are also associated with poor survival rates. Examination of the colon can provide some additional information. Return of a normal pink serosal color after volvulus correction suggests a viable colon, however does not indicate mucosal viability (see Chapter 28). Loss of the mucosa with damage of the crypt cells can result in severe postoperative endotoxemia. Visual examination of the mucosa made through a pelvic flexure enterotomy provides additional information. The presence of dark red or black mucosa with no active bleeding is a poor prognostic indicator. The use of frozen sections and calculation of the interstitial-to-crypt ratio and percent loss of epithelium correlates well with survival; an I:C ratio of 3:1 or greater, or loss of more than 95% of the epithelium was associated with 95% death in one study. However, this requires the presence of personnel able to perform this evaluation. Other tools that have been used to evaluate colonic viability include surface oximetry, fluorescein dye, and Doppler flow. None of these tools has gained popularity in a clinical setting. The decision to perform a colon resection should also be based on the location of the volvulus. If the line of devitalized bowel is located distal to the cecocolic ligament, the outcome of a large-colon resection is much more favorable, as resection of the affected bowel is possible. However, in most

instances, the line of devitalization is located at the base of the colon oral to the cecocolic ligament so that the resection must be performed in a compromised portion of the bowel, thereby increasing the risk for dehiscence. Surgeons who are advocates of large-colon resection for the treatment of large-colon volvulus make a case that removing the majority of the diseased colon decreases endotoxin absorption and, therefore, increases the likelihood of survival. In addition, removal of the large colon prevents recurrence of the condition. Surgeons who do not routinely perform large-colon resections for large-colon volvulus state that the procedure in itself has a high risk of complications and does not in most cases result in removal of all of the diseased colon; in addition, the increased anesthesia time may be detrimental to the animal. One report suggests that survival in horses undergoing a large-colon resection is not significiantly different compared with those without a resection.[87] Still these debates emphasize the complexity of the decision-making process in these cases, and the importance of experience, familiarity with surgical techniques, and the influence of types of cases on the decision-making process. For example, horses that are referred quickly and that have a short duration of illness seldom require a large-colon resection.

Preoperative parameters indicative of poor survival include PCV greater than 50%, rectal temperature higher than 102°F, and heart rate more than 80 beats per minute.[88] Intraoperative factors associated with poor survival include black mucosal color, poor return of perfusion after correction of the volvulus, an increasing PCV and decreasing total plasma protein concentration during surgery.[88] Abdominocentesis findings are usually normal in horses with large-colon volvulus; an increase in total protein concentration in the abdominal fluid is associated with decreased survival.[86] Abdominocentesis, therefore, does not usually provide information that will alter the decision for surgical treatment, and it presents an increased risk of enterocentesis or injury to personnel in horses in severe pain.

Reported mortality for large-colon volvulus varies from 56% to 65%. In one study, short-term survival rate was 84%; this higher survival rate was thought to be related to a shorter duration of illness and faster intervention time.[89] Although short-term mortality is high after surgical correction of large-colon volvulus, a long-term probability of survival of 80% has been reported once horses are discharged from the hospital.[90]

Right Dorsal Colitis

Prevalence, Etiology, Risk Factors

Right dorsal colitis is a specific type of ulcerative colitis observed in the right dorsal colon of the horse, specifically the aboral segment of the dorsal colon as it joins the transverse colon. This condition is recognized in association with administration of NSAIDs and has been reproduced experimentally by administration of phenylbutazone. Horses with a nervous predisposition seem more prone to the development of the disease even when appropriate dosages of NSAIDs are administered. Although NSAID administration is commonly associated with this condition, it also has been documented in the absence of NSAID administration.

Clinical Signs

Clinical signs of right dorsal colitis can manifest as acute colic, endotoxemia, diarrhea, and even death. The disease is more common in the chronic form, where horses are presented for weight loss, hypoproteinemia, intermittent signs of colic, and intermittent diarrhea.

Diagnosis

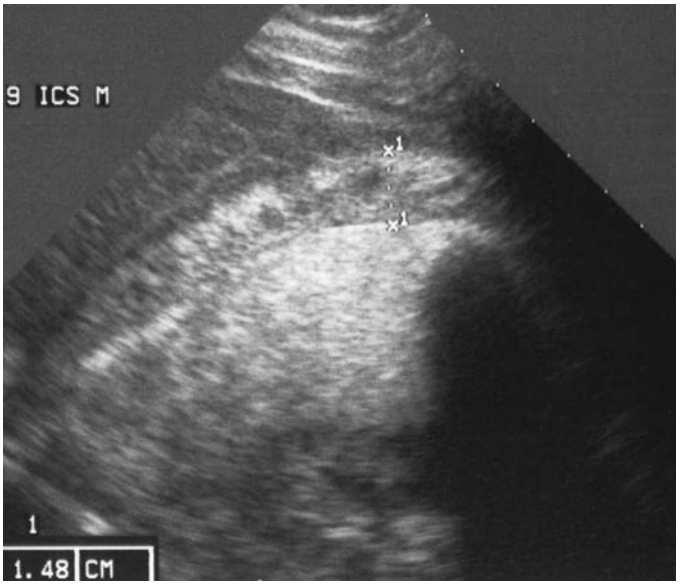
The diagnosis of right dorsal colitis is based on historical findings, particularly those of NSAID administration, and ruling-out other causes of weight loss, hypoproteinemia, and diarrhea. Diagnostic ultrasonography of the right dorsal colon can help identify the thickened colon wall (Figure 38-8).[91] More recently, scintigraphy with radiolabeled white blood cells has been used to diagnose the condition.[92]

Treatment

Medical management is initially recommended for the treatment of horses with right dorsal colitis. Medical management includes discontinuation of NSAID; initiation of dietary modifications; and administration of anti-inflammatory drugs, intestinal protectants, and metronidazole. Dietary modifications are important to help control the signs of colic.

In cases of protracted colic, or when intermittent colic episodes are so frequent as to prevent the horse from maintaining itself, surgical exploration can be recommended. At surgery, the right dorsal colon will feel markedly thickened, and may be strictured with scar tissue (Figure 38-9). Once the disease is identified at surgery, treatment options include right dorsal colon bypass, resection of the affected portion of the colon, large-colon resection, or large-colon resection and large-colon bypass.

Figure 38-8



Ultrasonographic image of the right dorsal colon at the 15th intercostal space using a 3.5 mHz probe illustrating the marked thickening of the intestinal wall.

Figure 38-9



Intraoperative photograph of the right dorsal colon of a horse with severe stricture secondary to ulcerative colitis.

Bypass of the affected area of the large colon is performed by exteriorizing the large colon on a colon tray. The small colon is then exteriorized and a 20- to 30-cm side-to-side anastomosis is made between the right dorsal colon oral to the lesion and the small colon approximately 1 meter distal to the transverse colon.[93] When this procedure is performed, transient diarrhea has been observed. This procedure does not remove the affected portion of the colon; therefore, the patient can continue to suffer from continued weight loss and hypoproteinemia until the colitis has resolved. Resection of the affected colon through a 16th rib resection has been reported in one horse.[94] This approach requires either prior knowledge of the disease, or a second celiotomy approach once the diagnosis has been made. Resection and end-to-end anastomosis will only be possible if the lesion does not extend too far aborally. In cases of severe right dorsal colitis with stricture of the right dorsal colon, large-colon resection and anastomosis in a side-to-side fashion can be performed to restore intestinal transit of ingesta; however, complete removal of the ulcerated area is not possible with this approach. Another approach, which has not been described for the treatment of this condition, is amputation of the large colon, particularly the dorsal colon as far aborally as possible, and performing an end-to-side anastomosis between the right ventral colon and the small colon. This approach has been reported for the management of nonfunctional dorsal colon lesions in two horses.[95,96]

Mural Infarction (Thromboembolic Colic)

Prevalence, Etiology, Risk Factors

Compromise of the mesenteric vasculature without evidence of strangulation has been described in association with arteritis resulting from *Strongylus vulgaris* larval migration or in horses with severe colitis and coagulopathies (Figure 38-10). Anecdotal reports and results from necropsy suggest that current methods used to control intestinal parasites have decreased the prevalence of this disease.

Cases of larval arteritis can be acute, with signs of ischemic bowel disease and peritonitis; or chronic, with signs of recurrent colic and weight loss. Horses with acute thromboembolic colic will have significant changes in their peritoneal fluid, consistent with peritonitis; horses with recurrent colic can have normal peritoneal fluid, although the results are variable.

Figure 38-10



Intraoperative photograph showing venous infarction of the cecum and large colon in a horse with necrotizing enterocolitis.

Clinical Signs

In acute cases, surgical intervention is indicated based on the signs of colic, and peritonitis. Pain is variable, and recurrence of pain and lack of response to treatment in horses with mild pain but lacking intestinal distention or gastric reflux may be the only signs indicating surgery.

Treatment

At surgery, mural infarction can be focal or involve an entire viscus, such as the cecum or large colon. If possible, resection of the affected segment of intestine is performed. Careful palpation of the cranial mesenteric artery should be performed; identification of severe enlargement, aneurysm, or abscessation are indications for a guarded to poor prognosis. A regular systemic deworming program should be instituted as part of the postoperative care.

Horses with colitis that show acute signs of abdominal pain and abdominal distention should be suspect for thromboembolic colic and necrotizing colitis, although a history of a comprehensive parasite control program makes this problem unlikely. Horses that have extensive lesions are not good candidates for surgical intervention. In addition, their systemic status, as a result of the primary colitis, makes them poor surgical candidates.

Other Strangulating Lesions of the Large Colon

Other strangulating lesions of the equine large colon have been reported. These include incarceration in the epiploic foramen,[97] the gastrosplenic ligament,[98] or a defect in the renosplenic ligament (see Chapter 21); large-colon intussusception;[99,100] and volvulus associated with abnormal mesenteric bands or defects.[101,102] Surgical intervention is dictated in these case by the increasing degree of abdominal pain, abnormal findings on rectal palpation, and results of abdominocentesis indicative of intestinal compromise. Resection and anastomosis of the affected colon is required to correct these conditions.

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Disorders of the Small Colon

Chapter 39

John F. Peroni

Of the horses with abdominal diseases referred to tertiary care facilities, 3% to 18% are evaluated because of abnormalities involving the small colon. The frequency of obstructive disorders of the small colon that require abdominal surgery is approximately 4%.[1-4] Successful diagnosis and treatment of diseases of the small colon depends on a thorough understanding of its anatomy and physiology (see Chapter 1). The mid-section of the small colon is relatively mobile within the caudal abdomen; however, its most oral and aboral segments are fixed in position. These anatomic features facilitate transrectal palpation of the majority of the small colon and are advantageous in the diagnostic approach to small-colon disease. In contrast, these same features hinder surgical access to the entire length of the small colon, making visual inspection of the proximal and distal aspects of the small colon impossible during a ventral midline laparotomy. These and other distinctive physiologic characteristics are important because they affect the approach to common diseases affecting the small colon.

Surgical Considerations Affected by Anatomic Features of the Small Colon

The small colon is occasionally referred to as the descending colon, a term that more accurately describes the corresponding portion of the gastrointestinal tract in humans. However, some specific points require mention here as they have important implications regarding the surgical approach to diseases of the small colon. For example, the transition between transverse colon and small colon occurs at a fixed point adjacent to the left kidney. The small colon is suspended from the sublumbar body wall by the mesocolon, which is the caudal continuation of the root of the mesentery. The duodenocolic fold is a narrow extension of the peritoneum and attaches the small colon to the terminal duodenum. This important anatomic landmark is used during exploratory celiotomy to identify the cranial-most portion of the jejunum. Because of these anatomic features, the most oral and aboral portions of the small colon cannot be exteriorized during a ventral midline celiotomy. During colic surgery it is, however, important to carefully palpate the transition between the transverse colon and the small colon as this is a frequent site of obstruction, particularly in enterolithiasis.

The vascular anatomy of the equine small colon has been described in detail.[5] Vascular arcades are concealed within the mesocolon by large amounts of mesenteric fat and originate from the cranial and caudal mesenteric arteries. The cranial mesenteric artery gives rise to the middle colic artery which supplies the cranial portions of the small colon, whereas the caudal mesenteric artery is responsible for the majority of the blood supply of the small colon via anastomosing branches of the left colic artery and the cranial rectal artery.[3] A marginal artery can be found 1 or 2 cm away from the serosal surface coursing parallel to the longitudinal axis of the small colon. From the marginal artery a secondary arcade of blood vessels arises to form a hemicircumferential arterial rete that forms anastomoses on either side of the bowel.[3] It is often reported that survival after small-colon resection and anastomosis may be complicated by a relatively poor blood supply.[2,6,7] It would appear instead that the merging cranial and caudal mesenteric vascular supply and the presence of 3 communicating intramural plexuses derived from the marginal artery would allow the formation of an effective collateral blood supply.[8]

Motility patterns of the equine small colon have not been elucidated in detail. Clinical evidence does exist, however, that horses possess a well developed gastrocolic reflex. This occurs after feeding when signals from the stomach follow the extrinsic innervation of the autonomic nervous system and cause evacuation of small-colon contents. Clinicians can take advantage of this physiologic mechanism to stimulate evacuation of the colon by offering small amounts of feed to horses receiving aggressive medical treatment for obstruction of the small colon. Mixing and propulsive movements occur in the small colon but are less active than those occurring in the small intestine.[9] The slower transit time of colonic contents allows absorption of water and electrolytes, which leads to progressive fecal dehydration. This may be compounded in dehydrated animals facilitating fecal accumulation and obstruction such as in the case of small-colon impactions.

The anatomic and physiologic details mentioned above form the basis for a few principles that should be observed when considering the surgical approach to the small colon. In horses with small-colon abnormalities requiring surgical intervention, it is commonly necessary to evacuate colonic contents or to remove foreign bodies via an enterotomy, which is best performed along the mid-portion of the wide antimesenteric band (taenia). Compared with an incision through the sacculations of the small colon, an enterotomy through the tenia is associated with less hemorrhage, edema, and surgery time and, at 96 hours after surgery, incisional strength is superior to an enterotomy through the sacculations.[10,11] The taenia can be partially incised to facilitate aboral advancement of an enterolith lodged within the most proximal aspect of the small colon. Because this segment of the small colon cannot be exteriorized through a ventral midline celiotomy, it is helpful to perform a seromuscular teniotomy that effectively widens the diameter of the bowel and allows enteroliths to be moved aborally up to 15 cm for safe removal.[12] Closure of enterotomies and teniotomies is usually performed with 2-0 synthetic absorbable monofilament, such as polydioxanone, in a single-layer inverting suture pattern. It appears from one study that separate mucosal apposition does not have a significant effect on healing time and effectiveness of closure.[11]

Strangulation-obstruction of the small colon may necessitate resection and anastomosis, which, in this location is usually performed with an end-to-end technique. A stapled anastomosis technique can reduce surgery time and has been used experimentally in the small colon; however, the hand-sewn technique is preferred because the intricate mesenteric vasculature can be more carefully preserved, larger luminal diameters are achieved, better healing is accomplished, and postoperative adhesion formation is minimized.[13,14] Although several anastomosis techniques are available, a few important principles of intestinal surgery should be followed to preserve the vascular supply, avoid compromising the luminal diameter, and minimize adhesion formation. If a two-layer closure is chosen, care should be taken to avoid excessive tissue inversion, which would considerably reduce luminal diameter, particularly in the first 7 to 10 days after surgery when edema formation may further restrict the size of the lumen.[15-17] In order to minimize adhesion formation, mucosal exposure of the peritoneal surfaces should be avoided by utilizing an inverting suturing technique such as a Cushing or Lembert pattern. Adhesions can be further minimized by covering the anastomotic site with a bioabsorbable hyaluronate membrane, which has been successfully used in adhesion prevention both clinically and experimentally.[18,19] A common anastomosis technique includes an initial simple interrupted layer oversewn with a Cushing pattern interrupted at 180 degrees at the mesenteric and antimesenteric edges. Suture bites should be placed with great care in the area of the mesenteric attachment because the small arterial rete, concealed by the large amount of adipose tissue, may inadvertently be damaged.

Knowledge of the distribution of the intestinal flora plays an important role in the decision-making process after small-colon surgery. Compared with the small intestine, the microflora of the cecum and colon is rich in aerobic and anaerobic bacteria.[20,21] The colonic microflora is dominated by strict anaerobic bacteria, including *Bacteroides sp.; Clostridia sp.* Facultative anaerobes occur in numbers 1000-fold lower and include lactobacilli, enterococci, streptococci, and Enterobacteriaceae.[21] These bacterial populations warrant the perioperative use of broad-spectrum antimicrobials, including metronidazole, which is specific for the prevention and treatment of anaerobic infections. The short mesentery of the small colon compels the surgeon to perform resection and anastomoses or enterotomies in close proximity to the celiotomy incision, thereby increasing the risk of inadvertent abdominal contamination.

Obstruction of the small colon often causes stasis of fecal material in the colon and cecum. For this reason, evacuation of the contents of the ascending colon via a pelvic flexure enterotomy should be performed to minimize fecal passage on a newly created small-colon anastomosis or on a small-colon enterotomy. The rationale for evacuation of these contents is supported by the fact that fecal material undergoes progressive dehydration in the small colon, a process that may further stress incisions that initially depend solely on the holding power of the suture material.

In addition to the high bacterial content of the distal intestine, small-colon anastomotic healing is thought to be hindered by the relatively high activity of collagen-degrading enzymes such as matrix metalloproteinases (MMPs).[2] Although specific studies addressing the effect of MMPs on healing of the equine colon are lacking, evidence exists that an abnormal regulation of these enzymes may lead to delayed anastomotic dehiscence in people.[22-24] Increased levels of collagenase, a specific collagen-degrading enzyme that is part of the MMP family, have been documented after venous strangulation obstruction of the small colon in ponies.[25] Despite these findings, the major determinants of a successful outcome after small-colon resection in the horse appear to be related more to the inability to exteriorize the proximal and distal ends of the small colon and to the presence of mesenteric fat, which obstructs the view of the intricate vasculature present at the interface between the bowel and the mesentery.

Obstructive Lesions

Obstructive diseases of the small colon have been associated with specific breed, sex, and age predispositions (see Chapter 5).[2,26-28] According to retrospective studies, the Arabian, American Miniature horse, and pony breeds are prone to small-colon disease and the female gender appears to be over-represented. The small colon may be predisposed to obstructive disease because of the nature of its function and location, but specific reasons for breed and gender predispositions are unknown.

Meconium Retention

Meconium is usually evacuated within the first few hours of birth and is composed of amniotic fluid, mucus, bile, and cells that have been shed from the skin and the intestinal tract. It is possible that the ingestion of colostrum promotes the evacuation of meconium in part because of hormonal stimulation of gastrointestinal motility and because it acts as a dietary laxative for the neonate.[29,30]

Clinical signs of meconium impaction depend on the degree and duration of the obstruction. As the degree of distention of the proximal bowel increases, foals will exhibit more obvious colic-like symptoms, ranging from restlessness, lack of interest

in suckling, and tail swishing to rolling, laying on their back, and tenesmus (see Chapter 6 Figure 10). Heart and respiratory rates will be increased because of pain but, most importantly, depending on the degree of hypovolemia and dehydration.

The diagnosis of meconium retention is not difficult to make in newborn foals that are well monitored because caretakers will be able to report lack of passage of meconium, thus aiding in the diagnostic process. In other less clear cases, progressive abdominal distention in a foal less than 48 hours old should prompt the clinician to perform a careful digital rectal examination, which in most cases reveals hard fecal material present at the pelvic inlet. In a recent retrospective review, most foals with retention of meconium were colts evaluated for signs of colic occurring before 24 hours from birth.[31] In the same study, the most common clinical signs were lack of interest in suckling, straining to defecate, absence of milk feces, and evidence of meconium on digital rectal examination.[31] The diagnosis of meconium retention and other small-colon obstructions in foals can often facilitated by the use of plain abdominal radiographs and retrograde contrast radiography (see Chapter 7).[32] Plain lateral and ventrodorsal projections may confirm the presence of impacted ingesta oral to the obstruction and in advanced cases, gas distention of the large and small intestine usually distinguishable by the characteristic hairpin turns (see Chapter 15, Figure 15-58). In a foal with a meconium obstruction, contrast radiographs are obtained after barium sulfate (5 mL/kg as 30% wt/vol solution) is administered by gravity flow into the rectum via a Foley catheter.[33] Typically, in affected foals the contrast material does not reach the transverse colon, which should be routinely demonstrable in normal foals, and reveals silhouetted fecal balls at the site of obstruction.[32]

Treatment of meconium retention is best accomplished using gravity-flow enemas consisting of soapy water, mineral oil, or phosphate-based products. The latter should be used sparingly to avoid hyperphosphatemia. The administration of 1 or 2 acetylcisteine enemas (40 mL of the commercially available 20% solution dissolved in 160 mL of water to yield a 4% solution) was proven successful in 87% of foals treated for meconium retention.[31] Surgical treatment of meconium retention may be necessary but should be used as a last resort option because of the risks associated with abdominal procedures in foals. Meconium obstruction requires prolonged intestinal handling, that predisposes to the formation of abdominal adhesions, which are a known complication in foals (Figure 39-1).[34] The goal of surgery is to gently manipulate the meconium towards the anus while an assistant provides lubrication via a small stomach tube placed in the rectum. Occasionally, the impaction may be extensive enough to require a small-colon enterotomy to evacuate the hardened fecal material.

Figure 39-1



Meconium impaction surgery. The small colon is inflamed from both distention and handling during surgery. Hyaluronic acid in the lavage fluid is recommended when handling of the bowel is necessary.

The prognosis for foals with meconium retention is generally good for those treated medically, barring the presence of concurrent disease such as septicemia or neonatal maladjustment syndrome.[3,31] A study assessing the outcome of surgical treatment reported that 8 of 24 foals evaluated for meconium obstruction required celiotomy and all were discharged from the clinic. Of the 6 foals available for follow-up, 2 developed intestinal adhesions and were euthanized.[35]

Small-Colon Impaction

Factors that may predispose to diffuse impaction of the small colon include poor quality or inadequate ingestion of hay, poor dentition or inadequate mastication, decreased water intake, and lack of consistent exercise.[2,4,36] Of the diseases of the small colon, impaction is the most common condition requiring veterinary intervention. It has been reported to be common in American Miniature Horses.[37] Impaction seems to be more prevalent in the cold months of the year and may be associated with colonic dysfunction or parasitism.[26] Feces obtained from horses with the condition, especially horses requiring surgical intervention, have a tendency to yield positive culture for *Salmonella species*. Therefore, horses with the disease should be considered potentially infectious and dealt with according to the appropriate infectious-disease protocols.[26] Factors associated with small colon impaction are listed in Table 39-1.

Table 39-1
Factors Reported to be Associated with Small-Colon Impaction.[2,3,26,37–39]

Signalment	Possible etiology	Predisposing factors
American Miniature Horse	Colon dysfunction	Fall and winter months
Shetland Pony	Submucosal edema	Decreased water intake
Female		Poor dentition
Horses older than 15 years		Inadequate mastication
		Poor quality roughage
		Parasitism
		Lack of regular exercise or turnout

Horses with small-colon impactions are often evaluated for signs of mild colic associated with the voiding of a scant amount of loose feces. Findings on rectal examination include a tubular small colon filled with firm and indentable feces (Figure 39-2). In one study, the condition was correctly diagnosed via transrectal palpation in 87% of cases.[40] The presence of impacted fecal material in the small colon may not allow thorough examination of the remainder of the abdomen, and in cases of extensive impaction, the small colon may be drawn over the pelvic brim into the caudoventral abdomen.

Small-colon impactions may be successfully treated with medical therapy that includes judicious use of nonsteroidal anti-inflammatory medications (e.g., flunixin meglumine at 1.1 mg/kg or 0.5 mg/kg), intravenous fluid therapy, and oral rehydration therapy, including fecal softening compounds such as magnesium sulphate or mineral oil. The medical treatment of horses with small colon impaction may not be straightforward because affected horses often exhibit signs of abdominal discomfort during the course of therapy, which may be caused by the peristalsis of the bowel against the impaction. In these horses, the clinician should carefully evaluate the use of analgesic medications, which may include the intravenous administration of 2% lidocaine (loading dose of 1.3 mg/kg, followed by a constant rate infusion of 0.05 mg/kg/min). Lidocaine has been shown to have an effect on gastrointestinal motility and may also provide analgesia by decreasing inflammation in the bowel through inhibition of prostaglandin synthesis or local anesthesia.[41-43]

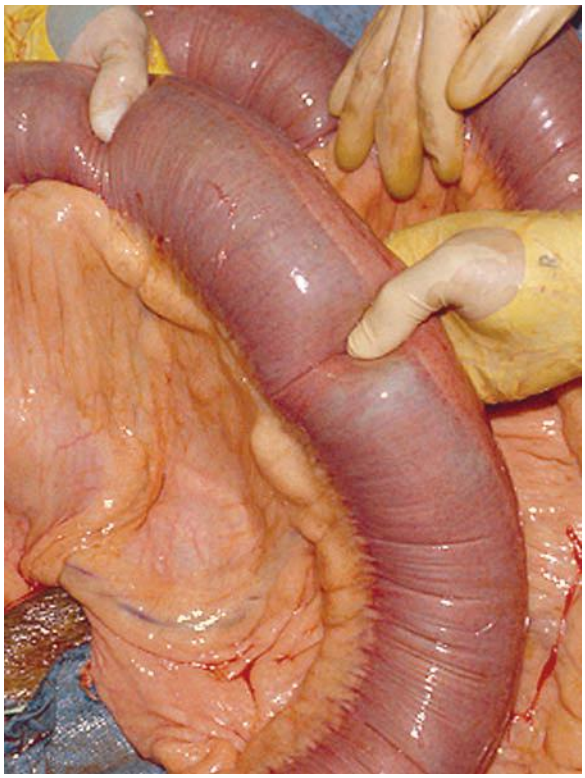
Surgery may be necessary when horses do not respond to medical therapy. It is accomplished via a ventral midline celiotomy. Following exposure of the impacted segment, the small colon is gently massaged while an assistant performs an enema with lubricated warm water (J-Lube, Jorgensen Laboratories, Inc.) aimed at softening the impaction. A stomach tube is passed into the rectum and carefully guided to the impacted segment while the surgeon controls the progress of the tube via transmural palpation. In instances in which the small colon is edematous and hyperemic or when there is concurrent rectal damage, it may be necessary to perform an enterotomy along the antimesenteric band to evacuate the impacted fecal material. The location of the enterotomy should be as close to the midpoint of the small colon as possible, because this section can be exteriorized away from the celiotomy incision to prevent inadvertent contamination of the abdomen.

The results of studies comparing medical and surgical treatments indicate that horses undergoing surgery tend to have longer hospitalization times and a tendency to yield postoperative fecal cultures positive for *Salmonella species*.[26,40] Two

studies reported a high success rate with medical treatment: in one of the two studies, the long-term survival was significantly lower for horses treated surgically than for those treated medically,[26] whereas in the other study, the long-term survival was similar irrespective of medical or surgical treatment.[40]

The prognosis associated with medical management of small-colon impaction is favorable (approaching 100%) whereas the outcome of surgery may be complicated by the trauma induced during bowel manipulation and a relatively higher concentration of anaerobes found in the distal intestine. For these reasons, perioperative broad-spectrum antimicrobial therapy should include the use of metronidazole as a preventative measure against anaerobic infection.[2-4]

Figure 39-2



Small-colon impaction causing the characteristic solid tubular shape devoid of normal fecal ball formation.

Isolated Intraluminal Obstructions

The most frequent discrete obstructions of the small colon are fecaliths, enteroliths, and ingested foreign bodies.[27,28,37,44-48] Fecaliths are hardened masses of fecal material, and result from poor mastication or digestion of hay. They are commonly diagnosed in yearling horses, particularly American Miniature Horses, transitioning to a forage diet, or in older horses with abnormal dentition. Other similar obstructive masses are phytobezoars and trichobezoars (Figure 39-3), which are formed by magnesium ammonium phosphate and contain poorly digested plant material or hair, respectively.

Enteroliths are a common cause of colonic obstruction in specific geographic areas such as the southwest regions of the United States, specifically California (see Chapter 14). Smaller sized enteroliths are more likely to move through the large colon and commonly become lodged at the transition point between the transverse and small colons. This area is particularly vulnerable to obstruction because of the sudden narrowing of the bowel lumen that occurs in this location.

Although uncommon, foreign-body obstruction of the small colon has been reported to occur, especially in younger, inquisitive-natured horses, who are prone to ingesting items such as rope halters, hay nets, bailing twine, and rubber fencing (Figure 39-4).[45] Over time, the irregular contour of these synthetic objects becomes encrusted with ingested fiber materials and minerals and can compromise the integrity of the bowel wall, increasing the likelihood of septic peritonitis.

The diagnosis of an isolated obstruction can occasionally be made by identifying the obstruction on transrectal palpation. Enteroliths can be palpated in the small colon in some cases. When an enterolith is in the transverse colon, ballotment may be possible just cranial to the mesenteric stalk. More often, however, the clinician will suspect this type of lesion because of the signalment of the patient, the history, and the clinical signs. An example of a clinical picture that may lead to suspicion of fecalith obstruction would be that of a yearling American Miniature Horse with colic-like symptoms, progressive abdominal

distention, and lack of fecal output.[49] Abdominal radiography is a sensitive ancillary diagnostic test used to identify enteroliths in the large and small colons (see Chapter 6).[50,51]

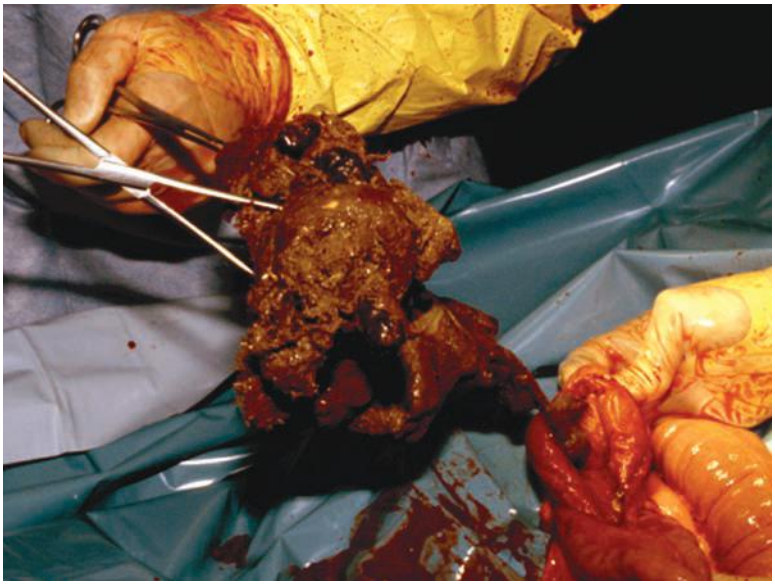
Medical treatment is unlikely to be successful, and the treatment of choice is an exploratory celiotomy for removal of the obstruction. The most successful approach is through an enterotomy placed along the mid-portion of the taenia of the small colon. However, on occasion, the obstruction may be located in the oral or aboral portion of the intestine, thereby hindering exteriorization of the mass. For orally located obstructions, the surgeon can attempt retropulsion of the mass into the right ventral colon and then proceed with removal via a pelvic flexure enterotomy.[4] In cases of enterolith obstruction, the teniotomy technique described earlier may lead to safe removal, allowing further advancement of the obstructing concretion.[12] Fatality from enteroliths is most often the result of rupture of the small colon around the enterolith; this has been reported to occur in 15% of cases.[50] Surgery is highly successful, with survival rates at greater than 90% and recurrence reported at 7.7%.[50]

Figure 39-3



Trichobezoar removed from the small colon of a horse.

Figure 39-4



An enterotomy of the small colon to remove a concretion made around a piece of rubber belting.

Vascular and Strangulating Lesions

Strangulation-obstruction of the small colon is an uncommon condition. However, the literature includes reports of several clinical cases in which the small colon was either affected by mural vascular lesions or entrapped in a variety of tissues including ovarian pedicle, teratomas, mesenteric rents, and the stalk of strangulating lipomas.[52-59] Lipomas may be predisposed to form in the descending mesocolon because of the large amount of fat in that mesentery, and are often encountered as incidental findings during celiotomy. Other than strangulating lipoma, polyps and leiomyomas have been associated with small-colon vascular compromise. In one horse, a leiomyoma within the lumen of the small colon had subsequently formed the lead point of an intussusception.[60] Other lesions that rarely affect this segment of the bowel include volvulus, herniation, and intussusception.[61]

The clinical signs consistent with vascular and strangulating lesions are associated with an acute obstruction of the small colon and lead to acute fecal stasis, progressive abdominal distention, and severe colic. Typical findings on rectal examination include large-colon tympany and difficulty in examining the entire abdomen because of a sudden obstruction of the small colon. The diagnosis of strangulating lesions may be aided by the use of transrectal ultrasound examination.[62] Compromised intestine leads to the development of toxemia, which increases heart and respiratory rates, causes progressive dehydration, and eventually, cardiovascular derangement and shock.

Mural Lesions

Submucosal hematomas have been speculated to occur as a result of parasitism (*Strongylus vulgaris* larvae).[52,53] Submucosal hemorrhage can be extensive and leads to secondary obstruction because the hematoma compresses the lumen of the small colon. Importantly, it has been noted that small-colon hematomas may sometimes rupture the mucosal lining, causing intraluminal hemorrhage.[53] This may be detected on the sleeve of the veterinarian after a rectal examination, and should not be mistaken for bleeding associated with rectal tearing, a more common cause of bleeding from the distal intestine after transrectal palpation. Treatment of choice for mural hematomas is surgery, which usually requires evacuation of the hematoma and resection and anastomosis of the affected small colon segment. When the hematoma can be completely exteriorized, the procedure is usually successful, although this depends on the length of intestine involved and the location of the hematoma.

Lesions Associated with the Reproductive Tract and Pregnancy

Strangulation of the small colon attributable to ovarian structures may be caused by an ovarian pedicle or entrapment of the colon between a granulosa cell tumor and the ovarian ligament. Strangulation of the small colon has also been reported to result from a testicular teratoma whereby the bowel was partially obstructed by the spermatic cord.[3,54,55,63] Because of straining that occurs during delivery, mares in the second stage of labor may incur severe abdominal trauma that may affect the viability of the small colon either by compromising the bowel directly or by damaging the mesocolon and associated vasculature.[64,65] This author has also seen two cases of uterine torsion complicated by concurrent entrapment of the small colon in the twisted broad ligament. Foaling injuries that may compromise the small colon are also associated with severe rectal prolapse (types II and IV), which causes rupture of the mesocolon, intussusception and disruption of the arterial supply, leading to ischemic necrosis of the bowel.[3]

Surgical treatment is necessary in these cases and is often performed as a true exploratory celiotomy since a preoperative diagnosis is rarely obtained. Careful evaluation of intestinal viability during surgery is important when the vasculature is only partially compromised and the lesion has not caused a clear line of demarcation between viable and nonviable intestine. An additional complicating factor to consider pertains to the removal of damaged reproductive structures such as ovaries or masses, thereby requiring a modification of the initial celiotomy approach. In cases in which involvement of the female reproductive tract is suspected, the surgeon may elect to perform a laparoscopic evaluation of the caudal abdomen prior to selecting the most appropriate laparotomy approach.

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Rectal Tears

Chapter 40

Peter C. Rakestraw

Anatomy

The rectum extends from the pelvic inlet to the anus, and is approximately 30 cm in length in the adult horse.[1] Because there is no apparent line of demarcation between the distal small colon and the proximal rectum, the plane of the pelvic inlet is used as the division between the small colon and rectum.[1] The rectum can be divided into two segments. The cranial (peritoneal) segment is proximal to the peritoneal reflection, and the caudal (retroperitoneal) segment is caudal to the peritoneal reflection and forms a flask-shaped dilatation called the rectal ampulla. The peritoneal reflection is approximately 15 to 20 cm proximal to the anus in an adult 1000-lb (450 kg) horse.[1-3] The peritoneal segment of the rectum is suspended by the mesorectum, a continuation of the mesocolon. As the rectum passes retroperitoneally, it is attached by connective tissue to surrounding structures in the pelvic canal.[1] The outer muscular layer of the ampulla is thickened where the longitudinal muscle of the taenia fans out to form thick, loosely bound bundles of muscle tissue.[2] The rectococcygeus muscle, which forms a large band on each side, originates from the longitudinal muscle and travels dorsocaudally, inserting onto the ventral surface of fourth and fifth caudal vertebrae.[1]

Etiology and Prevention

The majority of rectal tears are iatrogenic, occurring during rectal palpation. Most tears occur from pressure exerted by a contractile wave as it passes around the examiner's hand, or from stretching of the rectal wall when an examiner attempts to palpate a structure.[3-5] To decrease the likelihood of these occurrances, the examiner's hand should not be advanced during a rectal contraction, and the hand should be retracted as the contraction pushes it caudally. Excessive stretching of the rectal wall when attempting to palpate abdominal structures should also be avoided. The examiner's hand should be carefully advanced cranial to the area of interest and then brought caudally, releasing tension on the bowel wall when palpating intraabdominal structures.

