# INFECTIOUS DISEASE MANAGEMENT IN ANIMAL SHELTERS



LILA MILLER and KATE HURLEY

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# Dedication

This textbook is dedicated to the countless homeless animals in shelters everywhere, and the steadfast veterinarians and shelter staff who toil tirelessly on their behalf.

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# Preface

Shelter medicine is a relatively new specialty area in veterinary medicine. In the past, euthanasia has been the most common response to infectious disease in sheltered animals. Even when shelter staff had the desire and resources to seek alternatives, veterinarians and fellow shelter professionals may have advised depopulation. This did not reflect a lack of compassion, but simply a lack of knowledge regarding safe alternatives that addressed the needs of individual animals while protecting the health of the shelter population and surrounding community. Balancing these concerns in the resource-limited shelter environment is a complex task, but veterinary science need not shy away from complexity. The same principles of evidence-based medicine and herd health, applied so effectively in other settings, create a powerful set of tools to maintain the health of this most vulnerable population.

While the challenges inherent to shelter medicine are substantial, the potential rewards are great. Because so many animals pass through shelters, the effects of policies, both good and bad, are magnified. Effectively managing outbreaks, preventing infection, and establishing wellness programs in shelters have the potential to save countless lives, prevent tremendous suffering, and even save shelters money and staff time that can be devoted to other urgently needed programs.

*Shelter Medicine for Veterinarians and Staff* was the first textbook for veterinarians devoted solely to the care of animals in shelters. It was published in 2004 and very ambitiously tackled a variety of medical and management issues that veterinarians working with shelters would need to know, but only touched on the specifics of managing disease in shelters. It very quickly became clear that a textbook was needed that focused entirely on the management of infectious disease in animal shelters. This textbook was conceived in 2005 and work began shortly thereafter.

The purpose of this text is to provide detailed, practical information regarding fundamental principles of disease control in shelters and specific management of the most important diseases encountered in dogs and cats in shelters. The emphasis throughout is on strategies for the prevention of illness and mitigation of disease spread. Practical information on treatment and considerations for adoption are also included. This text is not intended to provide the reader with exhaustive information about each disease included nor does it cover every disease that may be encountered in a shelter animal. Other textbooks are available that focus on the details of disease pathogenesis, individual animal treatment protocols, and less common conditions in shelter dogs and cats as well as other species of importance. The reader is encouraged to use these resources in conjunction with this text. The recommendations contained herein are based on research coupled with the authors' collective experience. As in any practice setting, final decisions regarding selection of treatment protocols, safe drug use, and shelter practices are the responsibility of the clinician.

# Acknowledgments

This book is truly the work of many people. We would like to thank the contributing authors who provided their valuable time and expertise so freely to this project. We recognize that completion of the chapters was an additional project for individuals with extremely busy lives. Nevertheless, the authors worked unstintingly to provide the very best available resources, often gathering together information that has never before been presented in this format. Each chapter is a gift for the homeless animals we are all working to care for.

In reflecting on the circumstances that made this book possible, we must acknowledge all those pioneering veterinarians who established the integral role of the veterinarian in shelter animal care and who founded the field of shelter medicine. We must also gratefully acknowledge the shelter staff and volunteers who work tirelessly to care for homeless pets and who help make our work meaningful.

We recognize Wiley-Blackwell for their vision in supporting publication of this and the first textbook on shelter medicine, *Shelter Medicine for Veterinarians and Staff*. They courageously answered the need for a resource dedicated to a population of animals previously little regarded by veterinary publishers.

We would especially like to thank the ASPCA and UC Davis for recognizing the importance of the textbook. Our supervisors, colleagues, and residents have all contributed with their patience and support over the three years it took to bring this project to its completion.

Special thanks must also go to Diane Wilson, the project manager, whose excellent organizational skills, encouragement, and enthusiasm allowed us to focus on the process of assembling all the information contained in this text.

All the authors provided invaluable contributions, but two authors went above and beyond the call of duty: Sandra Newbury co-authored an epic four chapters, and Miranda Spindel, in addition to co-authoring two chapters, provided valued editorial assistance with several others.

Finally, we would like to extend a heartfelt thanks to our beloved families, friends, and pets, who tolerated our prolonged absence and neglect as we worked day and night on this book.

Kate would like to personally thank: Muggs the Terrier for being a warm anchor at my feet for the many hours I sat at my desk; Foss the Cat for refusing to take my angst seriously; my Mom for raising me to believe I could make a difference in the world; and all my wonderful family, friends, and partners in dance and crime who supported, amused, and distracted me throughout this project and who always remind me of how much more there is to life.

Lila would like to personally thank: my parents Virginia and Lonist, who have never wavered in their love and support over the years; my brother Rodney and his family; Corlette and Lila for their patience; Mr. Rusty and Miss Coco, two cats who always met me at the door on those late nights coming home from the office; and the many friends and colleagues who have cheered me along the way.

Without your support and encouragement this book surely would not have been possible. We missed you and are happy to be back, if only until the second edition is due!

# Infectious Disease Management in Animal Shelters

# Section 1
# Principles of Disease Management

# 1
# Introduction to Disease Management in Animal Shelters

*Kate F. Hurley and Lila Miller*

## SHELTER MEDICINE AS A SPECIALTY

The development of shelter medicine as a valued component of veterinary science reflects a variety of trends, including increased value placed on animals and a desire to seek alternatives to euthanasia as a response to companion animal homelessness; greater resources and sophistication on the part of animal-sheltering organizations, which create unprecedented opportunities for the design of quality facilities and health-care programs; and an explosion in the amount of evidence-based knowledge available to guide best practices for shelter animal care.

Although veterinarians have been working with shelters for years, it has only recently been acknowledged that this is a very complex field requiring special expertise. The first formal shelter medicine class at a veterinary college was offered by Cornell University in 1999; there are now shelter medicine programs, courses, and residencies offered at several universities. Many major veterinary conferences offer lectures in shelter medicine as well. There is an Association of Shelter Veterinarians whose membership is growing daily. As interest in the field steadily increases, more studies are being conducted to determine better ways of managing the health and welfare of shelter animals.

### Roles of veterinarians in shelters

Veterinarians work with shelters in a variety of capacities as volunteers, employees, or consultants. The range of authority can be very broad. They may be on the high end of the chain of command as shelter directors or board members, or they may enter the shelter merely to provide per diem surgical or medical services. Many veterinarians fall somewhere in the middle as regular or part-time employees in charge of the health-care program.

Employment and consulting opportunities for shelter veterinarians are rising, and these opportunities represent rewarding and challenging options for professional practice. However, currently only a small percentage of veterinarians have a specialized background or expertise in this area. There is a great need to expand learning opportunities so that veterinarians may better serve shelter populations.

### Herd health approach to shelter medicine

Simply stated, shelter medicine is herd health medicine for companion animals. The design of a comprehensive program to control, manage, and reduce the transmission of disease in animal shelters is a challenge for the veterinary professional. Current traditional clinical veterinary education focuses either on the design of cost-effective herd health protocols that emphasize disease prevention and maximize the production of animal products for food or that deliver sophisticated and potentially costly health care to individual companion animals. Shelter medicine requires a blend of these two approaches. Often the care of each individual shelter animal is best served by rigorous attention to the wellness of the group as a whole. When disease transmission is prevented, individual animals are spared serious illness that otherwise might not be treatable. When the population as a whole is healthy, more resources are available for those individuals requiring an additional level of care.

Another key historical difference in the two approaches to clinical practice revolves around the emotional bond and value attached to companion animals that do not exist to the same degree in large animal agricultural practice. This bond has a major impact on the ability to deliver science and evidence-based management

recommendations to shelters. In the past, euthanasia was the primary tool for managing population numbers and disease in shelters, just as slaughter is often used to manage disease in large animal herds. The increasing rejection of the routine use of euthanasia by animal shelters can be traced to a number of factors, the human–animal bond being at the forefront. Although animal welfare groups may complain that companion animals are considered "disposable," many people view them as family members. The same unprecedented interest in applying the latest medical advances to improve the health and well-being of companion animals applies to shelter animals as well.

Shelter medicine seeks to combine herd health management strategies and principles with individualized animal care in a way that has not been done before. Confronting shelter medical problems can therefore present a true quandary for the well-meaning companion animal practitioner who lacks a background in either herd health or shelter management. Conversely, the large animal herd health practitioner who tries to apply traditional methods of outbreak management in a shelter (i.e., depopulation, closing the herd down, and testing all newcomers) will find that in many cases these strategies will be rejected outright. This textbook was conceived to help veterinary professionals sort through the haze to find effective, acceptable, and workable solutions to disease problems and to promote health and wellness in shelter environments.

### *Unique aspects of the shelter environment*

One might argue that the design of herd health care for companion animals is not new, and that shelter medicine does not require all this attention. It is true that some of the basic principles of disease control that have been utilized for managing kennels, catteries, and research laboratories apply in shelters, but significant differences exist. The goals of breeding and research facilities can be uniformly defined, whereas animal shelters have unique goals and challenges related to their varied missions. Differences and fluctuations in funding, resources, philosophy, training, governance, and even community attitudes towards the shelter all play roles in the functioning and priorities of shelter health programs. Husbandry practices must often be implemented in shelters that have never been applied in any other communal housing situation, thereby forcing shelter veterinarians to be innovative, resourceful, and courageous in their decision making.

The disease prevention component of shelter medicine is integrated into a complex health-care program that extends far beyond simple recommendations about vaccinations and deworming. The range of knowledge and experience required to design a comprehensive shelter wellness program can be quite daunting. The health aspect of animal sheltering intersects with virtually every other program within a shelter, including adoptions, volunteer programs, foster care, stray animal management, zoonotic disease control, cruelty investigations, and even design of the shelter building itself. In other words, few if any shelter programs are not directly or indirectly affected by animal health considerations. In addition to an in-depth knowledge about infectious disease, shelter veterinarians must be knowledgeable about several other disciplines, including sanitation, animal behavior, nutrition, husbandry, stress reduction, data collection, veterinary forensics, high-volume, high-quality spay/neuter techniques, and so much more. For more comprehensive information about shelter medicine and shelter operations, the reader is referred to *Shelter Medicine for Veterinarians and Staff* by Miller and Zawistowski, and to www.sheltermedicine.com, the Web site of the Koret Shelter Medicine program at the University of California, Davis, School of Veterinary Medicine. Additional resources are listed in Appendix 1.1. Most of the information in this introductory chapter will be covered in more detail in Chapters 2, 3, and 4 on wellness, outbreak management, and sanitation, and in each of the various other chapters. This chapter serves as an overview and introduction to the concepts necessary for designing an effective health program.

## SHELTER MISSIONS AND GOALS

As noted above, an understanding of the shelter's mission is critical to the design of an effective shelter health program. A medical program that keeps animals healthy but fails to help meet the major goals of the organization – such as adoption of animals, increasing spay/neuter rates in the community, or reducing euthanasia – cannot be considered a complete success. Even advising on management of an outbreak or treatment of an individual animal requires an understanding of that particular shelter's goals and resources, both in general and for that individual animal or situation.

The American Society for Prevention of Cruelty to Animals (ASPCA) Community Outreach department estimates there are between 4,000 and 6,000 animal shelters in the United States alone. It is a mistake to assume that all shelters have identical goals. Although there is often an overlap in the provision of services, shelters tend to fall into two basic categories: they are either municipal shelters charged primarily with animal control responsibilities, or private, nonprofit shelters. Some communities have

1.1

1.2

**Figures 1.1. and 1.2.** Shelter resources, design, and mission vary widely. Figure 1.1 shows an overcrowded colony kennel for dogs. Figure 1.2 shows an enriched communal space for cats.

multiple shelters, both municipal and private, while others do not have shelters at all.

Not all shelters focus on adoption and rehabilitation of homeless animals. The allocation of municipal shelter resources may emphasize stray animal capture, protection of public health, complaint resolution, and law enforcement, whereas the private animal welfare organizations may dedicate larger expenditures to vaccinate, deworm, test for disease, treat, and neuter animals for rehoming. However, there is an increasing tendency for municipal as well as private shelters to work toward an increased adoption rate; seek alternatives to euthanasia as a strategy for disease management; and develop programs that emphasize public outreach and prevention of problems that lead to relinquishment. There is great variation within private shelters as well, ranging from those that provide lifelong sanctuary to a limited number of animals to those that accept all animals presented and euthanize those they are unable to place, and many variations on these strategies. Some of the different types of shelters are described in more detail below.

Just as it is important not to judge clients by their appearance, the breed of their pet, or the vehicle they drive, it is not advisable to make assumptions about shelter philosophy or resources based on shelter type, title, location, or history. Priorities may change and opportunities emerge with changes in management or philosophy. Even the smallest or poorest shelter may prioritize adoption, utilize progressive spay/neuter, volunteer, foster or other programs, or pursue alternatives to euthanasia for management of disease. Even if these possibilities are not available immediately, shelters may incorporate them into future plans. Therefore, all options should be offered to shelters and ideal standards explained, just as they would be for any patient. Figures 1.1 and 1.2 depict shelter housing for dogs and cats.

### Municipal shelters

It is a common belief that most municipal shelters operate chronically overcrowded, underfunded programs located in dilapidated facilities in undesirable sections of the community. While this model does exist, animal sheltering has undergone a fundamental change in many communities over the past 20 years as the human–animal bond strengthens and society becomes less tolerant of animal abuse and neglect. Shelters of all types have experienced increased internal and external motivation to upgrade the quality of care they provide. There has been a varied response to this pressure: many communities are renovating, retrofitting, and building new facilities with the latest innovations, consulting with veterinarians, expanding staff and services, etc. Veterinary expertise is required to effectively implement many of these changes.

Municipal shelter functions historically focused on stray animal pickup, control of dangerous animals, including quarantines of animals that may have bitten someone, capture of free-roaming animals, nuisance complaints,

investigation of animal cruelty complaints, handling of wildlife, etc. They may also offer adoptions, low-cost spay/neuter and vaccination clinics, humane education, and an assortment of volunteer, foster care and other community programs. Most municipal shelters are mandated to accept all animals regardless of their capacity to find homes or take appropriate care of them, and utilize euthanasia regularly for animals that cannot be safely placed for adoption and as a tool to manage the population numbers as well as disease.

### Private shelters

Private shelters are generally chartered as 501(c)3, not-for-profit organizations; they are privately funded and their policies are often set by elected or volunteer boards of directors. Private shelters may incorporate the words "humane society" or "SPCA" in their titles, but most private shelters operate independently and are not related to each other, nor are shelters titled "SPCA" related to the ASPCA. Some private shelters contract to provide animal control services to local government entities (county or city), although an increasing number have relinquished animal control contracts to focus on adoption, spay/neuter, behavior, and humane education programs.

One of the latest ongoing trends in animal sheltering is for humane societies to adopt policies known as "no kill," meaning they will not euthanize adoptable animals for lack of space to house them. This has a major impact on animal care programs: "no kill" organizations or limited admissions facilities may restrict their admissions and hold animals for longer periods, which can create unique challenges for maintaining animal health and mental wellness. Studies in United States shelters have shown that the longer animals remain in a shelter, the more likely they are to become sick, although a recent study completed in shelters in the United Kingdom showed the opposite trend with respect to feline upper respiratory infection (Edinboro, Janowitz, et al. 1999; Edinboro, Ward, et al. 2004; Edwards, Coyne, et al. 2008). This illustrates the impact that variations in shelter environments, management practices, and even cultural attitudes can have on animal health.

A great deal of variation can be found even within the scope of private shelters with similar titles. It should be noted that few if any descriptive terms can be assumed to have consistent meaning across all shelters. The term "no kill" is just one example. Some shelters that use this term do perform some euthanasia, while some shelters that follow similar policies to those commonly found in "no kill" shelters (e.g., they limit intake and/or do not perform euthanasia for population control) do not use the term.

### Other types of shelters

Not all shelters can be categorized as either strictly municipal or private. In addition to private shelters that accept the contract to provide municipal services, some municipal shelters solicit private donations to provide services not mandated or paid for by their contractual arrangement with the municipality. Other foster care and rescue groups may work out of private homes or focus on a specific breed, age, or special needs animals. They often work closely with shelters to rescue animals that can be rehabilitated and placed for adoption if provided with veterinary and behavioral care that cannot be offered by the shelter. A limited number of sanctuaries also exist that will provide lifelong care for animals that cannot be successfully or safely adopted.

## REGULATION OF SHELTERS

There is little, if any, accountability of shelters to any particular entity. There is no parent organization to which all shelters belong: the ASPCA and the Humane Society of the U.S. (HSUS) are autonomous, independent organizations that do not oversee or run local SPCAs, humane societies, or other animal rescue or adoption organizations. Most states do not regulate shelters, nor does the federal government. Only a few states have minimum standards of care for animals in shelters. Regulations pertaining to shelters are often limited to providing guidelines for euthanasia and mandating holding periods for stray animals and bite cases. However, the shelter veterinarian should become familiar with relevant local laws, as there is an increasing trend towards greater regulation and scrutiny of many aspects of shelter practice.

### Requirements for data reporting

While a few states do require reporting of certain statistics related to animal intake and disposition, this is not generally the case. Even the number of shelters operating in the United States is unknown. In addition to the lack of reliable data regarding the number of shelters in this country, the lack of reporting requirements makes it difficult to accurately determine the number of animals admitted or euthanized in shelters, or to establish norms for disease rates or other important measures of shelter animal health. However, while national or international figures remain elusive, individual shelters and communities are becoming increasingly sophisticated in tracking important data related to the well-being of animals in their communities. With the widespread use of computerized, and in some cases Web-based, shelter database programs, pooled data

collection and analysis from multiple shelters may become increasingly possible in the future.

## SHELTER CHALLENGES

Any veterinary professional who is working with a shelter must have an understanding of the obstacles and challenges the shelter faces in order to design an effective and comprehensive program that combines preventative health-care strategies with wellness protocols. Whatever the shelter's particular mission, one goal of every shelter should be to provide a clean, healthy, and safe environment that supports the maintenance and improvement of the health of all of its residents, regardless of the length of their stay or ultimate fate. Some of the issues that must be dealt with in order to achieve these goals will be touched upon briefly in this chapter.

### Shelter resources

Shelters, regardless of their mission or type, are often limited in the resources they can offer to provide animal control and welfare services. Human and animal services must often compete for sparse municipal funding, and private fundraising efforts may be insufficient to meet the targets and needs of the shelter program. Veterinarians can best serve shelters by advising on allocation of limited resources for maximization of shelter animal health in the context of the shelter's overall goals and mission. Even with limited funding, shelters can maintain a healthy environment for the animals with meticulous attention to management of population numbers, good sanitation, prompt isolation of diseased animals, stress reduction, and other practices described in this chapter and elsewhere in this text.

Veterinarians should take a broad view when advising on resource allocation in shelters. In many cases, when all costs are considered, prevention of illness is not only more humane for the animals and preferable for public health, it is more cost effective than the alternative. Even apart from ethical considerations, a modest investment in vaccination, diagnostic testing, or sanitation will be amply repaid if more animal lives are saved and more animals are adopted as a result: adoption fees can offset some of the costs of care, while the costs associated with euthanasia and disposal can be substantial. Thus the best approach for animal health and adoption can also prove to be a sound financial choice, especially when preventive measures are emphasized.

Fortunately, many of the practices that enhance shelter animal health are no more costly than less effective practices. For example, as described in Chapter 5 on vaccination and immunology, vaccinating animals at the time of admission is far more likely to confer protection than vaccinating them a few days or even a few hours later, and costs no more. In some cases, best practices are actually less expensive than the alternative. For instance, Chapter 4 on sanitation describes in-residence or "spot" cleaning as a preferred method of cleaning for cat cages. This takes less time and utilizes fewer costly chemicals than more intensive daily disinfection, while potentially reducing stress and limiting disease transmission among cats.

If resources are so limited that basic practices to protect animal health cannot be implemented, this should be brought urgently to the attention of management, funding entities, and the public. The inability to limit disease spread in the shelter can have substantial implications for public and community animal health as well as the welfare of sheltered animals, and should not be tolerated as a long term situation. Figure 1.3 is an example of inadequate care being provided to a puppy suffering from parvovirus.

Even shelters with ample resources may encounter problems if there is a failure to align expectations with the available facilities, staffing, and funds, with consequent compromises to animal and human health. Many ambitious and well-intentioned organizations, public and private, strive to take in more animals than they can properly care for, and the results are dirty, malodorous, overcrowded facilities with diseased and possibly dying animals. This in turn leads to animal pain and suffering, decreased visits from potential adopters, bad public relations (especially if there are disease outbreaks or diseased animals being released from the shelter), and increased

**Figure 1.3.** A fundamental goal of shelter health programs must be prevention of suffering. This puppy with parvovirus is suffering from inadequate care.

mortality and euthanasia rates. In some cases, shelters have actually been charged with cruelty to animals for their failure to provide the appropriate food, water, shelter, and veterinary care that is necessary to prevent suffering.

To prevent such harmful scenarios, veterinarians and managers should work together to perform a realistic assessment of how many animals can be humanely housed in the facility and then allocate resources to provide appropriate care and humane treatment. This forms the foundation for implementing many other practices described in this text: preventing disease, mitigating stress, and responding to outbreaks without resorting to depopulation are all far more readily accomplished when the shelter's fundamental capacity is not exceeded. Limiting the population within the shelter need not lead to any increase in euthanasia or decrease in the number of animals adopted. As described in Chapter 2 on wellness, population within the shelter can be limited either by reducing intake and/or by moving animals more rapidly through the shelter. Maintaining animal health is one powerful tool to ensure that animals move through the shelter to adoption without delay. Other methods to decrease shelter crowding include appropriate use of foster care and rescue groups, animal transport and transfer programs, and proactive adoption efforts that do not rely on shelter crowding as a trigger. Attentive management is the foundation of optimizing these programs, and is described in more detail in Chapter 2 on wellness. Although immediate results may not be seen, long-range strategic planning should aim to reduce intake through shelter and low-cost spay/neuter programs that are accessible to the community. The improved animal health and shelter conditions that result from working within a shelter's true capacity may actually lead to an increase in adoptions as well as improved quality of life for shelter animals and staff.

**Shelter administration**

As tempting as it may seem, it would be inappropriate to label all the problems in shelters as a by-product of inadequate funding. One potential barrier to an effective shelter health program is a lack of communication and understanding between the veterinarian and the shelter's management. Although it is increasingly recognized that the veterinary component forms an integral part of the overall shelter management team, some shelters still separate the medical program from general shelter operations, not realizing the impact of animal health decisions on all aspects of the shelter's programs. This segregation can result in misunderstandings that lead to shelter veterinarians being accused of being unsympathetic to the plight of the animals, not understanding the shelter's goals or problems, or of outright incompetence and cruelty when difficult health-care decisions are made that are not popular with staff or in keeping with past practices.

To help avert some of these issues, the role and expectations for the veterinarian should be clearly defined within each individual shelter (Miller 2007). It is important to establish chains of command, determine which areas are the domain of the veterinarian, and create levels of authority and decision making. For example, will the veterinarian determine which animals are suitable for adoption? How are euthanasia decisions made? Who performs behavior assessments? Who selects the diet? Who determines the movement of the animals within the facility or deployment of staff?

In some cases, shelter personnel may cling to the idea that certain elements of the shelter health-care program do not need the involvement of veterinarians. This may be particularly true if there has been a history of less-than-successful communication with community veterinarians who had limited knowledge of shelter considerations and constraints. However, staff should be made aware that stress reduction, sanitation, population management, facility design, etc., all require veterinary input as much as do conventional medical decisions about vaccinations and anthelmintics. The restriction of the veterinarian to medical decisions only without any role in strategic planning, administration, training, or management can render implementation of new health-care protocols difficult for everyone involved. To be effective, shelter veterinarians should be an integral part of the management team with the authority to make or participate in decisions on all matters that pertain to animal health and welfare. If the veterinarian is not a member of the management team, a clear method should be developed by which management and veterinary staff can communicate routinely regarding issues of mutual concern.

Problems may also arise when shelter staff consult with local practitioners who are uninformed about the differences between private practice and shelter medicine and are therefore critical of practices recommended by shelter veterinarians, especially when taken out of context. Although there is increasingly widespread awareness of shelter medicine, some private practitioners may still apply their standards of care to shelter animals, not realizing that the different recommendations regarding vaccinations, treatment, spay/neuter, etc., for this population are based on a different set of risk factors, assessment tools, circum-

stances, and resources. This different standard of care should not be interpreted to be lower but rather to be shelter specific, just as there are different but effective standards of care for large animal herds.

Shelter medicine is still in its infancy when compared to most other veterinary specialties; some practitioners are unaware of its existence or the existence of various resources designed to help them deal with the unique dilemmas often encountered in shelters. Whenever a new specialty is evolving, it should be expected that there will changes and updates of philosophies and practices, and indeed even disagreements among the "experts." Changes in or conflicting recommendations among shelter experts regarding shelter practices should not be seen as errors in judgment; changing priorities and population demographics, new research, and emerging diseases require that veterinarians be flexible in reassessing programs and permitted to change protocols without fear of recrimination. In recent years, several routine beliefs and common practices have come under increased scrutiny, especially as new research that is applicable to or targets shelters is performed. Just a few of these question marks include the routine use of quarantine for newly admitted animals, the value of footbaths under most circumstances, the role of aerosolization of certain pathogens in disease transmission, the importance of daily disinfection of cat cages, the value of a minimum number of air exchanges for good ventilation, and so on. These topics are all tackled in various chapters in this text, but it is clear that more studies that target shelters are needed.

**Disease transmission**

It is essential to have a thorough understanding of how disease is transmitted in order to design a program that can halt its spread in shelters. Each chapter in this textbook will address modes of transmission for the specific disease being discussed. While direct contact, droplets, and aerosolization play key roles in disease transmission, the most common method of spreading disease in shelters is via fomites. In addition to knowing which species (including humans) are susceptible to the pathogen, it is also critical to know the routes of shedding, i.e., in urine, feces, nasal, and ocular secretions, etc. When designing a sanitation program, staff and volunteers must be educated about the significant role they play in spreading disease via their hands, clothing, or other inadequately disinfected fomites and equipment. Workers are much more likely to adhere to strict guidelines regarding sanitation if they understand the consequences associated with taking shortcuts or failing to comply. (See Chapter 4 on sanitation.)

***Incubation period, shedding, and carrier states***

Attention must be paid to the incubation period, duration, and pattern of shedding and carrier states when addressing disease control. Knowing the incubation period helps determine whether an animal entered the shelter with a disease or acquired it in the facility. This information is essential for organizing appropriate quarantines, sanitation procedures, and other outbreak management strategies. For example, lack of knowledge about the viral shedding pattern of parvovirus can lead to serious problems if susceptible animals are exposed to recovered patients who may still be shedding virus. It is also essential to know about parvovirus shedding patterns for accurate antigen test interpretation and an understanding of how recent vaccination may affect the test. The control of feline upper respiratory infections in shelters can be especially frustrating if veterinarians are unaware that both herpesvirus and calicivirus have inapparent carrier states and that herpes recrudesces approximately 1 week after a stressful incident. This information is covered in more depth in each respective disease chapter.

**Shelter design**

There is no doubt that many shelters are housed in facilities that do not meet their needs. They are often found in buildings that were originally designed for purposes other than animal care, such as factories and warehouses. The shelter may have been designed at a time when the population demographics were different, or the shelter's mission may have dramatically altered since the facility was originally designed. Shelters that prioritize adoption and hold animals longer may find that they do not have adequate space to provide for isolation if animals become sick and require treatment. They may not have sufficient space to provide for the animal's emotional well-being as well as its physical needs, such as exercise and play space, grooming areas, etc. Shelters that were originally designed primarily to handle dogs or litters of puppies may now find the population has shifted to cats, kittens, and adolescent dogs with problem behaviors. Normal wear and tear on the building can create cracks and crevices on concrete surfaces that make disinfection difficult.

In order to implement a successful disease control program, physical and design flaws in the shelter should be addressed promptly whether through renovation or retrofitting. In some cases, it may be necessary to explore the need for capital improvements or even construction of a new facility in order to most effectively meet the shelter's overall mission and provide a safe, healthy environment for the animals. However, a dilapidated facility should

never be considered an "excuse" for poor animal care. Many steps can be taken to maintain animal health even in a building that is far less than ideal. Vaccination on intake, provision of toys and bedding, and careful population monitoring for disease are just a few examples of important components of a wellness program that are not building dependent. (See Chapter 2 on wellness.)

### *Special considerations for shelter facilities*

The design of animal shelters varies substantially from that of veterinary hospitals, breeding facilities, or laboratories. A properly designed shelter should be versatile enough to adapt to the various situations that it may have to deal with, whether it is a disease outbreak or the sudden influx of animals seized from a hoarding situation or disaster response. Instead of a few large, open areas for housing animals, there should be several smaller areas that can be adapted as needed for isolation, quarantine, or other specific uses. Traffic patterns in the shelter should be simple and direct people and animals from areas with healthy and juvenile animals first to areas housing high-risk or diseased animals last.

All areas in the shelter that house animals should have adequate drainage and be constructed of nonporous, durable materials that can withstand repeated applications of hot water, detergents, and disinfectants. The materials used routinely in veterinary hospitals are often selected as much for their aesthetic value as for practicality and may not be able to withstand the rigorous sanitation protocols employed by shelters.

One of the keys to managing the health of a confined population is to make certain there is adequate ventilation in the facility. Ventilation should be measured at the level of the animals; ambient room temperature should be species appropriate, comfortable, and avoid fluctuations. The value of fresh air, sunshine, indoor/outdoor runs, and open windows should not be underestimated. Many shelters resort to the use of fans and high-efficiency particulate air (HEPA) filters, and take other variably effective measures to augment deficiencies in their ventilation systems.

Other shelter design considerations include the use of materials that reduce noise; communal housing as well as individual cages; runs with guillotine doors that facilitate the safe cleaning of enclosures with dangerous dogs; housing for species other than dogs and cats; food preparation, laundry, and storage areas; and euthanasia facilities. Because of the special needs of shelters, it is advisable that architects and contractors who are experienced with shelters be consulted whenever designing or retrofitting a shelter. Issues related to shelter environment and design are covered in greater depth in Chapter 2 on wellness.

### Sanitation

One of the cornerstones of any shelter health program is its sanitation program. This principle is discussed in every chapter. The sanitation program should be tailored to each particular shelter environment, with attention to the training and knowledge level of staff, surfaces to be disinfected, level of repair (or disrepair), and common disease problems in that shelter's population. Even in less-than-ideal circumstances, a reasonably effective program can almost always be designed. The goal should be to remove as many pathogens as possible through vigorous cleaning of all contaminated surfaces and potential fomites with hot water, soap, and degreasers, and then to use the appropriate disinfectant to inactivate whatever pathogens remain. The veterinarian's role in the design of the sanitation protocol extends far beyond the selection of the proper disinfectant and writing down a few instructions. Staff training and periodic review and updating of procedures should occur regularly; hands-on review of sanitation procedures should be a priority whenever handling a disease outbreak. Sanitation protocols are covered in depth in Chapter 4.

### Stress

The role of stress in disease transmission is well established in both human and veterinary medicine. Unfortunately, it is frequently overlooked by many shelter employees and managers who are busy cleaning cages or attending to other more visible needs. The importance of controlling stress cannot be emphasized enough. Stress has a powerful impact on animal well-being. It may result in behaviors that decrease an animal's chance of adoption, and many diseases are recognized as being indirectly or directly associated with stress. In addition to broad effects on immunity and susceptibility to disease, of particular importance in shelters is the link between stress and reactivation of herpesvirus in cats leading to upper respiratory disease signs. Stress can also cause symptoms and lesions that are indistinguishable from true clinical disease such as depression, diarrhea, vomiting, acral lick nodules, etc. The role of stress in disease transmission and ways to minimize its impact on the shelter population are discussed in Chapter 2 on wellness.

### Treatment, adoptability, and euthanasia

No decisions in the shelter are fraught with more anxiety, heartache, frustration, anger, and dissension than those

involving euthanasia. One of the challenges that faces shelters is deciding when and how to treat disease when it occurs. Many infectious diseases that are not inherently dangerous or life threatening to individual animals, such as ringworm or upper respiratory infections, pose true ethical and moral dilemmas for shelters that do not have the resources to treat or otherwise manage them. These fairly benign diseases may be deadly in the shelter because they may be either zoonotic or highly communicable. It can be extremely difficult for shelter staff or the public to understand that managing to save the lives of a few affected animals sometimes consumes precious resources that could otherwise be used to save more lives. If appropriate isolation facilities or sufficient staff are not available, care of diseased animals can endanger the lives of many others by exposing them to infection. On the other hand, being able to treat at least some animals can enhance morale and public support as well as result in better disease reporting on the part of shelter staff and volunteers. Ideally, preventive programs should be implemented so that animals will stay healthy, and thus not require treatment, and isolation facilities or other alternatives (e.g., off-site care) are planned and designed so that treatment can be safely and humanely provided. In the meantime, it can be a delicate balancing act between implementing measures that benefit the individual animal and yet protect the lives of the entire population.

## Monitoring and measuring shelter animal health

Although much attention has been paid in recent years to measurement of outcomes such as adoption and euthanasia, less focus has been directed to measures that reflect the health or well-being of animals within the shelter. This is unfortunate, as it is difficult to identify emerging problems before they become severe, communicate challenges or success to stakeholders and the public, or judge the relative value of various investments in animal health without a plan for systematic measurement. Conversely, a system that documents the impact of procedural changes on disease control can help bypass much argument and enhance staff compliance. For example, if a change in cleaning procedure or vaccination practices can be demonstrated to have a positive impact on animal health, the additional cost and effort associated with this practice will be more readily accepted. A detailed description of disease surveillance systems is beyond the scope of this chapter, but several brief examples will be given below. More information on strategies for data collection and analysis in shelters is available in the textbook *Shelter Medicine for Veterinarians and Staff*.

### *Counting the number of cases of disease*

One of the most straightforward measures of shelter animal health is simply the number of cases of disease that occur over time. This requires a consistent case definition and a system to detect and record disease occurrence. In some cases, this can be accomplished through correctly used shelter software systems, provided a field exists to record a unique diagnosis linked to a date on which the diagnosis was made. The number of cases can be reported in relationship to the number of animals admitted during the same time period, the number of total "days at risk" (the number of animals present each day who are potentially susceptible to the disease in question), or ideally both.

The number of cases can be monitored for every disease or syndrome of concern, or only for a few "marker" diseases. For example, upper respiratory infection/kennel cough (URI) is the most common disease problem for cats and dogs in many shelters. Differences in URI levels over time can be relatively easy to detect compared to more sporadic conditions such as parvovirus or feline panleukopenia. An increase in URI can be used as a red flag that the population may be at risk for an outbreak of more serious disease. Conversely, a change in cleaning, housing, or other practices that leads to a reduction in URI is likely to reduce the risk of other disease problems as well. More detailed information about disease surveillance for URI can be found in Chapter 8 on feline upper respiratory disease.

### *Shelter-acquired disease leading to euthanasia*

In addition to counting cases of disease, many other measures of health are available. Perhaps one of the most important for shelters that perform euthanasia is the number of animals that arrive at the shelter in a "healthy, adoptable" condition and are later euthanized due to shelter-acquired illness. If an increasing percentage of animals fall into this category, it should be cause for serious concern. This can be reported by commonly used shelter software systems provided intake status and outcome fields are used correctly with the goal of tracking these data in mind.