Rectal tears occur more frequently in young horses (1 to 5 years), stallions, and geldings who are not accustomed to rectal palpation.[2,6,7] Increased nervousness leading to sudden movement and straining may predispose these horses to rectal tears. Arabian horses appear to be at an increased risk for rectal tears, with approximately 32% of reported rectal tears occurring in this breed.[2,8] This may be due to their smaller size or fractious nature. Horses examined for abdominal pain may also be at an increased risk. Horses with colic often have firm feces, which may cause the rectal mucosa to be dry and friable. These horses are also often subjected to multiple rectal examinations, thereby increasing chances for repetitive trauma to the rectum. Copious lubrication, sedation, adequate restraint, and epidural anesthesia should minimize the occurrence of these iatrogenic rectal tears.[2,6] Other causes of rectal tears that have been reported are sadism, misdirection of a stallion's penis during breeding, dystocia, trauma during enema administration especially in foals, sand impaction, thromboembolism, impaction at a stricture, and spontaneous tears.[2,9-11]

Iatrogenic rectal tears are an inherent risk during rectal palpations and can be caused by experienced equine practitioners as well as new graduates.[7,8] It is likely that all equine practitioners will be involved directly or indirectly with a rectal tear during their careers.[8,12] Explaining the risks and consequences of rectal tears to horse owners prior to palpation, although not required, may help avoid legal complications if a rectal tear occurs during palpation, assuming the palpation was performed with proper technique and restraint. An information sheet that describes the risks and benefits of rectal palpation can be distributed to clients before the examination, mailed as a part of new-client information packets, or used as a handout at colic or reproductive seminars.[8,13] If the above precautions are taken, the veterinarian should make no statements concerning admission of guilt or responsibility for payment. If a rectal tear occurs, the veterinarian is responsible to ensure that the holder of the liabilty insurance policy is informed promptly.[8]

Location and Classification of Rectal Tears

Rectal tears have been divided into grades I to IV based on the layers of the bowel wall involved (Figure 40-1).[4] Grade I tears involve only the mucosal and submucosal layers. Grade II tears involve only the muscular layers, with the mucosal and submucosal layers remaining intact. The grade II tear results in a mucosal-submucosal hernia because of lack of support from the muscularis externa. Grade II tears may form from second intention healing of grade III tears, where the longitudinal and circular muscles heal incompletely, leaving a muscular defect.[4] Grade III tears involve the muscosa, submucosa, and muscularis. They are further subdivided into grade IIIa and IIIb rectal tears.[5] Grade III tears involve all layers except the serosa. Grade IIIb tears involve all layers of the rectum, but are in locations where there is no serosa, and they are outside the peritoneal cavity. Grade IV tears involve all layers and communicate with the peritoneal cavity.

Figure 40-1A



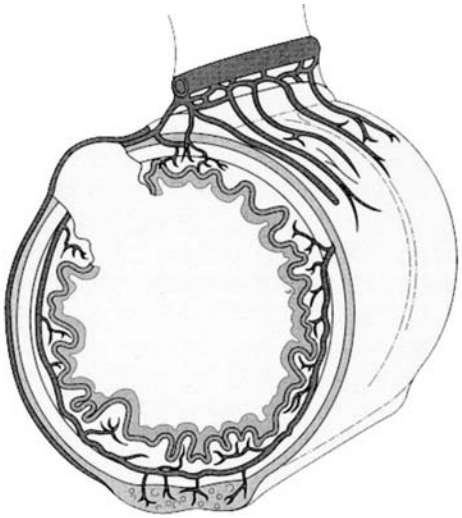
Grade I tear: involves only the mucosa or mucosa and submucosa.

Figure 40-1B



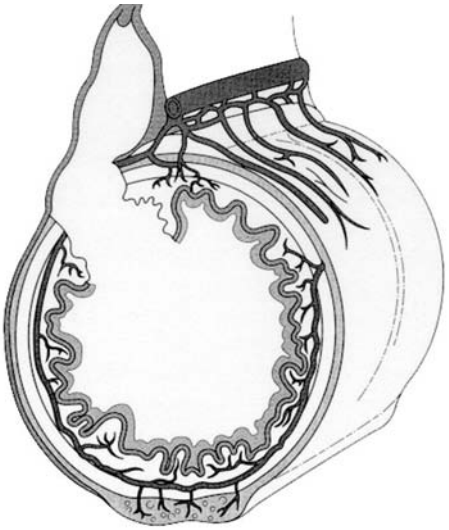
Grade II tear: involves only the muscularis.

Figure 40-1C



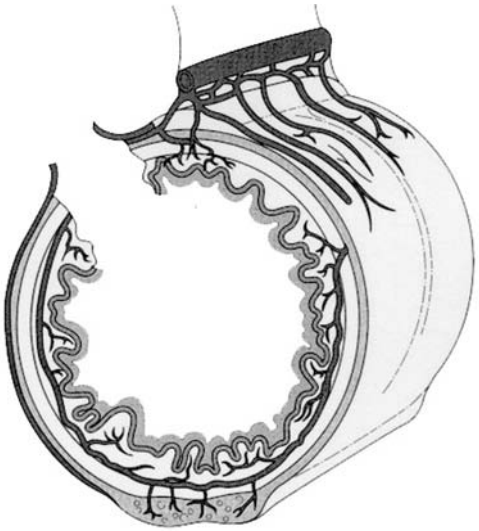
Grade IIIa tear: involves all layers except the serosa.

Figure 40-1D



Grade IIIb tear: dorsal tear involving all layers and extending into the mesocolon/mesorectum

Figure 40-1E



Grade IV tear: involves all layers and extends into peritoneal cavity.

Some ambiguity exists in the above classification scheme. Most references to grade IIIb tears refer to dorsal tears, which involve all layers of the rectum and extend into the space bordered by the mesorectum, which is not covered by serosa.[14-18] However tears distal to the peritoneal reflection may involve mucosa, submucosa, and muscularis and extend into the retroperitoneal space, which does not have a serosa. By the above definition retroperitoneal tears should be called grade IIIb tears.[5] This may be confusing when considering treatment and prognosis, as the recommended treatment and clinical course of the retroperitoneal tears can often be different, with a better prognosis for retroperitoneal tears in the pelvic canal than for dorsal peritoneal grade IIIb tears into the mesocolon.[4,19,20] Another classification ambiguity involves tears completely through the mucosa and submucosa and into the outer longitudinal muscle layer of the muscularis externa. These tears have muscularis externa between the defect and dorsal mesocolon in the dorsal rectum and between the defect and serosa for lateral and ventral tears. Because the tear is completely through mucosa and submucosa and involves the muscularis, these should be classified as grade III tears. The clinical significance of this modification in assigning the grade is unknown.

Most grade I tears occur ventrally, whereas most grade III and IV tears occur on the dorsal or dorsolateral aspect of the rectum between 5 and 55 cm (average 25-30 cm) proximal to the anus.[2,15] There is a narrowing and downward deflection of the rectum,[2] with thickening of the longitudinal muscle forming the mesenteric taenia and thinning of the circular muscle dorsally in this region of the rectum and small colon. Blood vessels that travel in the mesocolon penetrate the muscularis externa on each side of the mesenteric taenia approximately one fifth to one quarter of the circumference from the mesenteric angle.[2,21] Weakening in this an area of the human bowel wall has been suggested.[22] The bowel also lacks serosa dorsally between the two sheets of mesocolon attachment, further limiting its strength.

Because of direct fecal contamination of the peritoneal cavity, tears involving the intraperitoneal part of the rectum or small colon are more serious than tears distal to the peritoneal reflection. However, fecal accumulation in the pelvic canal from tears distal to the peritoneal reflection can also break into the peritoneal cavity or cause inflammation by transperitoneal migration of bacteria. Although the peritoneal reflection is approximately 15 to 20 cm proximal to the anus, this distance varies among horses, making it difficult to determine whether the tear is intraperitoneal based on the distance between the tear and the anus.[1,2]

Clinical Signs and Diagnosis

The person performing the rectal palpation does not always feel the tear when it occurs. Sometimes, a release of rectal pressure over the hand is felt when the tear occurs;[3,4] however, often the veterinarian appreciates no sensation that the rectum has torn. In these cases, blood on the rectal sleeve or the feces will be the first indication that a tear may have occurred. Although a blood-tinged sleeve may only indicate mucosal damage, any blood on the sleeve should be investigated to determine the cause and extent of damage. In some cases, no blood is seen and clinical signs of depression, colic, anorexia and fever are the first indications that a tear has occurred. Alternatively, the tear may be identified at necropsy.[2,20,23]

The speed of onset and progression of clinical signs depend on the severity of the tear. Horses with grade I tears may never develop clinical signs, especially if they are on a diet producing soft feces. Alternatively, horses with grade I tears may, over several days, begin to show signs of colic, anorexia, and depression as the tear progresses to a grade III or IV tear. Horses with grade III and IV tears rapidly develop clinical signs such as fever, colic, sweating, and depression within several hours as a result of peritonitis and endotoxic shock.[2,20]

Because the choice of treatment and the prognosis are dependent on the type of rectal tear, an accurate classification of the tear should be made as soon as possible. The horse should be adequately restrained and sedated before an examination. A nose twitch should be used and the horse should be placed in stocks, if available. Sedation may be achieved with either xylazine (0.3 - 0.6 mg/kg IV) or detomidine (0.01 mg/kg) in combination with butorphanol tartrate (0.01-0.04 mg/ kg, IV). Epidural anesthesia (5 - 7 mL 2% lidocaine) will decrease rectal straining and facilitate examination and emergency treatment of the tear (rectal packing). A lidocaine enema (12 mL of 2% lidocaine in 50 mL of water) will help desensitize the rectum and aid in reducing rectal straining. Some reports advocate use of paraympatholytic drugs (propanthelene bromide (0.014 - 0.07 mg/kg IV) or atropine (0.044 mg/kg IM or SC)) to relax the rectum and small colon and stop peristalsis.[2,3,20,24] Careful palpation with a bare hand covered with a water-soluble gel provides the most sensitive evaluation of the extent of the tear.

A thin, flap-like or undermined membrane is likely a mucosal-submucosal tear. A thick cavity-like depression lined by a thin tough membrane is most likely a grade III tear.[2] Speculum examination and endoscopy have also been used to assist in the evaluation of rectal tears. Speculums may not be long enough if the tear is proximal and the mucosal folds obscure the view.[5,8,20] If available, endoscopy with air insufflation of the rectum is very helpful in evaluating the tear (but care should be taken not to over-insufflate the rectum).

Rectal examination has been associated with 7% of legal claims involving medical procedures in horses.[12] Early diagnosis and appropriate first aid care will increase the chances for survival. Claims of negligence are more likely to occur because of poor management of the tear rather than the actual creation of the tear.[6] The owner should be informed of the potential problem as soon as a tear is suspected. The veterinarian should describe the steps needed to determine the extent of the tear and the importance of establishing an accurate diagnosis. Once the tear has been diagnosed and classified, the owner should be informed of the treatment options and associated complications. Appropriate communication with the owner will decrease the chances of claims of negligence.[17] It is often advantageous to call the referral hospital for advice on emergency treatment and transportation.

Emergency Management

Initial treatment is dependent on the severity of the tear. Grade I tears may be successfully managed medically by administration of antibiotics, nonsteroidal anti-inflammatories (flunixin meglumine 1.1 mg/kg every 12 hours, IV), tetanus antitoxin, and a laxative diet. Grade II tears usually are not identified at the time the tear occurs. Rather the horse presents later when the defect in the muscularis externa interferes with normal passage of feces, resulting in tenesmus and/or impaction. Grade III and IV tears require emergency management in the field to prevent further damage to the rectum leading to peritonitis, septic shock, and death. Broad-spectrum antibiotics such as potassium penicillin (22,000 IU/kg every 6 hours, IV), gentamicin (6.6 mg/kg every 24 hours, IV), and metronidazole (15 mg/kg every 6 hours, IV initially and then PO) should be administered. Flunixin meglumine (1.1 mg/kg every 12-24 hours, IV) is administered to prevent inflammation and to provide protection against endotoxins. Mineral oil should be administered via nasogastric intubation to soften the feces. All feed should be withheld.

Rectal packing with a "rectal tampon" is indicated to prevent feces from filling the defect and causing further contamination and expansion of the tear.[5,18,25] The packing is made from a doubled 3-inch stockinette filled with rolled cotton (Figure 40-2). The cotton should be moistened and the stockinette sprayed with povidone-iodine and covered with surgical jelly. The packing is placed after performing the epidural anesthesia. After placement of the pack, more cotton may be added as needed to fill but not distend the rectum. It is imperative that the oral end of the tampon be positioned proximal to the tear (approximately 10-20 cm) so that the tear can not be filled with feces. The tampon is maintained in place by closing the anus with towel clamps or with a pursestring suture. It is important that the epidural anesthesia be maintained to prevent straining until the definitive treatment is performed. Appropriate placement of the tampon will effectively prevent the feces from further damaging the tear. Inappropriate placement can potentiate further damage by diverting the feces into the tear. As a potential alternative to rectal packing, one report recommends repeated manual evacuation of the rectum during transit if the horse is more than 2 hours away from the referral hospital.[16]

Figure 40-2A



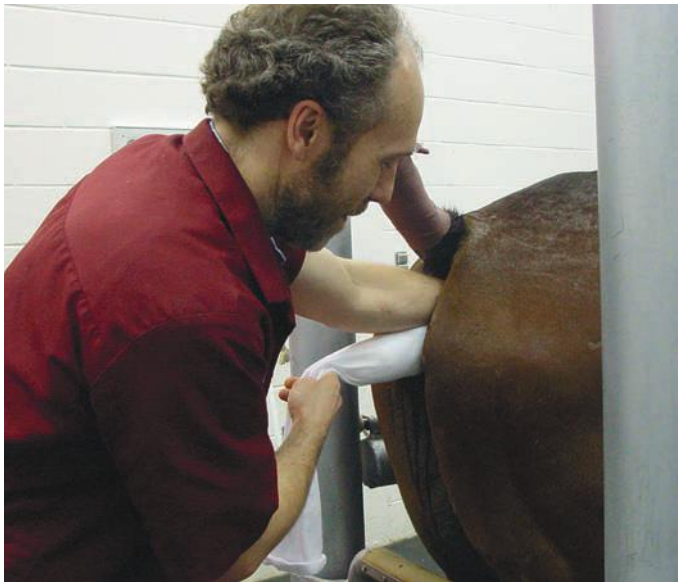
Rectal packing. A 3 inch stockinette loosely filled with cotton.

Figure 40-2B



Stockinette is covered with lubrication.

Figure 40-2C



Stockinette is inserted into the rectum with the proximal end positioned 10 cm cranial to the tear.

Figure 40-2D



Additional cotton is added to the stockinette so that it fills the rectum.

Medical Management

Grade I and II tears rarely require surgical treatment.[4,5,20,26,27] Grade I tears, involving only the mucosa or mucosa and submucosa, respond in most cases to antibiotics (e.g., trimethoprim sulfonamide, 20 mg/kg every 12 hours, PO), and flunixin meglumine (1.1 mg/kg every 12 hours, IV or PO), mineral oil (1 gallon via nasogastric tube every 24 hours), and dietary changes such as bran mashes, moistened pellets, or grass both to reduce the volume of feces and to keep the feces from becoming firm and impacted at the tear. Although some horses with grade I tears receive no form of treatment and heal uneventfully, it is recommended that, if there is any undermining of the mucosa or if the tear is larger than 2 cm, medical management should be initiated.[15] If all or a significant portion of the submucosal layer remains intact, grade I tears should heal with medical management without complications. However, if the tear extends significantly into the submucosa, the remaining submucosa and the underlying muscularis are at increased risk of progressing to a grade III and IV tear. The extent of the submucosal damage can be difficult to assess on palpation and visual inspection. If in doubt, grade I tears can be sutured per rectum. The clinical response to medical or surgical treatment should be monitored by physical examination, CBC, and peritoneal fluid analysis.

Grade II tears often present as an incidental finding. If the diverticulum or mucosal-submucosal hernia becomes large (>5 cm), affected horses may present with tenesmus or with a rectal impaction.[4,5,14,15,20,24] Medical management involves feeding a laxative diet to prevent impaction at the defect.

Although grade III tears usually require surgical intervention, there have been several reports of successful treatment with medical management alone.[16,17] In one case series of grade IIIb rectal tears, 6 of 8 horses were treated successfully by administration of broad-spectrum antibiotics and NSAIDs, maintenance of soft feces with a diet of grass and bran mashes, and daily administration of mineral oil by nasogastric tube, along with daily manual removal of feces from the rectum after sedation and epidural anesthesia.[17] Additional therapy for some of the horses included IV fluids, plasma, and heparin (40-80 IU/kg SQ every 8 hours). All horses had or developed septic peritonitis during the course of treatment. Of the 6 successfully treated horses, 3 developed a rectal diverticulum at the site of the tear without any obvious clinical problems. The successful outcome in 75% of these cases was attributed to early treatment and the use of broad-spectrum antibiotics (penicillin, gentamicin, and metronidazole) until the tear filled in with granulation tissue and the peritoneal fluid returned to normal (between 2 and 7 wks). The authors felt that manual evacuation of feces should be done only if the tear became impacted with feces, to avoid further trauma to the tear.

In another report of 4 horses with grade IIIb tears treated medically, frequent manual evacuation of feces was recommended.[16] Manual evacuation was performed every 1 to 2 hours for the first 72 hours, every 6 to 8 hours by days 4 and 5, with decreasing frequency to once a day as the tear healed. This necessitated repeated caudal epidural anesthesia initially, which was subsequently replaced with lidocaine and lubricant enemas. All 4 horses had tears of less than 10 cm in

diameter. Manual evacuation was discontinued between 9 and 21 days. All 4 horses were treated successfully by this approach. These results suggest that, in certain cases, early initiation of treatment including manual evacuation and medical therapy may be a viable alternative to surgical treatment of grade IIIb rectal tears.[16]

Horses with full-thickness tears into the retroperitoneal space should be treated with manual evacuation of feces (often required several times daily), antimicrobial therapy, and stool softeners.[4,19,28] In these cases the tear is into connective tissue, which allows the tear to be packed with gauze soaked in antiseptic solution until the defect fills with granulation tissue. Perirectal abscesses, which may result from the fecal contamination, can be drained into the rectum or perianally with a chest trocar. Ventral tears in mares can be drained through the dorsal vaginal wall.[4] In some cases, abscessation may dissect into the tissue layers of the inner thigh and require ventral drainage, broad-spectrum antimicrobials, and NSAIDs.[4]

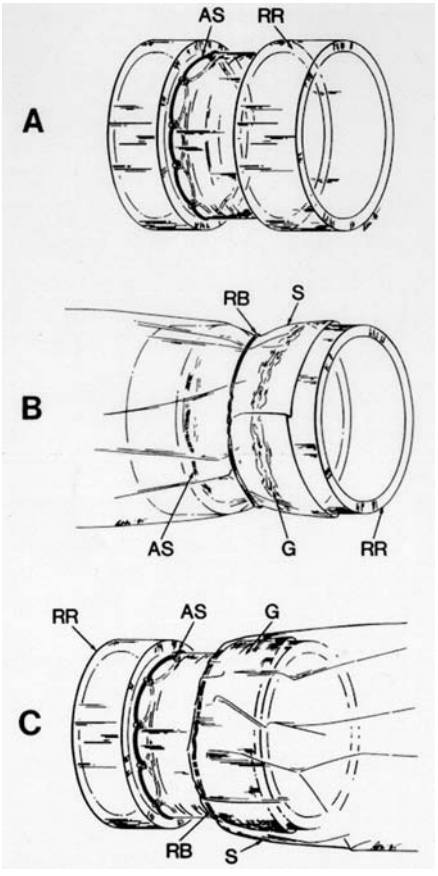
Surgical Management

The techniques described to surgically treat rectal tears are colostomy,[4,14,,29,30,31] insertion of a temporary rectal liner,[18,32] and direct suturing.[15,18,33] Each of these techniques can be used individually as the primary surgical repair. Both colostomy and temporary rectal liner techniques may be combined with direct suturing to decrease stress at the suture site.[15,18] Another surgical approach is to evacuate the large colon and small colon through enterotomies and withhold feed for 5 to 7 days postoperatively, allowing the tear to fill in with granulation tissue before starting the horse on a low-residue diet.[6] In most cases evacuation of the GI tract is combined with some surgical procedure.

Temporary Indwelling Rectal Liner

To protect a rectal tear from fecal contamintation during healing, a rectal ring with attached rectal liner is sutured to the distal small colon proximal to the tear.[5,26,32] The ring for the temporary rectal liner is made from a 5-x-10-cm plastic rectal prolapse ring that is trimmed at each end to form a 5-x 7-cm ring (Figure 40-3). Holes are then drilled 1.5 cm apart in one edge of the central groove and No. 5 dacron suture material is laced through the holes to form a continuous anchor suture. Originally, either a rectal sleeve or plastic cover used for an arthroscopic camera sutured and glued to the ring was recommended to form the rectal sleeve. Currently, a stronger arthroscopic sleeve is recommended.[5,32]

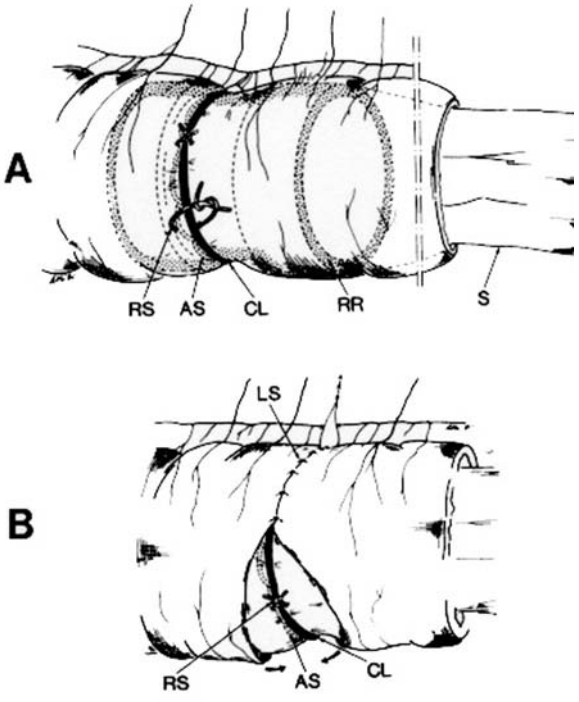
Figure 40-3



Diagrams indicating construction of a temporary in-dwelling liner. A. Shortened rectal ring (RR) with anchor suture (AS). B. The rectal ring (RR) is inserted into the end of the plastic sleeve (S), and the rubber band (RB) is placed around the sleeve and ring at the opposite end of the central groove from the anchor suture (AS). The sleeve is glued (G) to the circumference of the ring. C. The sleeve (S) is inverted over the distal end of the ring (RR), covering the rubber band (RB) and the glued (G) sleeve end. This leaves the anchor suture (AS) exposed.

To implant the rectal liner, a ventral midline celiotomy is made with the horse in dorsal recumbency. An assistant introduces the well lubricated rectal ring and attached sleeve into the rectum, while the surgeon carefully manipulates the small colon to move the ring in an oral direction. The surgeon continues the intraabdominal manipulations until the ring is positioned cranially to the tear but far enough caudally that the sleeve extends out of the anus when the horse stands.[5,26,32] A circumferential ligature of No. 3 chromic gut is placed tightly around the small colon over the central groove in the ring to begin constriction of the serosal surface (Figure 40-4). Four to 6 retention sutures (2-0 polyglycolic acid) are placed equidistant around the small colon to include the circumferential suture, all layers of the intestinal wall, and the anchor suture in the rectal ring. The retention sutures and the circumferential sutures are oversewn with a Lembert pattern. This creates an anastomosis to maintain continuity of the intestinal tract when the ring and circumferential ligature slough 9 to 12 days after surgery.[5,36-32] To reduce the volume of feces passing through the area in the immediate postoperative period, the large colon is emptied through a pelvic flexure enterotomy and the small colon is carefully emptied by flushing with a hose directed through the ring and liner from the anus. In most cases abdminal drains are placed for postoperative peritoneal lavage.[5,26,32]

Figure 40-4



Diagrams indicating the placement of the indwelling rectal liner. A. The circumference ligature (CL) is tied around the colon and the ring (RR) in the area of the anchor suture (AS). Four to 6 retention sutures (RS) are placed equidistantly around the circumference of the colon. Each suture is passed through the colon and underneath the anchor suture, out through the colon, and tied around the circumference ligature. Sutures should not be placed through the sleeve (S). B. Interrupted Lembert sutures (LS) are used to oversew the retention suture (RS) and the circumferential ligature (CL). Notice the location of the underlying anchor suture (AS).

Postoperative care includes continuation of broad-spectrum antbiotics, NSAIDS, and peritoneal lavage. The healing of the rectal tear is evaluated by careful digital palpation every 48 to 72 hours. To reduce the volume of soft feces, a pelleted ration is fed and mineral oil administered by nasogastric tube until the ring and liner detach and pass through the anus. Obstructions at the ring should be removed by retrograde flushing, which requires epidural anesthesia. To prevent retraction of the sleeve into the rectum, the horse should be cross-tied to prevent it from lying down. Approximately 60% of horses treated for grade lll tears were reported to heal using this technique.[32] Failures were due to serosal necrosis leading to peritonitis, tearing of the sleeve, retraction of the sleeve thus uncovering the tear, and formation of a rectoperitoneal fistula. Direct suturing of the tear in conjunction with the temporary rectal liner is recommended in order to prevent serosal necrosis leading to peritonitis.[18,32] The reduction in size and prevention of lesion expansion may aid in healing and reduce the potential of a grade lll rectal tear converting to a grade IV tear. Use of the liner by itself is inappropriate if the tear is greater than approximately 25% of the circumference of the rectum.[18]

Loop Colostomy

The goals of small colon colostomy for rectal tears are to divert feces to allow the tear to heal and then to restore normal anatomic function. Therefore, colostomy techniques require two surgeries: the first to construct the colostomy and the second to reverse the colostomy after the rectal tear has healed. Both end and loop colostomy techniques have been reported.[14,30,31] The end colostomy is performed by transecting the colon proximal to the tear and using this proximal end to form the colostomy stoma while the distal segment is oversewn and remains in the abdomen. The loop colostomy involves bringing a small intact loop of small colon out the flank and making a longitudinal enterotomy in the loop to construct the stoma. The end

colostomy has several disadvantages compared to the loop colostomy. First, it is more difficult to construct because the colon has to be transected. Second, during the time it takes for the rectal tear to heal, the distal blind end of the small colon atrophies. This makes the colostomy reversal procedure more difficult because of the discrepancy of size of the proximal and distal ends. Additionally, the atrophied distal segment may predispose to impaction at the anastomosis.

Atrophy of the small colon distal to the colostomy occurs to a lesser degree with the loop colostomy. Concerns about incomplete diversion of feces with a loop colostomy are not warranted as the correct construction of the stoma allows gravity to produce complete fecal diversion.[5,14,30] For these reasons, only loop colostomy techniques are described in this section.

The techniques used for constructing the loop colostomy vary depending on where the incisions are made, how many incisions are used, where the stoma is placed, and whether the procedure is performed in the standing or anesthetized horse.[5,26] If the rectal tear occurred during a colic examination, the surgeon needs to consider whether abdominal exploration is warranted to further diagnose and treat the colic. In this case, general anesthesia with a ventral midline incision allows the best chance to explore the abdomen and surgically treat the reason for the colic while also creating a colostomy. The colostomy in the left flank is then constructed, after closure of the ventral midline incision, by placing the horse in lateral recumbency. Alternatively, the colostomy is made with the horse standing after recovery from anesthesia. If the rectal tear occurred during a reproduction examination or during some other incident not requiring an abdominal exploratory, the colostomy can be performed in the standing horse, through either a single or double flank incision.

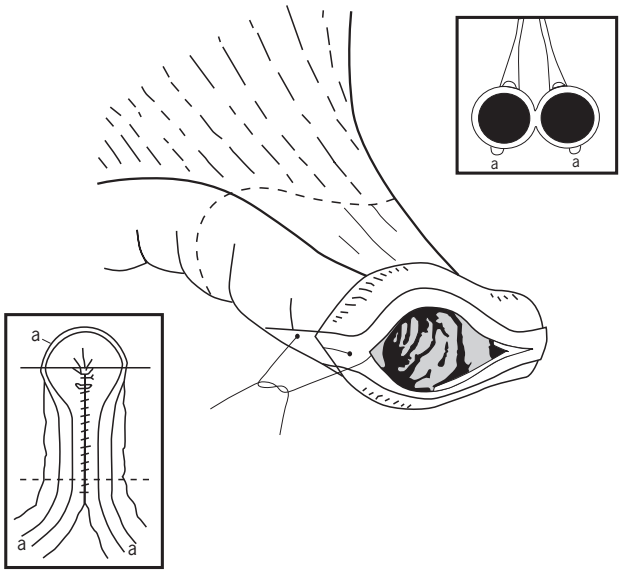
Single-Incision Loop Colostomy

This procedure has two variations.[5,30] In one technique, a 12 - 15-cm incision is made parallel to the costal arch at the level of the flank fold of the stifle.[26,30] The incision is made sharply through the external abdominal oblique fascia and continued bluntly through the aponeurosis of the internal abdominal oblique, the aponeurosis of the transversus abdominal oblique, and the peritoneum. The small colon at least 1 meter proximal to the peritoneal reflection is exteriorized through this incision. This distance is important because a significant number of adhesions may form between the body wall and the small colon during healing of the colostomy. If the colostomy is placed too far distally in the small colon, it becomes difficult to exteriorize sufficient distal small colon for resection and anastomosis of adhered small colon during the colostomy reversal procedure.

Once the segment of small colon is exteriorized, it is folded to form a loop. The two arms of the loop are sutured together for approximately 8 cm, using absorbable suture in a continuous Lembert pattern.[26,30] The sutures are placed half the distance from the mesentery to the antimesenteric taenia. As the suture apposition approaches the folded end of the loop, the sutures are placed closer to the mesentery so that the antimesenteric taenia is exposed (Figure 40-5). Suturing the two arms in this configuration facilitates the complete diversion of the feces at the colostomy stoma as well as stabilizes the two arms of the colon, reducing the chances of herniation at the stoma.[26,30] The prepared loop is then positioned so that the oral segment is at the cranioventral end of the incision with approximately 2 to 3 cm of the loop above the skin margin. The seromuscular layer of the small colon is sutured to the muscles of the body wall in an interrupted pattern with absorbable sutures. The dorsal part of the body wall incision is closed up to the loop, leaving approximately 6 to 8 cm of the cranioventral end of the incision to construct the stoma. A 6- to 7-cm enterotomy is made in the antimesenteric taenia and the edges of the enterotomy are sutured to the skin (Figure 40-6a).[26,30] Because this technique requires a longer incision to be made at the level of the fold of the flank than the two-incision colostomy, it is difficult to perform in the standing horse. Consequently, general anesthesia is required.

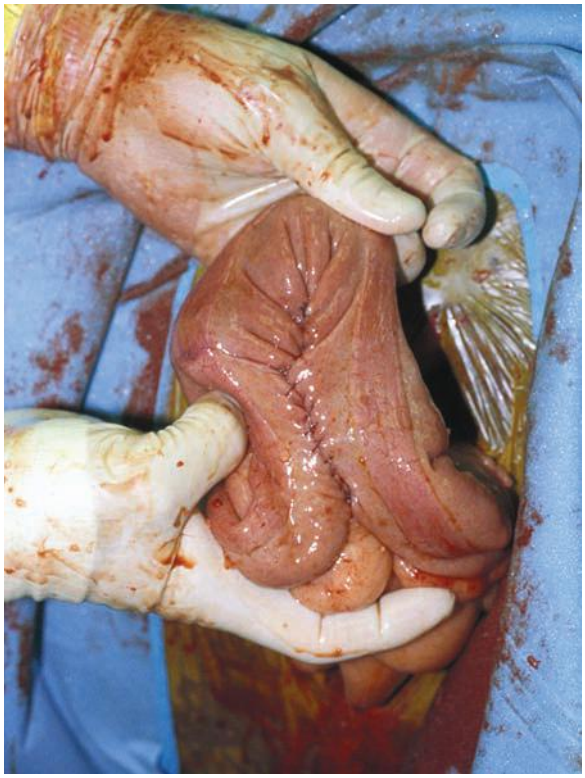
A variation of the above single-incision colostomy technique has been described.[14] In this technique, the incision is positioned midway between the level of the tuber coxa and the level of the coxofemoral joint and is not centered at the level of the fold of the flank. The subcutaneous tissue and external abdominal oblique musculature are transected sharply. The internal abdominal oblique and transverse abdominal muscles are bluntly separated parallel to their muscle fibers. A loop of small colon is exteriorized in the middle of its accessible length. The authors in this report did not suture the two arms of the small colon loop together. The seromuscular layer of the colon is sutured to the external abdominal oblique and/or to the subcutaneous tissue.[14] An 8- to 10-cm antimesenteric incision is made to create the stoma. The incision in this technique is in a more dorsal position than the single incision in the fold of the flank. Consequently, this colostomy technique can be performed in the standing horse.

Figure 40-5A



Method for preparing the colon and making the stoma. The same method is used for single- and double-incision colostomy techniques. Insets show method of apposing colon by suture to form the loop as viewed from the ventral aspect (lower) and in cross section (upper). As the suture line approaches the folded end of the colon, it should be closer to the mesentery so that the colon can be exteriorized with the antimesenteric taenia (a) exposed. The incision in the taenia is made as shown, and the cut edges are folded back as they are sutured to the skin. Broken lines represent the peritoneal opening, and the solid line in lower inset is the skin.

Figure 40-5B



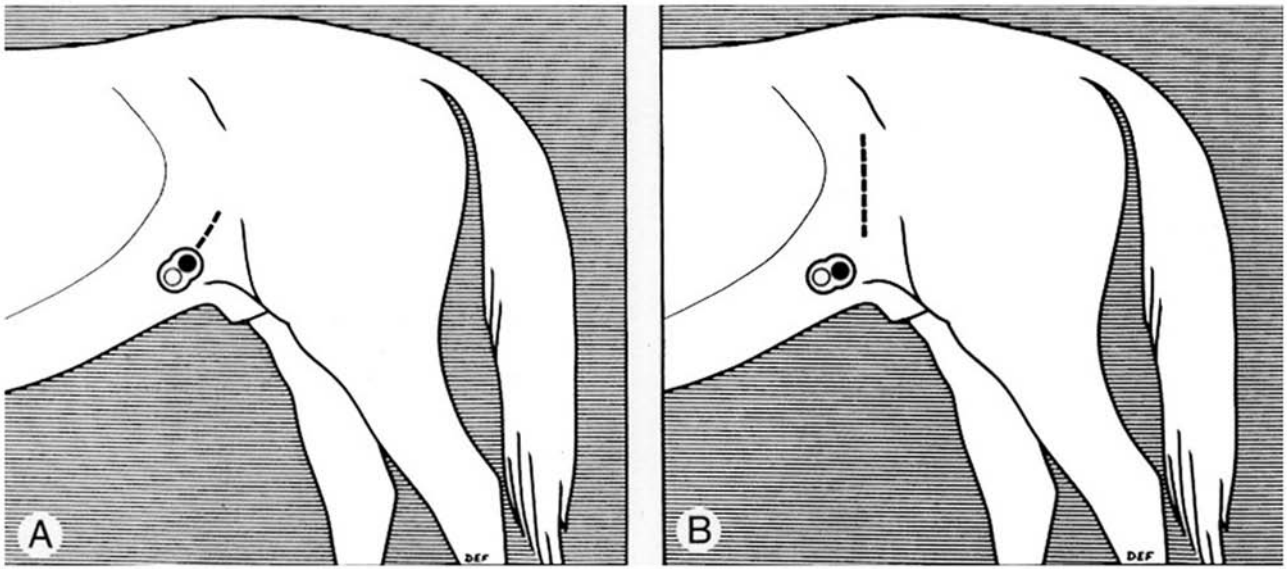
Two arms of the loop of small colon that has been prepared for loop colostomy through a flank incision. Notice how the suture line is placed closer to the mesentery at the end of the loop to expose the antimesenteric tenia for the colostomy stoma.

Standing Double-Incision Loop Colostomy

The first incision is made to construct the loop in the small colon that will be used for the colostomy.[26,30] Under sedation and local anesthesia, a 15-cm incision is made in the left flank starting about 10 to 12 cm below the tuber coxa. The small colon is identified and a section that is at least 1 m proximal to the peritoneal reflection is exteriorized. The small-colon loop is prepared as described for the single-incision loop. A second 6- to 8-cm incision angled dorsally 20 to 30 degrees at its caudal end is made for the stoma placement at the level of the flank fold of the stifle, midway between the fold and the costal arch (Figure 40-6b).[26,30] The incision is made through all layers, making sure to incise any potentially constricting tissue. If the incision is too small, it will constrict the proximal loop of small colon, predisposing to impaction proximal to the colostomy stoma. If the incision is too large, it will increase the risk of prolapse or herniation of small colon. The prepared small-colon loop is brought out of the lower incision aided by manipulation of the loop with the surgeon's arm in the high flank incision.[26] Approximately 3 cm of the loop should extend above skin level through the incision, with the proximal arm of the loop positioned at the cranioventral end and the caudal arm positioned at the caudodorsal end of the lower incision.