### *Sick animal care days*

Another important and accessible measure of shelter population health – and the cost associated with treatment rather than prevention – is the number of "sick animal care days." Sick animal care days can be determined by obtaining a daily tally, either by hand or by computer report, of all sick animals each day and adding this over time to provide the monthly and annual number of days

caring for sick animals. Alternately, this figure can be derived by tracking the duration of disease and adding disease duration for each case over time; again this may be accomplished by hand or computer report, provided date of onset and outcome are reliably entered.

Even if sick care days for only one disease, such as URI, are tracked, this can be very helpful as a likely reflection of overall shelter health. When the number of sick care days is multiplied by the average daily cost of care, an estimate can be made of the true cost of disease. In this context, investment in preventive measures may be more readily justified. For instance, an initial investment in cat housing that is likely to significantly reduce feline URI may be rapidly repaid in reduced staff time and costs associated with caring for ill cats.

### *Shelter death rate*

The number and percentage of animals that die (as opposed to being euthanized) in the shelter or foster care is perhaps the starkest potential indicator of urgent shelter health problems. This number should be tracked carefully, separately from all other "outcome" categories, and monitored over time. Monthly numbers should be compared to the same month for previous years, as death rate is normally liable to climb slightly in summer months in conjunction with kitten season. A small, informal survey of shelters by author Hurley revealed an average annual death rate of 0.75% (range 0.18–1.61%). Shelters with relatively high annual intake reported death rates toward the high end of this range. Death rates of over 2% to 3%, or any increase in death rate, should be cause for close examination. While increased death rates may occasionally arise as a result of a positive policy change (such as addition of a foster program for neonatal kittens, which are prone to relatively high mortality rates), the effect of increased animal death on foster, rescue, and adopter morale should be recognized and addressed even under these conditions. The circumstances of *each death* within the shelter or foster care should be carefully investigated and documented, including whether or not the animal was healthy at the time of admission; whether and when health problems were noticed or diagnosed; whether the animal was receiving appropriate treatment for the condition that caused its death; the location of death (specific area of shelter or foster care); how many days the animal was in the shelter (healthy and sick) before death; and the reason for death if known. Even a small increase in the number of animals admitted healthy and dying of shelter-acquired disease should be viewed with grave concern.

### *Other indicators of shelter animal health*

Other measures of health include the number of valid health-related complaints received after adoption; the number of recheck appointments seen for shelters that have a postadoption care program or the number of claims for pets insured under a shelter pet health insurance plan; days from intake to vaccination; number of vaccines used compared to number of animals admitted (if fewer vaccines are used than animals admitted, this suggests that not every animal is getting vaccinated); number of daily treatments; and amount of drugs used and cost thereof. Changes in these numbers should be analyzed in context. For example, an increase in the number of treatments, cost or amount of drugs used is not necessarily a bad sign. However, if this occurs not because of a specific plan to increase the range and type of treatments available but rather because more animals are entering healthy but later developing illnesses that require treatment, it suggests a breakdown in prevention that should be addressed.

Although the establishment of health monitoring systems may seem daunting in a busy shelter environment, this information should be considered a vital underpinning to a functional shelter health program. Just as individual animals cannot be diagnosed and treated without performing a physical exam and obtaining other measures of health, blindly investing in health practices directed at a population is likely to be suboptimally effective at best. Ultimately, a well-designed health measurement system is a humane and cost-effective investment, as it directs shelter management and veterinarians to the most successful methods of maintaining animal wellness and quickly identifies problems.

## SUMMARY OF SHELTER HEALTH PROGRAMS

There is no one single health-care protocol that is appropriate for every shelter. Programs should be custom made for each facility based on its goals, needs, and resources. The shelter health-care program itself should consist of several components. Minimally it should include physical examination of the animals on admission by medical staff or trained shelter personnel, vaccinations on admission, external and internal parasite control, well-managed foster care programs for underage animals or those with special needs, daily rounds, disease testing, isolation or removal of sick animals, prompt treatment to alleviate pain and suffering, and euthanasia when appropriate. Spay/neuter programs will not be covered in this textbook; although

they are a key component of many shelter health-care programs, they are not considered part of disease management. The importance of conducting a realistic assessment of the needs of the community and animals in order to allocate resources appropriately cannot be stressed enough. For example, routine feline leukemia virus (FeLV) and feline immunodeficiency virus (FIV) testing of every cat before adoption may not be the best use of resources in shelters that have a high turnover, euthanize for space, or house animals in individual cages. Testing all cats for these viral infections makes more sense for shelters that have low turnover, house animals long term or group house, or adopt out virtually all animals. Allowances should be made for budgetary adjustments required during a disease outbreak, for example, when disease testing or use of a more expensive or different vaccine or disinfectant becomes a priority. There should be a written health-care plan that undergoes regular reassessment and revision as conditions change. In terms that are analogous to agricultural herd health, instead of producing a healthy animal product for food consumption, the goal of shelter health programs is to provide a clean, safe, enriched environment for homeless animals that functions as part of the shelter's overall mission. More details on the overall approach to shelter animal health are provided in Chapter 2 on wellness.

## CONCLUSION

Shelter medicine is a challenging and rewarding field of veterinary medicine. The prevention of disease transmission and creation of effective wellness protocols require a multidisciplinary approach that is best achieved by a management and veterinary team that works together and understands the shelter's and the community's goals, limitations and opportunities, and respects the strengths and weaknesses of the team members. The ensuing chapters in this textbook will provide in-depth information on some of the concepts that were introduced here to help veterinarians offer effective solutions to disease problems in shelters.

## APPENDIX 1.1. SHELTER MEDICINE RESOURCES

### Documents

Richards J, et al. 2006. The American Association of Feline Practitioners Feline Vaccine Advisory Panel Report. *JAVMA* 229(9):1406–41. www.catvets.com/professionals/guidelines/publications/?Id=176.

American Animal Hospital Association 2006 Canine Vaccine Guidelines – Revised www.aahanet.org/PublicDocuments/VaccineGuidelines06Revised.pdf.

American Association of Feline Practitioners and American Animal Hospital Association Basic Guidelines of Judicious Therapeutic Use of Antimicrobials. http://www.avma.org/issues/policy/jtua_aafp_aaha.asp

### Books

Greene CE, ed. 2006. *Infectious Diseases of the Dog and Cat*, 3rd edition. Philadelphia: WB Saunders Co.

Peterson C, Dvorak G, Rovid-Spickler A, eds. 2008. *Maddie's Infection Control Manual for Animal Shelters for Veterinary Personnel*. Ames, IA: Center for Food Security and Public Health, Iowa State University College of Veterinary Medicine.

Rhoades R. 2002. *The Humane Society of the United States' Euthanasia Training Manual*. Washington, D.C.: Humane Society Press.

Miller L, Zawistowski S, eds. 2004. *Shelter Medicine for Veterinarians and Staff*. Ames, IA: Blackwell Publishing.

### Colleges of Veterinary Medicine with Shelter Medicine Programs

Contact regional colleges for diagnostic laboratory services and to determine if a shelter medicine program exists and can be of assistance. Several colleges now have programs, including the following as of this writing:

Colorado State University College of Veterinary Medicine
300 West Drake Road
Fort Collins, CO 80523-1620
http://csuvets.colostate.edu/shelter_medicine.htm

Cornell University College of Veterinary Medicine
Ithaca, NY 14853–6401
http://www.vet.cornell.edu/MaddiesFund/

Iowa State University
College of Veterinary Medicine
Iowa State University
Ames, IA 50010
http://www.maddiesfundisu.org/

University of California at Davis
School of Veterinary Medicine
Davis, CA 95616-8782
http://www.sheltermedicine.com

University of Florida
College of Veterinary Medicine
2015 SW 16th Avenue Room V2-110
Gainesville, FL 32610
http://www.ufsheltermedicine.com

University of Pennsylvania
School of Veterinary Medicine

Department of Clinical Studies
Philadelphia, PA 19104

**Other Organizations**

The American Humane Association
http://www.americanhumane.org/site/PageServer

The American Society for Prevention of Cruelty to Animals
http://www.aspca.org/site/PageServer?pagename=aspcapro_home

The Association of Shelter Veterinarians
http://www.sheltervet.org/

The Companion Animal Parasite Council
http://www.capcvet.org/

The Centers for Disease Control and Prevention
http://www.cdc.gov/

The Humane Society of the United States
http://www.hsus.org/

National Animal Control Association
http://www.nacanet.org/

Society for Animal Welfare Administrators
http://www.sawanetwork.org/

Veterinary Information Network
http://www.vin.com/

## REFERENCES

Edinboro CH, Janowitz LK, et al. 1999. A clinical trial of intranasal and subcutaneous vaccines to prevent upper respiratory infection in cats at an animal shelter. *Feline Practice* 27(6):7–13.

Edinboro CH, Ward MP, et al. 2004. A placebo-controlled trial of two intranasal vaccines to prevent tracheobronchitis (kennel cough) in dogs entering a humane shelter. *Prev Vet Med* 62(2):89–99.

Edwards DS, Coyne K, et al. 2008. Risk factors for time to diagnosis of feline upper respiratory tract disease in UK animal adoption shelters. *Prev Vet Med* 87(3–4):327–39.

Miller L. 2007. A blend of science and art: what every shelter should know about shelter medicine. *Animal Sheltering* January/February 2007:49–51.

# 2
# Wellness

*Brenda Griffin*

## WELLNESS DEFINED

Simply stated, the overarching goal of any animal shelter (no matter what resources, philosophy, or mission it possesses) must be for animals to be as "healthy and happy" as possible during their stays. In addition, the protection of public health and safety must always be central goals. In this way, shelters also achieve the goal of public education, leading by example as they model good animal care practices.

Wellness is defined as the maintenance of good health. Both physical health and behavioral (or emotional) health comprise wellness. For example, a dog may be physically fit, free from infectious or other physical disease, but suffering from severe separation anxiety. This animal cannot be assessed as truly healthy and his behavioral disorder must be addressed in order to ensure his well-being. A wellness program to optimize animal health in the shelter must therefore address both physical and behavioral health.

In addition to addressing the animals themselves, addressing the shelter environment is also critically important when developing a wellness program for an animal shelter. Even the best-designed facilities cannot manage or prevent infectious disease and problem behaviors without thoughtful implementation of environmental wellness protocols. In small animal practice, environmental wellness is frequently not emphasized simply because many owners are accustomed to providing a reasonably healthy environment for their pets. In contrast, a structured program to address environmental wellness is essential in the context of an animal shelter regardless of the actual physical plant of the facility. Proactive measures to maintain clean, sanitary environments that are not overcrowded where animals are segregated (by species and health status) and provided with regular daily schedules of care by well-trained, dedicated staff are essential.

### The critical importance of wellness protocols for shelters

Infectious diseases, stress, and problem behaviors are common in cats and dogs housed in animal shelters. Individuals with compromised physical or behavioral health are less likely to be adopted and more likely to be euthanized. Pets entering shelters are highly stressed and at significant risk of developing infectious diseases. The stress of even short-term confinement in a shelter can compromise not only physical health but also behavioral health, negatively affecting animal welfare and making cats and dogs less desirable to potential adopters.

The maintenance of good health or wellness of animals in shelters presents difficult challenges for obvious reasons. Shelters possess many risk factors for the development of infectious disease, including introduction of new animals to a facility, high-density housing, housing animals of different ages and susceptibility levels in close proximity, induction of stress, and lack of adequate vaccination or time to respond to vaccination. All of these risk factors, and others, exist in the shelter setting; therefore, a certain risk of infectious disease is inherent. In addition, certain diseases frequently become endemic in facilities where populations of animals are housed.

Confinement of pets awaiting adoption can result in a wide variety of behavioral indicators of stress and anxiety including activity depression, hyperactivity, stereotypic behavior (such as pacing or pawing), frustration, and barrier aggression, among others. Shelter environments must be enriched to prevent undue stress in housed animals. Programs that reduce stress also serve to

minimize the morbidity of endemic infectious diseases because stress has a profound influence on disease transmission as well as behavior.

Shelters have an obligation to provide humane care for animals; thus a critical need for a wellness program exists in every shelter. It is simply not humane to house animals under conditions likely to induce illness and poor welfare. These conditions can be expected when wellness programs are not in place and carefully monitored. In addition, if animal shelters are to compete with other sources of animals for adoption, they must be able to achieve the goal of presenting healthy animals in a healthy environment.

### Goals of a shelter wellness program

The goals of a shelter wellness program are to minimize infectious disease and problem behaviors while optimizing the physical and behavioral health of the animals and preventing transmission of zoonotic diseases. Concisely, a wellness program should be designed to keep animals "healthy and happy" and the public safe. When shelters meet these goals, both public relations and adoption rates may be positively impacted.

Shelter wellness programs should not be based on control of a single disease or problem, but should offer broad-based preventive strategies (a holistic approach). Furthermore, in the context of an animal shelter, wellness programs must address both the health of individual animals and the health of the population as a whole. Shelter medicine has been compared to herd health (Hurley 2004). Indeed, much like a herd health approach, population medicine in the shelter utilizes a systematic approach to optimizing animal health in the group. Unlike a herd health program for large animals, where production is the ultimate goal, ensuring the welfare of cats and dogs is the ultimate goal in the animal shelter. In the context of establishing and implementing a comprehensive wellness program for the shelter, establishing goals for and methods of monitoring the population is critical to ensuring animal health and welfare. Medical decisions must be weighed in the context of the population as well as the individual, while considering animal welfare and the availability of resources. Finally, assessment and follow-up is performed on a population level as well as on an individual level.

Although very few regulations and standards of care for animal shelters currently exist, it is the ethical responsibility of every animal shelter to provide for the well-being of each and every animal it handles to the best of its ability. Inadequate or delayed veterinary care constitutes neglect, which is illegal according to some state laws. Under no circumstances should a shelter engage in any practice or omission that would result in resident animals being allowed to suffer unnecessarily or unjustifiably.

When situations arise in which animal welfare cannot be managed, whether due to physical or behavioral disease or environmental conditions such as overcrowding, euthanasia must be employed if no other remedies exist within or beyond the shelter to relieve animal suffering. Euthanasia, however, should not be used as a substitute for providing animals with proper care while in the shelter and implementing earnest programs designed to decrease euthanasia of adoptable animals and feral cats.

Wellness programs will vary depending on the shelter's mission, philosophy, and resources, and may vary within shelters depending on such factors as intake rate and time of year. Keep in mind that the goal of optimizing the health and happiness of every animal during its stay, while maintaining the health and happiness of the population as a whole, is key to establishing effective protocols. Research is needed to better define protocols for limiting and treating physical and behavioral diseases common to shelter animal populations and to help better assess the welfare or quality of life of cats and dogs in animal shelters.

### Quality of life

Every attempt must be made to sustain quality of life for shelter animals. Like "happiness," quality of life remains difficult to define. Both physical and emotional factors contribute to quality of life, well-being, or welfare. These factors are broad, complex, and very individual. According to McMillan (2000), quality of life "is comprised of an array of affective states, broadly classified as comfort-discomfort and pleasure states. In general, the greater the pleasant and the lesser the unpleasant effects, the higher the quality of life."

Criteria are lacking for the objective measurement of the quality of life for cats and dogs; however, subjective assessments can and should be made by medical and behavioral personnel at regular intervals (weekly or even daily as indicated) considering the most information possible. Researchers are giving increased attention to validating quality of life measurements, which could help ensure humane end points for health care, define minimum housing standards, and be used for welfare audits in animal shelters as well as other settings where populations of animals are housed. The Farm Animal Welfare Council's five freedoms represent a benchmark for measuring quality of life or assessing animal welfare (see Table 2.1).

**Table 2.1.** The five freedoms.

1. Freedom from hunger and thirst by ready access to fresh water and a diet to maintain full health and vigor.
2. Freedom from discomfort by providing an appropriate environment, including shelter and a comfortable resting area.
3. Freedom from pain, injury, or disease by prevention or rapid diagnosis and treatment.
4. Freedom to express normal behavior by providing sufficient space, proper facilities, and company of the animal's own kind.
5. Freedom from fear and distress by ensuring conditions and treatment that avoid mental suffering.

### Considerations regarding infectious disease transmission

Despite the fact that infectious agents are always present in the environment, under normal conditions health is maintained. It is well recognized that the development of infectious disease is determined by a complex interaction of many factors surrounding the host, the infectious agent, and the environment. The species, age, sex, general health, and immune status, as well as stress level and genetic predispositions of the host are all known to be factors that influence animal health (Greene 1998a).

Infectious agents vary in virulence and modes of transmission. In many instances they persist in the environment because they are resistant to disinfection, and many produce carrier states that also contribute to continued environmental contamination or direct exposure of other animals. The amount and duration of exposure to an infectious agent, as well as methods of spread, routes of inoculation, carrier states, and mutation rates, will all affect the likelihood that disease will spread in the shelter environment. Disease may be spread by direct contact with infected animals or carriers, via inhalation, ingestion, and contact with feces, urine, other bodily secretions, fomites, or even vectors. Environmental factors also contribute substantially to disease, including housing density, ease of cleaning/disinfection, extremes or fluctuations of temperature, and air quality, among others. Thus no single factor results in disease; rather, disease results from a combination of factors.

#### *General principles of disease control*

It is important to recognize the general principles of infectious disease control:

1. Removal of infected animals (through isolation, foster care or euthanasia)
2. Mass vaccination
3. Mass treatment
4. Good husbandry practices (animals and environment)
5. Education of personnel
6. Quarantine of new arrivals

The importance of adhering to these general principles whenever possible must never be overlooked in the context of an animal shelter. Coupled with vigilant surveillance and early recognition of disease, these principles serve as the foundation of all disease control efforts when disease is present. It should be noted, however, that although mass vaccination, treatment, good husbandry, and staff education can be achieved in animal shelters, implementing true quarantine is problematic. Exercising careful biosecurity for those animals that are most susceptible to infectious disease (e.g., young puppies and kittens) may be the preferred practice in most situations, unless particular circumstances such as severe disease outbreaks necessitate true quarantine or even temporary closure to admittance. The single most important method of addressing disease control, however, remains prevention: designing and implementing comprehensive wellness protocols for the shelter animals and environment.

### Components of a wellness program

Wellness starts with prevention, including prevention of both disease and problem behaviors. Prevention is more time and cost efficient than treatment. In addition, it is simply kinder to the animals as well as to the staff that must care for them. Table 2.2 contains the recommended components of a wellness protocol for shelter cats and dogs, and Table 2.3 shows the recommended components of a wellness protocol for the shelter environment.

## THE PROBLEM-ORIENTED APPROACH TO SMALL ANIMAL MEDICINE

The "problem-oriented approach" to medicine is widely accepted as the gold standard for small animal patient care and assessment. In small animal veterinary medicine, a problem is defined as "any abnormality requiring medical or surgical management or one that interferes with quality of life" (Lorenz 1993). In the context of an animal shelter, problems are also defined as conditions that affect public health and safety (such as aggression).

The problem-oriented approach is used to systematically identify and address an animal's problems. With this approach, the clinical reasoning process is based on four

**Table 2.2.** Recommended components of a wellness protocol for shelter cats and dogs.

| Total Wellness | |
|---|---|
| Physical Health | Behavioral Health |
| History and physical examination | History and behavioral examination |
| Vaccination | Proper housing |
| Parasite control/prevention | Consistent daily routines |
| Spay/neuter | Proper exercise |
| Identification (collar/tags, microchip) | Mental stimulation |
| Proper nutrition and exercise | Social companionship |
| Grooming | |
| Periodontal disease prevention | Positive-reinforcement-based training |
| Breed-specific care | |

**Table 2.3.** Recommended components of a wellness protocol for the shelter environment.

| Environmental Wellness |
|---|
| Population density |
| Cleaning and sanitation protocols |
| Segregation and traffic patterns |
| Other facility operations [Heating, ventilation, and air conditioning (HVAC), light/dark cycles, regular schedules, building maintenance, etc.] |
| Staff training |

steps: (1) database collection, (2) problem identification, (3) plan formulation, and (4) assessment and follow-up. This approach enables the clinician to logically approach each patient to ensure thorough and accurate assessment so that appropriate actions can be taken.

In the context of an animal shelter where populations of animals are housed, it is important to have efficient systems that allow for assessment of individual animals while affording consideration to the population. Shelter medicine represents a unique blend of both individual patient and population medicine.

**Database collection**

An initial or guaranteed minimum database should be obtained on every patient. Although the size of the database is often debated, there is no disagreement that it must include a complete history and a complete physical examination for every patient whenever possible. From the perspective of a shelter, resources and philosophy must be considered when deciding what will be included in the guaranteed minimum database for each patient. The author's recommendations may be found in Table 2.4.

**Table 2.4.** Recommended minimum database for cats and dogs in the shelter.

| At Intake | Prior to Adoption |
|---|---|
| History | Behavioral examination and assessment |
| Determine if animal is safe to handle | Feline leukemia virus (FeLV)/ Feline immunodeficiency virus (FIV) testing (cats) |
| Physical examination (including scanning for a microchip) | Heartworm (HW) testing (dogs in HW endemic areas) |
| Problem identification | Fecal exam (If diarrhea is present) |
| Medical assessment | Geriatric patients*: Packed cell volume (PCV)/ Total solids (TS), urine specific gravity and dip stick |

*Geriatric: Small dogs (under 20 pounds) 10 years; medium and large dogs (21 to 90 pounds) 7–8 years; giant dogs (over 90 pounds) 6 years; cats 9–10 years.

With regard to senior animals in the shelter, the author recommends the addition of the following tests to the minimum database of geriatric animals that will be offered for adoption: PCV/TS (packed cell volume and total plasma solids) and urine specific gravity and dip stick. These procedures broadly screen many body systems and are very cost effective. These should be viewed as extensions of the physical examination for the senior animal. Whenever time and resources allow, the veterinary clinician should also consider fine-needle aspiration for in-house cytologic evaluation of all cutaneous and subcutaneous masses. This simple and inexpensive practice of evaluating "lumps and bumps" may identify potential malignancies that would otherwise go unchecked, or provide reassurance that any growths present are not cause for undue concern by potential adopters.

**History**

Next to physical examination, history is the most important aspect of medical problem solving. The history alerts the clinician to the presence of potential problems. Obviously, in the shelter setting, it may not always be possible to obtain an accurate history. Some animals will

be brought in by animal control officers or good Samaritans who have little if any information about the animal. Some shelters provide a location (e.g., drop-off cages or runs) where animals can be relinquished after business hours. In this case, every effort should be made to obtain a history through questionnaires that relinquishers can fill out when the animal is left. The presence of staff to directly accept the animal and obtain a history at the time of relinquishment is greatly preferred. Even so, surrendering owners may or may not provide thorough or accurate information fearing that if they are honest about a pet's problems, the pet may be euthanized.

Nonetheless, when available, a history can be extremely valuable and may save time, money, and stress on the animal and staff. Intake procedures should be in place to capture basic patient information, including both physical and behavioral data as well as the reasons for relinquishment. The importance of obtaining historical information cannot be overemphasized. In many cases, historical information may be used to expedite the disposition of the pet.

**Physical examination**

Every animal (that is deemed safe to handle) should receive a physical examination at or as close to the time of admission to the shelter as possible. In addition to the physical examination, a behavioral examination and assessment should be performed after the animal has acclimated to the shelter environment for 2 to 5 days. However, for high-volume shelters that lack the ability to hold animals for extra days while they adjust to the new environment, an alternative plan would be to evaluate and process apparently social, owner-relinquished animals with no history of aggression in their previous home as quickly as possible for immediate placement in adoptions, foster care, or with rescue groups. Physical examination is the single most important aspect of the guaranteed minimum database. Following a physical examination form will ensure a complete and systematic review of all body systems. Likewise, following a standardized behavior examination form will ensure that thorough evaluations are conducted.

Of particular importance in the shelter physical examination is an accurate physical description of the animal and careful inspection for the presence of identification, both of which may aid in pet–owner reunification. Examination should include careful inspection for the presence of a microchip or tattoo. Microchip scanning should be systematically performed on every animal at the time of intake and prior to the animal being made available for adoption or being euthanized.

Upon activation by a low-power radio frequency emitted by a scanner, microchips transmit a unique identification number that can be linked through a database to an owner. Currently there is no standard radio frequency used for microchips in the United Sates; three different frequencies are marketed. Because of this, it is essential to use a global scanner that will read the frequencies of all available microchips when scanning animals. In addition, the scanner must contain well-charged batteries for reliable identification of microchips. Furthermore, for an accurate reading, it is essential to scan the entire animal using a consistent technique described as follows. Rocking the scanner slightly from side to side will maximize the potential for optimal chip orientation and successful detection. Most scanners should be held parallel and in near or close contact with the animal during the scanning process; in other words, it should be very close to the animal either lightly touching the skin or held just over the skin less than an inch away from contact with the patient. The scanner speed should not be any faster than 0.5 feet per second. This is because global scanners must cycle through various modes to read all possible chip frequencies. Scanning should begin over the standard implant site, which is midway between the shoulder blades. If the microchip is not detected, scanning should continue down the back, sides, neck, and shoulders to the elbows cranially and stifles caudally. The scanner should be moved over the scanning areas in an S-shaped pattern in a transverse direction (from side to side). If no microchip is detected, the scanner head should be rotated 90° and then the scan should be repeated in an S-shaped pattern in a longitudinal direction on both sides.

The inner pinnae, abdomen, and the inguinal area are common locations for tattoos. For cats (even those which may be feral or too fractious to handle), visual evaluation of the pinnae should be performed to identify a cropped ear tip, which may indicate that the cat is a sterilized member of a managed cat colony.

An additional critical aspect of the intake exam for shelter animals is identification of conditions that require special housing considerations. Common examples include animals suspected of being infected with contagious diseases that would require isolation, pregnant animals that appear near term, and others that may possess special medical needs. Animals that are deemed unsafe to handle on entry should be identified so that they can be housed appropriately in enclosures that are especially secure and designed to minimize animal handling, such as those that contain guillotine doors or other separators.

**Plan formulation, assessment, and follow-up**

Once problems are identified, a plan can be formulated to address them within the mission, philosophy, and resources of the shelter, and with respect to the legal holding periods (which allow owners the opportunity to find and claim their pets) as prescribed by local and state laws. The plan should take into consideration three elements, including (1) any necessary diagnostic testing, (2) treatment, and (3) relevant staff or adopter education.

The final step in medical problem solving is the assessment and follow-up. Timely action is essential in the shelter where animals may be triaged to adoption, foster care, rescue groups, isolation, or euthanasia. For animals that undergo long-term stays in shelters, regular reassessment is imperative to identify new problems (medical or behavioral) that may develop so that these problems can be addressed in a timely fashion to ensure the welfare of the individual animal as well as that of the population and the shelter staff.

Some shelters may elect to house animals with existing medical or behavioral problems. When such "special needs" animals are housed in the shelter, it is imperative that a humane plan for diagnosis, treatment/management, monitoring, and housing be implemented. Special needs animals should not be kept in the shelter unless adequate medical care can be afforded to them, including pain control. When determining if animals with special needs can be humanely cared for in the shelter, the following goals and considerations should be addressed:

- Will the care provided to the animal result in a cure or adequate management of the disease or problem behavior?
- Will the animal be adoptable?
- What steps can be taken to minimize the holding time required for treatment?
- What measures must be implemented to prevent transmission of disease to other animals or people?
- Can the shelter afford the cost of and time for care? How will this impact resources available for other animals?
- Can adequate care realistically be delivered in the shelter or in foster care?
- What factors will be used to assess if the treatment plan is working or should be modified?
- If the animal is adopted, what can be done to decrease/eliminate return of the animal for its special needs?
- If the pet is not adopted, what welfare assessment will be used to measure quality of life in the shelter?
- Do humane long-term care options exist in the shelter?

A regular system of physical and behavioral health surveillance should be in place for follow-up of all animals. At a minimum, rounds should be conducted twice daily by medically trained staff or volunteers to observe each individual animal as well as its environment for signs of health problems. Early recognition and timely action are critical for effective control of infectious diseases.

**Medical record keeping and data collection**

Medical records are essential in order to assure quality and timely medical care. Record-keeping procedures should comply with state and local practice acts, guidelines provided by state and national veterinary medical associations, and with federal drug laws.

A medical record should be prepared for each animal and should include: the intake date; an animal ID number; signalment; physical description; historical and physical examination findings; results of microchip scanning; body weight and condition; names and dosages of all drugs administered or prescribed and routes of administration including vaccines, parasite control products, other treatments, and anesthetic agents; results of any diagnostic tests performed; surgical procedure(s) performed; any abnormalities that are identified; and any other pertinent information regarding the animal's condition.

Standardized examination and operative/surgical reports may be used but should allow for additions and medical updates when necessary and as appropriate. Standardized examination forms that document both normal and abnormal findings during a systematic body system review are particularly helpful. The medical record should also include the behavioral history, examination, and assessment findings, including a determination of the animal's adoptability.

In addition to the obvious need for medical record keeping in the context of individual animals, the population also benefits from thoughtful record keeping and data collection. For example, in the context of population medicine, several goals of the wellness program might include decreasing the incidence and prevalence of infectious diseases in the shelter and following adoption, decreasing the incidence of problem behaviors in the shelter, decreasing the rate of return of animals to the shelter for problem behaviors, increasing the adoption rate, and so forth. By identifying and tracking measurable factors (often called performance targets in large animal medicine), it is possible to measure progress toward these goals. In shelter medicine, such factors may be more appropriately termed "welfare targets." Once baseline data (such as disease rates) are established, it may be possible to measure the

impact of protocol changes on population health by evaluating individual welfare targets. A system for regular reporting will make it easier to identify both positive and negative trends in animal health.

### Policy and protocol development

Shelters should have written policies and protocols in place that detail how medical and behavioral problems will be handled (Hurley 2004). Policies and protocols should be based on research and facts as well as the individual organization's mission, philosophy, and the availability of resources (including facilities, staff, and veterinary care). Policies and protocols are best established by a committee that is responsible for shelter health issues, including the shelter director or manager, medical staff, or other key individuals. The goals of the committee should be to establish definitions or descriptions of the disease or problem behavior in question, a general policy regarding the disposition of animals affected by the condition, and a description of the methods that will be used to diagnose or recognize the condition. In addition, protocols should include details on notification of the appropriate parties, housing, decontamination, treatment, and documentation in each case. These written protocols should serve as guidelines for systematic triage and care of animals in the shelter.

## WELLNESS: PHYSICAL HEALTH

The basic physical health of cats and dogs should be systematically addressed through the wellness program. Protocols should include provisions for vaccination, parasite control, spay/neuter, identification, proper nutrition and exercise, periodontal disease prevention, and breed-specific care.

### Vaccination

The high likelihood of exposure and the potentially life-threatening consequences of illness in shelters make vaccination against certain diseases essential. Guidelines for the vaccination of cats and dogs in animal shelters have been well described by the AAFP and AAHA, respectively (Richards, Elston et al. 2006; Paul, Carmichael et al. 2006). Certain "core vaccines" are recommended for all cats and dogs that enter shelters. Core vaccines target diseases that represent significant morbidity and mortality, are widely distributed in shelters, and for which vaccination has been demonstrated to provide relatively good protection against disease. Core vaccines for shelter cats include feline parvovirus (FPV or panleukopenia), FHV-1 (feline herpes virus type 1 or feline rhinotracheitis virus), and feline calicivirus (FCV) (see Table 2.5). Although FeLV is not considered a core vaccine for shelter cats, vaccination against FeLV may be warranted when cats are group housed. When administered, injection of this vaccine should be performed in the left hind leg according to the AAFP guidelines, and initial vaccination should be followed by a booster in 2 to 4 weeks. *Chlamydophila felis* (*C. psittaci*) and *Bordetella bronchiseptica* are not recommended as core vaccines, but they may be of benefit when clinical signs of these diseases are present in the shelter and diagnosis is confirmed by laboratory evaluation. Their efficacy is moderate and reactions are more common than with most other feline vaccines; ongoing use should be periodically reassessed.

For shelter dogs, core vaccines include canine parvovirus (CPV), canine distemper virus (CDV), canine adenovirus (CAV-2, hepatitis), parainfluenza (CPiV), and *Bordetella bronchiseptica* (see Table 2.6).

Rabies vaccination is recommended in both cats and dogs prior to adoption when a licensed veterinarian is available to administer the vaccine (or by shelter staff in accordance with state laws), which should be injected in the right hind leg. Alternatively, a rabies vaccination may be administered by the new owner's veterinarian as soon as possible following adoption. This alternative may serve to encourage new owners to establish a relationship with a private veterinarian. New owners should be advised that rabies vaccination for dogs is mandatory in most jurisdictions, and proof of vaccination may be required for dog licensing. Rabies vaccination is also warranted when animals are housed long term in shelter facilities. Animals being held for rabies bite quarantines should be vaccinated for rabies by a licensed veterinarian in accordance with the guidelines provided by the current *Compendium of Animal Rabies Prevention and Control*. (Refer to Chapters 18 and 23 on rabies and zoonosis for more information.) Finally, rabies preexposure vaccination is highly recommended for shelter staff.

Some vaccines are not generally recommended for use in animal shelters because of either undemonstrated efficacy and/or low risk of disease transmission within shelters. For dogs, these include canine coronavirus, giardia, leptospirosis, *Borrelia burgdorferi* (Lyme disease), canine adenovirus type 1, crotalus atrox toxoid (rattlesnake), and *Porphyromonas* vaccine.

Vaccines not generally recommended for shelter cats include FIP and giardia. As previously described, vaccination against FeLV is considered a noncore vaccine and is not generally recommended except in shelters or foster homes where cats are group housed. Similarly, FIV

**Table 2.5.** Core vaccines for shelter cats.

| Core Vaccine | Type of Vaccine Recommended | Route/Frequency/Location of Administration | | Vaccine Prevents Disease Altogether or Reduces Severity of Disease | Comments |
|---|---|---|---|---|---|
| | | Kittens <4 Months of Age | Kittens >4 Months of Age and Adults | | |
| FPV | MLV | Administer SQ right dorsal shoulder as a 3-way vaccine (FVRCP) on entry and then every 2 weeks beginning at 4–6 weeks of age and continuing to 16 weeks of age or when permanent incisors erupt. | Administer SQ right dorsal shoulder as a 3-way vaccine (FVRCP) on entry. A single boost in 2 weeks is ideal; however, the vast majority of cats will respond to a single injection. | Prevents | Because intranasal vaccination may not provide reliable protection against feline panleukopenia, all cats should be vaccinated with a parenteral MLV panleukopenia vaccine, regardless of whether or not IN respiratory vaccines are used (Richards 2006). |
| FHV-1 | MLV | See above | See above | Reduces | Administration of an intranasal vaccine against FHV-1 and FCV in addition to the parenteral vaccine may provide extra protection presumably due to rapid onset of local (mucosal) immunity (Edinboro, Janowitz et al. 1999). Mild self-limiting reactions are common and manifest with transient coughing and/or sneezing, and/or mild nasal discharge, within days of vaccination. Reactions in brachycephalic breeds may be severe. |
| FCV | MLV | See above | See above | Reduces | |

**Table 2.6.** Core vaccines for shelter dogs.

| Core Vaccine | Type of Vaccine Recommended | Route/Frequency/Location of Administration | | Vaccine Prevents Disease Altogether or Reduces Severity of Disease | Comments |
|---|---|---|---|---|---|
| | | Puppies <4 Months of Age | Puppies >4 Months of Age and Adults | | |
| CDV | MLV or recombinant | Administer SQ right dorsal shoulder as a 4-way vaccine (DHPP) on entry and then every 2 weeks beginning at 4–6 weeks of age and continuing to 16 weeks of age or when permanent incisors erupt | Administer SQ right dorsal shoulder as a 4-way vaccine (DHPP) on entry. A single boost in 2 weeks is ideal; however, the vast majority of dogs will respond to a single injection. | Prevents | Recombinant distemper vaccine has been shown to provide the best protection in young puppies since maternal antibody interference does not occur (Larson 2006). |
| CPV | MLV | See above | See above | Prevents | |
| CAV-2 | MLV | See above | See above | Prevents | |
| CPiV | MLV | See above | See above | Reduces | |
| *Bordetella* | MLV | Administer a single intranasal dose in puppies as young as 3 weeks. Boost in 2–4 weeks. | Administer a single intranasal dose. A single boost in 2 weeks may be ideal. | Reduces | In general, intranasal vaccination is recommended due to rapid onset of local (mucosal) immunity. Mild self-limiting reactions are common and manifest with transient coughing and/or sneezing, and/or mild nasal discharge, within days of vaccination. Reactions in brachycephalic breeds may be severe. |

vaccination is not generally recommended in the shelter. An additional confounding feature of FIV vaccination is that cats vaccinated against FIV develop false positive test results. If FIV vaccination is elected, vaccinated cats should be permanently identified (e.g., by use of a microchip) to help clarify their status.