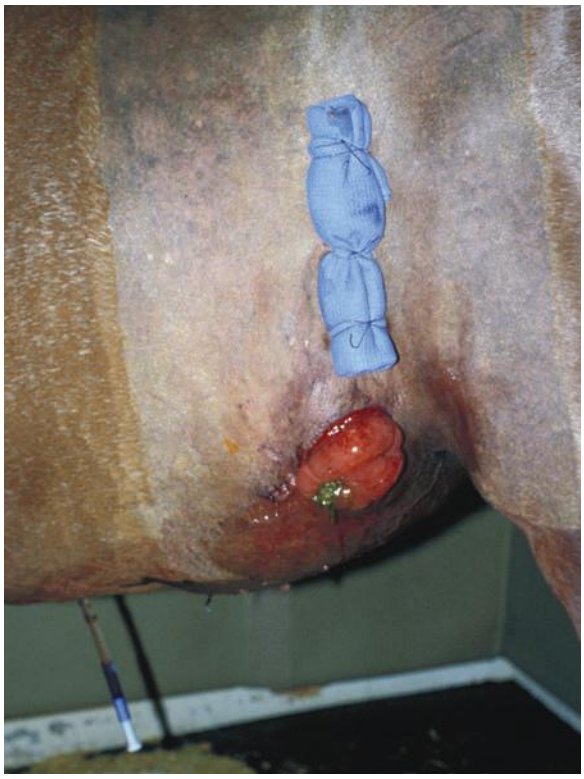
Interrupted absorbable sutures are placed between the seromuscular layer of the small colon and the muscle and fascia of the body wall. These sutures are important to anchor the colon loop to the body wall and to provide a seal to prevent potential peritoneal contamination that may occur from ingesta leakage between the skin and colostomy closure. A 6- 8-cm incision is made through the antimesenteric taenia into the lumen of the small colon, and edges of the colostomy incision are sutured to the skin with simple interrupted nonabsorbable sutures.[26,30]

Figure 40-6A & B



Methods for making a loop colostomy: A. Single-incision technique with stoma incorporated into the ventral aspect of the flank incision, used for all stages of the procedure (broken line). Open circle in stoma is opening of the proximal segment and solid circle is the distal segment. B. Double-incision technique. The colon is selected, prepared, and inserted into the lower incision from a flank incision (broken line). Open circle in stoma is opening of the proximal segment, and the solid circle is the distal segment.

Figure 40-6C



Double-incision colostomy with stent sutured over dorsal incision and a chest tube placed ventrally for peritoneal lavage.

Colostomy/Ventral Midline Celiotomy

In horses in which the rectal tear occurred during a colic evaluation, a ventral midline celiotomy may be required for abdominal exploration and treatment of the gastrointestinal problem. A ventral midline celiotomy also allows the large colon to be evacuated, thereby reducing the amount of feces passing out the colostomy in the immediate postsurgical period. If colostomy has been chosen as the technique to treat the tear, the loop for the colostomy should be constructed through the ventral midline incision. This will allow the colostomy incision for the stoma to be kept small. The ventral midline incision should then be closed and the stoma constructed through a small incision in the low flank as described in the two-incision technique. The stoma is constructed either with the horse repositioned in right lateral recumbency or in the standing horse after recovery from anesthesia. Stoma construction with the horse in dorsal recumbency may lead to obstruction of the stoma as the tissue layers change when the horse recovers.[26,30] Placing the horse in lateral recumbency decreases shifting of tissue layers in the body wall when the horse recovers, thereby decreasing the risk of stomal obstruction postoperatively.

Postoperative Management

Horses are maintained on a laxative and low-bulk diet of bran mash and moistened pellets, with increasing amounts of grass, if available, and/or alfalfa hay once the colostomy appears to be working effectively.[5,14,26,30] Antibiotics and NSAIDs are administered as necessary to treat peritonitis and any postoperative incisional infections. Placement of a drain for peritoneal lavage is predicated on the clinical condition of the horse and evaluation of the peritoneal fluid. Petroleum jelly is applied to the skin under the colostomy stoma to prevent scalding. Normograde flushing of the small colon distal to the colostomy is recommended to limit atrophy of the distal segment. Flushing should be initiated only after the tear has filled in with granulation tissue, approximately 5 to 7 days after colostomy.[5,26,30]

Colostomy Reversal

Once the tear has filled in with granulation tissue and has mucosa covering the defect, the colostomy can be reversed. Times reported for reversal have been 13 to 68 days.[14,15,26,29,30] If the horse has been on a grass and alfalfa hay diet, the horse should be switched to a low-bulk diet for 3 to 4 days prior to surgery. Feed should be withheld for at least 24 hours prior to surgery. The horse is placed on broad-spectrum antibiotics and NSAIDs. The surgery is performed with the horse under general anesthesia in right lateral recumbency. To minimize contamination, the stoma is first closed using inverting horizontal mattress sutures in the skin. An elliptical skin incision is then made around the closed stoma to initiate an “en bloc” resection.[14,30] One author recommends making the elliptical skin incision 1 cm from the edge of the colostomy and then inverting the skin margin over the colostomy.[14] Careful sharp and blunt dissection is required to separate the loop of small colon and stoma from the surrounding body wall. The dissection can be difficult because of significant adhesions of body wall to small colon around the colostomy. Once the stoma and adjacent small colon are completely separated from the body wall, the stoma, adhered small colon, and excised body wall are resected. The distal segment of the small colon will be smaller in diameter than the proximal segment because of atrophy. To correct for this size disparity, the distal segment is transected at an angle to the proximal segment to create a larger luminal opening.[30] A two-layer, hand-sutured, end-to-end anastomosis is preferred.[34] The first layer is a simple interrupted pattern that is oversewn with a Cushing pattern. The muscle and fascial layers of the flank incision are closed with a simple continuous pattern. The closure of the body wall is under considerable tension as a result of the amount of body wall and attached adhesions removed during the “en bloc” resection. Placement of Penrose drains has been recommended as incisional problems are common.[26,30] The skin is closed with simple interrupted sutures with periodic placement of vertical mattress sutures to relieve tension, if necessary. A stent is sutured over the incision. Postoperatively the horse is maintained on antibiotics and NSAIDS for approximately 5 days, and then is converted from the laxative diet to a normal diet, over a period of 3 to 4 weeks.

Complications and Prognosis

Peristomal herniation and small-colon prolapse through the stoma are reported complications after colostomy.[11,29,30] Increasing the size of the stoma may increase the risk of small-colon prolapse. For this reason, the stoma should be made with an opening no larger than the diameter of the colon proximal to the stoma.[5,26,30] The longer incision required for the single-incision colostomy may be associated with greater laxity in the periostomal body wall compared with that for the double-incision colostomy. The reduced support in the body wall around the stoma may predispose to peristomal hernia and prolapse formation. For these reasons, the double-incision colostomy has been recommended over the single-incision colostomy by some surgeons.[5,16,30]

Impaction proximal to the stoma is another reported complication of colostomy.[5,14,26,30] Making the stoma too small or leaving constricting bands of tissue in the body wall around the stoma may increase the risk of impaction at the stoma. These

impactions should be treated by carefully breaking them down digitally or with the aid of gentle lavage. Placing the horse on a laxative diet should decrease the occurrence of impactions. Partial dehiscence of the colostomy with mechanical separation of the colon and skin closure during recovery from general anesthesia is another reported complication. The dehiscence either should be treated by primary closure or allowed to heal by second intention.[14,30] Performing the colostomy in the standing horse avoids this problem. Incisional infection with abscessation and/or partial dehiscence are seen after colostomy and colostomy reversal.[14,30] Abscesses should be drained and partial dehiscence left to heal by second intention. Impaction after colostomy reversal should be treated with fluid therapy and laxatives and may require surgical correction.[14] Other complications reported are rupture of mesenteric vessels, spontaneous closure, adhesions and laminitis.[11,29]

Of 6 horses having colostomies to treat grade lll rectal tears, 2 survived in one report,[33] whereas 5 of 7 survived in another report.[14] The majority of deaths in horses in which colostomies have been performed to treat rectal tears were attributed to the peritoneal contamination associated with the rectal tear rather than technical difficulties related to the colostomy.[14,18,30] For this reason, it is important to perform the procedure as quickly as possible to divert feces and prevent further damage and fecal contamination of the tear.

Primary Repair

Several techniques for primary repair have been described. Instrumentation specifically developed to facilitate visualization and access for suturing tears per rectum, such as a long expandable speculum and pistol-grip needle holders, have been used successfully to repair rectal tears.[3,35] However, repairing rectal tears with the aid of these instruments is difficult and the instrumentation may not be available.[3] Primary repair of a rectal tear with the horse standing has been accomplished by intussuscepting the damaged segment through the anus, using traction sutures placed in the tissue around the tear and stapling the tear.[23] Caudal rectal tears have been repaired by placing the horse in lateral recumbency under general anesthesia and using long stay sutures placed at the end of the tear to prolapse the tear, allowing visualization while suturing.[3] Intussuscepting the damaged segment through the anus by intraabdominal manipulation through a ventral midline celiotomy has also been described.[4] In most cases the tear is too far cranial to the anus and the mesocolon is too short to allow exposure of the tear by these techniques. Laparoscopic techniques with sutured or stapled repair of iatrogenic tears have been described in an experimental model.[36] Tears into the dorsal mesentery would be difficult to repair with the laparoscope because mesentery prevents access to the tear. Laparoscopic repair of rectal tears has not been evaluated in clinical cases.

Nonvisual Direct Suturing Per Rectum

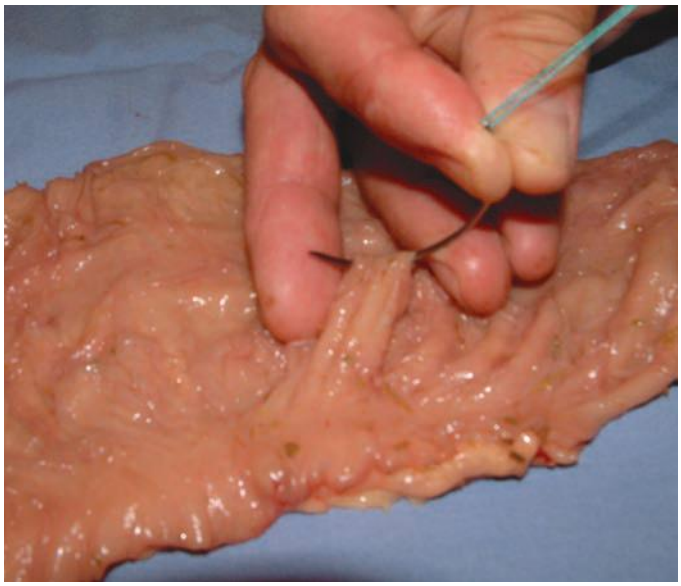
Direct suturing without visualizing the tear has been described in several reports with encouraging results.[15,18,33] In this technique the patient is restrained in the standing stocks. Caudal epidural anesthesia is administered, and rectal packing, if present, is removed. Fecal material is digitally removed from the rectum and distal colon. Careful cleaning of the defect is important prior to suture closure. Moistened 4x4 gauze sponges are used to remove manure from the lumen walls. If the tear is not full thickness, gentle gravity lavage should be used to assist in cleaning the tear. If the tear is a grade IV, assessment of the degree and duration of peritoneal contamination will aid in determining whether a repair should be attempted. Assessment of the tear by video endoscopy and/or digital palpation is more informative than speculum evaluation.[15] Digital assessment and repair are performed without gloves to improve tactile sensation.

The nonvisual technique is facilitated if the rectum is dilated with air, providing more space for the surgeon to maneuver his/her hand and needle when placing the sutures. Tying the tail in a dorsal position with the anal sphincter relaxed from the caudal epidural allows air to enter the rectum. Depending on the surgeon's preference, there may be some mechanical advantage to suturing tears on the left side with the right hand and tears on the right side with the left hand.[15,33]

For surgical repair, No. 5 dacron on a 6- to 8- cm, half circle cutting or trocar point needle in a cruciate or simple interrupted pattern is recommended. The suture length for each suture placed is 100 to 150 cm, with the needle placed in the middle of the suture. With both ends of the suture held outside the rectum, the digitally shielded needle is manually advanced to the tear. The first bite is positioned in the center of the caudal border of the tear, holding the needle with the thumb and first 2 fingers. The needle is inserted approximately 1.5 cm from the edge of the wound and guided to the center of the defect subserosally by the second and third finger (Figure 40-7A). The needle is pulled through this tissue and again grasped with the thumb and first 2 fingers. Next, the needle is placed in the center of the proximal edge with the bite beginning subserosally within the defect and guided to exit 1.5 cm from the defect's edge. It is helpful to use the third finger to press the tissue onto the needle (Figure 40-7B). The needle is then withdrawn from the cranial aspect of the defect and brought out the rectum. One side of the doubled suture is pulled through, leaving a simple interrupted strand suture in place with its distal

end extending 10 to 15 cm distal to the anal sphincter. The distal end of the needle is clamped on the needle side with a hemostat, leaving the needle threaded on the proximal one half of the suture. The clamped suture is held in place to one side by an assistant and the needle is moved near the opposite end of the suture strand and carried into the rectum. Placing traction on the placed suture will aid in closing the defect into a transverse plane. For the next bite, the suture is passed through both cranial and caudal edges of the defect without repositioning the hold on the needle. The needle is grasped in the same manner as before and the third finger is placed within the defect to provide guidance of the needle from the caudal edge into the defect and then positioned to press the tissue over the point of the needle as it travels out the cranial edge of the defect. The needle is then brought out the rectum. Releasing the previously placed hemostat and pulling the needle end of the suture through will form the cruciate suture. The knots are tied outside the rectum, pushing them inside with one hand while maintaining pressure on the suture with the other hand (Figure 40-7C). The ends of the sutures are left intact to retract the tissue for additional knot placement. Additional sutures are placed, working from the cranial portion of the defect caudally. In this way, as the rectal lumen decreases in diameter with suture placement, subsequent knots are placed in areas that have not been previously narrowed. After all sutures are placed (usually 4 to 6), the ends are cut with long tags to aid in identification and facilitate their removal.[33]

Figure 40-7A



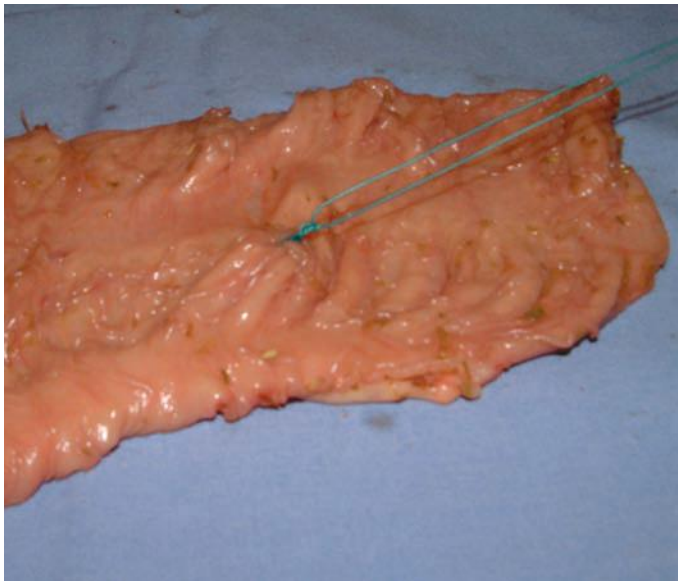
Nonvisual direct suturing technique. The needle is inserted 1.5 cm from the wound edge and guided to the center of the defect subserosally by using the second and third fingers.

Figure 40-7B



The second bite is started subserosally in the defect and exits 1.5 cm cranial to the defect edge, holding the needle with the thumb and first 2 fingers.

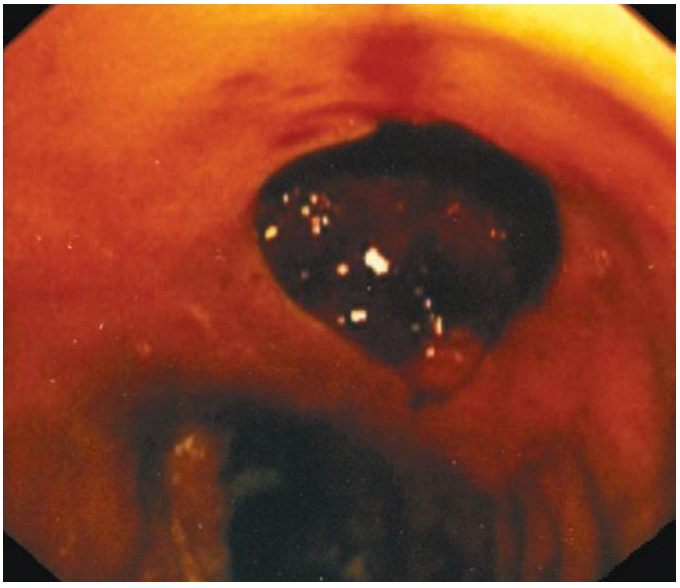
Figure 40-7C



The suture is tied by forming the knots outside the rectum and pushing them down tight with one hand in the rectum and one hand outside.

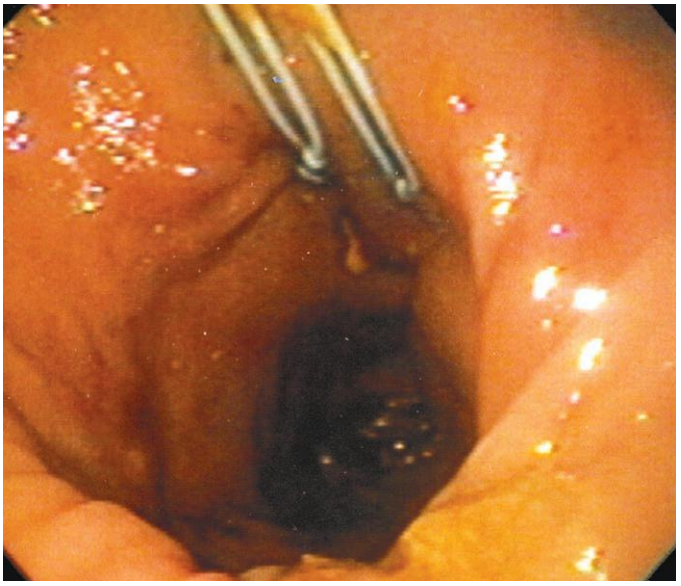
Intravenous fluids and broad-spectrum antibiotics are administered as indicated by clinical and laboratory parameters. The need for abdominal lavage is determined by peritoneal fluid analysis and evaluation of the horse's clinical status. The horse should be maintained on a low-bulk diet. The suture line is checked at 24- to 48-hour intervals (Figure 40-8). If defects are felt either from loosening sutures or reduction of edema, additional sutures should be placed. The sutures are removed 12 to 14 days after initial placement.[33]

Figure 40-8A



Direct suturing of a grade IIIb tear. A. Grade IIIb tear.

Figure 40-8B



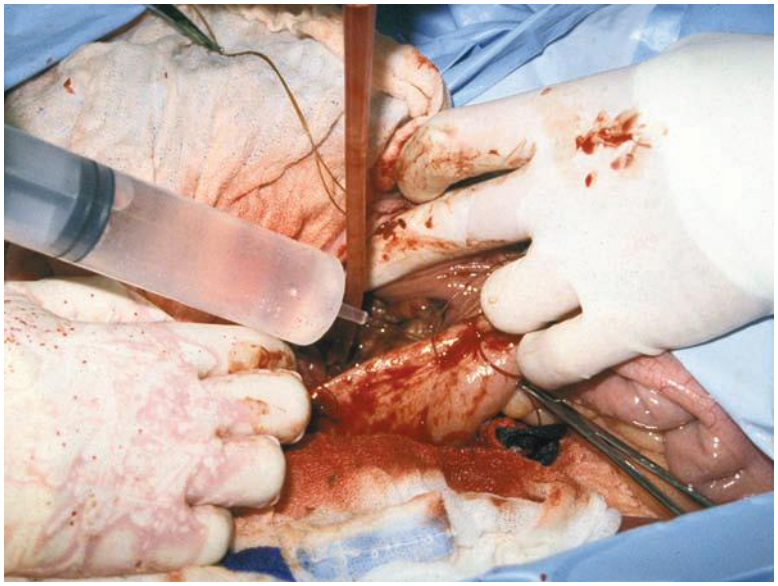
2 days after placing 2 cruciate sutures.

Ventral Midline Exposure and Antimesenteric Enterotomy for Suture Repair

It has been reported that tears more than 25 cm proximal to the anus may be amenable to primary closure through a ventral midline celiotomy.[4] In mares the ventral midline incision can extend between the mammary glands, improving access to the distal small colon. In geldings and stallions a paramedian incision is necessary to gain access to the affected small colon. Elevating the hindquarters may also improve surgical exposure to the tear.[3] If the tear is lateral or ventral, direct access for suture repair of the tear within the peritoneal cavity is possible. A glass speculum inserted up the rectum and positioned under the tear may facilitate visualization of the tear for suture placement.[4] Placing an arm up the rectum to move the bowel segment with the tear cranial and ventral may also improve visualization.[37]

If the tear is dorsal into the mesocolon, it can be approached through an antimesenteric enterotomy.[3,38] A ventral midline incision is made as far caudally as possible. Balfour retractors are placed to facilitate caudal retraction of the body wall. The caudal portion of the small colon is exteriorized and the tear is palpated within the abdomen. If the tear is dorsal it can be felt within the mesocolon. Traction on the small colon will bring the tear closer to the incision, but in most cases the segment of affected bowel will remain in the abdomen. Laparotomy sponges are used to pack off the surgical area, and a Penrose drain or Fogarty clamp is placed to occlude the proximal small colon. An antimesenteric incision is made as close to the level of the tear as possible. The surgeon will have to decide if the enterotomy can be made far enough caudally to provide sufficient access for surgical repair of the tear. Stay sutures are placed to retract the incised edges of the bowel. Feces from the enterotomy site to the tear are removed. Deaver retractors are inserted into the bowel in a caudal direction to facilitate visualization of the tear.[38] The tear should be meticulously cleaned, removing any feces within the tear and from within the dorsal mesocolon (Figure 40-9). The tear is then closed in a simple continuous pattern including the mucosa, submucosa, and muscularis, using 2-0 absorable suture. The antimesenteric enterotomy is closed in a routine fashion. Evacuation of the large colon should be performed to decrease fecal flow through the repair. Complications reported with this technique involve infection in the dorsal mesocolon leading to dorsal abscess formation. If this occurs, ventral drainage should be established into the lumen of the bowel once the abscess is walled-off.[38]

Figure 40-9



Antimesenteric enterotomy for primary closure of a Grade IIIb tear. The space into the dorsal mesentery is meticulously cleaned prior to suturing the tear.

Prognosis and Recommendations

The prognosis for horses with rectal tears depends on the severity of the tear, the degree of fecal contamination of the tear, the techniques used to treat the tear, and the experience and skill of the surgeon performing the repair. Most retrospective studies on rectal tears report on the outcome of a specific type of treatment for a relatively small number of cases.[14,16,17,19,23,29-32,38] Because of the small number of cases, the ability to predict prognosis accurately is somewhat limited.

Several reports exist regarding the outcome of larger groups of horses treated by several different methods.[15,18] These have provided some general recommendations about treatment, enabled comparisons of different individual or combined treatment techniques, and allowed predictions to be made concerning prognosis. In one report, multiple techniques used to treat 35 horses with grade III or IV rectal tears were evaluated.[18] Overall, 64 % of horses with grade III tears were discharged (74% of horses with grade IIIa and 44% of horses with grade IIIb). Neither of 2 horses treated for grade IV tears survived. In regard to technique for treatment, primary suture as the sole repair was successful in 6 of 7 horses in this case series. Fecal diversion was recommended if the tissue's ability to hold sutures was in doubt because of extensive tissue damage or edema. Fecal diversion was performed either by insertion of a rectal liner (19) or by colostomy (1). Of the 20 horses treated by fecal diversion, 50% survived. The combination of fecal diversion and suturing gave better results than fecal diversion alone. The authors also noted that appropriate first aid was important in influencing outcome. The first aid measures most important were those taken to protect the tear from contamination and further trauma as fecal balls packed into the tear. In horses in which the feces were removed from the vicinity of the tear and a rectal tampon was placed to protect the tear, there was less severe peritoneal inflammation with none of the tears progressing from grade III to IV prior to admission to the referral hospital. Horses without adequate rectal packing were more likely to present with grade IV tears and require euthanasia. A significantly higher number of horses was discharged that had had adequate first aid compared with those discharged without adequate protection of the tear (79% vs. 50%, respectively).

A review of 85 horses with rectal tears examined the outcome in horses treated with all grades of rectal tears.[15] Fifteen horses had grade I rectal tears. Medical management, which included maintaining soft feces and administration of antibiotics (9) or no treatment (6), allowed successful resolution of all cases except in one horse that suffered a catastrophic fracture while recovering from an elective surgery. Three horses had grade II tears: 2 were incidental findings, while a third involved three quarters of the circumference of the rectum. This horse was euthanatized because of chronic impaction colic. Twenty three horses had grade IIIa tears, of which 70% (16/23) were discharged. The majority of these were treated solely by direct suture per rectum (17/23), of which 82% were discharged. One of 2 horses treated by a combination of colostomy and direct suture was discharged, and 1 of 3 treated by combination of temporary indwelling rectal liner and direct suturing was discharged alive. Thirteen horses had grade IIIb tears. Six horses with grade IIIb tears were treated conservatively with antibiotics, NSAIDs, peritoneal lavage, and stool softeners. All 6 survived to discharge. Two of 4 horses treated by direct suturing survived, and 1 of 2 horse treated by direct suturing and temporary indwelling rectal liner survived. Of 31 horses presenting with grade IV rectal tears, 25 were subjected to euthanasia at presentation because of extensive fecal contamination of the

peritoneum. Neither of the 2 horses with grade IV tears treated by direct suturing only survived. One of 3 treated by loop colostomy and direct suturing, and 1 treated by temporary indwelling rectal liner plus direct suturing survived to discharge.

Deciding which technique or combinations of techniques to use is determined by multiple factors such as the time elapsed since the injury occurred, the degree of contamination, and the size and location of the tear. Some reports have cautioned against the use of one-handed suture attempts.[4] There is no doubt that this technique requires considerable manual dexterity combined with practice for the surgeon to become efficient; however, this procedure has been used on many horses with excellent results. If direct suturing cannot be performed or if the tear is sutured but the surgeon feels the repair is weak, we then recommend a standing two-incision loop colostomy to protect the repair.

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Colic and Pregnancy

Chapter 41

Elizabeth M. Santschi

Colic during Pregnancy

Diagnostics

Abdominal pain occurs frequently in pregnant mares, and most episodes resolve with minimal medical therapy. However, some colic episodes in pregnant mares are more severe and require surgical intervention. The first step in determining whether surgery is necessary is establishing the origin of the pain. The most common sites of colic in pregnant mares are the gastrointestinal tract and the uterus. Another less frequent cause of abdominal pain is damage to the abdominal tunic. Most colic episodes originate because of lesions involving the gastrointestinal tract, but abnormalities involving the uterus become more likely as the pregnancy progresses. Because the causes of uterine-related colic are few, and their occurrence relatively infrequent as compared with those involving the gastrointestinal tract, the easiest way to determine the colic source is to eliminate the uterine and abdominal-wall causes first. The first step is to palpate the uterus via the rectum to ascertain its shape, size, and orientation. If these findings are normal, the uterus is highly unlikely to be the source of abdominal pain. Occasionally, parturition or abortion can be confused with colic, so a cervical examination by speculum or by gentle palpation can be helpful. If the uterus is not the cause of pain, the location of colic is assumed to be gastrointestinal, as abdominal tunic disorders are readily apparent by visual observation.

The diagnostic work-up for a pregnant mare with gastrointestinal colic is the same as for a non-pregnant horse. However, in the late-term mare, the usefulness of palpation of the viscera per rectum and transabdominal ultrasound can be reduced as the large uterus obscures the viscera.

Decision-making in the pregnant mare with colic is further complicated because the health and maturity of the fetus is an additional concern. Selected laboratory tests and ultrasonographic examinations can be performed to get an estimate of fetal health, but decision-making can be simplified by following two guidelines. The first is that the best way to care for the foal is to care for the mare, and the second is that mares in pain need exploratory abdominal surgery.

Assessment of Fetal Health and Maturity

Accurate assessment of fetal health is a challenge, but there are guidelines, particularly for ultrasonographic examination, to assess fetal well-being.[1] Fetal death can be easily determined by visualizing asystole via transabdominal ultrasound in the late-term fetus, but less dramatic compromise of the fetus can be difficult to detect. Daily ultrasound examinations to determine fetal heart rate and movement and estimate fetal fluid is presently the best method of assessing fetal well-being. Fetal heart rates are most easily obtained by transabdominal ultrasound, and serial examinations are recommended. Fetal heart rates should range from 70 to 110 beats per minute. Repeatedly higher or lower rates are associated with fetal compromise and death. Detecting fetal death is important because dystocia can easily result from unassisted attempted delivery of a dead fetus.

Fetal maturity can be estimated by measuring electrolyte concentrations in mammary secretions, as concentrations of calcium, potassium, and sodium change as the fetus reaches maturity.[2,3] Before maturity, concentrations of sodium and potassium in mammary secretions are similar to those in serum (sodium concentration higher than potassium), but these concentrations invert about 3 days before birth (sodium concentration becomes lower than potassium), indicating accelerating fetal maturity. Although electrolyte concentrations in mammary secretions provide only an estimate of maturity, at present, this measurement is the best test available. If fetal survival is a primary goal, methods of assisting parturition, such as induction or hysterotomy, should be delayed if possible until the concentrations of the electrolytes in mammary secretions have inverted.

Gastrointestinal Colic

Medical

Colic occurs frequently in pregnant mares. As in non-pregnant horses, the vast majority of colic episodes in pregnant mares resolve with minimal therapy. These single colic episodes appear to have little effect on either the mare or the fetus. However, when abdominal pain is accompanied by signs of endotoxemia or is repetitive, there is risk to both mare and foal. Endotoxemia appears to have the greatest effect on the fetus in the last 60 days of gestation.[4] Although it is not known if endotoxin can cross the equine placenta, endotoxemia can cause uteroplacental perfusion abnormalities in cattle,[5] and this consequence and a concurrent cytokine release may be the mechanism for compromise in late-term pregnancies. Early in equine pregnancy, experimental endotoxemia can cause prostaglandin-mediated luteolysis and subsequent pregnancy loss.[6] It is not known if circulating concentrations of endotoxin in clinical cases are sufficient to result in luteolysis. Sustained signs of endotoxemia are most common in mares requiring intensive medical therapy for diseases such as proximal duodenitis/jejunitis or colitis. The appropriate therapy for endotoxemia includes correction of the inciting cause, administration of cyclooxygenase inhibitors such as flunixin meglumine, and appropriate fluid support.[7]

Surgical

When relatively small groups of pregnant and non-pregnant horses are compared, no significant difference is found between the types of lesions causing colic,[4] but a few colic lesions are frequently associated with pregnancy. In the early stages of pregnancy, the pregnancy itself appears to have little effect on the health of the mare, but a previous pregnancy may have some residual effect. During late pregnancy, the gravid uterus occupies a very large portion of the intraabdominal space, causes stretching of the abdominal wall, and leaves little room for colonic ingesta. After parturition, the colon has more space to move because of the laxity of the abdominal musculature and the empty colon. Additionally, it is common for recently foaled mares to receive fermentable feedstuffs such as concentrates or lush forage and pasture. The combination of an empty colon that is predisposed to tympany and the fact that it has more room for movement is believed to predispose postparturient mares to colonic displacements and large-colon volvulus.

Large-colon volvulus is of particular concern to broodmare owners as this condition occurs commonly in broodmares in early to mid gestation, recurs in some individuals, and is often deadly.[8] A plausible mechanism for large-colon volvulus is the shape of the post-parturient abdomen: it has a deeper ventral concave shape and the space for the large colon and cecum is larger. The apex of the cecum is on the midline, and the right ventral colon is pulled toward the midline via the cecocolic ligament which attaches to the ventrolateral band. This causes a slight clockwise (as viewed from behind) rotation of the colons, and results in an axial placement of the ventral colon relative to the dorsal colon. The oblique (as opposed to a vertical stacking) orientation of the colons is also promoted by concavity of the diaphragm. When the colons are in this position, gas in the ventral colon or the apex of the cecum or heavy feed in the dorsal colon can hypothetically promote rotation of the ventral and dorsal colons around their common mesentery. If the rotation continues, the twist becomes tighter, resulting in colic by obstructing gas and ingesta. Once the colon is distended, vascular compromise causing ischemia leads to severe colic and shock followed by death if the problem is not identified and treated immediately.

Surgical correction is essential to the treatment of large-colon volvulus. The colon is untwisted through a ventral midline celiotomy. A pelvic flexure enterotomy can be performed to evacuate the colon and inspect the mucosa for viability. If the colon is viable, it is replaced in the abdomen. If the colon is compromised, resection of 60% to 75% of the colon is possible.[9] Large-colon resections are performed to remove devitalized tissue, reduce the absorption of endotoxins, and reduce the dramatic loss of plasma protein that can occur after surgery. Although the mares will lose weight after surgery, they will gain it back in several weeks and can carry the present and any subsequent foals to term.

In response to the approximately 30% recurrence rate of large-colon volvulus in Thoroughbred broodmares, colopexy procedures to prevent colonic rotation have been developed;[8] however, these techniques have not been universally accepted. The development of large-colon volvulus in mares after foaling may be reduced by feeding forage rather than fermentable feeds, so as to fill the colon with ingesta rather than gas, and by promoting exercise to improve the muscular tone of the abdominal wall and to support normal gastrointestinal motility.

Two causes of colic that are specifically associated with pregnancy are small-intestinal entrapment over the broad ligament and through rents in the proximal duodenal mesentery. Both conditions are seen most commonly in mares in the last quarter of gestation The jejunum is the section of intestine that gets entrapped over the broad ligament. The distended small intestine is readily palpable per rectum, and because of concerns about small-intestinal strangulation, these mares often are subjected to an exploratory celiotomy. The bowel is usually not compromised, and the colic is resolved by correcting the entrapment and decompressing the intestine.

Rents in the mesentery generally involve the short axis of the mesentery from the root to its attachment to the intestine. Entrapment of the small intestine occurs because the available room in the abdomen is reduced by the enlarging uterus and the bowel is displaced through the rent. Because of the large size of the rent, intestine probably moves freely in and out of the rent. Presumably, however, as the uterus enlarges, the intestine cannot move as freely and gets entrapped, causing physical obstruction and colic. Strangulation of the entrapment is rare because of the large size of the rents. There is usually no fresh hemorrhage in the abdomen from the mesentery and the margins of the tears are healed, suggesting that the rent had occurred previously, perhaps during parturition. Mesenteric rents are most commonly found in the duodenum and small colon where the mesentery is short and perhaps more likely to be damaged; however, a distal jejunal rent has also been described.[10] Correction of mesenteric rents causing small-intestinal herniation requires removal of bowel from the hernia, resection of any damaged sections, and closure of the rent. Closure of the rent can be difficult as the proximal extent is deep in the abdomen and the uterus makes exposure difficult or impossible. It is generally accepted that leaving a big hole is better then a partially closed one; therefore, if the rent cannot be substantially closed, it is left undisturbed. Owners are

advised that another colic episode during this gestation is a possibility. Closure of the rent after foaling via celiotomy or by laparoscopy, with the horse standing to visualize the dorsal mesentery should be considered.

Hysterotomy during Colic Surgery

If the lesion causing colic cannot be accessed because of the enlarged uterus, removing the foal may allow the colic episode to resolve. This is an uncommon situation, never desired, and should be avoided if possible. If the foal is not ready for birth, the decision to remove the foal is essentially an abortion to save the life of the mare, and should only be done on that basis. If the foal is close to term and the mare's electrolyte concentrations in the mammary secretions are consistent with fetal maturity, the foal is delivered and sent to intensive care, the uterus closed, and the lesion causing the colic episode corrected. Because the survival rate of these foals is low, this procedure should not be done if the colic lesion can be corrected otherwise.