When the use of unnecessary vaccines is avoided, costs are reduced, which is essential when shelters possess limited resources. Furthermore, it serves to minimize the incidence of adverse reactions associated with vaccination. Serious adverse reactions from core vaccines are extremely rare and the risk/benefit ratio is overwhelmingly in favor of vaccination in the shelter setting.

There is no doubt that proper vaccination protocols substantially reduce disease in the shelter and improve animal health. That being said, it is important to understand the limitations of vaccines in disease prevention. Although they represent an extremely important component of a comprehensive wellness program for an animal shelter, vaccines are not "magic bullets" that can prevent disease altogether. Shelter staff should be educated regarding basic facts about vaccination. They need to understand that vaccines are health products that trigger immune responses in animals and prepare them to fight future infections from disease-causing agents; they do not treat disease or provide instant immunity. Furthermore, staff must understand that vaccines do not always provide sterilizing immunity or prevent disease altogether. In many instances, they provide only partial protection, lessening the severity of future diseases but not preventing them. Indeed, even the best vaccines take some time to provide protection; and vaccine failure may occur when animals enter the shelter already incubating disease. In particular, canine and feline upper respiratory disease cannot be prevented by vaccination (only limited), whereas canine distemper and canine and feline parvovirus can be effectively prevented when vaccines are used correctly. Even so, there may be sporadic cases of CPV, FPV, and CDV in shelters, especially in young puppies and kittens due to waning maternal antibodies and the window of susceptibility to these diseases. Finally, it is important to recognize that vaccine failure will occur in some individuals, regardless of the protocol used, and that vaccines are not available for all diseases seen in shelters.

Many variables affect an individual's response to vaccination including age, presence of maternal antibodies, concurrent disease, fever, nutritional status, and stress level, among others (Greene 1998b). In addition, the period between vaccination and exposure, the infectious dose to which the animal is exposed, as well as the particular disease agent in question influence vaccine response. Finally, the appropriate handling of vaccines is critical to their effectiveness. Because vaccines contain live or modified live agents, they are very sensitive to temperature changes and are unstable once reconstituted. Upon arrival of a shipment, vaccines should remain well chilled, be refrigerated immediately, and never be left unrefrigerated. Conversely, they should never be frozen, since both heat and excessive cold can result in inactivation. For best results, vaccines should be removed from the refrigerator only as they are used and should be administered within 30 minutes of reconstitution. The type of vaccine administered (including manufacturer and serial number), date, and the name of the person who administered it should be entered into a medical record for each patient.

In the majority of cases, modified live vaccines should be used in the shelter since they evoke a more rapid and robust immune response and are better at overcoming maternal antibody interference than killed products (Richards, Elston et al. 2006; Paul, Carmichael et al. 2006). In fact, a single dose of a modified live virus (MLV) vaccine can often offer protection to animals over 4 months of age, whereas killed products frequently require a boost to confer immunity. In general, parenteral vaccines are preferred, but intranasal vaccines may offer advantages for use in canine and feline respiratory disease because they have been shown to rapidly induce local immunity at the site of exposure.

The timing of the vaccination is critically important. Ideally, all animals would be vaccinated at least 1 week prior to entry to the shelter. Since this is usually not possible, vaccination immediately prior to or upon entry is the next best practice and can provide dramatic protection for the majority of cats and dogs admitted to shelters. In fact, immunity usually begins developing within hours of vaccination and if neither maternal antibody nor another cause of vaccine failure interferes, modified live vaccinations against canine and feline parvovirus will confer full protective immunity in only 3 days and 5 days, respectively (Brun, Chappuis et al. 1979; Carmichael, Joubert et al. 1983). Protection against CDV from modified live and recombinant vaccines may be conferred even more rapidly (Schroeder, Bordt et al. 1967; Larson and Schultz 2006). Intranasal vaccines against respiratory infections including FHV, FCV, and *Bordetella* may provide protection in 2 to 4 days (Cocker, Newby et al. 1986; Gore, Headley et al. 2005).

Upon entry to the shelter, all cats and dogs should be considered unvaccinated unless a medical record is available that clearly documents current vaccination by a

licensed veterinarian and is verified to belong to the animal in question. All incoming cats and dogs 4 weeks of age and older should be vaccinated immediately upon entry. A delay of even a day or two will significantly compromise the vaccine's ability to provide timely protection (Paul, Carmichael et al. 2006). In general, even injured animals and those with medical conditions should be vaccinated. In the majority of cases, vaccination will be effective at inducing immunity and any risk of vaccination reactions or adverse side effects is outweighed by the high risk of exposure and development of infectious disease in the shelter. In addition, a booster vaccination can be administered in 2 weeks to optimize response. Practical considerations dictate that if an individual is so severely debilitated that vaccination is deemed unsafe, exposure to infectious disease and stress in the shelter will likely result in decompensation and death or euthanasia of that animal.

Vaccine response has been shown to be impaired in animals with a temperature above 103.6° due to fever or hyperthermia (Greene 1998b). Cats and dogs with rectal temperatures above 103.6° should be cooled prior to administration of vaccines. Some risk to the developing fetuses is associated with the vaccination of pregnant animals with modified live vaccines, but the risks associated with vaccination must be weighed against the risk of disease exposure. Many shelters elect to vaccinate pregnant animals on intake and spay them prior to adoption. Finally, although vaccination of all cats and dogs (that are safe to handle) on entry is ideal in order to maximize disease prevention and control, it may not be financially feasible for all shelters to do so. In this case, all cats and dogs deemed adoptable at the time of entry, or animals that are likely to be in the shelter long term should be vaccinated immediately, while those that are likely to be euthanized after legal holding periods are not vaccinated. Whenever possible, vaccinated animals should be separated from those animals that will remain unvaccinated as soon as that determination can be made.

A series of vaccinations should be administered to kittens and puppies less than 4 months of age in order to minimize the window of susceptibility to infection and ensure that a vaccine is received as soon as possible after maternal antibodies have decreased sufficiently to allow vaccine response. For kittens and puppies, vaccines should be administered every 2 weeks until they are 16 weeks of age or until their permanent incisors erupt. A vaccination interval of less than 2 weeks is not recommended since it may actually blunt the immune response from previous vaccination (Greene 1998a). The author recommends that puppies/kittens less than 6 to 8 weeks of age not be housed in the shelter as they invariably become seriously ill from infectious disease despite aggressive vaccination procedures and environmental management. Underage puppies/kittens should be removed from the shelter and placed in foster care within 48 hours of arrival whenever possible.

Just as in owned pets, booster vaccines are generally not required before 1 year for modified live vaccines, but may be administered once in 2 weeks if resources permit. Revaccination in long-term shelter facilities should follow the guidelines set forth for pets (boost at 1 year, then every 3 years for feline viral rhinotracheitis, calicivirus, and panleukopenia (FVRCP) and distemper, hepatitis, parainfluenza, and parvovirus (DHPP) and according to local and state ordinances for rabies).

**Parasite control and prevention**

Parasite control and prevention represent essential components of shelter wellness programs. Both internal and external parasites are common in cats and dogs. In particular, roundworms and hookworms are common intestinal parasites that possess zoonotic potential. The Centers for Disease Control and Prevention and the Companion Animal Parasite Council strongly advise routine administration of broad-spectrum anthelmintics to control these potential zoonoses. Pyrantel pamoate is one of the safest, most cost-effective and efficacious anthelmintics for treatment of roundworms and hookworms. The author recommends administration of pyrantel pamoate at a dosage of 10 mg/kg on entry to all adoptable dogs and cats with retreatment in 2 weeks and then at monthly intervals. In addition, puppies and kittens should be treated at 2-week intervals until 4 months of age. For cats and dogs with diarrhea, a fecal flotation, direct fecal smear, and stained fecal cytology should be performed with treatment according to results. Even if results are negative, the administration of broad-spectrum anthelmintics should be strongly considered. Ectoparasites (including fleas, ticks, ear mites, lice, sarcoptes, and cheyetiella) are also common in dogs and cats entering shelters, and they require routine diagnosis and control measures.

In areas where canine heartworm disease is prevalent, the testing of adoptable dogs is highly recommended. For dogs, antigen testing is the gold standard for diagnosis, but may be cost prohibitive for some shelters. Microfilaria testing is much more cost effective; however, as many as 20% of dogs with heartworm infection may not be microfilaremic (Nelson et al. 2005). In areas where heartworm disease is endemic, many shelters perform a microfilaria test (direct smear and/or a concentration test), which costs only pennies per test. If this test is negative, then an invest-

ment is made in performing an antigen test to verify the dog's true status. Heartworm testing is not recommended for cats due to the difficultly of interpreting the results. Heartworm prevention is recommended for cats and dogs sheltered in endemic regions. For in-shelter use, 1% ivermectin solution can be diluted in propylene glycol and used very cost effectively at a heartworm preventive dose (6–12 mcg/kg orally (PO) once monthly) in dogs. Continuous monthly administration of prophylactic doses of ivermectin has been demonstrated to be highly effective against both early and late precardiac larvae and young adult heartworms; therefore this drug may offer better protection for dogs with an unknown exposure history and for those that have not been on preventive before (Nelson et al. 2005). Chapters 22 and 14 contain a detailed review of heartworm and parasite control and prevention in the shelter.

**Spay/neuter**

Another essential component of a shelter wellness program is ensuring that cats and dogs are spayed or neutered prior to adoption. Virtually all animal shelters require adopted pets to be sterilized; however, national compliance rates average only 50% to 60% despite implementation of spay/neuter contracts, coupons, other incentives, and time-consuming follow-up (Moulton 1990). To ensure compliance, the American Veterinary Medical Association advises that all pets be neutered before adoption, including young puppies and kittens (American Veterinary Medical Association 1999). Numerous controlled prospective studies and large retrospective cohort studies have been conducted to verify the safety of performing spaying and neutering in puppies as early as 6 to 8 weeks of age (Howe, Slater et al. 2000; Howe, Slater et al. 2001; Spain, Scarlett, Houpt 2004a, 2004b). In many states, sterilization of animals adopted from shelters is mandatory.

In shelters where pets awaiting adoption may be held for long periods, reproductive stress from estrous cycling in queens and bitches and sex drive in tomcats and dogs can decrease appetite, increase urine spraying/marking and intermale fighting, and profoundly increase social and emotional stress. Spaying and neutering animals awaiting adoption is essential in shelters where cats and dogs will be housed for periods of longer than 2 to 4 weeks. These procedures decrease spraying, marking, and fighting; eliminate heat behavior and pregnancy; and greatly mitigate stress. This facilitates group housing and participation in supervised playgroups for exercise and emotional enrichment. In addition, the medical benefits of spay/neuter have been well described, including dramatic reductions in the risk of mammary cancer, elimination of pyometra and ovarian cancer in females, and decreased risk of benign prostatic hyperplasia, prostatitis, perianal hernias, and tumors in males (Johnston, Kustritz, Olson 2001).

**Identification (collar/tags, microchip)**

Identification of animals in the shelter in the form of a neck band, collar and tag, and/or a microchip is essential for preventive health care and ongoing surveillance of individuals, particularly where animals are group housed. Over the past two decades, a variety of microchips have been introduced into the U.S. market without regard to creating any national standards for radio frequency. This has, unfortunately, created situations where available scanners could not detect the presence of certain microchips. Currently, there are efforts to standardize microchipping in the U.S., including widespread distribution of global scanners to ensure that all implanted microchips can be reliably identified. Once global scanners are widely available, the AVMA recommends adoption of the 134 kHz (ISO) microchip as the American standard since this frequency is recognized as the international standard for microchips in the rest of the world.

Although the use of collars and tags as visually obvious forms of identification is quite valuable, the provision of permanent identification in the form of a microchip may be extremely beneficial as a means of improving pet–owner reunification since collars and tags may be easily lost. Improving pet recovery following adoption is another important goal or welfare target for animal shelters to strive for; thus, applying collars and tags and implanting and scanning for microchips is another way for shelters to be proactive and to model excellent standards of pet care for the public.

**Proper nutrition and exercise**

Proper nutrition and exercise have profound implications on wellness. Not only are they essential for management of healthy body weight and condition, good nutrition is known to support immune function and regular exercise is closely associated with behavioral health and well-being. A regular diet of good-quality, palatable commercial food consistent with life stage should be offered, and appetite should be monitored to ensure the maintenance of an adequate nutritional plane. Animals that do not eat for more than 1 to 2 days should be evaluated for medical problems and stress, and appropriate action should be taken as indicated based upon the findings. In addition, fresh water must always be available. Finally, animals should be weighed at intake and at routine intervals throughout their

shelter stay. Ideally, body weight should be recorded weekly during the initial month of shelter care and then once a month or more often if indicated. This is especially important for cats since significant or even dramatic weight loss may be associated with stress or upper respiratory infection during the first few weeks of confinement. On the other hand, excessive weight gain may occur in some individual animals housed long term. Therefore, protocols must be in place to identify and manage unhealthy trends in body weight since both weight loss and gain can compromise an animal's health, well-being, and chances for adoption.

### Grooming

Attention must also be given to proper grooming of animals in the shelter, including bathing, brushing and removal of matted hair, nail trimming, and ear cleaning. Long-haired dogs and cats frequently enter animal shelters with heavily matted hair coats and/or overgrown nails that can be painful and can predispose them to skin infections. When animals are held in the shelter for long-term stays, a system of regular grooming must be implemented to prevent the accumulation of painful mats and overgrown nails. In many instances, dogs are housed in runs that are damp, which can predispose animals to pungent body odor and skin infections, especially pododermatitis. Care must be taken to keep animals clean and dry. The author has witnessed in long-term shelter facilities many animals that are extensively matted and suffering from chronic pyoderma. This represents an unacceptable level of care and should not be permitted. Such situations can often be prevented by routine grooming and keeping the environment clean and dry. Some animals will obviously require more grooming than others, depending on their type of hair coat and conformation. Regular grooming also provides an excellent opportunity to monitor health and body condition while checking for skin problems and lumps. In addition, some animals enjoy the contact and attention.

### Periodontal disease prevention

Dental health is another component of addressing wellness; it extends far beyond bad breath. Plaque and tartar buildup are known to contribute to serious health concerns ranging from oral pain to chronic, intermittent bacteremia and organ failure. In dogs, periodontal disease is one of the most common health problems, affecting an estimated 80% of canine patients over the age of 5. It is especially common in small breed dogs (Debowes 1998).

In the context of an animal shelter, periodontal disease prevention may be low on the list of priorities for wellness; however, it should still be a consideration regarding individual care. When painful dental disease is present and animals are to be kept for adoption or long-term stays, a plan for timely treatment should be identified and implemented.

In terms of simple and practical means of prevention, the use of products aimed at encouraging chewing activity are well recognized to be beneficial by maximizing self-cleansing and physiological stimulation of salivary flow. Furthermore, chewing is a normal behavior for puppies and dogs, and when dogs are confined, bored, isolated, or stressed, they may engage in chewing as a coping strategy. For these reasons, as well as to help maintain oral hygiene, dogs of all ages should be provided with a variety of chew toys appropriate for their size and age.

### Breed-specific care

Wellness protocols may also be dictated by specific needs of certain breeds of dogs. For example, caution must be taken with brachycephalic dogs to ensure they do not experience heat exhaustion, to which they are extremely sensitive given the conformation of their airways. This may affect selection of holding/housing areas and exercise routines for these individuals. Poor airway conformation also predisposes brachycephalic dogs and cats to more severe upper respiratory infections than other breeds. For these reasons, care should be taken to house brachycephalic animals in well-ventilated areas away from sick animals, and they should be prioritized for removal to foster care or rescue. In the author's experience, even intranasal vaccination of these breeds is best avoided because it can result in severe clinical signs of respiratory disease.

Similarly, certain other breeds require special care in the shelter depending on their medical or behavioral genetic predispositions. The pit bull is another example: Many of these dogs require extra attention regarding housing conditions in a kennel setting so that a propensity to learn or exhibit dog–dog aggression is not exacerbated through exposure to high levels of arousal and stimulation from other dogs. Their kennels should also be escape proof and built to withstand efforts by some of these high-energy animals to climb the walls, chew, break through, or otherwise damage the enclosure. This type of behavior may be exhibited by other breeds and individual dogs as well and similar precautions should be taken regarding their care and housing.

## WELLNESS: BEHAVIORAL HEALTH

Animal shelters are simply not normal or natural environments in which to house cats and dogs. They are meant to

serve as temporary housing for pets waiting to be reclaimed or rehomed, and in some cases temporary housing for animals that will be euthanized. Over the past decade, there has been a growing trend in animal sheltering to afford pets awaiting adoption longer-term stays. This is especially common in limited admission "adoption guarantee" shelters that do not euthanize cats and dogs unless medically or behaviorally indicated. If not chosen by an adopter, an animal may stay in the shelter for weeks, months, or even years.

Cats and dogs experience many stressors in animal shelters beginning at the moment of admission. Even under the best possible conditions, animal shelters are stressful by their very nature: Incoming animals are confined and exposed to varying intensities of new and novel stimuli as well as to a variety of infectious disease agents. When confined long term, cats and dogs often suffer from anxiety, social isolation, inadequate mental stimulation, and lack of exercise, all of which can adversely affect their physical and behavioral health and lessen their adoptability. This in turn may result in euthanasia of the animal in some shelters, or in others it will increase the length of their stay if they do not attract the interest of an adopter because of poor physical or behavioral health. Over time, the animal's emotional and/or physical well-being may be compromised even further.

When addressing behavioral health in the shelter, prevention is crucial. A behavioral wellness program starts with proactive strategies to decrease stress from the moment animals arrive at the shelter until the moment their stay ends. As previously described, a thorough behavioral history and examination are essential and will provide an important baseline for action and follow-up.

### The role of stress

Stress involves outcomes secondary to increased secretion of catecholamines and cortisol. The harmful effects of chronic activation of these hormones have been well described and include adverse metabolic responses that promote dehydration, mental depression, insulin resistance, peptic ulcer formation and susceptibility to infection (Moberg 1985; Greco 1991). Chronic stress can also alter metabolism sufficiently to cause weight loss, prevent normal growth, and result in abnormal behavior deleterious to the animal. Stress responses and immunity are also intimately related; stress compromises the immune response, lowering resistance to infection (Griffin 1989). In fact, stress can trigger shedding of certain viral pathogens, including reactivation of latent viral rhinotracheitis (feline herpesvirus) infections in cats (Gaskell and Povey 1977). In the context of an animal shelter, minimizing stress has the potential to greatly improve animal welfare, decrease infection rates and disease transmission, and enhance adoptability.

A stressor represents any stress-producing factor or stimulus. Housing cats and dogs in animal shelters presents enormous opportunities for introducing stressors and inducing stress. Stressors may include illness; captivity; transport; overcrowding; isolation; changes in environmental temperature, light pattern, and/or ventilation; strange smells; noises; other animals; diet changes; handling; restraint; irregular caretaking schedules; unpredictable daily manipulations; the absence of familiar human contact; and the presence of unfamiliar human contact. In fact, anything unfamiliar to a cat or dog can trigger apprehension and activate the stress response. The severity, chronicity, novelty, predictability, and duration of the stressor, as well as the individual's perception, influence the response to a stressor (Moberg 1985; McMillan 2002). An individual animal's perception of a stressor is influenced by its genetic makeup, personality, and prior socialization and experience.

If allowed, animals employ coping strategies in order to lessen the negative impacts of a stressor (Carlstead, Brown, Strawn 1993; McMillan 2002). Examples of behavioral coping strategies include hiding, seeking social companionship, and acquiring mental stimulation. There is marked variability among individual cats and dogs regarding their ability to cope. Those that are successfully able to cope will suffer less from the physical and mental impacts of stress and will adjust better to life in an animal shelter. That being said, rare is the individual animal that truly thrives when housed long term in a shelter.

When animals are housed in shelters, stress frequently originates from the lack of opportunities they possess for engaging in active behavioral responses that would serve as means of coping. When stress is perceived as inescapable or uncontrollable, the resulting stress response is most severe (Carlstead, Brown, Strawn 1993; McMillan 2002). This is an extremely important consideration when designing housing and husbandry protocols for cats and dogs in shelters.

### Behavioral needs of cats and dogs

In addition to basic physical needs (such as proper nutrition and shelter), certain behavioral needs are also fundamentally important for cat and dog wellness. Most cats and dogs do not thrive in isolation; indeed, they are social animals, and thus the opportunity for social interactions represents a basic behavioral need. Cats and dogs also

require the ability to create different functional areas in their living environments for elimination, resting, and eating. They require consistent routines or daily patterns of care, including consistent periods of light and darkness. Other important behavioral needs include the ability to find a hiding place, to sleep without being disturbed, and to be free of chronic harassment from humans, other animals, or environmental stressors. Cats and dogs also require mental stimulation and the ability to play and exercise at will. Finally, cats need to scratch and dogs need to chew. For cats, scratching is a normal behavior that conditions the claws, serves as a visual and scent marker, and is a means of stretching. For dogs, chewing is a normal behavior that conditions the teeth, serves as a method of investigating their environment, and can be a healthy coping strategy for boredom or mild anxiety.

Manifestations of normal and abnormal behavior can indicate how successfully an animal is coping with its environment. Behavioral expressions may manifest via inhibited or withdrawal behavior, defensive behavior, disruptive behavior, and/or stereotypic behavior (Overall 1997; Hubrecht 1993). Inhibited or withdrawal behavior refers to activity depression or the absence of normal behaviors (such as grooming, eating, sleeping, eliminating, stretching, greeting people, etc.) Defensive behavior involves characteristic postural and/or vocal responses, and is often motivated by fear. Disruptive behavior involves destruction of cage contents and/or creation of a hiding place. Pacing, pawing, and circling are anxiety-related stereotypic behaviors. Behavioral signs of stress may manifest as active communication signals or passive behaviors. Signals of anxiety, fear, aggression, and submission may be subtle or obvious and include vocalization (growling, hissing), visual cues (facial expression, posturing of the body, ears, and tail) scent marking (urine, feces, various glands of the skin), and overt aggression. Passive signs of stress include inability to rest or sleep, feigned sleep, poor appetite, constant hiding, the absence of grooming, activity depression (decreased play and exploratory behavior) and social withdrawal (Griffin 2006; Rochlitz, Podberscek, Broom 1998; Wemelsfelder 2005). High-density housing exacerbates these signs. When cats and dogs are well adjusted and their housing meets their behavioral needs, they display a wide variety of normal behaviors including a good appetite and activity level, sociability, grooming, appropriate play behavior and restful sleeping.

Proper housing, consistent daily routines, adequate exercise, mental stimulation, social companionship and positive-reinforcement-based training should comprise a behavioral wellness program (see Table 2.2). Understanding the importance of minimizing stress in cats and dogs and possessing the ability to recognize and respond to it are keys to maintaining proper behavioral welfare. Staff should be trained to recognize indicators of stress. Active daily monitoring is required to detect and respond to the needs of animals that are displaying behavioral indicators of stress and/or social conflicts including persistent hiding, agonistic behavior with conspecifics, activity withdrawal, or other markers as previously described. Staff should record their findings daily to ensure timely recognition of stress so that animal welfare can be ensured through appropriate actions to decrease stress and enhance the animal's ability to cope in the shelter environment. Although subjective, staff should also attempt to estimate the severity of stress and note trends: Is the animal acclimating to the environment? Becoming less stressed? More stressed? Assessment of the incidence and prevalence of stress among the population serves to measure the effects of the shelter's animal care protocols and establish important baselines to help measure the impact of changes in housing and stress reduction programs.

**Housing**

Proper housing meets the behavioral needs of the animals, thereby minimizing stress. The design of short-term housing should include provisions for housing individual animals, litters, or compatible pairs for intake evaluation, triage, isolation, and quarantine. Housing should be easy to clean and sanitize, well-ventilated, and safe for animals and caregivers. Even short-term housing should provide for the minimal behavioral needs of animals, affording animals with sufficient space to stand and walk several steps, sit or lay at full body length, and separate elimination, feeding, and resting areas. Resting areas should include comfortable surfaces and, to provide a refuge, a secure hiding place for cats or other visual barrier for dogs. The design of long-term housing (i.e., for confinement in the shelter of more than 2 weeks' duration) should provide space that is mentally and physically stimulating and preferably that which is esthetically pleasing to the public, especially in adoption areas.

For long-term housing of cats, alternatives to cage housing should be afforded, and enriched single or group housing is indicated. Although not always easy to accomplish in busy shelters, at an absolute minimum, cats that are cage housed should be released each day and allowed an opportunity to exercise and explore in a secure enriched setting. For long-term housing in most instances, cats will benefit from being housed together since they are social

animals, provided there is sufficient space, easy access to feeding and elimination areas, an adequate number of comfortable hiding and resting places, and careful activity monitoring by staff (Griffin and Baker 2002; Griffin 2006). Not every cat will thrive in a group housing setting, however, and certain individuals will require enriched single housing depending on their particular physical or behavioral needs. These may include cats that lack socialization with other cats, mothers that are nursing young kittens, or those with special medical needs. For social group housing, the author recommends housing cats in small groups of up to four to eight individuals since it is generally easier to monitor the health and well-being of individual cats in smaller groups and since larger groupings increase the difficulty and complexity of establishing successful social groupings. Tremendous individual variation exists among cats in the context of social relations with other cats. While the introduction of some cats will seem effortless and uneventful, introduction of others will result in considerable stress not only for the new cat, but for the entire group. In fact, bringing a new cat into an established colony is analogous to having a stranger move into your home and share your personal bath and living space. For this reason, the introduction of new cats should be done slowly under supervision, and group size should be kept small. For both enriched single and group housing areas, a variety of elevated resting perches and hiding boxes should be provided to increase the size and complexity of the living space, and to separate it into different functional areas, which allows for a variety of behavioral choices. The physical environment should include opportunities for hiding, playing, scratching, climbing, resting, feeding, and eliminating. In the author's experience, most cats can be divided into small amicable groups if the enclosure is not overcrowded. Small rooms or multiple runs within a room may be used for housing. The author recommends a minimum enclosure size of approximately 10–12 feet × 16–18 feet for colonies of up to a maximum of eight cats, or 3–4 feet × 4–6 feet long high for groups of two to four cats. When runs are used, they should be at least 6-feet high. Doubling the size of an enclosure does not necessarily allow a twofold increase in the number of cats that can be properly housed. Group housing requires careful monitoring by staff trained to recognize subtle signs of stress. The addition of new cats results in a period of stress, which can often be mediated through the provision of multiple hiding areas and multiple feeding and elimination areas as described. These enhance the ability of individuals to cope and adapt to their new surroundings. Bully cats and others who do not adapt or show significant progress toward adaptation to group housing after several days may best be served by enriched single housing. For shelters that do not routinely house cats for more than a few weeks, the cats may best be served by enriched single or pair housing to avoid the potential stress that may arise from social conflicts.

For dogs, maintaining an adequate kennel environment to meet their behavioral needs for long-term housing is particularly challenging (Overall 2005; Loveridge 1998; Hubrecht 1993). Indoor–outdoor access is generally preferred, but whatever the arrangement, dogs should be able to see out to observe their environment. Runs must be large enough to allow a dog to move about freely, and a clean, comfortable bed should be available for resting in a secure location. Visual barriers should be available to provide refuge from kennel mates. The addition of three-dimensional space (such as platforms, steps, or ramps) is beneficial, and periodic rearrangement of the structures can help to alleviate boredom and stereotypic movements. In addition, dogs must be provided with regular opportunities to exercise outside their runs each day. Supervised playgroups afford opportunities for exercise and social interaction. The provision of such items as kiddie pools, tunnels, and platforms in play areas may enhance interactions. If outdoor play enclosures are not available, dogs should be walked outside. Long lines or retractable leashes may provide greater opportunities for exercise during walks, but care should be taken to make certain that staff and volunteers are trained to ensure that animals do not escape or injure anyone. In some situations, outdoor enclosures may also be suitable for cats. Benefits include ample exposure to natural light, excellent ventilation, and mental stimulation. Galvanized wire chain link panels with 1-inch mesh (including a top panel) or specially designed fencing for cat enclosures (Purrfect Fence, www.purrfectfence.com) may be used (Griffin 2006). Finally, "real life" rooms (e.g., rooms with a homelike environment) away from the kennel or cattery may also be useful, especially for those animals that remain in the shelter for more than a few weeks.

The successful adaptation of cats and dogs to novel environments depends on both the quality of the environment and the adaptive capacity of the animal. Although most adapt to new environments over time, some never adjust and remain stressed indefinitely, ultimately resulting in decline of physical as well as emotional health. Even in modestly populated, carefully introduced, environmentally enriched cat colonies, behavior problems may occur. Manipulating the social environment by regrouping cats may help resolve these problems; however, many cats are

incompatible with one another as housemates. If only one or two cats are responsible for social destabilization of a colony, they can be removed and reassigned to another colony. Often it is the social grouping, not the individual, that is the problem.

In time, a careful observer will see that cats usually divide themselves into amicable groups. Observers should note feline personality types (e.g., bold versus shy) and watch for behavioral signs of stress as well as affiliative behaviors (e.g., those behaviors that promote social contact). The best colony environments are those that produce the most "normal" behaviors, including grooming, sleeping, playing, stretching, allorubbing and exploring. Colonies should be carefully monitored to ensure that all colony members are content in the social environment.

Novel environments tend to be especially stressful for poorly socialized and for geriatric cats and dogs. Housing of feral cats should be avoided whenever possible. Geriatric cats in animal shelters generally benefit from placement in foster care and feral cats from neuter and return programs. The author recommends that shelters maintain a variety of housing styles in order to meet the wide array of behavioral needs of individual animals. The importance of proper staff training to recognize and prevent stress is critical for animal welfare and cannot be overemphasized. Shelters that colony-house cats are cautioned that although this method of housing can enhance welfare when done well, it could also serve to increase stress when improperly managed. In particular, overcrowding of cats in colony housing must be avoided to ensure welfare, or an all-in/all-out approach should be used to prevent constant introductions of new cats, which induces stress. Likewise, care must be taken to ensure careful monitoring of dogs when housed in pairs or when in playgroups to recognize stress, prevent fighting, and ensure both animal welfare and staff safety.

### Behavioral care and environmental enrichment

Perhaps the most effective environmental enrichment is an animal care staff that enjoy working with animals and that are willing and able to spend ample quality time interacting with the animals on a daily basis to ensure social contact and tractability. Cats and dogs become entrained to daily routines and generally respond strongly to their human caregivers. Whenever possible, caregivers should be assigned to care for the same animals on a regular basis so that they become aware of the personality of each animal. This familiarity is necessary for detection of physical or behavioral problems, and enables staff to make better adoption matches. Caretakers should schedule time each day to interact with "their" animals in addition to the activities of feeding and cleaning. Some cats and dogs may prefer to be petted and handled while others will prefer to interact via a toy (e.g., cats chasing dangling feathers or dogs fetching a ball). Regular aerobic exercise is essential for dogs, the intensity and duration of which are defined by the individual's needs.

The provision of scratching boards is especially important for cats. Empty cardboard boxes and paper bags are inexpensive and disposable, and they stimulate exploration and play behavior in addition to scratching. Cats and dogs should be provided with sanitizable or disposable toys to stimulate play. Cat or dog treats or dry food can be hidden in commercially available food puzzle toys, cardboard boxes with holes, or empty soda bottles such that the cat or dog has to work to extract the food pieces. Similarly, dogs can be encouraged to chew by stuffing treats in commercially available chew toys. Making special toys or treats part of the daily routine helps give the animals positive events to look forward to and may help to alleviate boredom and frustration. For dogs, olfactory stimulation can be pleasurable and periodic application of commercially available scented room deodorizers (such as lavender) might provide a source of positive stimulation in the kennel.

Obedience training using clickers with food or play rewards can provide additional stimulation and activity and social contact for both dogs and cats. In addition to providing mental stimulation, teaching dogs good manners makes them more appealing to adopters and sets another example of good pet care. Finally, use of a commercially available feline facial pheromone spray (Feliway®, Veterinary Product Laboratories, Phoenix, AZ) or a dog-appeasing pheromone (DAP® Veterinary Product Laboratories, Phoenix, AZ) may be beneficial to cats and dogs, respectively, as these products have been shown to help reduce anxiety.

A sense of control over conditions is one of the most critical needs for mental health and well-being in animals (McMillan 2002). Cats and dogs need variety and choice, and individuals possess different preferences for environmental conditions, levels of activity, and social interactions with other animals and humans. The best environmental enrichment will provide for all of these choices.

## ENVIRONMENTAL WELLNESS

The shelter environment has a profound influence on animal health and well-being; thus systematic wellness protocols to address the shelter environment must be

established. Protocols should include provisions for maintenance of proper population density, cleaning and sanitation, animal segregation and traffic patterns, other facility operations, and staff training.

### Population density

Overcrowding is one of the most potent stressors recognized in housed animals (Griffin and Baker 2002; McMillan 2002). Overcrowding increases both the number of susceptible animals and asymptomatic carriers in a given group thus increasing the likelihood of disease transmission between group members through both direct contact and contaminated fomites. Overcrowding increases the magnitude of many stressors in the shelter environment including noise, air contaminants and infectious agents, and compromises animal husbandry, inflating the risk for serious outbreaks of disease in the population.

There is no simple formula available to determine the number of animals that a given facility should house. Crowding is not simply a matter of space available for animals, but also of the shelter's ability to provide proper care to meet their physical and emotional needs. Overcrowding negatively impacts the shelter staff by overwhelming their ability to provide proper care to the animals and good customer service to the public. Overcrowding can negatively affect adoption rates since potential adopters often find an overcrowded shelter to be an overwhelming and uninviting environment, further compounding the shelter's crowding problem. Shelters must limit the number of animals they house to the number for which they can provide reasonable care. At times, unexpected intake may result in temporary conditions of overcrowding, but a good wellness program dictates that protocols must be in place to alleviate overcrowding and maintain a modestly populated environment for the health and protection of the animals and staff.

Overcrowding may be reduced by euthanasia, limiting intake, and/or decreasing the average length of time animals remain in the shelter. Programs to increase and speed adoption, redemption, and transfer (to rescue or foster care) help to minimize euthanasia for space in open admission shelters and maximize intake in limited admission shelters.

Euthanasia decisions are always difficult but are part of the responsibility of every shelter. Euthanasia may need to be performed in consideration of the population in order to alleviate overcrowding or prevent disease outbreaks from spreading out of control. Euthanasia may also be necessary for individual animals that are suffering from physical or behavioral disease or that pose a risk to public health or safety. When a decision is made to euthanize an animal, it is imperative that the procedure be performed without delay. In many instances, this will serve to protect individual animal welfare and public safety as well as serve the population as a whole. For example, aggressive dogs that cannot be safely rehomed should not be held beyond their legal holding periods. Instead, they should be humanely euthanized as soon as possible to prevent undue stress and anxiety on the dog and risk for the shelter staff and public. No matter what the underlying circumstances are surrounding the euthanasia of an animal, these procedures are always difficult. Delays in action, however, often contribute negatively to population health and prolong the stress of individual animals in the shelter.