Anesthesia

Anesthesia of the pregnant mare is not substantially different from that in non-pregnant horses. However, risk to the mare's life is increased if anesthesia is performed in the last trimester of pregnancy.[11] The reasons for this increased risk are unclear, but are possibly due to the cardiovascular changes associated with late pregnancy, the challenge of ventilation, poor venous return because of the pressure of the uterus on the caudal vena cava, the weight of the mare, and perhaps some delay in therapy because of concerns about anesthesia. All anesthetic agents have an effect on the fetus,[12] so small alterations in protocol are considered practical. One consideration is to minimize the use of α-2 agonists such as xylazine and detomidine, because they increase uterine tone.[13] The author's preference is to use xylazine (0.3-0.5 mg/kg, IV for sedation), and then rely on additional agents such as 5% guaifenesin (100 mg/kg, IV) or valium (0.1 mg/kg, IV) for relaxation before inducing anesthesia with ketamine (2.0 mg/kg IV). Another anesthetic consideration in late gestation pregnancies is hypoxia. Hypoxia in the last 60 days of gestation has been associated with poor fetal outcome.[4] If possible, arterial oxygenation should be maintained at 80 mm Hg or higher during surgery; however, it can be difficult to ventilate mares positioned in dorsal recumbency when they have a large uterus and distended bowel. In such cases, the best way to prevent hypoxia is to diagnose the primary condition early, decompress the bowel quickly, and correct the lesion as soon as possible. Strict attention should be paid to proper padding and positioning of the late-term pregnant mare during general anesthesia, as the extra weight of the fetus and fluids will place extra stress on the muscles, making postoperative myopathy a possibility.

Abortion after Colic Treatment

There is little risk to the fetus in a pregnant mare that has responded well to minor medical therapy for a colic episode. The incidence of abortion increases for mares requiring surgery or intensive therapy.[4,14] The increased likelihood of abortion after surgery for a nonstrangulating colonic lesion is extremely low if no complications arise. Mares with strangulating colonic lesions or small-intestinal lesions appear to have about a 10% post-surgical abortion rate that can be attributed either to the colic or the treatment. Multiple bouts of colic, particularly if they occur after surgical interventions, seem to be associated with an increased incidence of abortion. To minimize the risk of abortion, surgical therapy for colic should be performed as soon as the need for surgical intervention is determined.

Abortions after colic episodes occur because of fetal death. Once the fetus dies, parturition should occur within 48 hours. Dystocia is frequent because the fetus cannot participate in parturition, thereby resulting in carpal and poll flexion in the mare. These malpositionings are readily corrected, and can be anticipated by checking fetal viability daily via transabdominal ultrasound. Mares will often deliver at night, so 24-hour monitoring of a mare with a dead fetus is necessary.

Pregnancy Maintenance

Adjunctive strategies directed at supporting the pregnancy are many, but evidence for their efficacy in clinical situations is mostly anecdotal. Experimental evidence exists that the administration of altrenogest (0.044 mg/kg) may have benefits.[15] For mares in early gestation, exogenous progestagens can be administered if the possibility of luteal compromise exists. Therapy can be continued until sufficient endogenous production of progestagens can be demonstrated. For mares in later gestation, stall confinement with light exercise, such as 1 to 2 hours' turn-out in a small paddock or round pen, is believed useful. Strict stall confinement of the late pregnant mare should be avoided as it can lead to accumulation of edema in the limbs and around the udder. For medical therapy, the author uses altrenogest 0.09 mg/kg, orally once a day and flunixin meglumine at 0.5 mg/kg, IV three times a day, or 1.0 mg/kg, IV twice a day. The altrenogest is used as a tocolytic, and the flunixin meglumine for its anti-inflammatory properties. Other clinicians use pentoxyphylline (12 mg/kg PO, b.i.d.) for its anti-inflammatory and rheologic properties, and provide intranasal oxygen to the mare to improve oxygen delivery to the fetus.

Uterine Causes of Colic

Uterine torsion

Torsion of the uterus occurs in mid- to late gestation.[16,17] The primary clinical sign is abdominal pain that is usually moderate in degree but occasionally can be severe. Portions of the gastrointestinal tract can be involved in the torsion.[18] Systemic compromise is rare, and when present, indicates uterine damage or gastrointestinal complications. The diagnosis of uterine torsion is made by palpation: one broad ligament is taut and passes over the uterus and the other is a band under the uterus. The cervix is rarely open and vaginal twisting is usually not apparent. The uterus can be twisted in either direction.

Treatment of mares with uterine torsion requires physical detorsion of the uterus. This can be accomplished either via a standing laparotomy, a ventral midline approach with the mare under general anesthesia, or by a non-surgical rolling procedure with the mare under general anesthesia.[16,17] The procedure chosen depends on the condition of the mare and her stage of gestation when the torsion occurs, financial constraints of the owners, facilities, and the clinician's preference. Early correction of the torsion is more important to maternal and fetal health than the method used. The prognosis for mares with uncomplicated uterine torsions treated early is very good. The survival rate for all foals presented in a torsed uterus is about 50%, and approximately 70% of foals that are viable at surgery or during the rolling procedure are born alive.[16]

The rolling procedure is often successful in affected mares in mid-gestation.[17] The mare is anesthetized and placed in lateral recumbency on the same side as the direction of the torsion. The purpose of the rolling procedure is to hold the foal and uterus in place and roll the mare to "catch up" with her uterus and fetus. A board can be used across the flank to hold the uterus and foal still while the mare is rolled. Correction of the torsion is determined by rectal palpation. The rolling procedure can be repeated, if at first unsuccessful. Once the torsion is corrected, the mare is allowed to recover from anesthesia.

Uterine torsions can be corrected by standing laparotomy at any stage of gestation, but correction can be somewhat difficult in late-term mares. Standing correction requires that the mare tolerates the procedure. It should not be performed in mares with suspected uterine damage. Sufficient sedation and analgesia are important. An inverted "L" block with local anesthetic is made in the flank on the side to which the uterus is rotated. A vertical incision is then made through the flank, and the abdomen is opened via a modified grid incision. The surgeon's arm is placed under the uterus and the uterus is gently rocked back and forth. The goal is to get sufficient momentum to "flip" the uterus into its normal position. The surgeon should be careful to only put pressure on the uterus with the flat of the hand to avoid tearing the uterus. If detorsion is difficult, the flank incision can be enlarged to admit both arms to allow manipulation of the uterus.

The ventral midline approach is used for later-term mares and for mares with suspected uterine damage; this is the author's preferred approach. The uterus is approached through a large caudal ventral midline incision. By placing the hands and arms under and around the uterus, the uterus is untwisted. Filling the abdomen with sterile saline will reduce friction in the abdomen and faciliate detorsion. In rare cases when the uterus cannot be detorsed, the fetus can be removed to facilitate detorsion. If the uterus is ruptured, the fetus is delivered, and the uterus sutured. Mares with extensive uterine damage should be euthanized.

Uterine Artery Hemorrhage

The majority of uterine artery hemorrhages occur during parturition, but they can occur during gestation and cause signs of colic. The diagnosis is made by physical examination, which will reveal pain, hypovolemia if the hemorrhage is severe, a hematoma associated with the broad ligament of the uterus, and blood in peritoneal fluid obtained by abdominal paracentesis.[19] Many treatments exist for uterine artery hemorrhage, most focusing on supporting the mare while the arterial defect seals. The most important therapy is probably gentle supportive care, mild sedation, and analgesia. Post-parturient mares with this condition have a 50% survival rate.

Hydrops

Hydrops refers to excessive production of fluid by the placenta. Most cases in horses are allantoic hydrops, although amnionic hydrops has also been reported.[20] Affected mares have massive abdominal enlargement out of proportion for their stage of gestation. They can develop respiratory distress, particularly when lying down, they move stiffly and have signs of mild abdominal pain. Rectal examination reveals massive fluid distension of the uterus; the fetus cannot usually be palpated. Mares with hydrops should have their fetus aborted because of the danger of uterine[21] or abdominal-wall rupture, the high likelihood of additional fetal abnormalities,[22] and to protect the uterus from over-stretching.

The massive fluid loss that accompanies the abortion of fetuses in mares with hydrops suggests that fluid preloading to minimize hypovolemia is indicated. Crystalloid fluids are administered IV to ensure good plasma volume. The abortion can usually be performed by manually dilating the cervix and rupturing the chorioallantois. Using gentle pressure, the cervix can usually be dilated, but if necessary, cervical softening with topical misoprostil can be considered. Insertion of a sterile large-bore tube such as a nasogastric tube can be used to remove the fluid in a slower controlled manner, but sometimes the fluid is violently released. Once the fluid begins to flow, a small fetus usually will present itself and can be delivered with gentle traction. Retained placenta is common, and should be treated appropriately.

Abdominal tunic disorders

Damage to the abdominal tunic occurs most frequently as prepubic tendon rupture or stretching, but can also present as muscular hernias in the abdominal wall.[23] Damage can occur in abnormal pregnancies such as hydrops, but more commonly occurs in apparently normal pregnancies. Diagnosis of a prepubic tendon rupture is made by observing an upward tilt of the caudal pelvis caused by a lack of tension on the pubic bone (Figure 41-1). Usually there will also be edema cranial to the mammary gland and a caudal orientation of the teats. Ruptures are thought to occur most frequently in draft mares, but are also seen in light breeds of horses. The most common clinical sign seen is colic owing to the pain associated with tearing of the support structures.

Figure 41-1



Prepubic tendon rupture in a mare. The displacement of the caudal abdomen hinders rear limb movement and distorts the mammary glands.

When the prepubic tendon is ruptured before the foal is mature, the likelihood of carrying the foal to term and saving the mare is very low. If the mare's life (without the ability to carry later foals to term) is important, pre-term induction with assistance in delivery may be considered. However, it is usually not clear whether induction or continuing the pregnancy is more injurious to the mare. If owners wish to continue the pregnancy, the mare is confined to the stall and given anti-inflammatory drugs. Mares with prepubic tendon ruptures often have trouble moving because of an inability to advance their hindlimbs appropriately. Abdominal supports can also be used, but are not of clear benefit. If such supports are used, they should be of stout construction, either heavy canvas or leather, and padded both over the back and on the ventral abdomen. Tape supports usually stretch and are of questionable benefit. Disadvantages to the use of abdominal supports include a frequent need to reset the support, and concentration of the abdominal mass in the center of the spine causing damage to the back.

If the mare completes her pregnancy, foaling should be attended, as she may not be able to provide sufficient abdominal contraction to deliver the foal quickly. Carrying future pregnancies to term is unwise, but has been accomplished.[24] Embryo transfer may be a reasonable option if reproductive capabilities are essential. For some abdominal hernias, surgical repair can be performed after the hernia develops a distinct fibrous border.[25]

Partial damage to the prepubic tendon can sometimes be managed successfully, and success is related to the amount of damage. Clinical signs include abdominal pain and edema in the area of the tear, but a normal orientation to the pelvis and mammary gland. Sometimes these mares have what appears to be a stretched prepubic tendon, with a lengthened distance

between the umbilicus and the base of the mammary gland. These mares should be stall-confined and given anti-inflammatory drugs as needed.

Mares with ruptures of the muscular support of the abdomen also exhibit edema and pain, but the swelling is greater on one side of the abdomen, usually ventral to the flank. Large tears usually progress, and require euthanasia of the mare. Small muscular tears can be managed successfully, using the therapy described for tendon ruptures. A common problem with mares with muscular hernias is that the hernias can entrap bowel and cause an abdominal crisis. If bowel is not present in the hernia, supports can be used to help obliterate the space. If a mare with a small hernia carries her fetus to term, surgical repair should be considered if further pregnancies are desired.

Colic in the Peripartum Period

Diagnostics

Evaluation of colic in recently foaled mares can be complicated by normal postpartum events such as uterine pain from delivery of the placenta and uterine involution. Just as in pregnant mares, the uterus and the gastrointestinal tract should receive equal attention to determine the source of the abdominal pain. Transabdominal ultrasound should always be a part of the examination of a depressed or painful postpartum mare to detect abdominal fluid accumulation and intestinal distention. If abdominal fluid is detected, abdominal paracentesis should be performed to determine whether peritonitis or hemorrhage is present. If peritonitis is present, there is little need to determine the specific source of the infection for mares with a surgical option. An abdominal exploratory surgery to determine the cause of the peritonitis, possibly correct it, and lavage the abdomen should be performed as soon as possible. For mares without a surgical option, sampling the abdominal fluid will provide information about the severity of infection, and whether euthanasia is appropriate. Some horses with peritonitis will respond to medical therapy only, but it can be difficult to predict success early in the course of the process (see Chapter 7). For valuable mares, an exploratory celiotomy can resolve most questions and prevent fatal peritonitis.

Gastrointestinal colic

Medical

The majority of episodes of post-parturient abdominal pain are mild to moderate in intensity and respond to medical therapy. For most post-parturient mares, the specific causes of colic are speculative, but bruising of the small colon and generalized ileus are relatively frequent. Treatment of these mares with laxatives, anti-inflammatory drugs, and oral or IV fluids is generally sufficient for the resolution of abdominal pain. Colic episodes with evidence of concurrent endotoxemia are frequently the result of ingesta leaking from small rents in the intestine. If the peritoneal cavity is contaminated with feed, these mares invariably die from peritonitis and adhesions. However, if peritonitis is diagnosed early, and there is movement of bacteria but not feed into the peritoneal cavity, surgical closing of the tear and lavaging the abdomen can be successful.

Rupture of the Small-Colon Mesentery

Rupture of the mesentery of the small colon occurs during the abdominal press of parturition.[26] Presence of a rectal prolapse during foaling should raise the suspicion of this injury, but rectal prolapse is not required for this condition to occur. Stretching of the mesentery during parturition tears the distal small-colon mesentery from the bowel for a variable length, causing intraabdominal hemorrhage, ileus, small-colon impaction, and eventually, bowel necrosis. Clinical signs associated with the rupture can be delayed for 24 to 48 hours after foaling, and the initial finding is a lack of fecal passage. A low-grade fever (102-103°F) usually develops, followed by bloating and colic. Rectal examination will reveal an impaction of the distal small colon. Differential diagnosis for mares with peritoneal effusion after foaling includes tearing of the wall or the vascular supply of the uterus or intestine.

Treatment of mares with small-colon mesenteric ruptures that result in compromised bowel requires surgery. Repair of the damage is limited by accessibility to the distal aspect of the mesenteric tear. If the necrotic small colon extends into the pelvic canal, euthanasia is necessary. If healthy bowel can be reached at the distal limit of the tear, resection and anastomosis of the damaged bowel should be performed. The relaxed abdominal wall after parturition, a large ventral midline incision, exteriorizing the large colon from the abdomen, and tilting the head of the surgery table forward can improve access to structures in the caudal abdomen. The small colon is transected at the distal limit of the damage. The compromised bowel is removed from the abdomen and is used as a conduit to relieve the impaction in the damaged section of the small colon and in the bowel oral to the damage. After a sufficient amount of ingesta is removed to allow anastomosis, an end-to-end hand-sewn double-inverting closure of the small colon is performed. The author prefers an Utrecht pattern using 000 monofilament absorbable suture. The mesentery that can be visualized should be closed using a simple continuous pattern. Closure

of the deeper mesentery is performed without visualization. Deep mesenteric closure is performed using absorbable suture material on a large-taper half-circle needle in a simple continuous pattern. Closure of the mesentery close to the dorsal body wall is performed first. The knot is made either by using a double strand of suture and looping the needle through the two strands after placing the first bites, or by a one-handed tie. By placing traction on the distal mesentery, both sides of the tear can be palpated in the abdomen and sutured using one hand. A moistened large laparotomy sponge positioned beneath the mesentery ensures that bites will grab the sponge (and be detected) rather than adjacent bowel. Before closure of the abdominal wall, the large colon should be emptied via pelvic flexure enterotomy and additional fluid added to the lumen to soften the remaining ingesta. This will reduce and soften the volume of feces that must immediately pass the anastomosis. An abdominal drain can be placed at surgery and used for abdominal lavage postoperatively.

Postoperatively, food is withheld until intestinal motility returns. Replacement fluids are given intravenously as necessary to maintain hydration. Feeding begins within 24 to 36 hours after surgery, and low-residue processed feeds, green grass, and moistened hay are fed to soften ingesta and reduce straining. Mineral oil is administered via nasogastric tube for its laxative effects. Perioperative use of antimicrobials, such as penicillin (22,000 IU/kg, IV, q.i.d.) and gentamicin (6.6 mg/kg, IV, s.i.d.), is recommended, and metronidazole (15-20 mg/kg, PO, t.i.d.) can also be administered to prevent anaerobic bacterial growth. Postoperative complications are common after repair of small-colon ruptures and include colic, colitis, peritonitis, and adhesions.

Diaphragmatic Hernia

Diaphragmatic hernias can occur after foaling and cause colic owing to bowel entrapment.[27] The diaphragm tears because of high intraabdominal pressure, and this can occur after normal foaling. Any part of the intestine can become entrapped through the tear. The most common clinical sign associated with diaphragmatic hernia is colic, but respiratory embarrassment can also occur. Diaphragmatic hernias are most often discovered during exploratory abdominal surgery, but can be identified preoperatively by ultrasound and thoracic radiographs. Surgical correction of the entrapment and closure of the tear are necessary. Closure of the diaphragmatic tear is usually difficult because of the size and location of the defect, and the damage to the tissue margins. The poor quality of the tissue margins of a fresh tear makes recurrence of the hernia highly likely either during recovery or soon thereafter.

Uterine Trauma

Uterine ruptures can occur before foaling, but most occur during parturition and become apparent in the immediate postpartum period. Clinical signs become evident within the first 24 to 48 hours after foaling and consist of depression, low-grade fever, and often, colic. Some mares with uterine tears will hemorrhage sufficiently to show signs of anemia, and if the tear involves a major artery, hypovolemia will be the predominant clinical finding. The diagnosis of uterine tears that do not involve major vessels is made by clinical signs, abdominal paracentesis, and occasionally, palpation of the tear either per rectum or through the uterus. Abdominal fluid analysis will indicate peritonitis that worsens over time. Mares with uterine ruptures tend to have large volumes of abdominal fluid with increased white cell counts that can resemble lochia.

Uterine tears are best treated by surgical correction.[28] Although some caudal tears can be sutured from the endometrial side per vaginum, most require general anesthesia and a ventral midline exploratory surgery to repair the rent and lavage the abdomen. Preoperative considerations should be directed at supporting the systemic circulation before anesthesia and may include administering whole blood or crystalloids. Mares that accumulate large amounts of fluid in the abdomen should have the fluid drained before anesthesia and circulating blood volume replaced. Surgical repair of the tear can be accomplished using either a single or double inverting suture pattern. Copious abdominal lavage is beneficial in reducing abdominal contamination. An abdominal drain should be placed to facilitate abdominal lavage postoperatively.

Postoperative care is directed at resolving the peritonitis and promoting uterine involution. Large-volume (10-20 liters) abdominal lavage for 2 to 3 days after surgery can assist in physical removal of debris and has been shown to reduce adhesion formation in horses after colic surgery. Anti-inflammatory drugs and broad-spectrum antimicrobials are indicated to treat the peritonitis, and oxytocin (20 IU, IM, every 2 hours) can be used to assist in uterine involution.

Major Artery Hemorrhage

Rupture of the uterine, iliac, or utero-ovarian arteries most commonly occurs in the peripartum period. Mares can show anxiety and depression as well as colic, usually within the first 24 hours after foaling.[19] Hemorrhage should be suspected if pale mucous membranes and subnormal rectal temperature are present. Other clinical signs seen are determined by the amount of blood lost and whether the hemorrhage is confined to the broad ligament or uterine wall or escapes into the

abdomen or uterine lumen. If the blood escapes from the broad ligament, the mare will be severely hypovolemic or can die suddenly. If the arterial rupture is confined by the broad ligament, the presenting clinical sign is abdominal pain. The hematoma can be palpated in the broad ligament and seromuscular surface of the uterus per rectum, and it is believed that stretching of these structures causes pain. Confirmation of the hematoma can be obtained using transrectal ultrasound, and intraperitoneal bleeding can be demonstrated by abdominal paracentesis. Mares with hemorrhage into the broad ligament predominantly show signs of pain, and treatment should be directed at relieving discomfort and reducing further hemorrhage.

Treatment of mares with blood loss into the peritoneal cavity or uterus is difficult owing to the rapid, acute blood loss and is directed toward treating circulatory shock and controlling hemorrhage. Crystalloid fluids, colloids, plasma, and fresh blood can all be used to restore vascular volume. Hypertonic saline (1-2 L, IV) can be used to rapidly increase circulatory volume, but must be followed by administration of isotonic fluids; however, over-dilution of blood is a concern. Initial determinations of packed-cell volume are unreliable indicators of the extent of hemorrhage because of the release of concentrated red blood cells from the spleen. The packed-cell volume and total plasma protein concentration should be closely monitored, as they can decrease dramatically during fluid therapy. If the packed-cell volume decreases to less than 15% and the plasma protein concentration decreases to less than 4.0 mg/dL (40 g/L), transfusion with 6 to 8 liters of cross-matched fresh whole blood should be considered. If whole blood is unavailable, fresh-frozen plasma can be used as a source of clotting factors. There is a concern that restoring blood pressure can exacerbate hemorrhage; however, hypovolemia is generally the cause of death in mares with these ruptures, so careful restoration of fluid volume is indicated. The author believes that stall confinement, intravenous administration of plasma, and light sedation combined with analgesics are the core of therapy.

Additional medical therapies for hemorrhage include naloxone (0.8 mg IV),[29] aminocaproic acid (20 g in fluids IV as a loading dose followed by 10 g every 6 hours),[19] flunixin meglumine (0.5-1 mg/kg, IV, b.i.d.), and butorphenol tartrate (0.03-0.07 mg/kg, IV or IM, p.r.n.). The opiate agonist/antagonists are used to treat hemorrhagic shock, the aminocaproic acid inhibits fibrinolysis, and the nonsteroidal anti-inflammatory drug reduces peritoneal inflammation and pain. These latter drugs should be used judiciously, as they can adversely affect platelet function and perhaps worsen hemorrhage. Intravenous administration of 10% formalin (10 mL in a liter of saline, IV) has also been used in horses because of its ability to decrease hemorrhage and may have a place in the treatment of arterial ruptures associated with parturition.

Surgical therapy for uterine artery ruptures has been attempted through both flank and ventral midline approaches. Surgical therapy is complicated by the hypovolemia and the difficulty in isolating the bleeding vessels because of the extensive tearing usually present in the broad ligament. Surgical treatment has not shown any clear advantage over medical therapy. Approximately 50% of mares that have severe postpartum bleeding survive with therapy. Subsequent fertility rates for these mares are unknown; recurrence of hemorrhage with subsequent pregnancies occurs, but some mares can foal without recurrence of hemorrhage.

Urinary Bladder Rupture

Rupture of the urinary bladder is uncommon in the post-foaling mare but should be considered when large volumes of fluid accumulate in the abdomen. Ultrasound will demonstrate the fluid, and measurement of creatinine in the abdominal fluid confirms the diagnosis if its concentration is twice that of serum creatinine. Cystoscopy of the bladder can allow visualization of the tear. Small urinary bladder tears can heal spontaneously if the bladder is kept empty using an indwelling urinary catheter, but larger tears require surgical correction. Surgical repair of urinary bladder tears can be performed via a ventral midline incision, but this approach does not allow access to the middle and caudal aspects of the urinary bladder. Standing repair of urinary bladder tears can be performed by directly suturing the tear by inverting the edges of the tear into the bladder through an incision in the urethra, or by retracting the bladder through a colpotomy.[30] Standing repair has the advantages of avoiding general anesthesia in a systemically compromised mare. Urine should be drained from the abdominal cavity in all cases of bladder rupture. This is an important preoperative consideration when general anesthesia is performed.

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Colic from Alternative Systems - “False Colics”

Chapter 42

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Colic is neither a specific disease nor a diagnosis, but simply represents the behavioral manifestations of abdominal pain. Although colic is generally associated with diseases of the gastrointestinal tract, diseases affecting other body systems can also cause pain that creates behavior similar to colic. These clinical signs can be difficult to differentiate from pain due to gastrointestinal disease. In addition, acute neurologic and muscular diseases may cause signs that can be confused with colic. These conditions are commonly referred to as "false colics." A list of differential diagnoses of the most common causes of "false" colic is shown in Table 42-1.

Table 42-1
Common causes of "False" Colic.

Female reproductive tract	Ovulation Post-ovulation hematoma Granulosa cell tumor Other ovarian tumors Vaginal (breeding) injuries Pregnancy Uterine torsion Dorsoretroflexion of the uterus and abortion Dystocias Arterial rupture and uterine hematoma Third-stage labor Perineal injuries Uterine rupture Inversion of the uterine horn
Male reproductive tract	Orchitis Testicular torsion Thrombosis of the spermatic cord vessels
Urinary tract	Cystic calculi Renal calculi Ureteral calculi Urethral calculi Pyelonephritis Cystitis Ruptured bladder
Liver	Acute hepatitis/hepatic failure Cholangiohepatitis Cholelithiasis
Pancreas	Acute pancreatitis Chronic pancreatic disease
Spleen	Splenic abscess Splenomegaly
Respiratory tract	Pleuritis Pleuropneumonia
Cardiovascular system	Aortoiliac thrombosis Aortic rupture Acute hemorrhage Myocardial infarction Pericarditis
Musculoskeletal system	Laminitis Acute exertional rhabdomyolysis Atypical myoglobinuria Rupture of the prepubic tendon and ventral hernias
Nervous system	Tetanus Botulism Seizures Hypocalcemic tetany Equine motor neuron disease

Differentiation between "true" and "false" colics depends on obtaining an accurate history and performing a careful physical examination, coupled, where appropriate, with further diagnostic procedures such as clinical pathology and diagnostic imaging. Although this is not invariably true, horses exhibiting colic caused by disorders of systems other than the gastrointestinal tract often show mild to moderate pain (e.g., pawing the ground, lying in sternal or lateral recumbency for prolonged periods of time, or exhibiting reluctance to move) but rarely demonstrate signs of severe pain (e.g., rolling violently).

Pain Associated with the Female Reproductive Tract

Ovulation Pain

Occasionally, mares demonstrate abdominal pain in association with ovulation during estrus.[1] Affected mares typically demonstrate mild to moderate colic signs similar to those demonstrated by horses with acute, short-lived gas colic or spasmodic colic. Rectal palpation and/or ultrasonography confirms that the mare is in estrus, with a large follicle or recent ovulation present in one or both ovaries. The affected ovary is painful to palpation. It can often be difficult to be certain that colic in a mare identified during estrus is indeed caused by ovulation pain rather than a nonspecific or spasmodic colic. Further credibility is given to the diagnosis by demonstrating a low concentration of blood progesterone at the time of the colic and by documenting a cyclic recurrence of the colic episodes every 18 to 21 days, coinciding with the mare's estrus periods.

Affected mares usually respond well to intravenous treatment with analgesic doses of phenylbutazone or flunixin meglumine and intragastric administration of laxatives (e.g., mineral oil) to lessen the possible discomfort associated with defecation. Usually the signs resolve immediately with medication or within a few hours if the mare is left unmedicated. Long-term solutions include treatment with supplemental progesterone (altrenogest 0.044 mg/kg PO s.i.d.) to prevent ovulation during the physiologic breeding season (i.e., Spring and Summer). In extreme cases, where chronic medication is not possible and the mare has no potential value as a broodmare, ovariectomy could be considered.

Post-Ovulation Hematoma

Occasionally, the normal ovarian hemorrhage that occurs post ovulation to form the corpus hemorrhagicum is excessive and a large hematoma forms. These structures can become quite large (10 to 30 cm in diameter). The mare generally shows no clinical signs and continues to cycle normally as the hematoma slowly regresses over weeks to months.[2] Occasionally, however, affected mares may develop acute pain.[1] Ovarian hematomas have been reported in at least one mare to cause recurrent colic. Management is aimed at alleviating the mare's pain during the acute episode (as for ovulation pain). If a recurrent problem arises, the use of altrenogest as previously described to prevent ovulation during the physiologic breeding season may be considered.

Granulosa-Thecal Cell Tumor

The granulosa-thecal cell tumor is the most common ovarian tumor in the mare, and accounts for 2.5% of all equine neoplasms.[3] These tumors are usually benign, but often are hormonally active. Clinical signs vary, depending on the hormonal pattern of the tumor, but commonly include stallion-like behavior, nymphomania (prolonged periods of estrous behavior or shortened inter-estrus periods) or anestrus. Occasionally, the presence of a large tumor may result in intermittent colic, especially associated with exercise. Some affected mares may have a history of reluctance to train and/or poor performance.[1] It is likely that the pain associated with the enlarged ovary is the result of tension in the broad ligaments as the tumor moves with the mare's movements. Rectal palpation typically reveals the presence of one enlarged ovary that has lost its normal bean shape and a small, inactive contralateral ovary. Most granulosa-thecal cell tumors are 10 to 20 cm in diameter (although they may be larger). Ultrasonography can be helpful, although the ultrasonographic appearance of granulosa-thecal cell tumors is variable depending on their structure and composition. They may be uniformly echogenic, heterogenous with a honeycomb appearance, or largely hypoechoic or anechoic. Treatment is ovariectomy of the affected ovary. If surgery is not performed, the owner should be warned of the mare's possible future discomfort, and a small risk of hemorrhage from ruptured ovarian ligaments. Metastasis is rare.

Other Ovarian Tumors

Other ovarian tumors occur less frequently than granulosa-thecal cell tumours, but can be associated with abdominal discomfort. These include ovarian teratoma,[3] dysgerminoma,[4] and serous cystadenoma.[5]

Vaginal (Breeding) Injuries

Trauma to the vagina can result from breeding, especially in situations where the stallion's penis is long relative to the mare's vagina or the stallion is excessively forceful and vigorous during intromission and thrusting.[1,6] The severity of the damage can vary from bruising to lacerations to rupture where the stallion's penis penetrates into the peritoneal cavity through the cranial vaginal wall. Such injuries may be suspected when fresh blood is noted on the stallion's penis or draining from the vulva of the mare immediately after dismount. These findings warrant an immediate manual vaginal examination of the mare to ascertain the degree of injury. Sexual rest of the mare is indicated even if the damage is considered to be minor, as a full rupture may occur if the mare is covered again during that estrus period. Colic signs may be mild to severe, depending on the degree of damage, and are sometimes accompanied by tenesmus. Alternatively, the mare may develop signs of depression and endotoxic shock after the traumatic cover. A potentially severe peritonitis may occur after gross contamination of the peritoneal cavity by the stallion's penis, his ejaculate, or vaginal flora. Acute and severe colic signs may also develop if a portion of the mare's viscera becomes entrapped through the vaginal rent. Eventration of bowel or the urinary bladder may also occur.[7]

Treatment of minor injuries to the vagina includes sexual rest (30 to 60 days), broad-spectrum antibiotics, and a Caslick procedure to prevent further peritoneal contamination via possible pneumovagina. The rent in the vagina is usually small and dorsal to the cervix and is left to heal by secondary intention. The mare should be prevented from lying down for the first few days after the injury to reduce the risk of secondary herniation of viscera. If the rent is in the vaginal floor or if it is excessively large, an attempt to suture and close the defect should be made.

Pregnancy

Many pregnant mares show signs of abdominal pain intermittently during the course of gestation. These episodes are typically brief and mild. Such bouts of discomfort may be attributed to uncomfortable, vigorous movements of the foal, mild stretching of the broad ligaments upon the movement of the mare or the foal, or mild digestive upsets.[1] In most instances the signs resolve spontaneously.

Mares in late gestation may also be found lying down and groaning, which can be confused with colic. The large size of the gravid uterus in such late-term mares can put pressure on the diaphragm; this pressure increases when the mare lies down, thereby causing some difficulty in breathing and a groaning noise.

Uterine Torsion

Uterine torsion usually occurs before the end of gestation, generally within the last trimester.[8,9] Torsions from 180 to 540 degrees can occur in either direction, with the site of the twist usually being cranial to the cervix within the uterine body. Affected preterm mares typically present with signs of persistent/recurrent mild to moderate colic (restlessness, sweating, anorexia, frequent urination, turning the head toward the flanks and kicking at the abdomen).[10] The severity of the pain sometimes seems to be related to the degree of torsion, and in cases where bowel becomes entrapped by the twisted uterus, severe pain may be present. Occasionally, affected term mares present at parturition with dystocia caused by uterine torsion.

Diagnosis of uterine torsion is made by rectal examination as the twist is usually cranial to the cervix and, therefore, not readily palpable *per vaginum*. In normal late pregnancy, the broad ligaments are pulled tightly downwards in front of the pelvic brim by the gravid uterus. Torsion of the uterus causes asymmetry of these ligaments. The broad ligament from one side of the uterus is pulled over the top of the uterus past the midline toward the side of the direction of the uterine twist. The other broad ligament is pulled ventrally beneath the uterus and away from the side of the twist. Careful palpation will confirm the diagnosis, determine the direction of the torsion, and give some idea of the severity of the torsion. The compressive forces of the displaced broad ligaments may cause a degree of constriction of the small colon, which sometimes makes rectal palpation difficult.

The fetus will typically be displaced cranially in the abdomen by the twist in the uterine body and may be out of reach during rectal palpation. In this instance, fetal viability should be assessed by transabdominal ultrasonography. The blood supply to the uterus may become compromised enough to cause fetal death. The uterus may also become edematous and friable, and in some extreme cases necrotic, thereby leading to a risk of uterine rupture and peritonitis. Mild uterine torsions (180 degrees of twist or less) do not alter the color, cellularity, or protein concentration of the peritoneal fluid.[11]

Treatment options include rolling the mare,[12,13] performing standing flank surgery, ventral midline laparotomy, and in the case of foaling mares that have an open cervix and a less than 270-degree twist, manual rotation of the foal through the cervix to return the uterus to a normal position.[14]

Correction by rolling the mare under general anesthesia is controversial, and potential complications include displacement of the colon, worsening of the uterine torsion, placental detachment, and uterine rupture.[8,9] Two methods of rolling have been described. In both methods the mare is placed in lateral recumbency on the same side as the direction of the twist. The mare is then rolled from one side, into dorsal recumbency, and then over onto her opposite side and then into sternal recumbency. In the first method, this maneuver is done quickly with the thought that the weight and inertia of the heavily gravid uterus will hold it still while the mare is quickly rolled around it. In the second method, a plank is positioned in the mare's flank and weighted down by a person sitting or standing on it, and then the mare is slowly rolled over as previously described. The idea is to use the plank to hold the gravid uterus still as the mare is rolled carefully around it, effectively untwisting it. Once the maneuver has been completed, the mare is reexamined rectally to ascertain whether the uterus has been successfully untwisted. If the uterus is still in torsion, additional rolling attempts may be made.

When the mare is tractable and there is no indication of uterine rupture, correction can be accomplished via a standing flank laparotomy.[10] An incision is made through the mare's flank (preferably on the same side as the direction of the twist) using a grid approach. The uterine torsion is corrected by carefully reaching underneath the uterus, gently holding part of the fetus through the uterine wall, and gently rocking the fetus back and forth to gain momentum until it can be rotated. A combination of lifting and rotating movements usually results in correction of the torsion. If the pregnancy is advanced, a second incision may be required in the opposite flank to allow two surgeons to work simultaneously (one pushing and the other pulling) to untwist the uterus and return it to its normal position. After the torsion has been corrected, the surface of the uterus is carefully palpated for the presence of any tears (especially where it was twisted), and an assessment of fetal viability is made by trying to detect spontaneous fetal movement or the presence of a heart beat in the foal's chest. Usually, the uterus is not compromised, and slight discoloration and edema do not signify a poor prognosis for continued pregnancy. A cesarean section should not be performed, regardless of stage of pregnancy, because this would introduce risk of complications that could be avoided by uninterrupted gestation and natural delivery. If the foal is dead, the mare should abort naturally once the torsion has been corrected or delivery can be induced. However, the mare should be closely monitored and obstetrical assistance should be available to correct any malpositions. If the foal is alive and has not been compromised, the pregnancy usually progresses uneventfully and successfully to term after surgical correction. If derotation of the uterus via the flank approach is unsuccessful, the incision(s) should be closed and the procedure performed via a midline laparotomy with the mare placed under general anesthesia.

In the foaling mare, it may be possible to correct a uterine torsion per vagina provided the twist is less than 270 degrees and the cervix is dilated enough to permit the clinician to reach the foal and place his or her arm ventrolaterally along the foal's body. The foal is then grasped and manipulated so as to rock it from side to side progressively in the opposite direction of the twist until enough momentum is achieved to flip the foal up and over, taking the uterus with it to resolve the twist. Once the twist has been fully corrected and the foal repositioned as needed to achieve a normal presentation, the foal may be delivered.

A ventral midline celiotomy is indicated to correct uterine torsion when the uterus is already believed to be severely compromised or when the gastrointestinal tract has become entrapped by the uterine torsion. This approach is also indicated when other correction techniques have failed, and there is the advantage that a cesarian section can also be performed during the course of the procedure to facilitate delivery of the foal if needed. The risk of incisional complications after this procedure in a heavily gravid and subsequently foaling mare must be recognized.

The prognosis for uterine torsion depends on the degree of vascular compromise. Potential complications after resolution of the uterine torsion using any of the described techniques include rupture of the uterus and resultant peritonitis in the mare, and premature placental separation and subsequent death and abortion of the foal. The prognosis for both the mare and the foal is generally good provided no severe uterine damage or peritonitis have occurred. A chronic form of uterine torsion has been described as a cause of weight loss, anemia, fever, and mild colic. This can only be treated by ovariohysterectomy.