As a part of rounds for routine daily surveillance, thoughtful consideration should be given as to why each individual animal remains in the shelter and what could be done to optimize or hasten a successful outcome for that animal (Hurley 2004). When shelters avoid overcrowding, they potentially have more time to properly care for and market resident animals, which may decrease shelter stays and ultimately allow them to serve more animals. In addition, funds saved on housing costs may be redirected to programs that increase adoption or contribute to prevention and decreased intake (such as spay/neuter programs).

### Cleaning and sanitation

For wellness programs to be effective, a clean and sanitary environment must be maintained. Not only does this promote pet health, but it also promotes staff pride and public support. In addition to protocols for routine daily cleaning and sanitation procedures, protocols should be in place for periodic deep cleaning and disinfection as well as procedures to be used in the event of disease outbreaks. Chapter 4 provides a more detailed discussion of cleaning and sanitation practices for animal shelters.

### Segregation of animals

The segregation of animals entering shelters is essential for proper welfare, infectious disease control, staff safety, and compliance with animal control procedures. Incoming animals should be separated by species (e.g., cats, dogs); age group [e.g., preweaning (less than 6–8 weeks of age); pediatrics (6–16 weeks of age); juvenile (4–12 months of age); and adults (older than 1 year of age)]; sex or reproductive status (e.g., in heat, pregnant, nursing); and physical and behavioral health status (e.g., apparently healthy, signs of contagious disease, dangerous, feral). Thus, a variety of holding, adoption, and isolation areas is necessary for proper segregation.

Quarantine areas should be used to segregate healthy animals for observation. The use of such areas not only allows apparently healthy animals to be observed for developing signs of disease, but it also allows time for response to vaccination in a highly biosecure environment where exposure risks are minimized. Where quarantine facilities are limited, they should be preferentially used for the most susceptible animals that enter the shelter (usually young puppies and kittens). Although quarantines have been routinely recommended as a mainstay of any population health disease control program, their effectiveness in shelter health programs has been called into question because shelters have constraints placed upon them that preclude the implementation of conventional quarantine protocols. The fact is, most shelters are unable to implement a proper quarantine where an all-in/all-out system is utilized. In most shelters, incoming animals are added to the quarantine group on a daily basis, effectively defeating the purpose and merely prolonging the stay of the animals, which contributes to the development of infectious disease. Quarantines can be of considerable value when used to observe animals involved in transport programs or during disease outbreaks, but the routine use of conventional quarantines may be of limited value, if not detrimental in many shelters.

When quarantine is used, the length of time recommended depends partly on the availability of space and resources, the prevalence of infectious disease in the population, and/or the geographic region and the incubation period of the disease in question. For example, strict quarantine or enhanced biosecurity measures for young puppies may be more important in shelters in the southern U.S., where there are large numbers of puppies and canine parvoviral infections are extremely common. Ideally, a 14-day quarantine will be sufficient to determine that animals are not incubating common infectious diseases such as canine parvovirus or feline panleukopenia that could be introduced into the shelter environment. However, length of stay has been linked to an increased risk for the development of respiratory disease in cats (Scarlett 2006) and in dogs (Edinboro, Ward et al. 2004), so an abbreviated quarantine period may be preferred. In addition, studies indicate that unless maternal antibody interference or recent exposure (incubation of the disease) prevents response, both cats and dogs develop protection against parvovirus within 72 hours of vaccination with a modified live product (Brun, Chappuis et al. 1979; Carmichael, Joubert et al. 1983), further negating the necessity of a lengthy quarantine or holding period.

General holding areas may be used for adult animals at intake that are less biosecure than quarantine areas. Holding time may also be influenced by the length of legal holding periods prescribed by state and local laws that allow owners a chance to reclaim lost animals. A legal holding period is not mandated for owner-relinquished pets, but a medical hold for evaluation and triage is almost always warranted.

Isolation areas are used to segregate sick animals from the general population. Immediate isolation of sick animals is critical for effective disease control. Isolation should be targeted by species, age, and disease. For example, separate isolation areas should be available for cats and dogs with respiratory disease. In addition, separate isolation areas should be available for cats and dogs with nonrespiratory infections. Strict biosecurity in quarantine and isolation areas, with attention to traffic patterns and the use of protective clothing such as shoe covers and gowns, is essential. Whenever possible, designated staff should care for animals in these areas. Traffic patterns should move from the healthiest and most disease-susceptible groupings to the least susceptible, and finally to the isolation areas housing sick animals. Observation windows and signage can be used to reduce traffic flow into quarantine and isolation areas. Staff hygiene is extremely important and the importance of diligent hand washing cannot be overemphasized. Where space or facilities are not available, foster care may represent a viable and medically sound option for quarantine or isolation of some animals, particularly preweaned kittens and puppies. Such situations must be monitored to ensure foster animals are receiving sufficient care, pet animals in foster homes are protected from disease exposure, and foster parents are not becoming overwhelmed.

**Other facility operations**

The success or failure of virtually every aspect of a wellness program depends on housing design and facility operations. Adoption of strict management protocols, thorough training, and supervision of personnel with oversight by a knowledgeable professional are required for success. In addition to proper housing design, segregation, and sanitation procedures, there are several other very important aspects of facility operations to consider when designing a wellness program for the shelter environment. Animal health can be compromised by inadequate ventilation or by ill-considered air pressure gradients that recirculate or cause exchange of air between rooms. Poor ventilation and high humidity contribute to disease by promoting accumulation of infectious agents as well as dust and fumes that

may be irritating to the respiratory tract. Thoughtful consideration must be given to strategies to maintain good air quality (Hurley 2005). These include improving ventilation, regular maintenance of filters, good cleaning practices including routine or as-needed vacuuming to control dust and dander, periodic deep cleaning, and the use of dust-free litter (or simply dumping dusty litter boxes outside). The best case scenario, and what is typical in laboratory animal settings, is for the heating, ventilation, and air conditioning (HVAC) system to allow for 100% fresh (e.g., nonrecycled) air in each room so that the air entering a given room is exhausted out of the building and not recirculated to another room. The standard recommendation for an animal room is 10 to 15 air changes per hour, but more or less airflow may be acceptable or necessary depending upon the species housed and the anticipated housing density (ILAR 1996). Even when ventilation systems provide 10 to 15 room air changes per hour, this may not occur at the level of the cages or other animal enclosures. Ventilation may be improved by housing design; for example, the use of flow through cages, runs (especially the indoor–outdoor type), or colony housing for cats may help. Another standard recommendation has always been to have separate ventilation systems for the various functional areas of the shelter to prevent exchange of air among them. However, some experts have recently called this recommendation into question because few diseases in shelters are truly transmitted via aerosolization but instead are primarily spread via fomites. Although this recommendation seems prudent to consider whenever possible, it is very expensive to install and operate this type of ventilation system. If air quality remains good and the shelter maintains effective comprehensive wellness protocols, this recommendation may not be necessary for maintaining animal health. More research is needed on this subject but in the meantime, the author recommends consulting with an HVAC specialist to analyze the shelter's needs and maximize the potential of the shelter's system.

Temperature and humidity should be controlled to keep animals comfortable. Drafts should be avoided. The recommended temperature range for cats and dogs is between 64 °F and 84 °F with a temperature setting in the low to mid 70s being typical (ILAR 1996). However, the temperature setting should match the animals' needs. For instance, sick animals, puppies, kittens, and animals recovering from surgery are more susceptible to lower temperatures than healthy animals. The location of the animal should be considered since cages located closer to the floor are always a few degrees colder than the ones above the floor level. In addition, it is important to consider the particular shelter situation, finances, and location. For instance, power companies recommend keeping the temperature between 78 °F and 79 °F during hot weather because this potentially could save 10% or more on the electricity bill. Regarding humidity, the laboratory standards for cats and dogs state 30% to 70% humidity is desired (ILAR 1996). Higher humidity (70%) may be advantageous in URI treatment areas, whereas less humidity (40% to 50%) in other areas may help with disease control by curtailing airborne transmission. Although the range considered acceptable is large, a given room should have a fairly constant humidity (e.g., it should not have large fluctuations). It is recognized that hosing or even mopping a room will cause humidity spikes, but they should be short-lived with a well-ventilated room.

Regular light and dark cycles are especially important, and staff should be trained to ensure that lights are on by day and off by night, or timers may be used to ensure control. Exposure to natural sunlight offers the advantage of curtailing disease transmission. The importance of regular schedules of feeding, cleaning, exercise, and play cannot be overemphasized. Even stressful events are less stressful if they are on a schedule. When aversive stimuli are unpredictable, chronic fear and anxiety may result. Conversely, predictable stressful events allow a period of calm and comfort between stress responses (McMillan 2002). Animals also respond to positive experiences in their daily routines; feeding time and playtime may be greatly anticipated.

Noise control is another important consideration in shelters, and housing design and soundproofing can help. For barking dogs, an examination of the motivation of the barker may help to solve the problem and alleviate the individual's stress as well as the impact on the environment. Regular pest control and all aspects of building maintenance are important considerations for the maintenance of a healthy environment. Developing and following written standard operating procedures and daily, weekly, monthly, and quarterly checklists will ensure systematic schedules of maintenance are carried out.

### Staff training

Regular staff training is essential to implement effective wellness programs. Staff must be trained in all areas of animal care from intake to adoption, redemption, transfer, or euthanasia. Staff knowledge, attitude, and skill will largely determine the success or failure of every aspect of the shelter's wellness program. Staff must be taught how to gather the essential historical information at the time of intake; to attend to all aspects of animal care including

feeding, cleaning, disease recognition, and behavioral enrichment; and to offer adoption counseling that will help ensure a successful match. Adopters should receive written records and instructions for follow up with their veterinarian. In addition, postadoption counseling and follow-up should be offered. The importance of regular staff training and assessment, and effective staff management and leadership cannot be overemphasized. The best-run shelters are ones with competent, compassionate, well-trained staff that work cooperatively in efforts to provide excellent animal care and public service.

## CONCLUSION

Today more than ever, society expects high-quality care for animals in shelters. Indeed, shelters have a moral obligation to provide for the health and welfare of animals entrusted to them. Shelter animal health is dependent on implementation of comprehensive wellness protocols, systematic surveillance, and excellent management. Shelters must establish solid goals for animal health and measure welfare targets. Wellness protocols and management practices must be regularly evaluated and revised to meet these targets. The bulk of the effort must focus on preventive strategies to ensure both physical and behavioral health of cats and dogs. Staff education is critical since a dedicated and well-trained staff is essential for success. In addition, the shelter environment must support opportunities for animals that promote pleasurable feelings and experiences whenever possible. "Healthy and happy" cats and dogs are highly desirable pets; thus wellness programs help shelters meet their ultimate welfare target: successful adoption.

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# 3
# Outbreak Management

*Kate F. Hurley*

## INTRODUCTION

Even in the face of rigorous precautions within an animal shelter, there will always be some risk for disease outbreaks. In most shelters, animals are admitted on a daily basis, potentially carrying with them infectious conditions reflecting the prevalence in the surrounding community. Many of these animals have an uncertain health history at best and often have received little or no preventive care. The frequent entry of especially vulnerable puppies and kittens creates further opportunity for potential outbreaks. Even in multianimal environments where the animals have a history of vaccination and good care, outbreaks of emergent disease are a very real threat. In recent years there have been reports of fatal outbreaks of virulent systemic calicivirus, canine influenza, and *Streptococcus zooepidemicus* in kennels and veterinary clinics as well as shelters. In this context, every veterinarian should understand the basic tools for outbreak management.

While in past years draconian measures such as total depopulation have often been utilized in shelters to control outbreaks, these are not viable when infectious disease invades a veterinary clinic, boarding facility, or sanctuary, and are becoming increasingly unacceptable at shelters as well. Fortunately, with a well-thought-out and systematic approach, most outbreaks can be controlled successfully with far less drastic measures.

Planning prior to an outbreak can greatly enhance the opportunities to control disease spread, minimize mortality, reduce the possibility of panic, and protect the organization's reputation. Researching diagnostic options, identifying off-site housing possibilities for exposed animals or designing on-site isolation and quarantine facilities, developing contact lists, and preparing a general communication plan are all better accomplished proactively before an outbreak takes place. This chapter will cover the basic tools to plan for and respond to outbreaks. Detailed information pertaining to specific diseases can be found in the relevant chapters elsewhere in this text.

## RISK FACTORS FOR OUTBREAKS

The ideal disease control strategy will always be prevention of outbreaks rather than reaction and, at best, damage control. Strategies for prevention of specific diseases commonly encountered in shelters are emphasized in each chapter of this text. However, it is unrealistic to suppose a specific preventive strategy can be prepared for every pathogen that may enter a shelter environment. Therefore, general preventive strategies must be in place. Many of these strategies are described in Chapter 2 on animal wellness and include stress reduction, vaccination, good nutrition, proper housing and ventilation, maintenance of a sanitary environment, and attention to mental as well as physical health of animals. Conversely, risk factors for outbreaks are predictable and include both animal and environmental factors. Some of the most important animal risk factors include stress, lack of vaccination, concurrent disease or parasitic infestation, and a history of predation or scavenging. Important environmental risk factors include failure to isolate animals that show signs of disease; lapses in sanitation; some-in/some-out housing, in which animals are added and removed from group housing without ever creating a clean break; mixing of species (e.g., housing dogs and cats in the same area); and widespread, nonjudicious antibiotic use.

Crowding is a common and very important risk factor for outbreaks that often underlies many of the other factors listed above. This is true in kennels and clinics as well as shelters; often outbreaks are reported at holiday seasons

when kennels are relatively full or within clinics running at (or beyond) maximum capacity. Increased population density in itself increases both the opportunities for disease introduction and the contact rate between animals, resulting in increased spread of any pathogen that might be present. When increased population density crosses the line to crowding such that animal care is compromised and stress levels for animals and staff spiral upward, the risk for disastrous outbreaks is dramatically elevated. Serious disease spread in turn can destroy rescue relationships, paralyze adoptions, and damage community and veterinary support, which can lead to further shelter crowding and disease issues. The ideal time for response, then, is when these risk factors are detected and before the actual occurrence of an outbreak.

## BASIC TOOLS FOR OUTBREAK MANAGEMENT

In spite of the best-laid plans, occasional outbreaks continue to be a reality for many shelters and other animal populations. Even the definition of an "outbreak" may vary from shelter to shelter. For some, virtually any occurrence or spread of serious disease is considered unacceptable and preventable, while for others, serious disease is brought in so commonly from the community that the term "outbreak" may not be invoked until extensive spread within the shelter is observed. Common conditions involved in shelter outbreaks include canine parvovirus, canine distemper, canine influenza, and canine infectious respiratory disease complex in dogs; and feline panleukopenia, calicivirus, upper respiratory disease complex, and ringworm in cats. Outbreaks of infectious enteritis from various causes are also common in shelter animals. In addition, uncommon or normally mild pathogens may mutate or partner with other pathogens to cause severe outbreaks, especially in crowded environments. Regardless of the definition or cause, outbreak management requires six main tasks:

1. Diagnosis and isolation of diseased animals
2. Identification and management of exposed/at-risk animals
3. Environmental decontamination
4. Protection of newly admitted animals
5. Documentation
6. Communication with staff, stakeholders, adopters, and the public

Although presented in sequential fashion in this chapter, in reality these six steps must often be accomplished virtually simultaneously as new, vulnerable animals continue to arrive throughout the day at most shelters and must be protected.

### Diagnosis and isolation of diseased animals

Animals caught up in an outbreak can be divided into four categories:

1. Those that are infected (and subclinically or clinically ill)
2. Those that have been exposed and are at risk of developing infection in the future
3. Those that have been exposed but are not at risk for developing infection (either due to previous vaccination or other factors)
4. Those that have not yet been exposed

Distinguishing among these groups is essential in managing an outbreak. Diseased animals need to be promptly identified and immediately removed from the general population. In order to be effective in halting an outbreak, rapid and sensitive diagnostic methods are needed. If it takes days or weeks to obtain answers, disease may continue to spread while veterinarians await results. For this reason, whenever in-house options are available for diagnosing relatively common conditions, these should be kept on hand, even when other diagnostic alternatives exist and may be used as adjuncts. This includes enzyme-linked immunosorbent assay (ELISA) snap tests for canine parvovirus and feline panleukopenia; Wood's lamp, direct exam, and fungal culture supplies for ringworm; and supplies to diagnose common enteric protozoal and parasitic infections. Polymerase chain reaction (PCR) panels are becoming more commonly available and turnaround time may be as little as 24 hours, making these another realistic option for diagnosis of some conditions. Specific testing strategies for common shelter conditions are given elsewhere in this book. If animals die or are euthanized due to severe illness of unknown etiology, necropsy can be an extremely helpful tool to rapidly arrive at a definitive answer. Additional details on sampling for necropsy specimens are provided in Chapter 7.

In most cases, diagnostic testing should focus on symptomatic animals or those with a highly suspicious exposure history. It is often costly and unnecessary to screen every animal in the shelter and doing so may lead to a high rate of false positives. For instance, in an outbreak of canine parvovirus, testing should generally be reserved for animals with diarrhea or other signs of systemic illness, puppies from high-risk areas of the community, and littermates or puppies very closely exposed to affected

animals. For a few conditions where clinical signs may be subtle and testing is relatively accessible, however, screening of the whole population is indicated. For example, this is sometimes the case when confronted with an outbreak of dermatophytosis: rather than risk missing a subtle lesion, it may be preferable to examine and screen the entire population via fungal culture.

When obtaining diagnostic samples in an outbreak of unknown etiology, acutely affected animals should generally be sampled (those that have not been extensively treated). Ideally, 10% to 30% of the population should be sampled; at minimum, three to five animals should be sampled, as results from one individual may not be generally applicable.