Dorsoretroflexion of the Uterus and Abortion

Dorsoretroflexion of the uterus is a rare cause of colic in the gravid mare (typically between 7.5 and 11 months of gestation).[1] Affected mares present with acute, moderate to severe colic signs, abdominal straining, constipation, and swelling of the vulva and perineal region. Administration of analgesics is typically ineffective in controlling the mare's pain.

Diagnosis is made by rectal palpation: a tense uterus is felt within the pelvis with the fetal head and limbs in a normal birth presentation overlying and obscuring the cervix. Vaginal examination is required to differentiate this condition from abortion. In the former case, the cervix will be closed in the cranial extent of the vaginal canal and ventral to the fetus, which is palpable dorsal to the vagina through the vaginal wall. In the aborting mare, the cervix will be dilated and the fetus and its membranes will be readily palpable within the vaginal canal through the dilated cervix.

Treatment of dorsoretroflexion of the uterus includes the administration of uterine relaxants (200 mg isoxsuprine IM or 200 μg clenbuterol slow IV or IM once or repeatedly over 3- to 6-hour intervals for 1 to 2 days), and repelling the relaxed uterus containing the fetus back into the abdomen via careful rectal manipulation. Resolution of colic signs usually occurs within 15 minutes of administration of the uterine relaxants, and it has been reported that restricting the mare's food intake and regular hand walking help to return the mare to normal within a few days.

Arterial Rupture

Rupture of a Major Vessel

Rupture of the middle uterine artery, uteroovarian artery, or the external iliac artery at or around the time of foaling is a significant cause of colic and death in older (> 11 years) multiparous mares.[15-22] The condition can also occur before foaling. Usually no evidence exists of a predisposing aneurysm, but an association with low serum concentrations of copper has been proposed as a reason for vessel fragility in aged mares. There appears to be a predilection for right-side uterine vessels.[16,19] Arterial rupture may occur after normal parturition or dystocia.[18,19]

The mare may be found dead or moribund with pale mucous membranes, tachycardia (up to 140 bpm), and tachypnea. If the bleeding is contained within the broad ligament, the mare may demonstrate signs of colic, sweating, tachycardia, tachypnea, pale mucous membranes, thready pulse, cool extremities, depression and weakness. Often these initial signs are mistaken for the typical discomfort experienced by postpartum mares as the uterus contracts (third stage of parturition). However, physical examination reveals pale mucous membranes with delayed capillary refill. These mares must be monitored closely as the hematoma can subsequently rupture out of the mesometrium and lead to rapid exsanguination.[16]

If a ruptured artery is suspected, the mare should be kept as quiet as possible and not stressed by the veterinary examination. Often, postponing palpation per rectum may be prudent. Although an internal examination will yield valuable diagnostic information, transabdominal ultrasound, abdominocentesis, and a hemogram may be all that is necessary to confirm that an acute hemorrhagic episode has occurred. If palpation is performed, the large firm swelling within the broad ligament is readily detected; palpation of the hematoma may be associated with a violent pain response by the mare.[23,24]

Transabdominal ultrasonographic evaluation will reveal free blood in the abdominal cavity if the hematoma and broad ligament have ruptured.[25] Abdominocentesis will yield blood or blood-stained fluid in such cases. If the hematoma is contained within the broad ligament without rupturing it, peritoneal fluid commonly shows increased total protein concentrations (up to 5.0 g/dL; 50 g/L), with a WBC count within the normal range (<5,000 cells/μL; < 5.0 x 10^9 /L).[11] The initial hemogram during an acute hemorrhagic episode can be confusing as the relative loss of erythrocytes and plasma may not immediately alter the hematocrit. Splenic contraction will also temporarily increase the hematocrit.[25] Over the following 12 to 24 hours, however, the hematocrit and total plasma protein concentration will decrease as the intravascular fluid volume is replaced.

If possible, affected mares should not be transported because movement could destabilize the clot, which could prove to be fatal. Any supportive therapy should be administered in the stall until the mare's condition has stabilized. The foal should be kept safely nearby so that the mare does not become unduly distressed. Removal of the foal will generally upset the mare, and can increase the risk of further hemorrhage.

Treatment of mares with uterine artery rupture that has resulted in extensive or uncontained hemorrhage is often unsuccessful. Surgical ligation is unlikely to be possible because of poor surgical access and the difficulty in actually finding the damaged arterial site within the large hematoma. Additionally, affected mares are poor anesthetic risks due to their poor cardiovascular status.

Treatment by volume expansion will aid tissue perfusion and counteract hypovolemic shock, but this will also lead to an increase in the mare's blood pressure, which may renew or worsen blood loss with potentially fatal results. The use of crystalloid fluids to effect volume expansion may also dilute blood coagulation factors and decrease blood viscosity at a time when

both are needed to promote hemostasis. As a direct result of this therapeutic challenge, there are two approaches to managing affected mares that survive the initial stages of the hemorrhage – one conservative, the other more aggressive.

The conservative approach involves minimizing stress or excitement of the affected mare. The mare is kept in a quiet, darkened stall. Tranquillizers are used judiciously as needed to help keep the mare calm and, with acepromazine, to help reduce mean arterial pressure directly. Naloxone (8-32 mg/500 kg, IV) has been anecdotally reported to be helpful in some mares.[18,24,25] Analgesics (butorphanol 0.01-0.04 mg/kg, IM) are also used as needed to control the mare's pain. Supplemental oxygen can be provided via nasal insufflation at a flow rate of 5 to 10 L/min.

The more aggressive therapeutic approach involves using all of the above treatments as well as volume expansion with crystalloid and/or colloid fluids to support tissue perfusion, and whole blood transfusions or synthetic oxygen-carrying fluids (oxyglobin) as indicated to support tissue oxygenation. It is important to remember that anemia is well tolerated provided blood volume is maintained, and that autotransfusion of approximately two thirds of the red blood cells lost into the abdominal cavity will occur over time. For this reason, whole-blood transfusion to affected mares is not advocated until the mare's PCV is less than 15% to 20%. If the hematocrit continues to decrease to that 15%, then whole-blood transfusions (6 to 8 liters over several hours) may be warranted.[25] Benefits include provision of oxygen-carrying cells, clotting factors, and oncotic pressure (albumin). A further consideration is that all mares must be carefully cross-matched with donor blood to avoid sensitization to incompatible blood types and possibly cause the occurrence of neonatal isoerythrolysis in future foals. In this regard, the use of synthetic oxygen-carrying fluids (Oxyglobin 7.5 to 10mL/kg) may have advantages over whole blood transfusion (see Chapter 17).

Serial blood samples from a mare that has recently hemorrhaged can be misleading if fluid therapy has been initiated. A decreasing hematocrit in these cases may be a result of the diluting effects of plasma expansion, and not necessarily of on-going blood loss.[25]

Hemostatic-promoting agents such as aminocaproic acid (10-20 mg/kg slowly IV), IV 10% formalin (anecdotal reports of efficacy), and conjugated estrogens have also been used. Anti-inflammatory agents (flunixin meglumine and glucocorticoids) as well as antioxidant drugs (Vitamin E) may lend supportive effects. Pentoxifylline (7.5 mg/kg PO) is purported to increase RBC deformability and may increase oxygen delivery to ischemic tissues, and therefore, may be of benefit.[25] Low-dose (10-20 IU) oxytocin therapy may be useful to promote uterine involution and thereby reduce the weight supported by the ligaments. Higher doses should be avoided as an induced colic episode may precipitate a fatal hemorrhage. Broad-spectrum antibiotics should be administered to prevent infection of the hematoma.[22]

Hemorrhage of the Uterine Wall and Pelvic Canal

Much of the caudal portion of the reproductive tract is supplied by the internal pudendal artery and the vaginal artery.[20,26] A hematoma arising from these vessels may dissect along the fascial planes within the pelvic cavity and present as a large unilateral vulvar swelling.[21] Affected mares typically show violent colic. Treatment involves the judicious use of analgesic drugs and anti-inflammatory agents. Abscessation of such retroperitoneal hematomas can become a life-threatening complication after dystocia, and thus prophylactic broad-spectrum antibiotic coverage is warranted.[19]

Third-Stage Labor

Stage III labor (passage of the placenta) normally causes some degree of discomfort and pain to the mare.[1] The signs associated with the uterine contractions that occur at this time range from mild discomfort (e.g., occasional kicking at the abdomen, stretching out and posturing as if to urinate, lying down quietly in sternal recumbency, or flank watching) to more dramatic signs of pain (e.g., agitation, frequently getting up and down, or rolling). The majority of mares pass their placentas within 30 to 60 minutes of the foal's delivery, but it is not unusual for signs of discomfort to persist (usually for no more than an additional hour) after passage of the placenta as uterine contractions continue as the mare's uterus begins to involute. Hand walking to provide the mare with relief and distraction from her discomfort may be helpful, but analgesic treatment is rarely necessary. Typically throughout these episodes, the mare's vital signs are stable, and she remains bright, with a good appetite and interest in her foal.

Perineal Injuries

Perineal damage (1st, 2nd, and 3rd degree perineal lacerations, vestibular bruising, hematomas, etc.) occurring during parturition can lead to a reluctance to defecate, secondary constipation, and low-grade colic. Anti-inflammatory drugs (phenylbutazone or flunixin meglumine) as well as local treatment with topical anti-inflammatory ointments are indicated to relieve pain and

swelling of affected tissues. Administration of oral laxatives (mineral oil) and laxative feeds (bran mashes, grass, etc) may help to soften the feces and make their passage less painful to the mare so that she is more willing to defecate.

Uterine Rupture

Rupture of the uterus at or near foaling can cause peritonitis and abdominal pain. Although tears in the uterine body are generally associated with dystocia, occasionally mares may sustain a uterine rupture during an uneventful foaling.[18] Large tears are likely to result in the rapid development of shock and signs of peracute peritonitis.[27] Occasionally visceral herniation may complicate the condition.[28] Any involved bowel should be examined and rinsed with sterile saline before being replaced. A ventral midline celiotomy may be warranted to fully evaluate the degree of intestinal damage, and repair the uterine laceration.

Tears that are not associated with dystocia tend to occur toward the tip of the gravid horn, and are often not detected until the mare develops clinical signs associated with peritonitis. Affected mares generally experience bouts of colic and become depressed, febrile, and anorectic as peritonitis develops. The interval from occurrence of the tear to diagnosis and initiation of therapy has a marked impact on the prognosis for survival.[11,19,21,24,29]

Diagnosis of uterine rupture is achieved by a combination of rectal palpation, ultrasonography, abdominocentesis, and direct palpation *per vaginum*. However, it may not be possible to ascertain uterine integrity by vaginal palpation alone.[21] The tips of the horns may be especially difficult to palpate from within the postpartum uterus. If a defect is detected, the clinician should be extremely cautious in exploring the laceration. A laceration that only extends into the myometrium can easily be converted into a full-thickness tear by injudicious palpation. In some instances, simultaneous palpation *per vaginum* and *per rectum* may be useful in evaluating the severity of a tear.[29,30] Laparoscopic evaluation of the uterus may confirm the diagnosis and provide useful information when determining whether surgery is indicated.[31]

If a uterine laceration (partial or full) is suspected, the mare should receive systemic broad-spectrum antimicrobials. Nonsteroidal anti-inflammatory medication may help to prevent the development of severe shock associated with endotoxemia. Oxytocin therapy (10-20 IU every 2 hours) promotes uterine involution. The dose can be increased if the mare does not become uncomfortable. Fluid therapy should be administered as necessary, ensuring that serum calcium concentrations are within the normal range. Intensive medical management may suffice for mares with small dorsal uterine tears.[29,31] Opinions vary on the need for, and usefulness of, peritoneal lavage.[31] Mares with large, full-thickness tears warrant surgical intervention. In some instances, the laceration can be sutured blindly in situ, but often a ventral midline laparotomy is the treatment of choice.[24,29,32,33]

Inversion of a Uterine Horn and Uterine Prolapse

Inversion of a uterine horn (intussusception) frequently results in acute pain within the first few hours after foaling, and often is unresponsive to administration of low doses of analgesics.[1] Pain is the result of the ovary and tip of one horn becoming inverted and entrapped within the uterine lumen. The myometrium proceeds to spasm resulting in an intussuscepted ring. In response, many mares begin to strain and the condition may progress to a complete prolapse of the uterus through the vulvar lips if left uncorrected.[24] Invagination of a uterine horn most commonly occurs in conjunction with a retained placenta. It may occur secondary to the weight of the placenta pulling on the horn in which it is retained and/or being suddenly pulled on during attempts at manual removal. Dystocia has also been cited as having a predisposing association with uterine prolapse.

Diagnosis of an inverted uterine horn is based on a rectal palpation finding of a blunted uterine horn with a tense mesovarium disappearing into the center of the blunted tip.[22,23,27] In minor intussusceptions, the ovary may not yet be entrapped and is still palpable at the tip of the blunted horn.[1] Palpation of this area is often painful to the mare and sedation is recommended. The inverted horn can also often be palpated *per vaginum* within the lumen of the uterus.

If possible, any retained placenta should be gently removed if it will come away readily so as to decrease the tension on the horn. However, if it cannot be easily detached, it may be preferable to cut off the majority of the exteriorized hanging placenta at a level just below the vulva so as to decrease the strain on the invaginating horn. Direct treatment and correction of the invaginated uterine horn includes controlling the mare's straining and pain (sedation, epidural anesthesia), manual reduction of the inverted horn *per vaginum* (may require the use of uterine relaxants such as acepromazine and clenbuterol), and full replacement of the previously invaginated horn and ovary to their normal position (manually or using intrauterine sterile saline to fully dilate the uterine horns). Supportive therapy in the form of intravenous fluids, NSAIDs, antimicrobials, and tetanus prophylaxis may also be indicated (especially in cases complicated by retained placenta). Careful use of low doses of oxytocin (10-20 IU IM) once the horn has been returned fully to its normal position may also aid in rapid normal involution and prevention of a recurrence.

If the invaginated tip is not identified and is left in place, necrosis may ensue. This is usually associated with a decrease in the mare's discomfort, but with the development of septic peritonitis. Surgical intervention is necessary in such cases.

Pain Associated with the Male Reproductive Tract

Orchitis

Orchitis is an inflammation of the testis, characterised by a painful, warm swelling of the affected testicle. It is generally traumatic in origin, resulting in sterile inflammation, and may be uni- or bilateral. Infectious orchitis is uncommon in the stallion, but may occur as a result of ascending infection (e.g., *Klebsiella pneumoniae*) or localization of systemic disease (e.g., *Streptococcus equi*). Penetrating wounds can result in localized swelling and abscessation. The affected testicle is often hot, painful, and tense because of swelling that is confined by the tunica albuginea. Superimposed edematus swelling in the scrotal skin makes palpation difficult. The stallion is likely to be febrile and may demonstrate colic-like signs of pain. Systemic antimicrobials, anti-inflammatory medication, and hydrotherapy are indicated, but often prompt unilateral orchiectomy is necessary to minimize damage to the contralateral testis.

Testicular Torsion (Torsion of the Spermatic Cord)

Acute testicular torsion is rare.[34,35] The condition is caused by torsion of the spermatic cord and results in signs similar to acute orchitis (severe colic, scrotal swelling, mild pyrexia). The condition is usually unilateral, but may be bilateral. The testicle is usually rotated by 180°, but can be rotated by 360° or more, with occlusion of spermatic vessels. The clinical signs depend on the severity of the torsion. In many cases, 180° torsions are subclinical, or the stallion may demonstrate mild, intermittent scrotal pain that becomes most pronounced during exercise. In contrast, 360° torsions, which are usually unilateral, generally cause acute severe testicular pain with scrotal edema and hemorrhage. Persistent colic and a stilted hind leg gait are observed. Obstruction of the venous drainage (pampiniform plexus) by a 360° torsion leads to hemorrhagic infarction of the testicle and severe edema. Arterial obstruction leads to ischemic necrosis of all ipsilateral scrotal contents located distal to the site of torsion.

Diagnosis of a 180° spermatic cord torsion is achieved by palpating the caudal epididymis (tail of the epididymis) and scrotal ligament within the cranial rather than the caudal scrotum. With a 360° torsion, these structures are located in their correct (caudal) location, but there is acute scrotal pain and unilateral swelling. The spermatic cord is thickened. The condition must be differentiated from inguinal or scrotal hernia, and palpation of the vaginal ring *per rectum* should be undertaken to establish the presence or absence of herniated intestine. Unilateral castration is indicated in most cases because of ischemic damage to the testis.

Thrombosis of the Spermatic Cord Vessels

This is a rare disease associated with thrombosis of vessels within the pampiniform plexus and the testicular artery.[35,36] The cause has not been established. The clinical signs are similar to those of 360° torsion of the spermatic cord. Definitive diagnosis is only achieved during exploratory surgery. Unilateral castration with excision of the cord proximal to the site of the lesion is required.

Pain Associated with the Urinary Tract

Urolithiasis

Most cases of obstructive urinary tract diseases in horses are caused by urolithiasis.[37,38] Incomplete obstruction of the urinary tract can cause dysuria, incontinence, and mild abdominal pain, whereas complete urinary obstruction results in moderate to severe pain.

Nephroliths develop around a nidus associated with a variety of renal diseases, including pyelonephritis and renal papillary necrosis. Although nephrolithiasis and ureterolithiasis are painful conditions in people, horses with these conditions often remain asymptomatic until bilateral obstructive disease leads to the development of chronic renal failure.[39] However, specific signs of upper urinary obstructive disease (i.e., colic, stranguria, hematuria) may be present in some horses. Diagnosis is based on rectal palpation, diagnostic ultrasonography, and clinical pathology.

Cystic calculi are the most common recognized form of urolithiasis in the horse.[37,40] The most common type of equine calculus is the spherical stone composed of calcium carbonate, having either a spiculated or smooth surface. Clinical signs may include hematuria, stranguria, pollakiuria, urinary incontinence, and low-grade, recurrent abdominal pain. Hematuria may be most obvious after exercise. Diagnosis is achieved by palpation and diagnostic ultrasonography of the bladder *per rectum*. Cystoscopy can also be helpful. Treatment involves surgical removal.

Urethral calculi are most commonly seen in male horses. These calculi probably originate in the bladder, and pass down the urethra until they lodge where the urethra narrows as it passes over the ischial arch. In some cases, the calculi may lodge further distally in the penile urethra. Complete urinary obstruction results, and this causes signs of colic with frequent straining and posturing to urinate. Rectal palpation reveals a distended, turgid bladder. The diagnosis is confirmed by passage of a urinary catheter or endoscope, which becomes obstructed by the urolith. Treatment of calculi lodged at the ischial arch involves removal via a perineal urethrotomy. Calculi lodged in the distal urethra can sometimes be grasped with forceps and crushed prior to removal. In some cases, surgical removal of the stone with the horse under general anesthesia is required.

If the bladder ruptures consequent to urethral obstruction by a calculus, signs of colic will disappear, but be replaced by progressive depression and anorexia due to post-renal acute renal failure.[40]

Cystitis

Cystitis is uncommon in horses.[41] It occurs most often secondary to conditions that cause urine stasis or urinary tract trauma. Cystitis is more common in females than males, probably because of the shorter urethral length in females. Predisposing conditions include trauma sustained at parturition, neurologic dysfunction of the bladder or urethra, and cystic calculi. The clinical signs include frequent urination, pollakiuria, tenesmus, and abdominal pain. Diagnosis is achieved by a combination of rectal palpation, diagnostic ultrasonography, cystoscopy, and urinalysis. Treatment involves the use of appropriate antimicrobial drugs and treatment of the predisposing cause.

Pyelonephritis

Inflammation of the renal parenchyma, calyces, and pelvis resulting from bacterial infection (i.e., pyelonephritis) is rare in the horse.[41] It has been described in association with urolithiasis, recurrent cystitis, and bladder paralysis. Concurrent nephrolithiasis or ureterolithiasis may be present. Affected horses generally present with fever, signs of depression, low-grade abdominal pain, inappetence, and weight loss. Hematuria or pyuria may be seen, but there is no stranguria or pollakiuria unless concurrent lower urinary tract infection is present. Diagnosis is achieved by a combination of rectal palpation, ultrasonography, urinalysis, ureteral catheterization, bacteriology, hematology, and serum biochemistry. Treatment involves prolonged courses of appropriate antimicrobials and treatment of any underlying disease. In selected cases, unilateral nephrectomy may be considered.

Bladder Rupture

Rupture of the urinary bladder is rare in adult horses, but has been associated with urethral obstruction (especially in males) and foaling trauma in mares.

Ruptured bladder and uroperitoneum are more commonly recognized in neonatal foals.[42,43] Although there are several different possible sites of urine leakage leading to uroperitoneum, including the urachus, ureter, and urethra, the most common site is the bladder. Colts and fillies can be affected, however, colts are more commonly affected.[42] The pathogenesis of uroperitoneum includes increased abdominal pressure during delivery, external trauma, infection within the urachus, or necrotic cystitis. Tears or defects within the bladder occur most commonly on its dorsal aspect.

Foals that develop uroperitoneum may not show clinical signs until they are 2 to 3 days of age. Clinical signs include progressive abdominal distention, tachycardia, tachypnea, depression, low-grade colic, and decreased interest in nursing. Although many foals have stranguria or oliguria, some affected foals will appear to urinate normally.

Diagnosis of uroperitoneum is made by a combination of physical examination, diagnostic ultrasonography, abdominal paracentesis, and clinical pathology. Percutaneous ultrasonography over the caudoventral abdomen usually shows excessive peritoneal fluid; a defect in the bladder wall may also sometimes be seen. Serum electrolyte abnormalities classically include hyponatremia, hypochloremia, hyperkalemia, and azotemia. The peritoneal fluid should be evaluated by cytology, as the presence of calcium carbonate crystals in the peritoneal fluid is a strong indication of bladder rupture. Creatinine concentrations in serum and abdominal fluid also should be compared. The diagnosis can be confirmed when the creatinine concentration of the abdominal fluid is twice that of the serum concentration.

Treatment of foals with uroperitoneum almost always requires surgical repair of the defect. However, stabilization of the electrolyte and acid-base abnormalities must be performed prior to surgery to prevent anesthetic complications or even

death. Medical stabilization should include drainage of the excessive abdominal fluid, either through a teat cannula or small chest trocar. Replacement fluids should be administered intravenously to correct hypovolemia and electrolyte abnormalities. Normal saline can be administered with dextrose to combat hypoglycemia and promote intracellular movement of potassium (see Chapter 17). Severe or nonresponsive hyperkalemia can also be treated by intravenous administration of calcium or subcutaneous injection of insulin.

Liver Diseases

Diseases of the liver are discussed in Chapter 35.

The Pancreas

Acute Pancreatitis

Acute pancreatitis is a rare cause of severe abdominal pain in horses.[44] The cause is uncertain, and antemortem diagnosis is rarely made because the clinical signs mimic other gastrointestinal diseases producing acute colic (especially small-intestinal strangulating obstructions and proximal enteritis). The pancreas is not easily visualized during routine surgical exploration of the abdomen and may be overlooked at necropsy, especially if gastric rupture has occurred.

The precise cause of acute pancreatitis often remains undetermined; however, it can sometimes occur in association with hyperlipemia. It has been speculated that excess lipid is deposited in and around the pancreas in hyperlipemia. This lipid is subsequently hydrolyzed by pancreatic lipase, and released as free fatty acids. Free (unbound to albumin) fatty acids are cytotoxic and, when the albumin-binding capacity is exceeded, pancreatic vascular injury occurs, resulting in necrotizing pancreatitis.

The clinical signs of acute pancreatitis in adult horses include severe abdominal pain, hypovolemic shock, tachycardia, tachypnea, pronged capillary refill time, sweating, cold extremities, and gastric distension with voluminous nasogastric reflux. Specific diagnostic features are not evident from the clinical signs or clinical pathology findings. Abdominal sounds are variable but are often reduced or absent. No specific abnormalities are detected by rectal examination. Peritoneal fluid may be serosanguinous or frankly hemorrhagic.

Most affected horses appear to die within 24 hours. No specific therapy apart from symptomatic treatment for abdominal pain and hypovolemic shock has been described.

Chronic Pancreatic Disease and Insulin-dependent Diabetes Mellitus

Insulin-dependent diabetes mellitus is rare in horses. However, adult horses and ponies may develop signs of exocrine pancreatic insufficiency, with or without associated insulin-dependent diabetes mellitus, after destruction of the pancreas by diseases such as neoplasia (pancreatic adenocarcinoma) and chronic pancreatic necrosis. Chronic eosinophilic pancreatitis has been reported, and is assumed to be caused by parasite (*Strongylus equinus* and *S. edentatus*) migration through the gland.[45,46] The clinical signs associated with chronic pancreatic disease may include chronic weight loss despite good or increased appetite, depression, inappetence, intermittent colic, persistent or recurrent pyrexia, and jaundice. If insulin-dependent diabetes mellitus is concurrent, polyuria and polydipsia may also be observed.

Clinical pathologic abnormalities are inconsistent, but may include the following: increased serum concentrations of amylase and lipase, increased peritoneal fluid amylase concentrations, hypocalcemia, hyperglycemia, glucosuria, hypertriglyceridemia, increased serum gamma glutamyl transferase, and hyperbilirubinemia. Reference values for amylase and lipase activities should be established by each laboratory.[47] Serum amylase activity for normal horses usually ranges from 14 to 35 units/L; values less than 50 units/L are generally considered to be normal. Peritoneal fluid amylase activity is usually slightly lower than serum activity. Serum lipase activity is normally less than 87 units/L.

Interpretation of pancreatic enzyme activity in horses can be difficult because the enzymes are not exclusively of pancreatic origin and may be released from other tissues such as the gastrointestinal tract. In addition, renal disease may result in decreased excretion of amylase and, therefore, lead to increased serum activities. In the diagnosis of acute pancreatitis, secondary damage to the pancreas from hypovolemia or reflux of duodenal contents up the pancreatic duct can result in release of pancreatic enzymes into the circulation.

The diagnosis of insulin-dependent diabetes mellitus can be confirmed by performing either an oral glucose tolerance test or intravenous glucose tolerance test. The intravenous glucose tolerance test is performed by administering glucose

intravenously (0.5 g/kg) as a bolus (e.g., 40% or 50%), and collecting blood samples at times 0, 15, 30, 45, 60, 120, 180, and 240 minutes for glucose and insulin estimations. Insulin-dependent diabetics will have high plasma glucose concentrations, which fail to decrease as fast as normal, with little increase in insulin concentrations. Confirmation of chronic pancreatitis or pancreatic carcinoma is generally made either at exploratory laparotomy or at postmortem examination.

Owing to the difficulties in diagnosing chronic pancreatic disease in the horse, treatments have rarely been attempted. Once the horse has developed insulin-dependent diabetes mellitus because of the destruction of the islets of Langerhans, the only effective treatment is the exogenous administration of insulin. The insulin dosage should be assessed by monitoring the response to small doses administered initially, and then gradually adjusting the dosage.

The Spleen

Primary diseases affecting the equine spleen are rare. The most common clinical disease that involves the spleen is renosplenic entrapment of the large colon (left dorsal displacement of the colon; (see Chapters 21 and 38). Other reported splenic conditions include splenic abscess and hematoma, splenic rupture, and neoplasia.

Splenic Abscess

Splenic abscesses may be confined to the spleen or arise in association with other abdominal abscesses.[48] Such abscesses usually cause signs of weight loss, inappetence, fever, and variable abdominal pain. Commonly identified clinicopathologic abnormalities include leukocytosis, neutrophilia, hyperfibrinogenemia and hyperglobulinemia. Total bilirubin concentrations may be increased because of inappetence. Peritoneal fluid often has an increased total protein concentration and an increased nucleated cell count with increased percentage of neutrophils. Free or intracellular bacteria may also be observed on cytologic examination of the fluid. Peritoneal fluid should be submitted for bacteriologic culture; commonly identified organisms include *Streptococcus equi subspecies equi*, *Streptococcus equi* subspecies *zooepidemicus*, *Salmonella* species, *Clostridium* species, *Bacteroides* species, and *Corynbacterium pseudotuberculosis* (the latter is confined to specific geographical locations such as the western United States).

Splenic abscesses may be palpable *per rectum* and may be visible by ultrasonography. They may also be visualized using laparoscopy. Treatment may include long-term antimicrobial therapy (based on the results of culture if possible), drainage of the abscess (surgically or using ultrasonographic guidance) or splenectomy. Splenectomy is usually carried out via a flank incision involving resection of the 16th or 17th rib; this approach often involves penetration of the diaphragm and the thoracic cavity.[49]

Splenic Rupture

Splenic rupture is rare in horses. It may arise secondary to direct trauma (e.g., kicks or vehicular accidents) or may be associated with a primary disease involving the spleen, such as hematoma or neoplasia. Most of the reported cases have involved rupture of the visceral surface of the spleen. In many cases, the affected horse is found dead as a result of exsanguination. Clinical signs in less severe cases include signs of hypovolemic shock (weakness, trembling, sweating, dyspnea, pale mucous membranes, tachycardia) and colic. Diagnosis is aided by the identification of hemoabdomen by abdominal ultrasonography and abdominocentesis. Treatment is supportive (i.e., therapy for hemorrhagic and hypovoemic shock), followed, if appropriate, by splenectomy.

Splenic Hematoma

Like splenic rupture, splenic hematoma is uncommon in horses, although transient hematomas secondary to trauma may be present subclinically. Large hematomas may be associated with abdominal pain. Diagnosis may be achieved by ultrasonography, rectal palpation, or laparoscopy. Treatment is supportive.

Pain Associated with the Respiratory Tract

Pleuritis and Pleuropneumonia

Primary pleuritis (i.e., pleuritis unassociated with underlying pulmonary disease) is unusual, but may arise from penetrating thoracic trauma. More commonly, pleuropneumonia develops secondary to bacterial pneumonia, with extension of the infection into the pleural space.[50] The history of horses with pleuropneumonia often includes events or factors that suppress pulmonary defense mechanisms (such as viral respiratory infection, long-distance transportation, general anesthesia, and strenuous exercise).[51]

Horses with bacterial pleuropneumonia usually present with fever, depression, lethargy, and inappetence. Many horses demonstrate signs of pleural pain (pleurodynia), respiratory difficulty, and endotoxemia. Horses with pleural pain have an anxious facial expression, stand with their elbows abducted, and are reluctant to move, cough, or lie down. Affected horses walk with a stiff, stilted gait, and some will grunt in response to thoracic pressure, auscultation, or percussion. These signs may be mistaken for signs of abdominal pain. The severity of respiratory difficulty depends on the volume of effusion and the extent of pulmonary consolidation. In most cases, the respiratory pattern is characterized by rapid, shallow breaths as a result of pleural pain and restricted pulmonary expansion by pleural effusion. A plaque of sternal edema is observed in horses with a large volume of pleural effusion.

Auscultation of horses with pleuropneumonia reveals a lack of breath sounds in the ventral lung fields and abnormal lung sounds (often crackles) in dorsal lung fields. Cardiac sounds may be muffled or absent, or may radiate over a wider area. Although uncommon, pleural friction rubs are most prominent at end-inspiration and early expiration, and are detected in horses with peracute disease (prior to development of effusion) or after thoracic drainage. Identification of dull areas on thoracic percussion indicates pulmonary consolidation, abscessation, or pleural effusion. Horses with pleural effusion typically have a horizontal fluid line, below which all pulmonary fields are dull, and above which resonant sounds are produced. Horses with pleurodynia object to this procedure, and may grunt in response to examination.

Clinicopathologic abnormalities vary with the stage and severity of disease. In horses with peracute pleuropneumonia, laboratory findings reflect bacterial sepsis or endotoxemia, and include abnormalities such as leukopenia, neutropenia, left shift, hemoconcentration, and azotemia. Horses with more stable disease have leukocytosis, mature neutrophilia, hyperfibrinogenemia, hyperglobulinemia, hypoalbuminemia, and anemia.

Ultrasound examination can identify gas echoes, fibrin, loculation, and fluid within the pleural space. Transudative pleural fluid (peracute pleuropneumonia, neoplastic effusion) appears anechoic, whereas more cellular exudate appears echogenic. Ultrasonographic evidence of large areas of pulmonary consolidation, in conjunction with serosanguinous suppurative pleural effusion, is consistent with pulmonary infarction and necrotizing pneumonia.[52]

Thoracocentesis is performed for diagnostic and therapeutic purposes in horses with pleuropneumonia. Malodorous pleural fluid is associated with necrotic tissue and anaerobic infection and indicates a more guarded prognosis. Serosanguinous pleural fluid has been observed in horses with necrotizing pneumonia, pulmonary infarction, thoracic trauma, and thoracic neoplasia. Thoracocentesis samples are submitted for cytologic evaluation (EDTA), anaerobic-aerobic bacterial culture and sensitivity, Gram stain, and biochemical analysis. Polymicrobial and mixed anaerobic-aerobic infections are common. Aerobic bacteria are isolated in more than 90% of cases, and the most common organisms are *Streptococcus zooepidemicus*, *E. coli*, *Actinobacillus* species, *Klebsiella* species, *Enterobacter* species, *Staphylococcus aureus*, and *Pasteurella* species.[51] Anaerobic bacteria are isolated from 40% to 70% of horses with pleuropneumonia and include *Bacteroides* species, *Clostridium* species, *Peptostreptococcus* species, and *Fusobacterium* species.

Medical therapy for bacterial pleuropneumonia requires broad-spectrum antimicrobial therapy, anti-inflammatory drugs, and supportive care.[52] The combination of penicillin, gentamicin, and metronidazole is often used for initial therapy. The antimicrobial regimen may require adjustment as the results of bacterial culture and sensitivity become available. Intravenous administration of antimicrobials is preferable in the early stages of treatment (i.e., first 14 to 28 days) to ensure adequate drug concentrations. Oral antimicrobial therapy can be instituted as the horse becomes more stable and production of pleural fluid subsides. Thoracic drainage using repeated thoracocentesis or indwelling thoracic drains is helpful in most cases.

Some horses fail to clear the pleural infection over the course of weeks to months despite antimicrobial therapy and drainage via indwelling chest tubes. Thoracostomy allows manual removal of organized fibrinous material and necrotic lung, and is sometimes needed in chronic cases that fail to respond to more conservative treatments. Two options exist for creating a thoracostomy in horses with pleuropneumonia: a rib resection or dissection through the intercostal space (i.e., finger-hole). The intercostal approach heals more quickly and usually allows adequate drainage, but manual access to the thoracic cavity is limited and resection of necrotic lung is difficult. Rib resection creates a larger defect for more effective drainage and debridement, but heals more slowly, is more painful after surgery, and may develop a chronic draining tract. Both procedures are performed in standing, sedated horses, using local anesthesia. Postoperatively, debris can be removed from the pleural cavity by manual debridement and lavage (sterile, isotonic fluids) on a daily basis. After adequate granulation of the incision (7 to 10 days), hydrotherapy of the wound and thorax can be performed with tap water.

Pain Associated with Cardiovascular Disease

Arterial Rupture

Rupture of the aorta is uncommon, but has been associated with an aneurysm and/or rupture and aortopulmonary fistula, and aortic ring rupture.[53] These vascular accidents may result in sudden death or, less commonly, in signs of acute thoracic pain.

Aortoiliac Thrombosis

Thrombosis of the terminal aorta and its major branches (the iliac arteries) is an unusual condition of unknown etiology that can result in exercise-associated pain and lameness or stiffness that disappears with rest.[54] The disease is associated with the development of a thrombus at the aortic quadrification with secondary embolization of the vascular tree of the hind limbs. The clinical signs are variable. The course of the condition can be chronic, with initial signs of vague hind-leg lameness. As larger vessels become involved, more severe clinical signs appear, including exercise-induced stiffness, weakness, and pain. Signs are usually asymmetric and resolve with rest. Clinical examination immediately after exercise may reveal a cold limb, but this sign is inconsistent. Occasionally, horses present with an acute and severe problem with marked pain, sweating, and severe lameness. Diagnosis is aided by palpation of the peripheral pulses, rectal palpation, and ultrasonography.

Pain Associated with the Musculoskeletal System

Severe musculoskeletal pain, as may occur with acute laminitis, exertional rhabdomyolysis, and atypical myoglobinuria may all produce signs that can, at least initially, be confused with colic. However, careful clinical examination will usually reveal the musculoskeletal system to be the site of pain rather than the abdomen.

Exertional Rhabdomyolysis

Horses with exertional rhabdomyolysis usually present with stiffness, sweating, and distress during or after exercise.[55] Affected horses may stretch out as if to urinate, become reluctant to move, and in severe cases, become recumbent. Attempts to move affected horses may result in their experiencing severe pain and anxiety. The affected muscles (commonly the back, hindlimb, and shoulder muscles) are often firm and painful when palpated. Myoglobinuria may be present in severe cases.

The diagnosis of exertional rhabdomyolysis is achieved by a combination of the history (the disease usually follows exercise or exertion) and clinical findings. Confirmation of muscle damage can be achieved by measuring serum concentrations of creatine kinase (CPK) and aspartate aminotransferase (AST).

Atypical Myoglobinuria (Atypical Myopathy)

Atypical myoglobinuria is more likely to be confused with colic than exertional rhabdomyolysis because of the absence of any history of preceding exercise. This is an unusual form of acute myopathy, of unknown etiology, that affects grazing horses, usually less than 6 years of age.[56,57] The clinical syndrome is characterized by sudden onset of stiffness, weakness, and sometimes recumbency, with passage of dark brown urine. Affected horses may be found recumbent and unable to rise, and may initially look as if they are suffering from colic. However, on careful examination most will not appear to be in distress or pain. Adverse climatic conditions often occur prior to an outbreak, and clinicopathologic evaluations reveal markedly increased serum concentrations of CPK and AST. Treatment is supportive, but the condition carries a high mortality rate.

Prepubic Tendon Rupture and Ventral Body Wall Hernias

Rupture of the prepubic tendon or other abdominal wall musculature is most commonly seen secondary to trauma or to the stress of the weight of a normal or abnormal pregnancy (e.g., hydrops or twins). The pain demonstrated by the affected mare is a direct result of the tearing of the abdominal support structures and/or the possible herniation and strangulation of bowel through the rents.

The prepubic tendon attaches to the cranial border of the pubis. Pregnant draft mares and older mares close to term may be predisposed to prepubic tendon rupture. In some cases, rupture may lead to hemorrhage, shock, and death.[24] More commonly, affected mares demonstrate pain, reluctance to move, and ventral edema. If the prepubic tendon is ruptured, the pelvis will appear tilted, and the mammary gland may be displaced cranially and ventrally as a result of the loss of the caudal attachment to the pelvis.[58] The pain associated with such ruptures can cause tachycardia and tachypnea. Confirmation of the diagnosis is not always easy. Palpation of the defect *per rectum* is usually not possible because of the advanced stage of pregnancy. External palpation is hindered by the thick plaque of subcutaneous edema. Ultrasonographic examination may be helpful in some cases. Often, an accurate assessment of the size of the defect cannot be made until the mare has foaled.

In most cases, treatment is aimed at managing the mare until term in order to salvage a viable foal. Anti-inflammatory drugs should be administered to keep the mare comfortable. The mare should have stall rest and only allowed gentle walking exercise. An abdominal sling or bandage can be applied to attempt to provide support. Since the mare is likely to experience difficulties during parturition (because of her inability to mount sufficient abdominal pressures to expel the fetus), assisted delivery should be anticipated. Surgical repair is unlikely to be possible or successful (see also Chapter 43).

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Abdominal Injuries

Chapter 43

John F. Peroni

The diagnostic approach and management of abdominal injuries in horses represents a clinical challenge. Injuries can range from uncomplicated external trauma without visceral involvement to severe penetrating or nonpenetrating injuries involving major abdominal organs. Timely identification of internal damage represents the most challenging aspect of managing horses with abdominal injuries. This is particularly true in horses with blunt injury when obvious abdominal wounds are not present.

Abdominal injuries can be of different etiologies and may involve the abdominal wall alone or abdominal viscera such as intestine and portions of the urinary and reproductive tracts. Intraabdominal injuries commonly occur in mares during parturition. These injuries can occasionally be fatal or may result in mesenteric tears, intestinal injury, and hematoma formation, leading to colic-like symptoms.[1-3] Prepubic tendon rupture and injury to the uterus can also occur in the parturient mare.[4,5] Penetrating trauma may result from horses impacting sharp objects or from gun shot wounds or may be iatrogenic.[6,7] As an example, injury to the abdominal wall blood vessels has been reported to occur during the percutaneous placement of trocars during laparoscopy.[8]

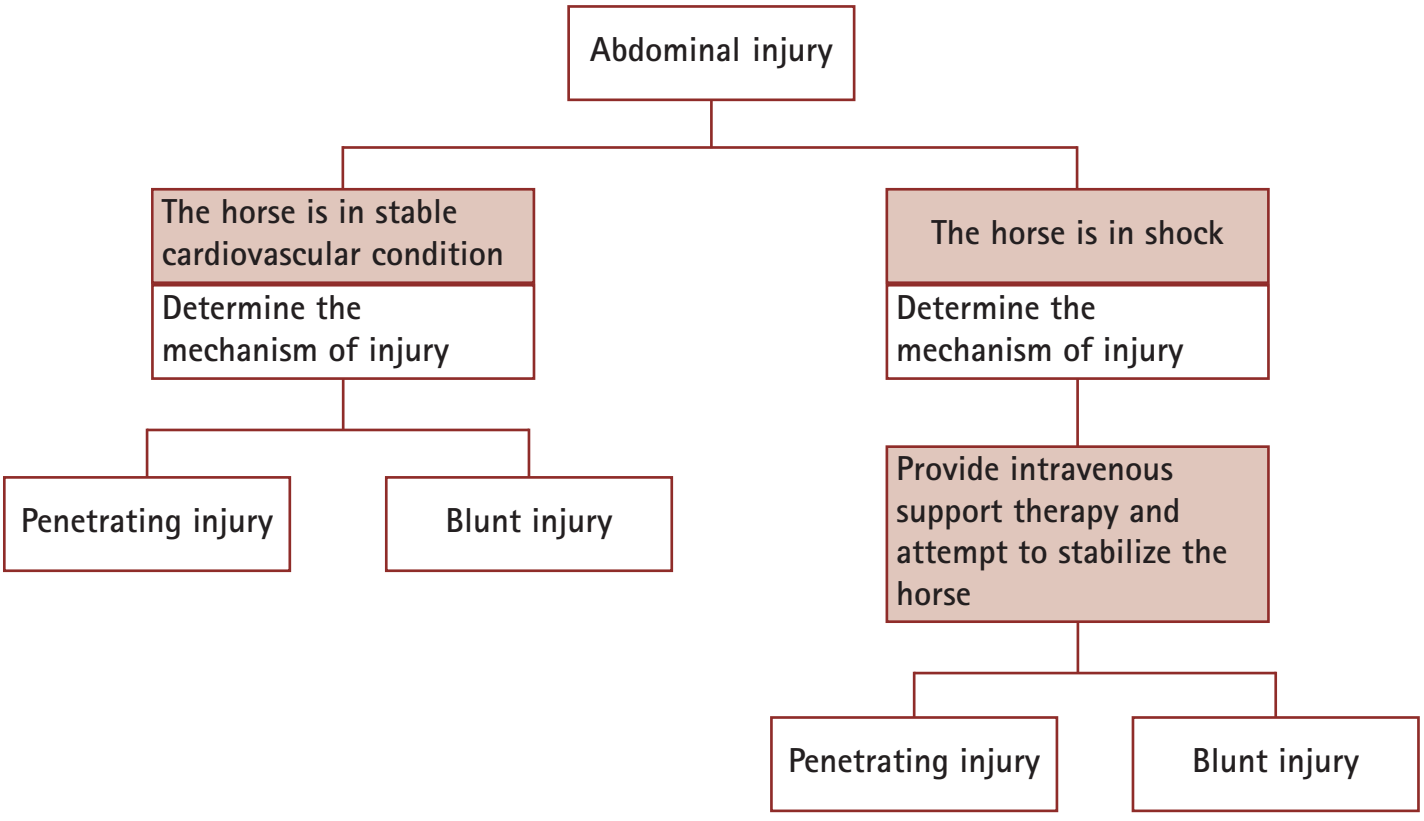
Initial evaluation and treatment of the horse depend on the mechanism of injury (i.e., penetrating or blunt) and on the hemodynamic status of the horse. The priorities for evaluating and treating horses with penetrating injuries differ from those for horses that have sustained blunt trauma because the respective patterns of injury are markedly different. Penetrating trauma typically results in an externally localized injury that may lead to massive abdominal contamination if the gastrointestinal tract is injured or penetrated. Conversely, blunt trauma may result in injuries that involve several organs. Regardless of the mechanism of injury, it is critical that hypotension and hypovolemia are identified and appropriate treatments initiated promptly to increase the horse's chance for survival.

Diagnostic Approach

The diagnostic approach to horses with abdominal injuries may be facilitated by following an algorithmic approach. One of the first priorities is to determine whether the horse is in a stable cardiovascular condition and if the injury is open or closed (Figure 43-1).

Subsequently, the type of injury will dictate further diagnostic and therapeutic decisions that must be considered.

Figure 43-1



Algorithmic approach to assessing a horse with an abdominal injury prior to initiating specific trauma therapy.

Physical Examination

Most horses with abdominal injury exhibit varying degrees of colic-like signs, the intensity of which range from mild to intense. Pain may result from the injury itself or from the presence of free blood in the abdomen, which causes distention and chemical peritonitis. Hemorrhage associated with an organ, as in the case of splenic hematoma, or involving support structures (e.g., broad ligament, mesentery) will also be accompanied by signs of pain.[9] Blood losses exceeding 25% of the horse's blood volume will result in clinical signs of restlessness, recumbency, and pawing, which can be confused with colic. Inconsistencies in the clinical picture, such as marked tachycardia associated with mild and intermittent abdominal pain, should alert the clinician to the possibility that the underlying problem may not be gastrointestinal in origin.

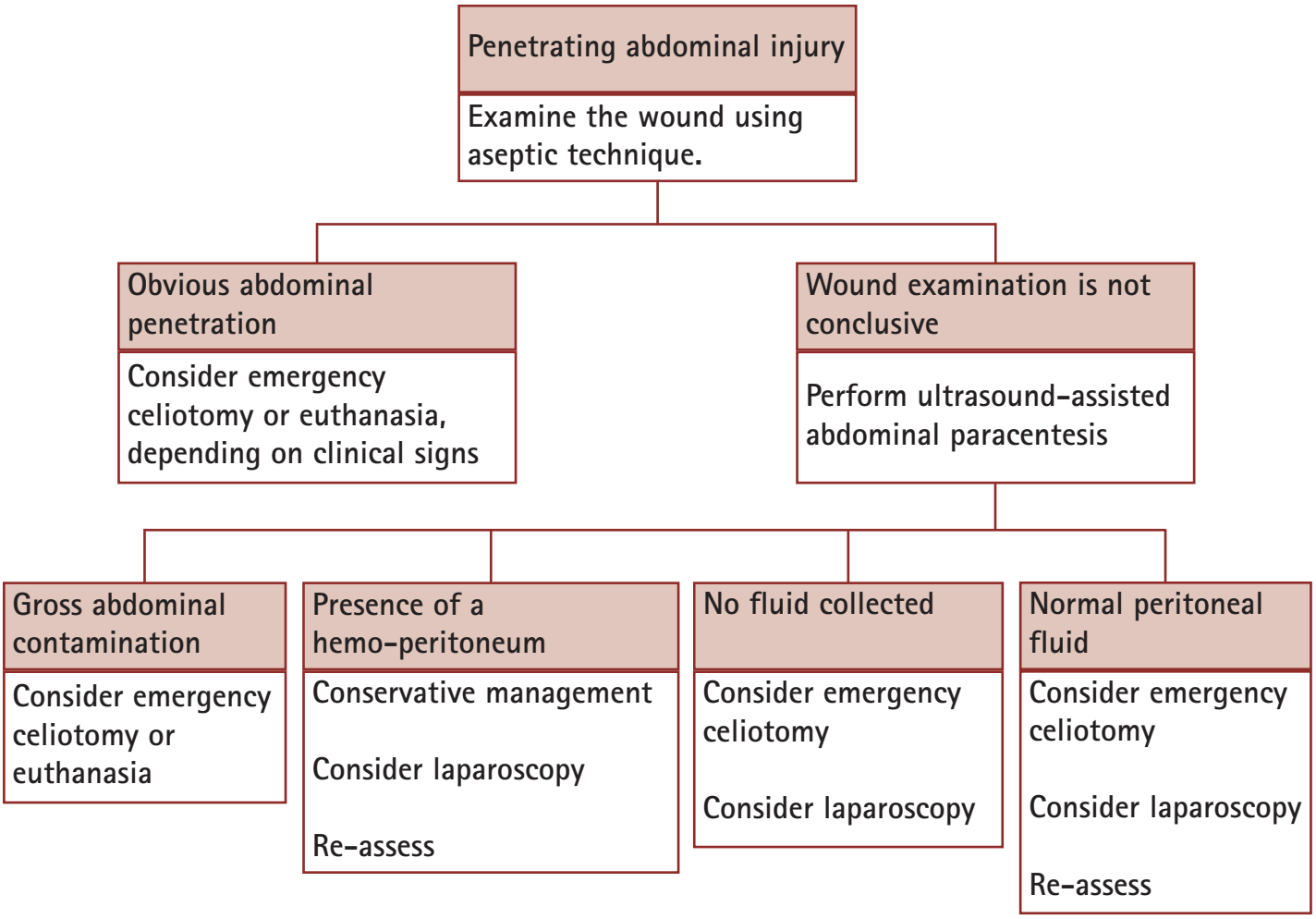
Evidence on physical examination of dehydration and hypovolemia accompanied by tachycardia and tachypnea indicate the presence of circulatory shock, and call for aggressive supportive therapy. Shock may result from one or more of the following: violent circumstances surrounding the injury (traumatic shock), acute blood loss (hemorrhagic shock), or visceral rupture (endotoxic shock). Catecholamine release and sympathetic stimulation result in peripheral vasoconstriction and splenic contraction, leading to pale mucous membranes and cold extremities (limbs, ears, and muzzle). As a result of splenic contraction, initial values for packed cell volume and plasma protein may be normal and will be unreliable indicators of the severity of blood loss. In fact, within the first 24 hours, the packed cell volume may be increased transiently owing to the release of erythrocytes from the spleen. Decreased capillary hydrostatic pressure will also allow fluid to move into the vascular space, assisting in the temporary restoration of blood volume.

Wound and Abdominal Examination

A thorough assessment of the wound is critical, particularly if a penetrating abdominal injury is suspected. The diagnostic approach should be directed toward determining whether the abdominal cavity has been penetrated, and if so, which of the abdominal organs has been injured (Figure 43-2). Thus, if the entry point is near the diaphragmatic reflection, the horse should be examined for possible thoracic injury. A thoracic radiograph may be helpful to identify either pneumothorax or hemothorax.[10] Examination of the wound should be carried out via careful digital palpation using aseptic technique. An abdominal wound may not necessarily correlate with abdominal penetration and care should be taken not to inadvertently penetrate the peritoneum while examining the site of injury. Although local anesthesia may facilitate the examination, ventrally located wounds can be edematous and painful to the touch, thereby complicating completion of the examination. If obvious evidence of abdominal penetration exists, the horse should be prepared for emergency celiotomy. When the findings of the external examination are inconclusive, additional diagnostic measures are warranted.

Abdominal paracentesis is an important part of the diagnostic work-up, and obtaining a representative sample of peritoneal fluid may greatly facilitate the diagnostic process. The use of transabdominal ultrasonography during collection of peritoneal fluid offers several advantages: Fluid can be identified ultrasonographically and sampled accurately without risking inadvertent perforation of an abdominal organ. Avoidance of abdominal organs during the paracentesis also facilitates interpretation of the laboratory results. Ultrasonography also may allow detection of excessive free fluid (e.g., hemoperitoneum) and identification of free-floating fibrin or fibrinous tags on serosal surfaces (peritonitis). Abdominal ultrasonography has been used to determine the size and location of splenic hematomas in horses.[11,12] The superficial location of the spleen renders this organ prone to blunt trauma such as kicks from other horses. More invasive diagnostic procedures may be warranted, particularly if the result of peritoneal fluid analysis is inconclusive or a sample cannot be obtained.

Figure 43-2



Algorithmic approach to assessing a horse with a penetrating abdominal injury.

Laparoscopy

The use of laparoscopy in horses with abdominal injury has been reported and is becoming more useful as surgical methods are refined and more surgeons gain experience with the technical aspects of the equipment and the proceedure.[13] When performed in the standing horse, laparoscopy may yield conclusive information, thus avoiding the risks of general anesthesia. This is especially useful in animals requiring treatment for shock. An exploratory celiotomy may be required after laparoscopy, either because the clinician fails to recognize an abnormality or the abnormality cannot be addressed via laparoscopy.

Reports present in the human literature document a reduction in hospital stay in patients with negative laparoscopic findings compared with patients with negative celiotomy findings.[14] In those studies, reduced hospitalization correlated with a significant reduction of the overall costs. Similarly, use of laparoscopy in horses can avoid the aftercare and the expenses associated with celiotomy. In humans, the use of laparoscopy in abdominal injury has been advocated as either a screening, diagnostic, or therapeutic tool.[15] In horses, laparoscopy is a useful screening and diagnostic tool to exclude or detect specific abdominal problems, such as hemoperitoneum, splenic injury, and intestinal perforation, and to confirm peritoneal penetration. In horses with blunt injury, laparoscopy may be useful in determining the source of abdominal hemorrhage when conservative management fails to improve the hemodynamic status of the horse and the cause for the symptoms remains unclear. When the external features of an abdominal wound are equivocal, laparoscopy can confirm or exclude peritoneal perforation. Injury to the upper abdominal quadrants can be assessed in the standing horse.

Laparoscopy can play a useful role in case of injuries requiring celiotomy. General anesthesia and emergency celiotomy are elected when the abdominal wall is structurally disrupted without the presence of a laceration. In such cases, the surgeon can explore the abdomen laparoscopically before proceeding to an exploratory celiotomy. The laparoscopic examination of the peritoneal aspect of a wound may suggest an approach to the abdomen different from the standard ventral midline celiotomy, thereby targeting the abdominal incision to a location that best suits the individual case (e.g., away from contaminated areas).

The assessment of ventrally located abdominal lacerations can be problematic because of the rapid development of dependent edema, which complicates the external evaluation of the wound. In addition, the planes of the subcutaneous fascia and of the abdominal musculature may ride over each other when the force of impact is tangential to the abdomen. This produces a disruptive and disorganized pattern of injury, making it difficult to determine whether the abdomen has been penetrated. With the horse under general anesthesia, the laparoscope can be placed distant from the area of injury, allowing a safe assessment of the visceral surface in the region of the wound. This evaluation may help the surgeon decide whether an open procedure is needed. This may allow the surgeon to avoid the potential complications and extended recovery period associated with celiotomy incisions. Table 43-1 summarizes laparoscopic applications in abdominal injury.

Table 43-1
Uses of Laparoscopy in Abdominal Injury

Diagnose hemoperitoneum
Detect source of hemoperitoneum
Identify mesenteric hematoma
Detect injury to the spleen, liver, and kidneys
Identify diaphragmatic hernia
Locate abdominal penetration
Detect intestinal perforation
Perform intraabdominal assessment of the peritoneal aspect of a ventrally located wound
Screen injuries prior to celiotomy.

Therapeutic applications of laparoscopy in horses with traumatic injuries are less obvious. However, in horses, certain operations such as diaphragmatic hernia repair, targeted abdominal drain placement, and hemostatic procedures involving the mesentery may be easier to perform laparoscopically because of the improved visibility compared with open techniques.[16] Laparoscopy alone does not represent the gold standard in the clinical approach to abdominal trauma in horses. Nonetheless, its use in combination with diagnostic modalities, such as abdominal ultrasound and paracentesis, can add valuable information to the diagnostic process. In addition, the use of laparoscopy prior to celiotomy in the assessment of ventral abdominal trauma can help the surgeon assess the peritoneal injury, target the open approach, or simply avoid a celiotomy.

Treatment

Treatment of abdominal injury should be conservative at first unless abdominal penetration is obvious, in which case an emergency celiotomy (with or without laparoscopy) is a necessary choice. Injured horses should be treated as needed for the systemic effects of trauma with intravenous fluid therapy and nonsteroidal anti-inflammatory drugs. Additional resuscitative measures may be warranted, such as the administration of hypertonic (7.2%) saline solution (5mL/kg) to correct severe dehydration and restore cardiovascular function (see Chapter 17). As with any wound, a tetanus booster or antitoxin should be administered.

Debridement of abdominal wounds is done with care to avoid inadvertent penetration of a compromised abdominal wall. Fresh wounds should be closed primarily, although in most cases wounds are heavily contaminated and are configured as skin flaps, which may be dealt with by promoting second-intention healing or delayed primary closure. The judicious use of drains promotes ventral drainage of the wound, thus avoiding seroma and possible abscess formation. A tendency exists for abdominal wounds to favor the formation of subcutaneous emphysema, which can diffuse along the subcutaneous plains distant from the wound area. This condition is usually benign and resolves with wound healing. It may be aided by placing a pressure bandage around the horse's abdomen and reducing movement, which creates a portal for entry of air into the wound.

Penetrating abdominal injuries can be fatal if the integrity of the bowel is compromised, leading to spillage of large amounts of fecal material and subsequent massive peritonitis. The goals of an exploratory celiotomy are to verify the presence of injured intestine, restore its integrity, remove damaged intestine, and repair the abdominal defect associated with the wound. Survival of horses with penetrating injury may depend on the intestinal segment involved. It appears that contamination resulting from traumatic perforation of the small intestine is more forgiving than that from similar wounds of the large colon. As a result of the low pH of the stomach and the small bowel, the stomach and the proximal portions of the small intestine

(duodenum and jejunum) contain low numbers of microorganisms. In the distal small intestine (ileum) and large colon, bacterial numbers are much higher, and lead to greater contamination in case of spillage.[17] During a celiotomy, devitalized intestinal segments must be removed and puncture wounds restored by over-sewing with healthy serosa. Sources of hemorrhage should be located and controlled via hemostasis. Finally, a thorough abdominal lavage should be done to reduce contaminants; this may be followed by placement of an abdominal drain. Specific techniques for treating peritonitis are described elsewhere (see Chapter 19).

In horses with blunt injury, the main goal should be to stabilize the horse and carefully monitor its progress. Blunt injury may be limited to only superficial bruising, requiring minor local and systemic anti-inflammatory therapy; but in severe cases, the abdominal organs may suffer significant damage. Splenic, hepatic, or diaphragmatic injuries, as well as peritonitis or hemoperitoneum, may not be clinically obvious on presentation, warranting monitoring of the horse until the wound is considered nonlife-threatening.

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Laminitis Associated with Acute Abdominal Disease

Chapter 44

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Pathogenesis

Physiologic Considerations

Although numerous diseases ranging from acute metritis to pleuropneumonia can predispose horses to the development of acute laminitis, the most common instigator of laminitis is acute abdominal disease.[1] Acute laminitis is commonly associated with horses exhibiting signs consistent with endotoxemia owing to compromised bowel in diseases that require surgical intervention (e.g., intestinal strangulation obstruction) and horses with severe inflammatory bowel diseases (e.g., colitis, proximal enteritis).[2]

Theories regarding the pathophysiology of laminitis were originally based on clinical and post-mortem findings in horses that developed the disease. Using two experimental models of laminitis that have been established over the last 30 to 40 years, new theories have emerged and old theories have been consolidated or modified through histologic, physiologic, pharmacologic, and, most recently, molecular examination of the developmental and acute stages of laminitis. These experimental models involve intragastric administration of either an excessive amount of carbohydrate[3,4] or the aqueous extract of the heartwood of black walnut trees.[5,6] In the carbohydrate overload model, a well described developmental stage (prior to clinical lameness), characterized by a decrease in central venous pressure, occurs approximately 12 hours after administration of the starch mixture.[3] Clinical lameness occurs approximately 40 hours after administration of the mixture. A variation of the same model involves the administration of oligofructose, a carbohydrate present in grasses.[4] Laminitis develops more rapidly in the black walnut extract model than in the two carbohydrate models, with less severe signs of systemic compromise and lameness. The developmental stage (characterized by leukopenia) occurs approximately 3 to 4 hours after administration of the extract, and onset of clinical lameness occurs approximately 12 hours after administration.[5,6] Data from numerous studies using these models, as well as from clinical experience with the disease, have culminated into three main theories regarding the pathophysiologic mechanisms leading to acute laminitis: 1) a vascular theory based mainly on ischemia, 2) a toxic/metabolic theory, and 3) an inflammatory theory. These theories overlap each other, and components of all three theories are likely to be involved in the pathophysiology of laminitis.

Vascular Compromise of the Digital Circulation

The importance of alterations in the equine digital vasculature in the developmental and acute stages of laminitis has been the subject of intense study for 4 decades. The first concrete experimental data indicating that a disruption in normal digital blood flow occurs in the acute stage of laminitis were obtained approximately 35 years ago using the carbohydrate overload model of laminitis. Contrast radiography of the digit demonstrated a decrease in perfusion of the digital lamellar region at the onset of clinical laminitis.[7] In a subsequent study, isotope-labeled macroaggregated albumin (large enough aggregates to reportedly become trapped in the lamellar capillaries) was injected into the digital arteries of horses in the acute phase of laminitis, and scintigraphy was used to assess changes in delivery of the isotope-labeled material to the digit.[8] Little radioactivity was detected in the digit, whereas radioactivity was marked in the thorax (indicating lodging of aggregates in pulmonary capillaries after bypassing the laminar capillaries). These data were interpreted as indicating that arteriovenous shunting of blood was occurring in the digit, possibly resulting in ischemia of the lamellar tissues. Using the same experimental approach, evidence was seen for increased delivery of the radio-labeled macroaggregates to the digital circulation once the clinical signs of lameness had dissipated.[8] The proposition that arteriovenous anastomoses existed in the digit was originally supported by histopathology,[9] but was later exquisitely demonstrated by scanning electron microscopy of corrosion casts of the lamellar microvasculature. In that latter study, a high density of arteriovenous anastomoses was documented both in the lamellae themselves and at the base of the lamellae.[10]

In an attempt to characterize the basic physiologic mechanisms regulating hemodynamics in the normal and laminitic equine digit, an extracorporeal organ perfusion model was used in both the carbohydrate and black walnut extract models of laminitis.[11] Using this extracorporeal technique, the digit is disarticulated and denervated, with the horse under general anesthesia, and the horse's blood is perfused through the digital vasculature at a controlled arterial pressure. A circulating pump is used to return the blood to the jugular vein while maintaining venous pressure at a set value. Investigators using this technique determined that the normal equine digit has much higher capillary pressure than that reported in other species, but that this high pressure does not result in accumulation of excessive fluid (i.e., edema) in the normal lamellar tissue.[12] This high capillary pressure is offset by a high tissue pressure and low microvascular permeability (and/or low capillary surface area). In the same experimental model, a marked increase in capillary pressure occurs in horses in the developmental stage of carbohyhydrate overload-induced laminitis.[11] This increase in capillary pressure is most likely the result of a 20-fold increase in post-capillary resistance (probably caused by constriction of the venous side of the microvascular bed). Other findings in that study included increased capillary filtration, most likely from the high capillary pressure, leading to increased lamellar tissue pressure. Thus, the investigators concluded that venoconstriction in the digital microvasculature leads to

increased capillary pressure, lamellar edema, and possibly, capillary collapse owing to the inability of edematous lamellar tissue to expand against the constraints of the inelastic hoof wall and distal phalanx. In a subsequent study, similar, although somewhat milder, changes in digital hemodynamics were shown to occur in the black walnut extract model of laminitis.[13] A possible mechanism by which black walnut initiates these changes in the digital microcirculation includes the release of vasoactive amines, which are formed by bacteria in the gastrointestinal tract. When administered to normal horses, these amines decrease blood flow to the digit and increase plasma concentrations of 5-hydroxytryptamine.[14]

Laser Doppler flowmetry is a technique used to monitor blood flow in the microvasculature. This technique has been adapted to the horse by placing small Doppler ultrasound probes in holes drilled through the hoof wall and directing these probes toward the lamellae. Using this approach, changes in lamellar blood flow have been monitored in standing horses before and after onset of experimentally induced laminitis. Although considerable variability in the measurements was present, one investigator reported a significant decrease (approximately 20%) in lamellar blood flow in the standing horse at the same developmental time-point in the black walnut extract model at which hemodynamic derangements were identified using the extracorporeal model.[15] The results of another study using hoof wall temperature as an indicator of lamellar perfusion were consistent with a decrease in lamellar blood flow occurring immediately prior to the onset of clinical signs in the carbohydrate overload model of laminitis.[16] In contrast to the results of this study, another investigator, also using hoof wall temperature as an indicator of lamellar perfusion, reported that lamellar perfusion increases during the entire developmental stage of carbohydrate-induced laminitis.[17]

In addition to the conflicting results obtained in the experiments described above, the techniques for measuring changes in the digital vasculature of horses with developmental or acute laminitis have limitations. For instance, recording total digital or lamellar blood flow (or calculating vascular resistance) cannot differentiate arteriovenous shunting of blood from lamellar capillary perfusion. Furthermore, it is likely that changes in hoof wall temperature reflect the degree of arteriovenous shunting rather than capillary perfusion, as shunting of blood in the extremities appears to have evolved for thermoregulatory control.[18] Finally, denervation of the digit for assessment of digital hemodynamics in the extracorporeal perfusion model is likely to have an effect on vascular regulation because arteriovenous anastomoses are richly innervated.[19] Thus, evidence appears to be insufficient to determine whether the blood supply or delivery of oxygen to the distal limb is reduced sufficiently to cause ischemia during the developmental stage of laminitis.

In an attempt to determine whether hypoxia or ischemia occur in the lamellae without having to rely on measurements of blood flow, investigators have used molecular biologic and protein biochemistry techniques to compare levels of expression of several genes that respond to hypoxia or ischemia in lamellar tissues from healthy horses and from horses administered black walnut extract. These investigators also determined activities of xanthine dehydrogenase and xanthine oxidase in the lamellae at the developmental stage of experimental laminitis (ischemia causes xanthine dehydrogenase to be converted to xanthine oxidase).[20,21] No evidence of ischemia was identified in the lamellar tissues by either of these techniques. Although these studies further question the role that ischemia plays in the initiation of lamellar pathology in laminitis, these results remain tentative. Interestingly, in the same study, the investigators also found minimal superoxide dismutase activity in the equine lamellae when compared with other equine tissues, suggesting that lamellar tissues may have little endogenous protection against oxygen radicals.[20] As oxygen radicals are not only produced by ischemia but also by leukocytes recently detected in affected lamellae, lamellar susceptibility to oxygen radical damage may contribute to the apparent increased susceptibility of endotoxemic or septic horses to develop laminitis.

The importance of coagulopathy and the formation of thromboses in the pathogenesis of laminitis is controversial. Although thrombi have been identified in the lamellar microcirculation of horses with either naturally occurring or experimentally induced laminitis,[22,23] detection of microthrombi in individual horses in the different models of laminitis has been inconsistent. This has led some investigators to conclude that thrombus formation may be a secondary phenomenon in laminitis and may not be necessary for induction of the disease. A role for thrombosis in the development of laminitis is supported by evidence of platelet adhesion in the digital circulation in the early stages of experimental laminitis[22] and by a reduction in the incidence of laminitis in two different experimental studies, one by heparin and the other by an inhibitor of platelet aggregation.[24,25] The development of platelet-neutrophil aggregates in the circulation in the early stages of laminitis suggests that platelets play a role (as occurs in organ damage in human sepsis) in the development of laminitis, for example, by promoting emigration of neutrophils into the lamellae in the early stages of laminitis.[26] No consistent evidence exists that coagulation is impaired in the developmental or acute stages of laminitis.

Toxic/Metabolic Theory

The second theory regarding the pathogenesis of acute laminitis is the toxic/metabolic hypothesis that states that bacterial toxins absorbed into the systemic circulation from the compromised gastrointestinal tract (or other organs such as the uterus or respiratory tract) reach the digital circulation, where they initiate the associated molecular and cellular events. This same theory has included the controversial hypothesis that an increase in digital blood flow in developmental laminitis enhances the delivery of these toxins to the digit. This theory proposes that these bacterial toxins activate metalloproteinases. Metalloproteinases are destructive enzymes that break down extracellular matrix proteins including those present in the basement membrane that bind the dermal and epidermal lamellae. The central hypothesis of the toxic/metabolic theory is that increased metalloproteinase activity resulting from exposure of laminar tissue to blood-borne toxins results in the physical destruction of the lamellar basement membranes and collapse of the lamellar support of the distal phalanx.

One of the main areas of controversy in laminitis is the involvement of gram-negative or gram-positive organisms in the disease process. Clinically, laminitis characteristically occurs subsequent to disease processes involving gram-negative sepsis or acute abdominal crisis, which are commonly characterized by clinical signs of endotoxemia. However, in only one report were endotoxins detected in the circulation of horses with experimentally induced laminitis using the carbohydrate overload model.[27] Attempts to detect endotoxins in the circulation of horses early after administration of the black walnut extract have been unsuccessful.[13,28] Failure to detect endotoxins in the systemic circulation in the majority of studies using either model may reflect clearance of endotoxins by the liver or lung; in a bovine grain overload model, endotoxins could be detected in the portal but not in the systemic circulation.[29] Although laminitis has never been induced by systemic administration of endotoxin, investigators using Doppler ultrasonography have reported that lamellar blood flow decreases in horses after intravenous administration of endotoxin.[30] In contrast to the increase in postcapillary resistance reported in horses in early laminitis subsequent to either carbohydrate overload or black walnut extract administration, the decrease in lamellar blood flow secondary to endotoxin administration appeared to be caused by an increase in precapillary resistance in the extracorporeal digit perfusion model.[31] Consequently, although signs of endotoxemia are present in the prodromal stage of most clinical cases of laminitis, the failure to induce laminitis experimentally with endotoxin suggests that endotoxin is associated with laminitis but that it requires the presence of other mediators or toxins to induce the disease process.

Increased attention has been paid to the gram-positive bacteria, *Streptococcus bovis*, which undergoes marked proliferation in the intestinal tract of horses in the carbohydrate model of laminitis.[32] Supernatant from broth cultures of *Streptococcus bovis* recovered from the compromised gastrointestinal tract and from several other gram-positive and gram-negative bacterial broth cultures causes separation of the dermal and epidermal tissues in an in vitro model of laminitis using hoof explants.[32,33] The separation of the epidermal and dermal components of the explants is reportedly caused by cell-dependent activation of metalloproteinases.[33] However, the link between the presence of these bacteria in the intestinal tract of horses after carbohydrate overload and the activation of metalloproteinases has not been demonstrated in vivo. Therefore, although *S. bovis* toxins may play a role in laminitis subsequent to severe gastrointestinal diseases, it is currently difficult to place the importance of this organism above that of gram-negative toxins because gram-negative sepsis or clinical symptoms of endotoxemia is the common factor in many diverse diseases associated with naturally occurring laminitis.

Regardless of the controversy regarding the role that different bacterial toxins may play in the activation of metalloproteinases, the histologic evidence of disintegration of the basement membrane between the dermal and epidermal lamellae in the acute stage of laminitis has spawned interest in the pathophysiologic role of this family of over 20 proteins that participate in degradation of extracellular matrix. The different matrix metalloproteinases (MMPs) use distinct proteins in the extracellular matrix as their substrates. MMP expression is induced by many stimuli reported to be present in laminitis, including bacterial toxins, inflammatory cytokines, and ischemia. Generally, MMPs are secreted as inactive proenzymes that require proteolytic cleavage by other MMPs or extracellular proteases (e.g, plasmin) for activation. MMPs are proposed to cause degradation of the basement membrane between the dermal and epidermal lamellae, thereby disrupting adhesion of the dermal and epidermal lamellae, resulting in lamellar separation and loss of support of the distal phalanx.[34] MMP-2 (a collagenase) and MMP-9 (gelatinase) are two metalloproteinases that break down components of the basement membrane; these two MMPs play a pathologic role in matrix disruption in several disease processes including vascular disease, cancer, and numerous skin diseases in humans. Increased MMP-2 and MMP-9 activity has been demonstrated in lamellar tissue from horses with either naturally occurring or experimentally induced laminitis, and increased expression of MMP-2 has been reported in the developmental stage of an experimental model of laminitis.[35] Whereas no study has yet attempted to inhibit the onset of laminitis with an MMP inhibitor, the nonspecific MMP inhibitor, balmistat, reportedly inhibits lamellar separation in the previously cited in vitro model of laminitis.[33] As the activation of MMP activity has been noted at the onset of clinical signs of laminitis, it is likely to occur secondary to the production of a variety of inflammatory mediators in the lamellae expressed at the developmental stage of the disease.

Inflammation in Laminitis

Inflammation has long been implicated in the pathogenesis of laminitis because of the histologic evidence of inflammatory cells present within the lamellae of acutely laminitic horses. Recently, neutrophils, which are not present in the lamellae of normal horses, have been demonstrated in the lamellae during the developmental stage of black walnut extract-induced laminitis. Conclusive evidence of the role of inflammation in the developmental and acute stages of laminitis has come from studies that have identified molecular indicators of the inflammatory response. Using the black walnut extract model, perivascular cells with marked expression of the central proinflammatory cytokine interleukin-1 beta (IL-1β) were identified in the dermal lamellae coincident with the onset of the leukopenic response to the extract.[28] Investigators have since found a 30-fold increase in expression of IL-1β and a 160-fold increase in expression of the potent inflammatory cytokine IL-6 in the developmental stage of experimental laminitis.[36] Similarly, lamellar expression of the inducible cyclooxygenase gene, COX-2, was increased approximately 10-fold in the developmental stage,[36] and at the onset of clinical signs of laminitis. Although COX-2 protein levels were also increased in the prodromal stage of laminitis, COX-2 was identified immunohistochemically in lamellar venules and arterioles of normal horses, indicating this central enzyme in the prostaglandin cascade may also have a homeostatic role.

The inflammatory response in developmental laminitis does not appear to be limited to the lamellae; recently, investigators have presented data indicating that neutrophils and monocytes in the peripheral blood are activated during the developmental stage of laminitis.[37] Thus, as clinical laminitis is usually associated with systemic signs of endotoxemia or gram-negative sepsis, it is possible that, similar to human sepsis, a systemic inflammatory response results in activation of leukocytes, followed by migration of these cells into the tissues with the local release of inflammatory mediators.

Reconsidering the Pathogenesis of Acute Laminitis

Based on evidence presented so far, it appears that the three theories are not mutually exclusive; interdependence among them is apparent. In attempting to coalesce the above data into a unifying pathophysiologic mechanism, the findings would best support a sequence of events similar to that reported for human systemic sepsis. In human systemic sepsis from gastrointestinal disease, bacterial toxins are translocated from the intestinal tract into the systemic circulation, which results in systemic activation of leukocytes, platelets, and the microvascular endothelium, leading to adhesion of platelets and leukocytes to each other and to the endothelium. These responses are then followed by transendothelial migration of the activated leukocytes, primarily the neutrophils, into the tissues. The leukocytes would then express inflammatory mediators, which induce the further expression of inflammatory mediators and enzymes (e.g., IL-6 and COX-2) by cellular constituents of the lamellae. Production of vasoactive mediators, including prostaglandins, by activated leukocytes and platelets may then lead to vascular disturbances, including arteriovenous shunting of blood and changes in lamellar microvascular flow, but possibly not total lamellar ischemia. These changes in blood flow may lead to further margination of leukocytes and platelets with attachment to the endothelium. Production of oxygen radicals by activated leukocytes may add to the damage, as there appears to be minimal endogenous superoxide dismutase (SOD) in the lamellar tissue to neutralize the oxygen radicals. Expression of inflammatory mediators by the leukocytes and possibly the resident cells in the lamellae may then result in marked induction/activation of MMPs, resulting in breakdown of the basement membrane, leading to lamellar separation and the displacement of the distal. As evidence of ischemia and thrombus formation in the lamellar vasculature appears to be reported more consistently at later time points (at the onset of clinical lameness or later in acute laminitis), it is possible that, as occurs in multiple organ dysfunction syndrome in human sepsis, ischemia and thrombosis may be important as secondary or "downstream" processes in lamellar failure.

Structural Considerations of the Equine Digit

The stresses on the lamellae are related to weight-bearing and locomotion. The forces coming to bear on the lamellae include the downward force of the horse's weight through the osseous structures of the digit, the torque (or moment) around the distal interphalangeal joint created by the ground reaction force, and the tension of the deep digital flexor tendon exerted on the caudal aspect of the distal phalanx (see Figure 44-1). It would appear that the more weight-bearing is concentrated on the distal wall (vs. the solar ground surface) the greater the stresses in the lamellae. At rest, the center of weight-bearing is approximately at the center of the ground surface of the foot, but the distribution of weight-bearing on the ground surface of the foot is related to the nature of the ground surface. On flat hard surfaces, including the artificial surfaces upon which we commonly force horses to stand, weight-bearing is through the ground surface of the wall and adjacent sole, which puts tremendous stress on the lamellar attachments. On a yielding surface such as sand, weight-bearing is more broadly distributed across the surface of the foot, with the sole bearing significantly more weight than the wall; thus, the sole can directly support the distal phalanx, resulting in decreased stress to the lamellae.[38] In the routinely shod horse, the stress on the lamellae is exacerbated by having the only contact of the shoe with the distal hoof wall, which results in a decrease in sole

support because of the elevation of the sole above the ground. Thus, it is usually detrimental to leave shoes with no sole support on the acutely laminitic horse.

During locomotion, the stresses associated with weight-bearing are also centered on the ground surface of the foot for most of the stride. However, during the break-over stage of the stride, the stresses are concentrated at the toe. Consequently, at break over, the ground reaction force is located at the toe of the hoof, so the length of the moment arm and hence the torque or moment is increased compared with what it is at rest and at the middle of the stance phase (Figure 44-1).

Figure 44-1A

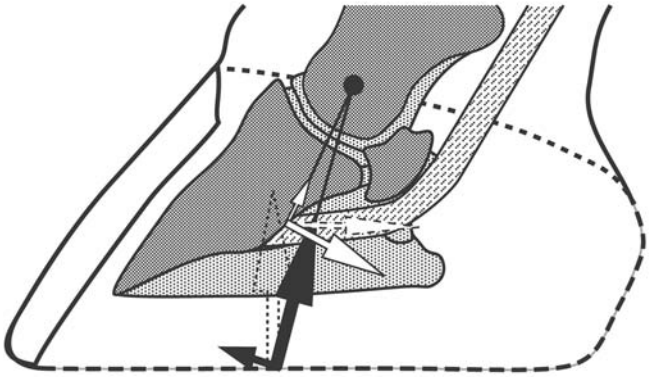


Figure 44-1B

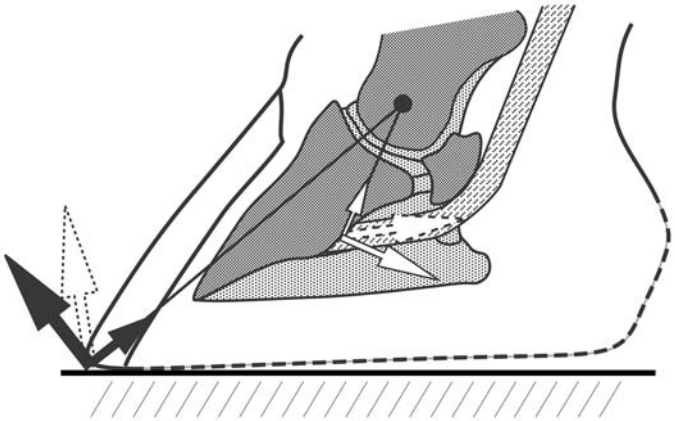


Figure 44-1C

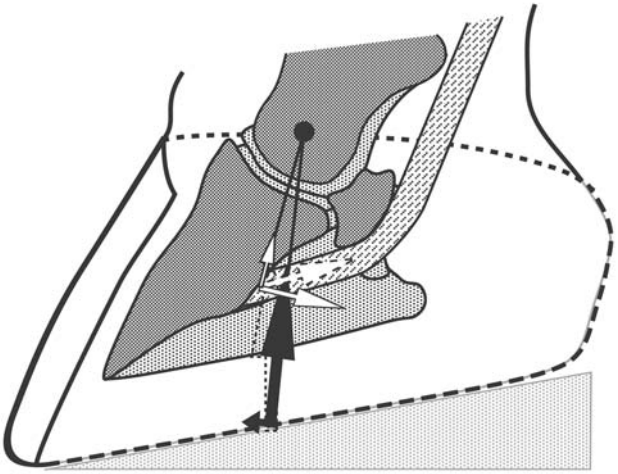
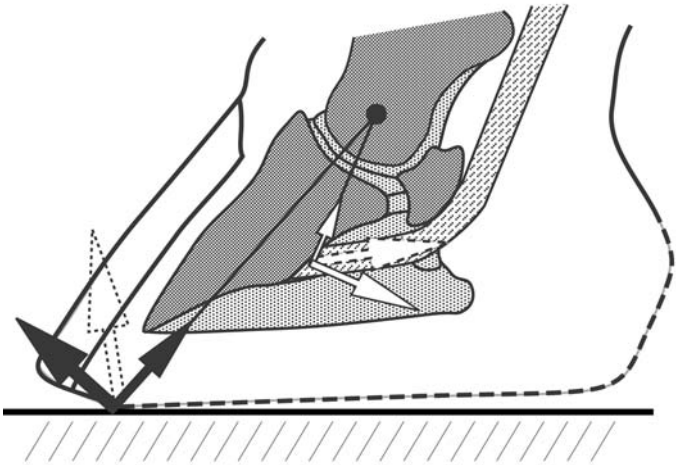


Figure 44-1D



The effects of heel elevation and moving the breakover palmarly on the moments about the distal interphalangeal joint. The thin black lines extending from the center of rotation represent the moment arms for the ground reaction force (dotted arrow with no fill) and the tension in the deep digital flexor tendon (dotted arrow with white fill). Each of these forces has been broken into a component perpendicular to the moment arm and a component parallel to the moment arm (black for the ground reaction force and white for the tension in the tendon). **A.)** normal foot at rest; **B.)** normal foot at breakover – note that the ground reaction force is no longer vertical; **C.)** 10 degrees heel elevation (assuming the point of action of the ground reaction force remains constant) – note that the component of the ground reaction force perpendicular to the moment arm is reduced compared with (A) and hence the torque about the distal interphalangeal joint is reduced; **D.)** breakover moved palmarly - note that length of the moment arm of the ground reaction force and the force perpendicular to it are both decreased, and hence the torque about the distal interphalangeal joint is reduced. (All the vectors illustrated by the arrows are for illustrative purposes only and are not meant to indicate actual values.)

In a healthy horse, the strength of the lamellae greatly exceeds the stresses applied, thereby allowing the distal phalanx to be retained in its normal position. However, in horses with laminitis, the strength of the lamellar attachment to the distal phalanx is reduced, most likely because of destruction of the basement membrane and, possibly, because of necrosis of lamellar epithelial cells. Once lamellar integrity is diminished during the developmental and acute stages of acute laminitis, partial loss of the lamellar attachments causes the remaining intact lamellae to endure the entire load of weight-bearing and locomotion, so that the remaining lamellae are potentially exposed to a cycle of exacerbated mechanical injury. The transition from acute/subacute laminitis to chronic laminitis is partially defined by displacement of the distal phalanx within the hoof capsule. Displacement of the distal phalanx occurs when there is an imbalance between the mechanical properties of the dermal and epidermal lamellae and the stresses imposed on them. The pattern of displacement of the distal phalanx within the hoof capsule varies among horses, and sometimes among an individual horse's feet. The distal phalanx may displace evenly around the circumference of the hoof wall, which is usually termed distal displacement or sinking (Figure 44-2). Alternatively, the distal phalanx may displace unevenly in relation to the hoof wall, the most common pattern of which is seen when the dorsal distal margin of the distal phalanx descends and the parietal (commonly termed "dorsal") surface of distal phalanx diverges from the dorsal surface of the hoof wall distally (Figure 44-3). This pattern is termed rotation of the distal phalanx. When treating horses with laminitis, it is advantageous to subdivide rotation into two categories: capsular rotation, which describes divergence of the parietal surface of the distal phalanx from the dorsal hoof wall (with or without flexion of the distal interphalangeal joint), and phalangeal rotation, which describes palmar rotation of the distal phalanx (flexion of the distal interphalangeal joint with or without capsular rotation) in relation to the axis of the phalanges. Occasionally, the distal phalanx displaces asymmetrically in a dorsal (frontal) plane, either medially or laterally (Figure 44-4). In most horses, the pattern of displacement is a combination of distal displacement and rotation of the distal phalanx, although one pattern is usually dominant.

After displacement has occurred, the space created by separation of the damaged lamellae between the hoof wall and the parietal surface of the distal phalanx is filled with blood and necrotic tissue. As the injured tissues heal, the coronary dermal papillae may not realign with the parietal surface of the distal phalanx, and the space between the wall and distal phalanx fills with hyperplastic tissue (commonly termed the lamellar wedge). Both of these changes may prevent the realignment of the dorsal hoof wall with the distal phalanx with new wall growth.

Figure 44-2A

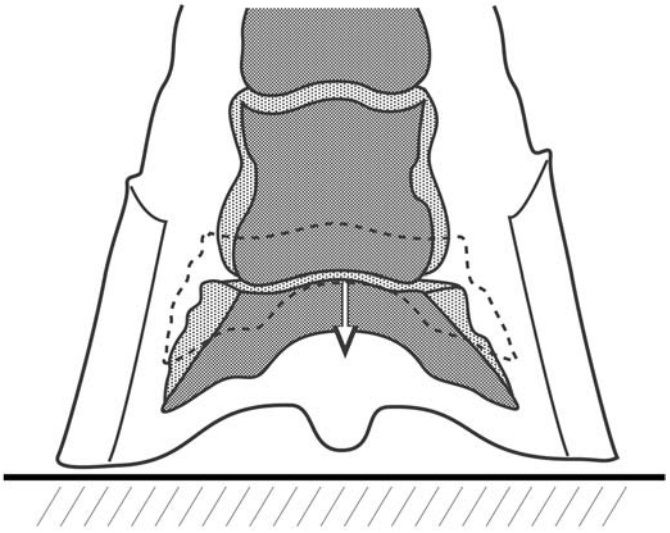
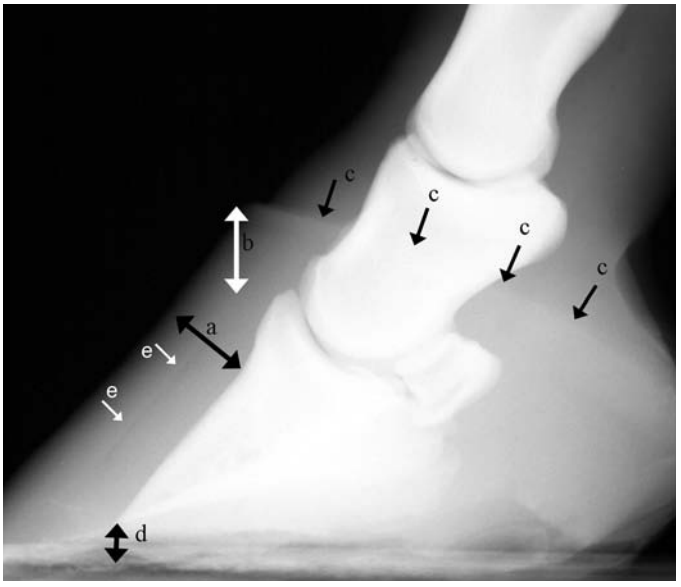
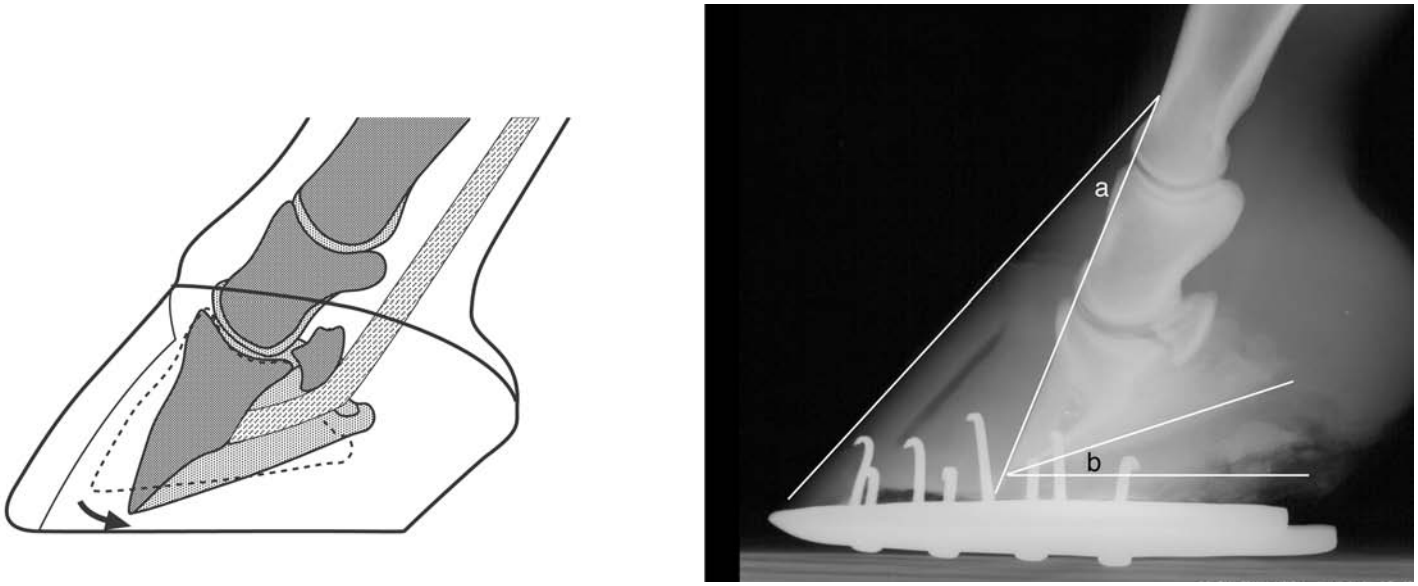


Figure 44-2B



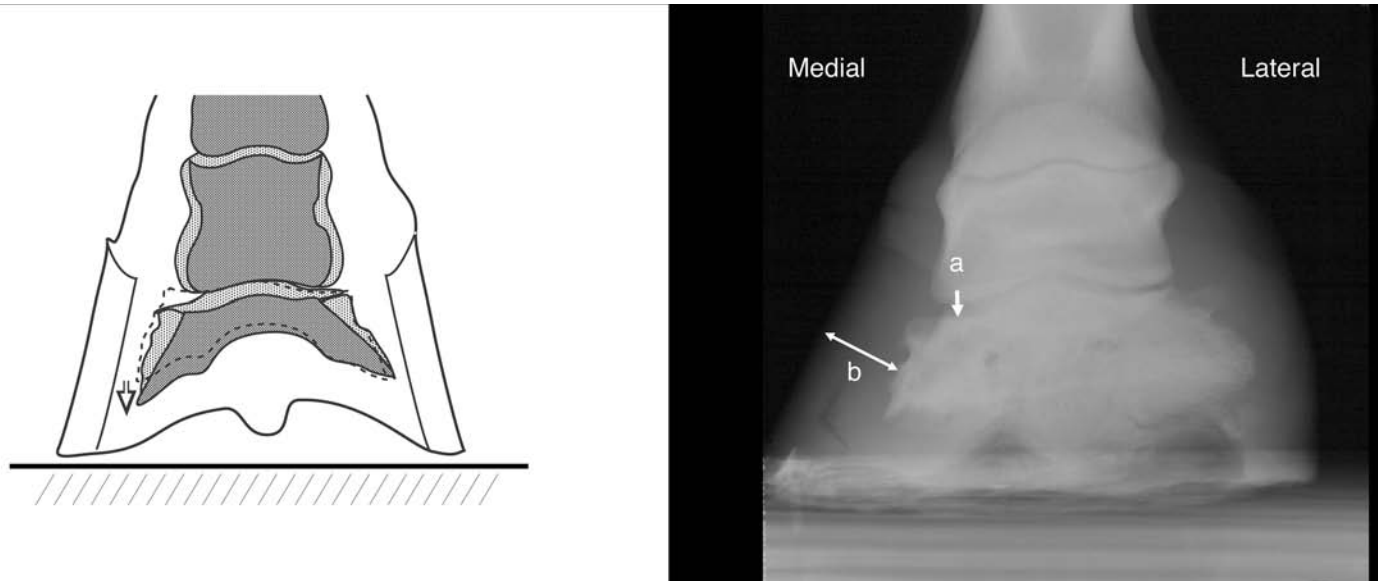
Distal displacement. **A.)** Schematic illustration shows descent of the distal phalanx from the dorsal perspective. **B.)** Radiograph shows features of distal displacement from the lateral perspective, including increased width of the dorsal hoof (a), increased distance between the coronary band and the extensor process of the distal phalanx (b), a prominent "sinker" line (c), reduced thickness of the sole (d), and a prominent radiolucent line between the dorsal hoof capsule and underlying tissues (e).

Figure 44-3



Rotational displacement.The parietal surface of the distal phalanx is diverging from the dorsal hoof wall (a, capsular rotation), and from the axis of the phalanges evidenced by an increased angle of the solar surface of the distal phalanx to the ground (b, phalangeal rotation).

Figure 44-4



Asymmetrical mediolateral distal displacement. The distal phalanx has distally displaced medially (a), and the medial wall is increased in thickness (b).

Clinical Presentation

History

The history of horses with laminitis may vary considerably; however, distinct patterns are recognizable in horses with either acute or chronic laminitis. In most diseases, the terms acute and chronic are used solely to designate temporal characteristics of the disease. However, in laminitis the term acute not only denotes laminitis of short duration, (specifically less than 3 days), but it also indicates that displacement of the distal phalanx has not occurred. In contrast, the term chronic with reference to laminitis is used to indicate that the distal phalanx has displaced regardless of the duration the disease process. Disease of longer than 3 days in which displacement has not occurred is called subacute. Thus, while the acute phase is truly acute, the subacute phase may refer to a horse that has survived the acute phase without rotation of the distal phalanx, but whose symptoms have not resolved for several weeks. Furthermore, the chronic phase may extend indefinitely from as little as 1 or 2 days after the onset of the disease. This classification does not reflect the amount of inflammation within the laminae.

Horses with acute laminitis usually have a history of a prior or concurrent disease for which laminitis is a recognized sequel; the onset of signs is usually rapid. Horses with chronic laminitis are likely to have the disease as a direct sequel to acute

laminitis, or to have a history of recurrence or continuation of chronic laminitis of a long-standing nature. Either acute or chronic laminitis may present with no history of a prior predisposing disease process.

Clinical Signs

The clinical signs of acute laminitis are characterized by lameness, increased temperature in one or more hooves, increased digital pulses, and elicitation of a painful withdrawal response to hoof-testers. Any combination of feet may be affected, although both front feet are most frequently affected. The magnitude of lameness may vary from mild to severe. Horses with mild lameness demonstrate repeated shifting from one foot to another, whereas horses with severe lameness may stand planted, refusing to move or even to permit a foot to be picked up off the ground. The characteristic stance of a laminitic horse with both forefeet affected is placement of the forefeet well in front of the normal position in order to bear more weight onto the palmar half of the feet, and anterior placement of the hind feet in order to shift more weight to the hindlimbs (Figure 44-5).[39] The characteristic gait of a laminitic horse includes stiff limb movement, including an arched back, appearing to shift weight to the hind limbs, short strides, and landing on the heels, all of which are exacerbated when the horse is turned. However, horses with milder forms of laminitis may not have this characteristic gait. Horses with distal displacement of the distal phalanx more frequently have a more normal stance and gait but are usually intensely resistant to movement as all four feet are equally affected. It is at times difficult to determine whether just the forefeet or all four feet are affected; anesthesia of the forefeet with abaxial sesamoid nerve blocks will help determine whether any lameness exists in the hind feet, or if any abnormality noted in hindlimb gait is merely compensation for the painful forelimbs. Horses in which hind foot pain predominates may occasionally have a hypermetic gait with quick withdrawal of the rear limb on weight bearing that is similar to the gait of a horse with stringhalt.

Figure 44-5



Classic stance of a horse with laminitis. The front feet are placed forward while the rear limbs are brought under the body to accept more weight.

Increased hoof temperature and the strength of digital pulses must be interpreted in the context of the lameness and other systemic symptoms, because it is not unusual for an increase in hoof temperature to be transient, and the interpretation of digital pulses is highly subjective. Application of hoof-testers is useful to confirm the presence of pain around the dorsal margins of the sole in a horse that is suspected of having laminitis.

Horses with long-standing chronic laminitis usually present with a combination of lameness and characteristic deformation of the hoof capsules. However, they may present with lameness without deformation of the hooves, or deformation of the hooves with minimal signs of lameness. The lameness varies from being barely detectable to the characteristic gait previously described. Changes to the hoof capsule vary with the duration of the disease and may be visible in both the wall and the sole. Immediately after a horse has suffered rotation of its distal phalanx, the wall is unchanged. However, depending on the degree of rotation, the sole dorsal to the apex of the frog may be flattened, and, especially with distal displacement of the distal phalanx, there may be a palpable groove at the junction of the skin of the pastern and the coronary band. In horses with prolonged chronic laminitis, the dorsal wall may assume a characteristic concave appearance, and the heels may be elongated (Figure 44-6). The disparate growth of the hoof wall between the toe and heels is visible in the growth rings, which are more widely spaced at the heels than at the toe. The texture of the hoof wall may also be duller or rougher than normal.

The sole may be flatter than normal, show evidence of bruising around its dorsal margin, and may be softer than normal. The white line may be wider than normal, frequently with elongated keratinized lamellae, and contain old hemorrhages.

Figure 44-6

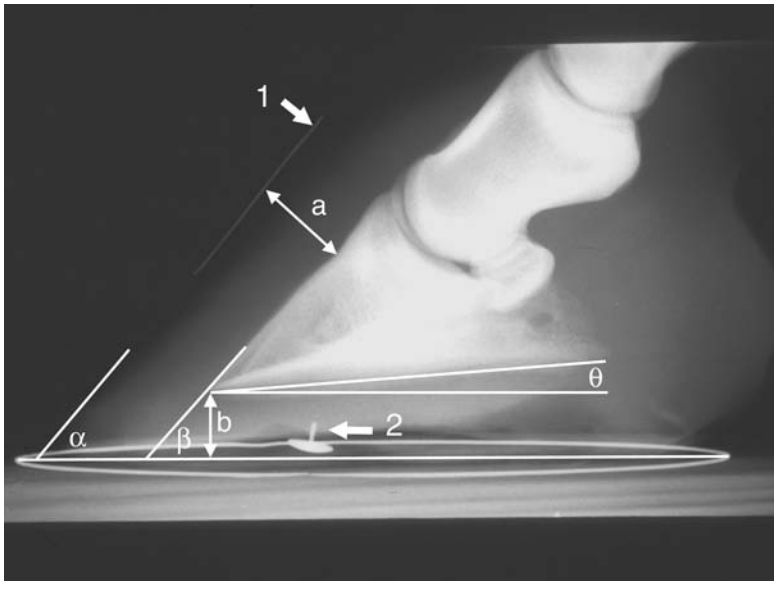


Prolonged chronic laminitis has caused foot deformity with dishing of the front of the foot and wider growth rings in the horn at the heels.

Radiography

Radiography is important in laminitis as a diagnostic tool, to monitor progress of the disease, and to guide treatment. Radiographs demonstrate the position of the distal phalanx in relation to the hoof capsule, and changes in the shape and density of the distal phalanx. Three main radiographic projections are used: lateral, dorsopalmar, and 45-degree oblique. For the lateral and dorsopalmar projections, it is important that the foot is placed on a block and that the x-ray beam is centered as close as possible to the solar margin of the distal phalanx (approximately 1.5 cm proximal to the weight-bearing surface of the hoof capsule). It is important to ensure that the radiograph is a true lateral; rotation of the axis of the foot by more than 10 degrees will cause the degree of rotation to be underestimated.[40] Because of the extreme difference in density of the hoof capsule and the distal phalanx, the lateral and dorsopalmar views may be obtained using two different exposures to discern the position of the distal phalanx in relation to the hoof capsule and the radiographic morphology of the distal phalanx. Additionally, it is helpful to define the position of the hoof capsule in relation to the distal phalanx by placing a linear marker on the dorsal hoof wall with the proximal aspect of the marker touching the coronary band, and a point marker at the apex of the frog (Figure 44-7).

Figure 44-7

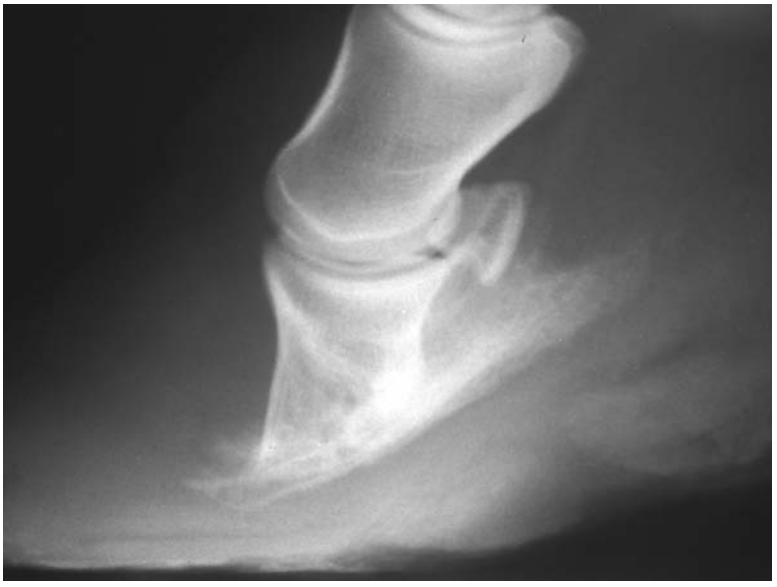


Lateral radiograph of the foot. (1) linear radioopaque marker on the dorsal hoof wall, (2) marker to identify the dorsal extent of the frog, (a) thickness of the dorsal hoof, (b) thickness of the solar hoof, (α) angle of the dorsal hoof wall to the ground, (β) angle of the dorsal parietal surface of the distal phalanx to the ground (β-α = degree of capsular rotation), (θ) angle of the solar margin of the distal phalanx in relation to the ground surface of the hoof.

Assessing the position of the distal phalanx in relation to the hoof capsule is dependent on the duration of the disease. Immediately after the distal phalanx has rotated or displaced distally, the external contour of the hoof capsule is not changed, whereas, after much greater duration, the deformation of the hoof capsule changes the interpretation of the radiographs. Immediately after distal phalanx rotation, the most useful radiographic signs are the degree of rotation between the dorsal hoof wall and the parietal surface of the distal phalanx (capsular rotation, β-α in Figure 44-7), the angle of the abaxial solar margins of the distal phalanx to the ground (θ in Figure 44-7), and the distance between the dorsal-distal margin of the distal phalanx and the ground (b in Figure 44-7). In horses in which the distal phalanx has displaced distally, the distance between the dorsal surface of the hoof capsule and the adjacent parietal surface of the distal phalanx (a in Figure 44-7) is a relatively repeatable measure of the displacement (13 to 20 mm in normal horses depending on size);[41] in horses in which the distal phalanx has rotated and displaced distally, this measurement should be made at the base of the extensor process. Other clinicians have used the distance between the proximal limit of the extensor process and the coronary band as a measure of distal displacement (–2 to 10 mm in normal horses depending on size) (see Figure 44-2).[42]

After prolonged chronic rotation of the distal phalanx, frequently remodeling or resorption of the distal aspect of the dorsal solar margin is visible on the lateral and dorosopalmar oblique views, and a lip of new bone on the dorsal aspect of the dorsal solar margin is visible on the lateral view (Figure 44-8). Additionally, small tangential fractures may be present at the dorsal solar margin of the distal phalanx and seen on the lateral and dorsopalmar oblique views. Ideally, the same measurements would be used to indicate the position of the distal phalanx in relation to the hoof capsule following prolonged rotation as would be used after recent rotation. However, distortion of the contour of the dorsal hoof capsule may make it impossible to obtain a precise measurement of capsular rotation. Therefore, measurement of the angle that the top one third of the hoof capsule makes with the parietal surface of the distal phalanx most likely provides the closest indication of what the rotation would be without the dorsal concavity. Unfortunately, resorption of the dorsal margin of the distal phalanx makes it harder to measure the angle of the solar margin of the distal phalanx to the ground, but by extrapolating from the palmar processes, an approximate angle can be obtained.

Figure 44-8



Lateral radiograph of prolonged chronic laminitis. Remodeling of the dorsal tip of the distal phalanx is due to pressure and bone lysis.

Digital venography in the standing horse has been developed as a prognostic aid to assess the vasculature of the digit. Venograms in which contrast dye does not fill the lamellar vessels, the circumflex area, and the terminal arch are reported to indicate an extremely poor prognosis for recovery.[43]

Treatment

The treatment of horses with laminitis varies according to the phase (i.e., acute or chronic) of the disease process. In horses with acute laminitis, the goals of treatment are (1) to halt or limit any systemic disease process that predisposed the horse to laminitis, (2) to prevent or limit the digital changes leading to separation of the injured lamellae, and (3) to control pain. Therefore, in the acute phase, therapy is primarily medical and supportive. In horses with chronic laminitis, the treatment goals are (1) to realign the solar margin of the distal phalanx with the normal weight-bearing surface of the hoof, (2) to encourage realigment of the dorsal surface of the hoof capsule with the parietal surface of the distal phalanx, (3) to control

pain, and (4) to manage secondary complications such as distal phalanx sepsis. As such, treatment of the chronic phase consists primarily of foot care, pain medication, and if necessary, surgery. The boundaries between the treatment of acute and chronic laminitis are more blurred than their definitions might suggest. Medical therapy initiated in the acute stage of the disease continues into the subacute and early chronic stages, and occasionally, surgical treatment, which is usually reserved for chronic laminitis, may be used in the acute stages.

Medical Therapy

The medical therapy of acute laminitis is ambiguous at best and contentious at worst, because no controlled clinical studies indicate which therapies are effective. Medical therapy for laminitis associated with acute abdominal disease is directed at the pathogenic processes presumed to be involved in the disease, namely, vascular dysfunction, coagulopathy, inflammation, and toxemia.

Vascular Dysfunction

Two types of pharmacologic agents have been used to improve digital blood flow, vasodilators and rheologic agents (agents that increase the malleability of red and white blood cells). Three types of vasodilators have been examined, α-adrenergic antagonists, isoxuprine, and nitrovasodilators. Of these, α-adrenergic antagonists (i.e., acepromazine) have received the most attention because (1) experimental evidence suggests that administration of such agents improves blood flow to the lamellae in normal horses,[44] (2) these agents are considered to be safe, and (3) subjective clinical impressions support their use. In contrast, it is difficult to justify the use of isoxsuprine because, although it causes dilation of digital vascular rings ex vivo, it is poorly absorbed and does not increase lamellar blood flow at suggested oral dosage (1.2 mg/kg b.i.d.).[44] Likewise, evidence supporting the use of nitrovasodilators is controversial. Early studies suggested that application of nitroglycerine over the palmar digital vessels caused both an increase in lamellar blood flow and clinical improvement in horses with laminitis;[45,46] however, the results of subsequent studies failed to document an increase in blood flow either in normal horses or horses with experimentally induced laminitis.[15] Pentoxifylline, a rheologic agent originally used to treat obstructive arteriosclerosis in humans, has been used clinically to treat laminitis. However, no data from either experimental or clinical studies support the contention that pentoxifylline increases blood flow in either humans or horses.[44,47] Isoxuprine has also been reported to have rheologic properties in addition to being a vasodilator, but as previously mentioned, it does not increase digital blood flow in the horse.

Coagulopathy

Several drugs have been used to address the possible involvement of thrombus formation in laminitis; these drugs include anticoagulants, such as heparin and aspirin, and a platelet aggregation inhibitor. As has been described, prophylactic administration of heparin before induction of laminitis reduced the severity of laminitis in one study.[24] However, two retrospective clinical studies provide conflicting evidence regarding its efficacy. Whereas one study reported a trend for decreased incidence of laminitis in horses with proximal enteritis treated with heparin,[48] a second study reported no impact of heparin therapy on the incidence of laminitis in equine small-intestinal surgery cases.[49] As heparin has also been reported to cause agglutination of erythrocytes in horses,[50] it is possible that heparin-induced RBC aggregates may lodge in the lamellar capillaries and impair blood flow within the lamellae. Aspirin has been proposed as a treatment for laminitis because of its ability to prevent platelet aggregation induced by arachidonic acid metabolism, and aspirin has been reported to effectively decrease thromboxane generation in equine blood ex vivo.[51] However, other stimuli exist that cause platelets to aggregate that are not affected by prostanoids. No clinical or experimental studies have been performed to determine the efficacy of aspirin in the treatment of laminitis. A novel platelet aggregation antagonist has been shown to reduce the incidence and severity of experimentally-induced laminitis,[25] however, this drug has not been used in clinical cases.

Inflammation

The increasing evidence that the inflammatory response is important early in course of experimentally-induced laminitis provides a clear rationale for the use of anti-inflammatory drugs for the treatment of acute laminitis. The nonsteroidal anti-inflammatory drug phenylbutazone is the most widely used because of its anti-inflammatory and analgesic properties; in the latter case the clinical evidence for its benefit is overwhelming. Other NSAIDs used in the treatment of laminitis include flunixin meglumine and ketoprofen. Flunixin meglumine has been reported to be effective for the treatment of musculoskeletal pain, but less so than phenylbutazone. Ketoprofen was found to be as effective as phenylbutazone in amelioration of chronic foot pain at a dose of 3.6 mg/kg, but in the experience of one of the authors, ketoprofen's analgesic effects appear to be short-lived. Phenylbutazone has a much higher clinical incidence of gastrointestinal and renal toxicity when compared with the other commonly used NSAIDs, including flunixin meglumine and ketoprofen.[52-54] As phenylbutazone is a less potent inhibitor of cyclooxygenase-1 (purported to be the protective isoform of cyclooxygenase) than either flunixin or ketoprofen,[55] phenylbutazone's increased incidence of toxicity

is most likely owing to the accumulation of the active metabolite oxyphenbutazone with chronic administration.[56] Many clinicians have used a combination of phenylbutazone and flunixin meglumine to maximize the anti-inflammatory effect of these compounds while attempting to avoid their toxic effects. Concurrent administration of flunixin meglumine and phenylbutazone experimentally at the suggested dosages (1.1 mg/kg and 2.2 mg/kg, respectively) resulted in no effect on drug clearance, but resulted in prolongation of the effect of the 2 individual drugs in blocking thromboxane synthesis.[57] Thus, it seems probable that decreasing the phenylbutazone dosage in combination with flunixin meglumine treatment would obtain adequate efficacy with decreased NSAID toxicity. Similarly, as ketoprofen has a high therapeutic index (no toxicity noted at 5 times the suggested dose for 15 days),[58] it has been suggested that the drug may be given at more frequent intervals to improve its long-term efficacy. One of the authors has used ketoprofen at 2.2 mg/kg dose q.i.d. in horses without renal compromise and no observed signs of toxicity. The main disadvantages of this drug are its cost and the lack of an oral form, although anecdotal evidence exists that the intravenous preparation will be absorbed if administered orally. As phenylbutazone is still the most valuable NSAID for prolonged treatment of laminitis owing to its efficacy and reasonable cost, clinicians (including the authors) have attempted to decrease the toxicity by not administering the drug for a 24-hour period 1 out of every 5 to 7 days to allow a "wash out" of the phenylbutazone that has accumulated in the tissues. If the animal is in too much pain to tolerate a 24-hour period without an NSAID, flunixin or ketoprofen can be administered for that 24-hour period without affecting phenylbutazone clearance.

Bacterial Toxemia

The frequent occurrence of laminitis as a sequel to conditions associated with endotoxemia suggests that plasma or serum with high antibody titers against endotoxin may be appropriate in the treatment of horses at risk for developing acute laminitis. While conflicting data exist regarding the efficacy of these antibodies in treatment of horses with endotoxemia,[59,60] its effect on the development of laminitis is unknown. In addition to the controversy regarding its efficacy, the expense of endotoxin antiserum can limit its use. Polymyxin B, which binds endotoxin, is used more frequently than anti-endotoxin antibodies largely because it is much less expensive. However, even though polymixin B does improve clinical parameters in experimental endotoxemia,[59] it has little beneficial effect in experimentally induced laminitis.[61]

While the advantages of flunixin meglumine are not as apparent to the clinical observer as the analgesic effects of phenylbutazone in horses with acute laminitis, flunixin meglumine is more effective than phenylbutazone in inhibiting endotoxin-induced synthesis of prostanoids,[62] and may, therefore, be a superior drug to use in the horse at risk for laminitis (i.e., the horse exhibiting signs of endotoxemia). Although a reduced dose of flunixin meglumine (0.25 mg/kg t.i.d.) significantly reduces endotoxin-induced prostanoid synthesis,[63] one of the authors uses the maximal dose of 1.1 mg/kg t.i.d. in most horses at risk of laminitis for two reasons: 1) COX-2 is markedly up-regulated in the developmental stage of laminitis, and 2) the reduced dose of flunixin meglumine does not always prevent development of the clinical signs of endotoxemia as effectively as the recommended dose (1.1 mg/kg). However, if the animal at risk is given the higher dose, close attention must be paid to hydration status, renal function, and gastric protection.

Pentoxifylline has been studied in human and veterinary endotoxemia/sepsis cases because of its ability to inhibit tumor necrosis factor-α (TNF) expression. Although the drug was found to effectively decrease TNF expression in an ex vivo equine endotoxemia model,[64] little efficacy was noted in experimental endotoxemia in horses or food animals.[65-68] Thus, the value in treating bacterial toxemia with pentoxifylline in the horse is questionable.

Dimethyl sulfoxide is widely used in the clinical treatment of horses with acute laminitis, primarily because of its purported value (mainly owing to anecdotal observations) as an oxygen free-radical scavenger. Although efficacy of dimethyl sulfoxide has not been tested experimentally, the report that digital lamellae have little endogenous SOD activity provides an additional rationale for its use. Metalloproteinase inhibitors are being investigated as potential therapeutic agents for certain human diseases, including cardiovascular disease and many types of cancer.[69] Although the metalloproteinase inhibitors may offer great potential for the treatment of laminitis in the future, they have not yet been evaluated in vivo either experimentally or clinically.

The pharmacologic control of pain in horses with laminitis has historically been limited to NSAIDs, particularly phenylbutazone; however, new analgesics should become available in the future. As COX-2 expression has been reported to increase in the developmental and acute stages of laminitis,[70] it may be possible to replace phenylbutazone with a COX-2 selective inhibitor. Clinicians are exploring alternative pharmacologic strategies including continuous intravenous infusions of lidocaine and epidural administration of morphine, and although both would avoid the toxicity of the NSAIDs, their effectiveness remains undetermined. Anecdotal reports suggest that the intravenous administration of lidocaine is a beneficial analgesic in horses in the early stages of laminitis.

Supportive Hoof Care

It appears that the pain experienced by horses with chronic laminitis reflects the stresses to the injured lamellae and/or pressure on the solar surface of the hoof. Therefore, appropriate foot support can provide relief from pain in conjunction with stabilizing the distal phalanx within the hoof capsule. In the acute phase of laminitis, supportive therapy is primarily directed at preventing or minimizing displacement of the distal phalanx. In the chronic phase, supportive therapy is also directed at preventing further displacement of the distal phalanx, but an important component in the chronic case is the realignment of the distal phalanx to both decrease solar pressure (and related pathology) by the displaced distal phalanx and to encourage new hoof growth to realign the wall with the parietal surface of the distal phalanx. The goals of supportive therapy in acute and chronic laminitis are sufficiently similar to allow the same biomechanical principles of stabilizing the digit to be applied to horses with either form of the condition. These basic principles are 1) reduce weight-bearing by the wall and lamellae, 2) decrease the moment about the distal interphalangeal joint during locomotion, and 3) decrease the tension on the deep digital flexor tendon. The stresses in the wall caused by weight bearing may be decreased by moving stresses from more severely affected wall to less affected wall, and by recruiting the sole and frog to bear weight. The forces applied to the distal interphalangeal joint may be decreased by elevating the heels and moving the point of break-over palmarly (Figures 44-1C and 44-1D). Primary differences exist between the supportive foot care of horses with acute or subacute laminitis and horses with chronic laminitis. First, the pattern of displacement cannot be predicted in the horse with acute laminitis, whereas the displacement has already occurred in horses with chronic laminitis. Second, the clinician is more likely to apply temporary types of foot support in the acute stage (i.e., Redden Ultimate or Styrofoam pads - “support blocks”) that can be rapidly applied with mimimal concussion and can be easily interchanged if there is a lack of response. Third, application of corrective shoes with nails is usually tolerated better by horses with chronic laminitis of several weeks’ duration.

Horses with acute laminitis should have stall rest to diminish the trauma caused by locomotion. In the acute stage, the shoes should be removed to decrease the concentration of stress around the periphery (i.e., wall) of the foot. The simplest way to redistribute weight from the wall to the sole and frog is to stand the horse on a surface that conforms to the ground surface of the foot. In this regard, sand is significantly superior to shavings because the granular nature of sand will conform better to the ground surface of the foot and, therefore, provide better support to the frog and sole in addition to the wall, and it will more readily allow the horse to adjust the position of the feet to find the stance that is most comfortable while it is standing. However, it is critical to use a bedding material in which the horse is willing to lie down to take the stress off the affected feet for extended periods of time. If a horse will not lie down in sand but will in shavings, it is may be best to use deep shavings and support the feet by application of the preferred type of digital support.

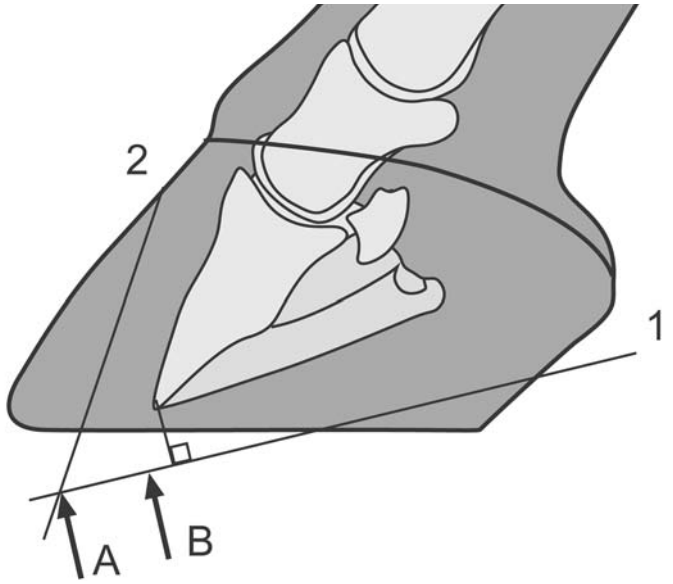
The simplest of digital support devices are frog pads, either commercially available pads or those made from rolled up gauze. Because response to such devices tends to be highly variable, the authors use them infrequently. Weight redistribution to a greater area can be achieved by filling the concavity of the ground surface of the foot with a 5 cm thick high-density Styrofoam support block (the Styrofoam used for insulating house foundations, also called blue board). The Styrofoam crushes readily (usually over 24 hours) and conforms to the ground surface of the foot. It is advantageous to continue to apply additional Styrofoam blocks as the prior ones are compressed until there are commonly 3 to 4 layers of Styrofoam on the bottom of the affected feet. It is possible to achieve elevation of the heels if the toe section is removed from the first 1 to 2 blocks after they are compressed. In addition to application of the Styrofoam blocks, the distal border of the wall at the toe may be beveled with a hoof rasp to move the point of break-over palmarly. It is advisable to avoid filling the concavity of the sole with hard, rigid filling materials, but commercial silicon putties, which are more pliable, are useful for applying sole support. A commercial cuff-wedge pad combination (Redden Modified Ultimate) used in conjunction with silicone putty (also termed digital cushion support or impression material) will redistribute weight-bearing to the sole and frog, elevate the heels, and move the point of break-over palmarly. Obtaining the best results from these techniques may require some trial and error because the areas of greatest stress within the lamellae cannot be identified unless the distal phalanx has displaced. If the lameness does not improve or becomes worse with the heel elevation caused by the commercial shoe (or Styrofoam wedge), one of the authors will apply an even layer of digital cushion support substance (approx. 1 inch thick) to the entire ground surface of the foot because some horses are more comfortable without heel elevation. Because of the broad range of severity of the lamellar damage among affected animals (and the fact that more severely affected horses take longer to heal), the duration of use of this initial foot support can vary from weeks to months.

In horses that progress from acute or subacute laminitis to chronic laminitis, the initial form of supportive therapy is usually continued for 3 to 5 weeks. During this period, the distal phalanx usually becomes more stable within the hoof capsule as evidenced by a decrease in lameness and the absence of continued displacement. At this juncture, it is appropriate to initiate corrective trimming and shoeing. The most important aspect about trimming and shoeing is that these procedures should be

guided by the position of the distal phalanx within the hoof capsule, particularly in horses with rotation of the distal phalanx. The relative position of the distal phalanx must be determined by radiography rather than based on the external surface of the hoof capsule (Figure 44-9). The objectives of trimming are to realign the solar margin of the distal phalanx with the ground surface of the hoof capsule, to preserve the thickness of the sole dorsal to the frog, and to position the point of break-over in relation to the dorsal margin of the distal phalanx. This can either be done by taking measurements from a radiograph or repeating radiographs after trimming and shoe placement. The normal thickness of the sole is approximately 15 to 20 mm, and the ground surface of the foot is trimmed accordingly. After the distal phalanx has rotated, it may not be possible to trim the sole or walls dorsal to the mid-quarters while maintaining optimal thickness of the sole; in this case, the foot is only trimmed from the mid-quarters palmarly (Figure 44-10A). This results in an uneven ground surface of the foot that may necessitate building up the wall dorsal to the mid-quarters with a composite before a shoe can be fitted (Figure 44-10B). If trimming the foot in this manner results in increased discomfort, the height of the heels should be increased during shoeing and subsequent realignment of the distal phalanx should be completed over an extended period of time.

The shoe is positioned so that its dorsal margin is no further dorsally than the point at which a shoe would normally be placed in relation to the distal phalanx. This point can be determined by drawing a line that is parallel and 15 to 18 mm dorsal to the dorsal parietal surface of the distal phalanx and that intersects the plane of the newly trimmed hoof (Figure 44-9). The point of break-over can be positioned by either placing the break-over approximately 5 to 7 mm dorsal to the dorsodistal margin of the displaced distal phalanx or by drawing a line extending down the dorsal surface of the distal phalanx to where it intersects the ground (Figure 44-10C). However, some clinicians are more aggressive in moving the point of break-over further palmarly.

Figure 44-9



Schematic of a radiograph illustrates how the shoe should be positioned in relation to the distal phalanx: (1) a line drawn approximately 15-20 mm distal to the solar margin of the distal phalanx to guide trimming the hoof capsule; (2) a line parallel to and 15-18 mm dorsal to the parietal surface of the distal phalanx; (A) intersection of lines 1 and 2, which marks the dorsal-most position for shoe placement; (B) a point approximately 6 mm dorsal to the dorsal margin of the distal phalanx (after trimming) that marks the approximate location for optimal breakover.

Shoeing the Horse with Rotation of the Distal Phalanx

In the long-standing chronic case of laminitis, one of the authors determines whether the pain is solar pain, lamellar pain (indicating a continued instability of the lamellae), or both. The author uses a combination of hoof testers and nerve blocks. In his experience, the palmar digital nerve block will alleviate solar pain (i.e., from solar pressure from the displaced distal aspect of the distal phalanx),[71] but will not alleviate pain emanating from the dorsal lamellae. If the majority of the lameness is alleviated with palmar digital nerve anesthesia, the author feels that the lamellae are most likely stable and, therefore, the entire hoof wall is potentially available to support the foot (along with the caudal sole and frog), and the focus of the shoeing will be on taking the pressure off the cranial sole. If lamellar pain is present, the author will also attempt to ensure that minimal pressure is applied to the dorsal hoof wall.

The type of shoe used can vary from open heeled to closed heeled, as long as they are all positioned in a similar manner. Although numerous clinicians use reverse shoes (and both authors have used them in the past), neither author currently uses them because of the belief that the toe of the shoe provides stability and protection to the dorsal sole and toe region, the area that is commonly the principal source of digital pain and solar compromise in the horse with chronic rotation of the distal phalanx. One of the authors prefers wide-web open-heel shoes, whereas the other author prefers a closed-heel (egg bar) shoe. Regardless of shoe type, it is important that no contact exists between the shoe and the sole at the toe. Redistribution

Figure 44-10A

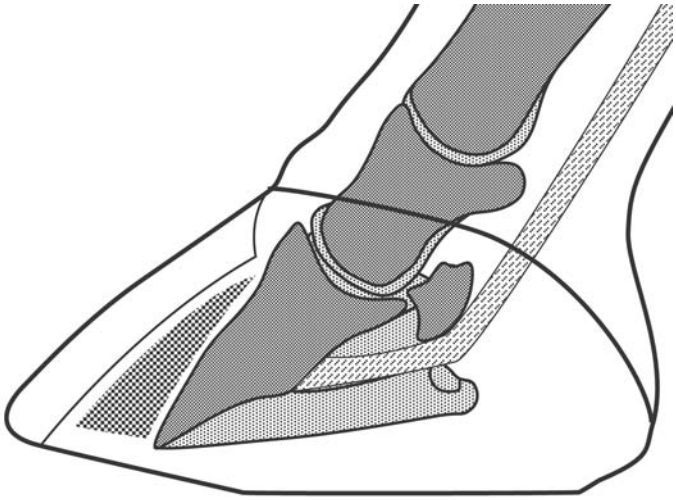


Figure 44-10B

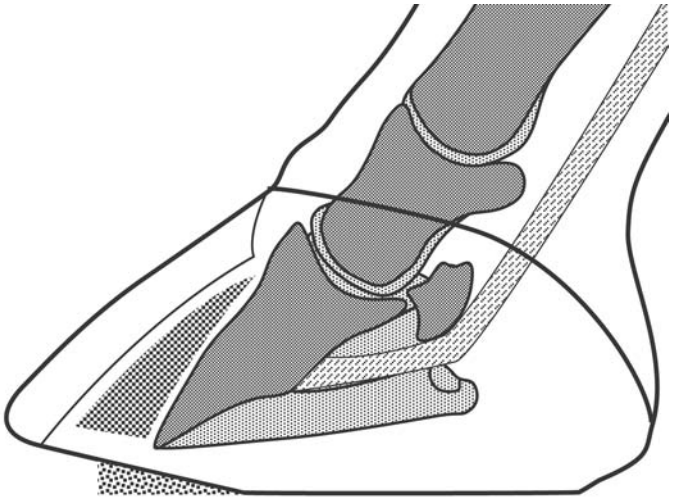


Figure 44-10C

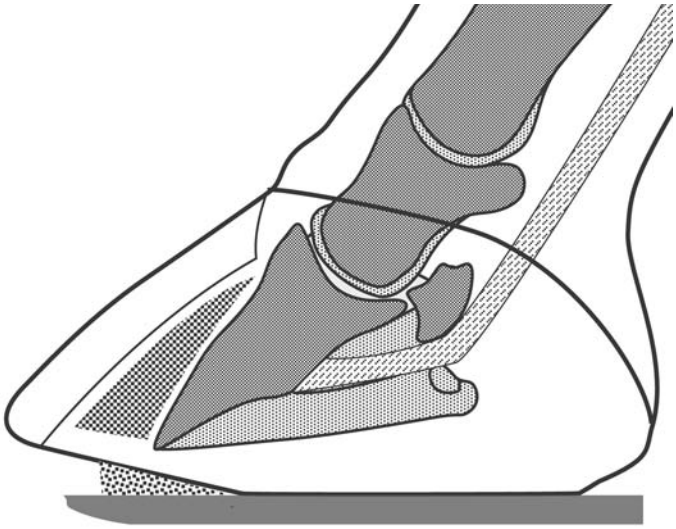
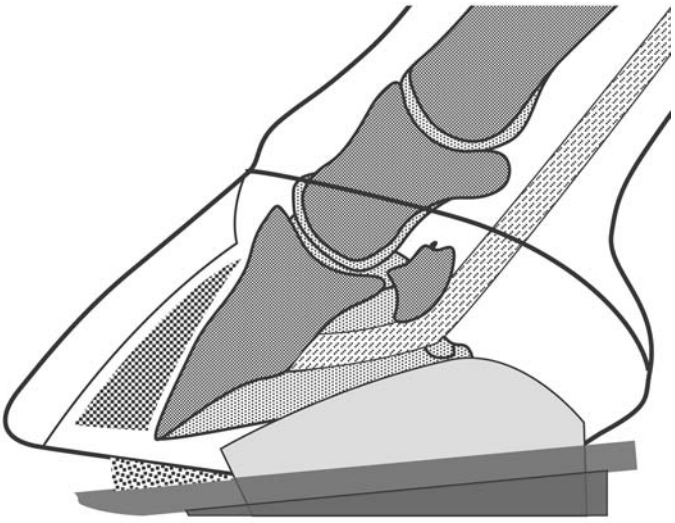


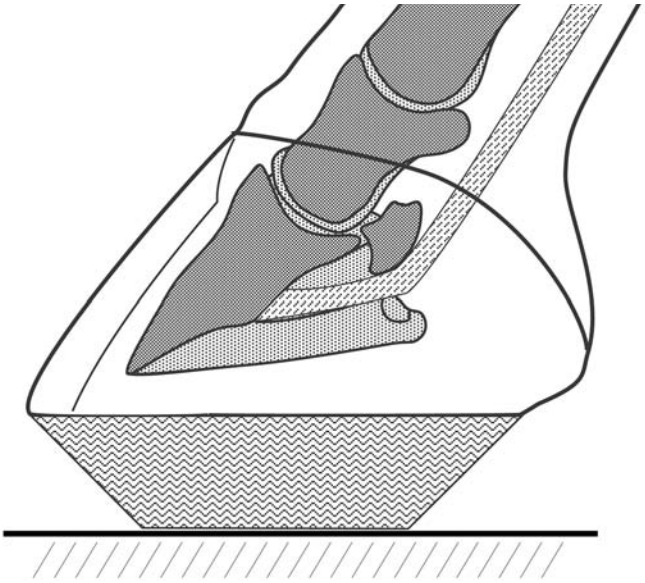
Figure 44-10D



Trimming and shoeing of a horse's foot with rotation caused by chronic laminitis: **A.)** immediately post trimming, **B.)** following application of synthetic composite to build up the wall dorsal to the mid-quarters, **C.)** position of the shoe in relation to the distal phalanx, **D.)** following application of rails and silicone putty.

of weight from the wall to the sole and frog may be obtained by inserting silicone putty under the frog and sole between the branches of the shoe or by applying a heart-bar to the shoe. Both authors prefer a general support of the frog and caudal sole with a resilient substance (e.g., silicone putty) instead of the heart-bar shoe. Two important goals are associated with the use of cushion support material: 1) to cover the entire heel and frog to approximately 15 mm dorsal to the tip of the frog (the toe is not covered in horses with rotation of the distal phalanx in order to avoid putting excess pressure on that region), and 2) to ensure that the cushion support is even with the ground surface of the shoe so that the solar surface is always supported when the limb is bearing weight. Heel elevation is commonly needed to decrease the tension on the deep digital flexor tendon and to decrease the stress on the dorsal hoof wall; this is particularly important when the heels have been selectively trimmed to realign the distal phalanx with the ground surface of the foot. Heel elevation may be achieved by interposing wedge pads (either as rim or full pads) between the shoe and the ground surface of the foot, using a shoe forged with an elevated heel (i.e., a 3-degree egg-bar shoe) or by attaching rails to the ground surface of the shoe (Figure 44-10D). In the latter instance, if commercially available detachable rails are used, heel elevation can be adjusted after the shoe has been applied. One development includes the use of devices such as full-rocker shoes, roller-motion shoes, or beveled wooden or synthetic blocks (Steward Clog) attached with screws that position the point of break-over nearer to the center of the foot (Figure 44-11).[72] The Steward Clog functions as an extreme roller-motion shoe and is designed to allow the horse to vary the angle of the foot in relation to the ground for improved comfort. The shoe has been used most commonly for horses that suffer primarily from distal displacement of the third phalanx.

Figure 44-11



The position of the Steward Clog in relation to the ground surface of the foot and the distal phalanx.

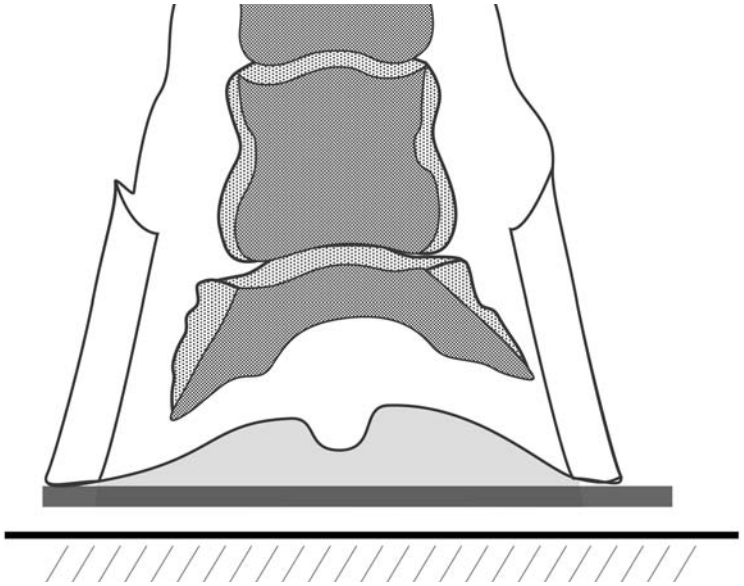
Because the severity of chronic laminitis varies, the shoeing must be tailored accordingly. While all horses require accurate positioning of the shoe, the most severely affected horses require redistribution of weight-bearing to the frog and sole plus heel elevation. Horses that are intermediately affected require redistribution of weight away from the walls, but do not require heel elevation. If response to treatment proceeds according to plan and the soft tissues between the hoof capsule and distal phalanx heal, the severity of symptoms decreases and the shoeing may gradually return toward a more routine type of shoe. However, the veterinarian and farrier must keep these animals on an aggressive trimming and shoeing schedule for the rest of the animal's life to ensure that the foot does not "re-contract."

Chronic capsular rotation may persist after phalangeal rotation has been corrected; this is characterized by convexity of the dorsal hoof wall. This convexity is usually associated with deviation of the middle and distal thirds of the hoof wall away from the parietal surface of the distal phalanx. This condition appears to be compounded by disparate growth rates of the hoof wall, the toe growing slower than the heels. Attempts to improve hoof wall growth have included either removing weight-bearing from the toe or grooving the coronary band. Additionally, rasping the dorsal hoof wall parallel to the parietal surface of the distal phalanx may be successful in exposing abnormal lamellar tissue and encouraging the new hoof wall to grow parallel to the distal phalanx. However, any of these measures is unlikely to be successful at redirecting hoof-wall growth if the coronary papillae (which direct horn tubule growth) are no longer parallel to the dorsal surface of the distal phalanx or the dermal lamellae have been displaced away from the surface of the distal phalanx.

Shoeing the Horse with Distal Displacement of the Distal Phalanx

Horses with distal displacement of the distal phalanx or displacement involving only the medial or lateral side of the digit have different treatment needs than horses with rotation of the distal phalanx. For example, supportive therapy must usually be continued for a longer period of time in horses with distal displacement of the distal phalanx. When these horses are ready to be shod, the shoe should be positioned and additional ground surface recruited to bear weight in a manner similar to that used for horses with rotation. However, horses with distal displacement of the distal phalanx do not appear to benefit from heel elevation, which in fact may worsen the lameness. One of the authors uses an egg-bar shoe and applies digital cushion support to the entire ground surface of the foot if there is no concomitant rotation of the distal phalanx. Horses with distomedial or distolateral displacement of the distal phalanx require appropriate positioning of the shoe, heel elevation, and recruitment of ground surface for weight bearing. Additionally, in order to reduce the stress in the wall of the affected side, an abaxial extension should be applied contralaterally (Figure 44-12). This is most easily achieved by spreading the branches of the shoe and setting the contralateral branch wide.

Figure 44-12



Unilateral distal displacement of the distal phalanx shows the approximate position of an extension on the side contralateral to the displacement. The concavity of the sole is packed with silicone putty.

Surgery

Surgery is seldom warranted in the treatment of horses with acute laminitis, but deep digital flexor tenotomy and surgical drainage and debridement of septic tissue may both be needed in the treatment of horses with chronic laminitis. Deep digital flexor tenotomy is performed to achieve greater reduction in the moment about the distal interphalangeal joint than is possible with corrective trimming and shoeing alone in horses with rotation of the distal phalanx. This procedure is indicated 1) when the distal phalanx continues to rotate within the hoof capsule despite attempts to stabilize it, 2) when a horse with rotation of the distal phalanx has unremitting pain that cannot be managed with trimming and shoeing alone, and 3) to treat secondary flexural deformity of the coffin joint. The tenotomy is usually performed in the mid-metacarpal region with a guarded bistoury in the standing horse. Tenotomy in the mid-pastern region is usually reserved for a repeat tenotomy, and is usually performed with the horse under general anesthesia because the presence of the tendon sheath requires more stringent aseptic technique compared to the procedure in the mid-metacarpal region. Realignment of the solar margin of the distal phalanx with the ground surface of the hoof capsule (commonly termed "derotation") is performed immediately after the tenotomy. It is critical to realize that the veterinarian and farrier only have a 4- to 6-week window to achieve optimal realignment of the distal phalanx. Slight, but significant, subluxation of the coffin joint occurs in most horses following deep digital flexor tenotomy, which necessitates corrective shoeing to prevent the development of degenerative joint disease. In order to minimize subluxation of the distal interphalangeal joint after tenotomy, one of the authors uses a combination of a slightly extended heel (i.e., with egg-bar shoe) and heel elevation, whereas the other author uses only heel elevation. It is best if radiographs are taken with the shoe and pads temporarily attached in order to determine the appropriate amount of heel elevation to avoid subluxation of this joint (the amount of heel elevation needed may vary from 3 degrees to over 10 degrees). An additional benefit of deep digital flexor tenotomy is accelerated growth of the sole. Although some clinicians perform a tenotomy of the inferior check ligament initially as a more conservative surgical approach to decreasing tension on the deep digital flexor tendon, neither author uses this approach.

Surgical drainage is indicated when abscessation occurs. However, both authors feel it is important to preserve as much integrity of the sole as possible because large solar defects permit prolapse of the solar dermis; this prolapsed tissue is extremely sensitive. Additionally, defects in the solar integument heal far more slowly in laminitic horses than they do in healthy horses. One author preserves solar integrity by making one to four small holes in the sole, whereas the other author prefers to preserve the full thickness of the sole and drain the abscess dorsally or abaxially through the distal hoof wall at its junction with the sole. Debridement of the distal phalanx is indicated whenever septic pedal osteitis is present. However, establishing the presence of septic osteitis can be problematic because many horses with drainage that have radiographic evidence of pedal osteitis do not have septic osteitis. It is the experience of one of the authors that many solar lesions dorsal to the frog caused by pressure on the sole from the distal phalanx will heal without debridement of the soft tissues or distal phalanx by altering the biomechanics of the foot. To accomplish this, appropriate biomechanical principles are used to decrease the downward pressure by the dorsal margin of the distal phalanx to relieve the solar pressure, usually by elevating the heels and/or performing a deep digital flexor tenotomy combined with corrective trimming to realign the distal phalanx with the solar surface. If conservative drainage, systemic and local antibiotics, and corrective shoeing do not resolve the problem, then surgical debridement is warranted.

Historically, dorsal hoof wall resection was performed when more conservative treatments failed to encourage new hoof-wall growth from the coronary band to progress parallel to the parietal surface of the distal phalanx. The rationale for performing hoof-wall resections was to encourage hoof-wall growth by removing hyperplastic keratinized lamellar tissue and by removing distracting forces within the hoof wall. However, the authors believe that this technique further destabililzes the distal phalanx because it removes any remaining dorsal lamellar attachments and concentrates stress at the abaxial margins of the resection. Partial hoof-wall resection involving only the distal half of the wall is more acceptable because it offers relief of pressure at the coronary band while maintaining sufficient hoof to support the foot. Alternatively, the coronary band may be grooved by creating a horizontal full-thickness groove through the stratum medium of the hoof wall parallel to and approximately 1 cm distal to the coronary band from one toe-quarter junction to the other. This technique mechanically dissociates the new wall from the old wall, thereby reducing any distracting forces in the dorsal wall from weight-bearing and locomotion. Unfortunately, neither technique restores normal orientation of the dorsal hoof wall in relation to the distal phalanx if the coronary band horn tubules are not aligned with the distal phalanx or if a wedge of dermal tissue has developed dorsally between the bone and the lamellar epithelium. The dorsal hoof wall can be dressed back so that the exterior surface of the hoof wall is nearer to being parallel with the dorsal surface of the distal phalanx, but the wall will subsequently be thinner and not as strong.

Other Supportive Care and Miscellaneous Therapies

Several other aspects of care for laminitic horses need to be considered, including nutritional needs, limb edema, and pressure sores. Although the nutritional needs of the laminitic horse have not been determined, the practice of starving laminitic horses for fear of exacerbating the laminitis is unwarranted. The only exception might be the first 1 to 3 days after the gastrointestinal disease that may have precipitated the laminitis. It is more appropriate to provide good quality hay supplemented with a complete ration if necessary; feeding grain is inadvisable in most active cases of laminitis. If supplemental feeding is necessary (because of inablility to masticate hay, or severe loss of body condition), it is best to feed small amounts of a pelleted complete ration several times during the day to avoid the disruption of the flora in the gastrointestinal tract that can occur with one or two large feedings. It is imperative that animals be deeply bedded if there is a firm surface (concrete or rubber) in the stall.

Limb edema should be controlled in acutely laminitic horses with bandages. Pressure sores in chronically laminitic horses should be kept clean, debrided if necessary, and dressed with a topical medication such as zinc oxide. Horses that develop flexural deformities at the metacarpophalangeal joint may respond with increased comfort and mobility if the lower limb is splinted soon after the symptom is observed. Cryotherapy (placement of the affected limbs in ice) performed on horses in the developmental stages of laminitis (using a grain overload model) reportedly decreases the basement membrane separation observed in laminitic horses and limits or delays the onset of clinical signs.[73] However, the effectiveness of this therapy in acutely laminitic clinical cases and the manner in which it should be applied have yet to be investigated. Contrast venograms performed for diagnostic purposes have also been reported to have beneficial therapeutic effects,[74] including an improvement in lameness and an increase in hoof growth. Both of these benefits are temporary. The explanation for these purported effects is unknown but warrants further investigation.

Summary of Proposed Treatment Regimens for the Different Stages of Laminitis

Treatment of laminitic horses must take into account the variety of ways in which horses with the disease present and the ambiguities surrounding the benefits of many of the pharmacologic agents that have been advocated for use in treatment of the disease. Obviously, prevention of laminitis through appropriate prophylactic therapy is ideal. Unfortunately, it is difficult to predict accurately when acute laminitis will occur even when a horse is known to have a disease known to increase the animal's risk of developing acute laminitis. Therefore, treatment is frequently not started until a horse shows clinical symptoms of acute laminitis, and when treatment is started, it is not on an aggressive scale because such therapy is time-consuming and expensive.

Overall Prophylactic Therapy for the Horse at Risk of Laminitis

Most horses undergoing gastrointestinal crisis are at risk of developing laminitis (i.e., they may be in the developmental stage of laminitis). Horses exhibiting more severe signs of systemic compromise (i.e., high heart rate, injected membranes) appear to be at greater risk. The recommended treatment is aggressive supportive therapy (i.e., IV fluids, etc.) to maintain adequate circulatory function, and aggressive use of flunixin meglumine and possibly polymixin B to combat bacterial toxemia and inflammation. For horses with severe symptoms of endotoxemia, treatment with endotoxin antiserum may be warranted. Broad-spectrum antibiotics should be used if systemic sepsis is suspected or should the primary condition warrant it. Shoes should be removed if present and the front feet (or all four feet) should be supported, most commonly with either Styrofoam

support blocks, silicone putty, or silicone putty in conjunction with Redden Modified Ultimates. As clinical laminitis usually ensues 2 to 3 days following the initial systemic insult, it is advisable to provide aggressive prophylactic medical and foot care for at least 3 days following a gastrointestinal crisis.

Overall Therapy of the Horse in the Acute Stage of Laminitis

Horses in the acute stages of laminitis may be treated with flunixin meglumine (if moderate systemic compromise still exists), or phenylbutazone (if the horse is systemically stable but lame), or a combination of the drugs. Ketoprofen is an excellent alternative in horses with compromised kidneys or a history of gastrointestinal ulceration. Acepromazine can be administered to address vascular concerns, and to decrease stress levels for the horse. Dimethyl sulfoxide (DMSO) is frequently used for its anti-inflammatory effects and purported action against free radicals. Foot support is critical using Styrofoam support blocks, level rubber pads made from cushion support, or Redden Modified Ultimates.

Overall Therapy of the Horse in the Chronic Stage of Laminitis

The horse with chronic laminitis will be addressed with a combination of NSAIDs (most commonly phenylbutazone), corrective shoeing, and possibly surgery. The choice of shoeing will depend, as described above, on the stability of the lamellae, the pattern of displacement, and how the animal moves. Deep digital flexor tenotomy will most likely be used in the horse with severe rotation, and surgical debridement of the distal phalanx will most commonly be performed on those horses in which there is persistent drainage with radiographic evidence of lysis of the distal phalanx that has not responded to corrective shoeing.

Prognosis

The prognosis for survival and return to work has been correlated in one report to the degree of the dorsal rotation of the distal phalanx visible on radiographs.[75] In another study, the prognosis has been correlated to the severity of clinical symptoms, but not severity of rotation; in that study distal displacement negatively impacted the outcome.[76] Another report suggests that the vertical distance between the coronary band and the proximal aspect of the extensor process is the most useful prognostic indicator.[42]

In horses with acute laminitis, the best prognostic indicator for survival is the severity of the initial lameness, which appears to correlate with the severity of the lamellar injury. However, the prognosis varies considerably among horses, and many horses with severe acute laminitis will improve dramatically over 2 to 3 weeks if rotation of the distal phalanx is prevented. If displacement of the distal phalanx occurs, stabilization of the degree of lameness (and displacement) over a 2- to 4-week period may be a suitable goal as we continually improve our ability to address chronic laminitis.

In the authors' experience with chronic laminitis, numerous factors must be considered when assessing the prognosis, including capsular rotation, phalangeal rotation, the thickness of the sole distal to the dorsal margin of the distal phalanx, and the presence of complications including infection and secondary flexural deformities. The severity of capsular rotation is a better indicator of how much corrective shoeing will be required. The severity of phalangeal rotation is a better indicator of whether tenotomy will be necessary to facilitate the realignment of the distal phalanx. The response to corrective shoeing over 3 to 6 months is the best indicator of how close to normal the final appearance of the foot will be and the likelihood that the horse will return to some form of exercise.

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