Unfortunately, quick and accurate tests are not always available. Although ideally the cause of every outbreak would be discovered, control measures may need to be implemented prior to reaching a definitive diagnosis. When this is the case, it is often necessary to proceed under the assumption that all animals with suspicious clinical signs are infected. In a shelter suffering an outbreak of canine distemper, for example, all dogs with respiratory signs must be considered potentially infected (and infectious) with distemper virus; no currently available antemortem test is sufficiently reliable to rule out distemper infection in a clinically affected dog. A common and potentially dangerous misapprehension is the belief that mildly diseased animals do not pose a great risk to others. While this may be the case for some conditions, often the severity of disease manifestations in an individual animal reflects more upon that individual's immunocompetence rather than the severity of the infecting pathogen. Transmission of severe and even fatal disease by mildly infected animals is commonplace with some important diseases such as canine distemper, canine influenza, and virulent systemic feline calicivirus.

### *Isolation and treatment of suspect cases*

Animals diagnosed with infection based on testing or clinical signs and history must be suitably isolated to protect the rest of the population. Shelter veterinarians should carefully evaluate whether adequate isolation and treatment can be delivered in house. The level of required isolation depends to some extent on the ease of spread and route of transmission of the disease. Pathogens that are extremely durable in the environment (such as canine and feline parvovirus and dermatophytosis) or that are spread via airborne transmission (such as canine distemper and canine infectious respiratory disease complex) require the most rigorous precautions. Ideal isolation entails complete physical separation, including separate housing, equipment, and supplies. Full protective garments should be worn in isolation areas, including long-sleeved tops and long pants or jump suits, gloves, and shoe covers or dedicated boots. Footbaths are not sufficient to reliably prevent transmission of serious disease (Stockton, Morley et al. 2006). Equipment and supplies used for isolation should be clearly marked and used only in that area.

If resources are such that adequate isolation cannot be performed at the shelter, or staff is not available to deliver adequate and humane treatment, off-site options can be considered. Particularly with advance planning and discussion, it may be possible to arrange for treatment of some animals at local veterinary clinics or transfer of affected animals to shelters with greater resources. Some rescue groups or foster homes can be set up to provide adequate isolation and treatment for mildly ill animals, particularly if the required treatment is limited to oral or topical medications and the disease is neither highly contagious to other pets nor poses a serious zoonotic risk.

Release of infected animals to foster or rescue groups should only be done in conjunction with the provision of written information regarding risks to pets and humans in the household and a clear understanding of who will be responsible for costs associated with the animal's medical care. Foster homes and rescues should be monitored as necessary to ensure that ill animals are indeed receiving adequate treatment and that care providers are not becoming overwhelmed. The release of ill animals may carry the risk that the animal will become more severely ill or even die. In some cases, it also carries a significant risk of disease transmission to other pets (especially for conditions for which vaccination is unavailable or unreliable, such as feline calicivirus). For those reasons, willing foster care providers and rescuers with good isolation facilities may be better reserved for exposed animals that are not yet ill, but cannot safely remain in the shelter for a quarantine period (see below). If neither on- nor off-site facilities exist for adequate isolation and treatment of affected animals, euthanasia may be the only option to avert suffering and prevent further spread. Allowing clinically ill animals to remain in a general shelter population without adequate treatment is not an acceptable option.

### Identification and removal of exposed/at-risk animals

Removing clinically ill animals will have little benefit in controlling an outbreak if exposed animals remain within the general population, only to break with illness in the subsequent days or weeks. Animals that are not yet symptomatic but that may be incubating disease must be

identified and quarantined for a suitable period (or possibly euthanized if no other method exists to control spread). Quarantine can be costly and labor intensive, and euthanasia is obviously a last resort; therefore, it is important to distinguish those animals for whom such special precautions are genuinely indicated. Not every animal residing within a facility at the time of disease occurrence in another animal is necessarily at a meaningfully increased risk of infection. Risk level depends on both degree of exposure and level of susceptibility of the individual animal.

### *Limitations of risk assessment*

Even when a concerted effort is made to thoughtfully evaluate risk as described below, it is rarely possible to establish that an animal is at zero risk. This is even true under nonoutbreak conditions. In most animal populations, there is always some small risk of infection. The goal of risk assessment, then, is to identify those animals that are at relatively low risk, ideally at no greater risk than during baseline operations for that particular shelter. Risk assessment standards should be most rigorous when the potential consequences of adopting out an infected animal are very severe. For instance, cats harboring virulent systemic feline calicivirus or dogs shedding canine influenza may transmit these potentially deadly infections to pet animals in homes; animals infected with multidrug resistant *Salmonella* may transmit severe or even fatal disease to humans. On the other hand, a somewhat greater risk may be tolerated when there is little possible harm to other animals or humans. For instance, an incompletely vaccinated dog exposed to canine distemper may develop the infection, but is very unlikely to spread it to well-vaccinated adult dogs in an adoptive or rescue home. The risk in releasing a distemper-exposed dog is primarily limited to the potential that it will become ill itself, leading to possible expense and heartache for the adopter or rescuer. While not a trivial concern, this risk must be weighed against the known perils of euthanasia or prolonged quarantine. In some cases, release of low- to moderate-risk animals with suitable disclaimers is the better choice.

### *Assessing environmental exposure*

Transmission of disease to other animals is by no means guaranteed every time an infected animal enters a shelter. Environmental exposure risk and likelihood of spread depends on cleanliness and routine disinfection practices, durability of the pathogen in question, and route of transmission. Factors that *reduce* the likelihood of spread include:

- Animal housing areas constructed of stainless steel, sealed concrete, or other nonporous, nonscratched surfaces that can be successfully disinfected
- A disinfectant proven effective against the pathogen in question is used on a daily basis
- Animals are infrequently or never moved from one kennel to another (especially if they are not moved on a daily basis for cleaning, e.g., double-sided runs or spot cleaning are correctly used)
- Common rooms, exam surfaces, and carriers are effectively disinfected between each use
- Sick animals are promptly identified and isolated
- Separate equipment and protective clothing is used between handling healthy and sick animals
- The facility is not overcrowded

The above-listed environmental factors have the greatest impact on conditions spread primarily via fomites or direct contact. For such conditions, if a single animal develops a serious disease, it may not be necessary to implement outbreak control measures unless there is evidence of additional spread. This is particularly true if a single case occurs soon after intake, suggesting that the animal may have been incubating disease at the time of admission rather than having acquired the infection during its shelter stay. Serious disease is bound to enter shelters from time to time, and implementing a full-scale response with each case can be nearly as crippling as blithely ignoring a serious outbreak. On the other hand, if a condition is spread via aerosol transmission, if environmental conditions are substantially less than ideal, or if there is evidence of spread within the shelter, a more detailed risk assessment of individual animals will be required to determine which animals can be released without special precautions and which will need to be quarantined or otherwise removed from the population.

### *Assessing individual animal risk*

Just as transmission is not inevitable if exposure can be prevented, exposure does not necessarily lead to infection. The two most important factors in determining the outcome of exposure are generally the dose to which the animal is exposed and the immune status of the exposed animal. For example, adult cats that have been fully vaccinated against feline panleukopenia at the time of exposure are very unlikely to become infected and need not be quarantined. This assumption can also be made regarding adult dogs fully vaccinated against parvovirus and canine distemper. On the other hand, vaccine protection against respiratory infections tends to be mediocre at best, and all exposed

animals must be assumed to be at risk regardless of vaccine status. Likewise, protection from vaccination is never 100% reliable in puppies and kittens under approximately 16 weeks of age.

Proximity also plays a role in individual animal risk, as it often affects the dose to which an animal is exposed. Canine respiratory pathogens can be transmitted 25 feet or more, while feline respiratory disease droplet spread is thought to be limited to approximately 5 feet (Gaskell and Povey 1982). Though fomite spread can cover long distances, proximity may still play some role: For example, one would expect the amount of parvovirus tracked on a shoe sole to be higher when entering the run next door versus a run 50 yards away. Clearly, animals directly cohoused with an affected animal will be at greatest risk. Littermates are at particularly high risk, as they share a common immunological background as well as exposure history. However, even littermates may not all have the same outcome from an exposure: Due to either protection from maternal antibodies or interference with vaccination, even within a litter some animals may become severely ill or die, some may become infected and shed while showing minimal signs of illness, and some may never become infected at all. It is worthwhile to quarantine exposed littermates if resources exist to do so safely and humanely.

*Use of serology for individual animal risk assessment*

The risk assessment process described above is imprecise but still often preferable to implementing blanket measures without regard to individual risk profile. For a few diseases in which serologic status correlates well with protection, serological testing offers a more precise guide to risk of infection. Diseases for which this is the case include feline panleukopenia, canine parvovirus, and canine distemper. For these conditions, positive titers at the time (or within a few days) of exposure in asymptomatic animals correlate well with protection. Negative titers do not necessarily mean the animal is susceptible and certainly do not mean it will become infected but indicate that it still must be treated as potentially at risk. While there is a modest cost associated with such testing, this must be balanced against the potentially substantial cost of quarantine or euthanasia (from both a financial and animal-welfare perspective). In many cases, serological testing will prove the more humane and cost-effective option. If some animals can be categorized as low risk based on serological testing, quarantine or rescue options for the remaining higher risk animals may become a more viable prospect. More details on serologic testing are provided in Chapter 5 on vaccination and immunology.

***Management of exposed/at-risk animals***

Animals that are at moderate to high risk of infection should be immediately removed from the general population in order to prevent continued disease spread. If resources permit, these animals should be held for a quarantine period equal to or longer than the longest probable incubation period of disease. Generally, this period must be restarted with each new case of disease that occurs in a quarantine area. Quarantine is thus a practical option primarily for conditions with a short, defined incubation period, such as canine influenza, canine parvovirus, and feline panleukopenia. Even in such cases, if serological testing is available, this may be a more cost-effective and appealing choice, as noted above. For conditions with a prolonged or variable incubation period (such as canine distemper or dermatophytosis) or for conditions for which development of clinical signs is not a highly reliable indicator of infection (such as virulent systemic feline calicivirus), quarantine alone may not be sufficient. As described above, diagnostic testing of all exposed/at-risk animals may be a preferred option, or even the only choice to rule out some infections.

If quarantine is utilized, the same precautions regarding separate housing, equipment, and caretaker clothing apply as described for isolation. In addition, vaccination, parasite control, and other preventive health measures should generally be continued for animals in quarantine as per the shelter's usual policy. In a few situations, prophylactic treatment of exposed animals is indicated (see the section on environmental decontamination regarding protection of naïve animals). As described above for isolation of ill animals, off-site, foster care, and rescue options may be considered for quarantine of exposed/at-risk animals with suitable precautions, including a written description of the possible risks and costs. Foster care and rescue groups interested in helping a shelter get through an outbreak may serve better by providing quarantine housing for exposed animals rather than attempting isolation and treatment of sick animals, since merely exposed animals generally do not require any special medical care. Off-site care is particularly desirable when a prolonged quarantine is required, as a foster home or rescue may be better able to provide an enriched environment. Off-site care will also relieve the nearly inevitable strain on a shelter that would otherwise be created because a number of kennels devoted to quarantine would thus be unavailable for incoming or adoptable animals. However, the risks of quarantine should not be understated. Off-site quarantine providers must be aware that the animal was exposed to a serious illness and could break with disease at any time. Animals

in quarantine must be kept in easily disinfected areas and should not be directly or indirectly exposed to potentially vulnerable animals.

If no safe facilities for quarantine can be identified on or off-site, an option to consider in some cases is adoption to appropriate homes *with full written and verbal disclosure of the animal's exposure history and risk.* Although not always appropriate, this may be an option for managing diseases that are usually self-limiting in individual animals but highly problematic in populations. Adoption should be limited to homes with no other potentially susceptible pets, and in the meantime, these animals must be kept separate within the shelter from new incoming animals. The risk to community animals must also be addressed. If indicated, adopters should be asked to abide by an in-home quarantine and refrain from taking the animal to areas where it might be exposed to other susceptible pets for the duration of the incubation period. If the animal is taken to a veterinary clinic during this period, the clinic staff should be advised of the animal's exposure history at the time the appointment is made. Because this voluntary quarantine cannot be strictly enforced, adoption of exposed/at-risk animals should only be considered for illnesses that pose little risk to community pets or people. Because special adoption restrictions and warnings may deter adopters, another risk of this approach is that exposed animals will linger for prolonged periods in the shelter and ultimately perpetuate the outbreak.

For these reasons, adopting out exposed/at-risk animals is not always a safe or realistic option. If resources do not permit on- or off-site quarantine, euthanizing exposed, at-risk animals may ultimately save more lives overall than allowing these animals to remain in the general population and perpetuate a serious outbreak. It is potentially devastating to euthanize healthy animals simply because they may be incubating an illness. Even in a shelter that euthanizes a high percentage of animals, it may help morale – and save lives – to be able to quarantine at least some animals, and animals still in their stray holding period must be held to allow owners a chance to reclaim them. Investment in quarantine facilities in preparation for a possible outbreak is therefore indicated for every shelter.

**Environmental decontamination**

Once diseased and at-risk animals have been identified and removed, the environment will need to be decontaminated before admission of naïve animals can safely resume. In some cases minimal cleaning with almost any disinfectant will suffice to render a contaminated environment safe again. For example, canine distemper and influenza do not persist for very long in the environment. Sanitation for these conditions is not a major challenge, and outbreaks are unlikely to be resolved through improved cleaning efforts (although of course such efforts are never contraindicated). However, several of the infectious agents associated with outbreaks in cats and dogs are extremely durable and resistant to all but a handful of disinfectants. These include the unenveloped viruses (canine parvovirus, feline panleukopenia, and calicivirus), ringworm (*Microsporum canis* et al.) and assorted protozoal and parasitic pathogens such as coccidia and whipworms. Once a clinic, home, or shelter is contaminated with one of these pathogens, careful mechanical cleaning followed by effective disinfection is imperative before naïve animals can be reintroduced.

An often overlooked source of ongoing contamination is subclinically affected or carrier animals. For example, feline respiratory infections are notorious for establishing carrier states, and this can be an issue in resolving a feline calicivirus outbreak. If an outbreak recurs following concerted efforts at decontamination, it may be necessary to revisit the exposure/risk assessment described above. Resolution of some outbreaks, such as coccidiosis, may require prophylactic or metaphylactic treatment concurrent with environmental decontamination. Animals may also physically harbor infectious organisms, even if not infected themselves. For instance, bathing to remove cysts from the hair coat was found to be an important component of resolving *Giardia* reinfection in dogs (Payne, Ridley et al. 2002).

Specific details for cleaning and decontamination are provided in other chapters. Basic steps for environmental decontamination following any outbreak include the following:

- Identify and treat or isolate carrier or subclinically affected animals.
- Mechanically clean the environment as well as possible. Steam clean carpeting, furniture, and other items that can be neither fully disinfected nor discarded. Clear all surfaces of clutter, wash with detergent and hot water, disinfect, and rinse to the extent possible. Irrigate outdoor areas such as lawns and gravel yards (in some cases, resurfacing may be required). Allow all areas to dry thoroughly between cleaning and maximize exposure to sunlight where possible. Often environments can be rendered safe through careful mechanical cleaning, even following contamination with highly durable agents such as parvovirus.

- Where possible, clean animal-use surfaces with a degreaser, followed by application of a broad-spectrum disinfectant. If contamination with a known pathogen has occurred, use a disinfectant proven effective against that or closely related pathogens by independent studies. For unenveloped viruses, this includes sodium hypochlorite (5% household bleach diluted at 1:32) and potassium peroxymonosulfate (e.g., Trifectant®). If dealing with an unknown pathogen, consider using an additional disinfectant to that normally utilized: For example, if a quaternary ammonium disinfectant is normally used, follow use of this product by disinfection with bleach, or vice versa (check to ensure compatibility, or rinse thoroughly between disinfectants). In areas where organic debris cannot be removed, choose a disinfectant with relatively good activity in the face of organic matter and leave it in contact with the surface for 24 hours.
- Review all areas for any possible fomites or surfaces that may have been bypassed in the initial decontamination process. Often a tremendous effort is expended cleaning animal areas, but key locations or items are missed. Especially important are animal transport vehicles (potentially including those belonging to rescue volunteers as well as field officers), carriers, exam surfaces, and equipment. In one shelter, an outbreak was apparently sustained for several months by a contaminated "rabies pole"; in another, contamination was detected in the siphon hose used to dispense disinfectant. It may be necessary to discard items such as scratched plastic carriers, beds, and litter pans if these cannot be successfully disinfected.
- Carefully evaluate whether closure of an area for an extended time is necessary or beneficial as part of the decontamination process. It is a common practice to empty a cage or facility for some time following a disease outbreak, but this often unnecessarily reduces shelter capacity without any real benefit. While simply holding an area empty may be helpful for relatively fragile pathogens such as canine influenza or distemper, it is not necessary if careful mechanical cleaning and disinfection has been accomplished. In some cases, it may even lead to a false sense of security: A couple of weeks are insufficient to eliminate durable agents such as parvovirus or ringworm. In these cases, the only real benefit of holding areas closed is to allow multiple cleaning cycles to take place; this process can be accelerated by cleaning and drying repeatedly at shorter intervals.
- Where possible, verify successful decontamination by environmental culture. This is possible for any organism that is readily cultured, including dermatophytes and many bacterial pathogens.

**Protection of newly admitted animals**

Protection of newly admitted animals must often take place simultaneously with the steps to identify and isolate at-risk animals outlined above. Ideally, intake will be halted until the outbreak is resolved, or at least until initial control measures have been put in place and a clean, safe area is created. To facilitate this, ideally "worst case scenario" plans should be made ahead of time: contact other shelters, rescue groups, and even veterinary clinics or kennels in the area, and determine who can help should intake need to be temporarily diverted (and offer the same, if possible, should other organizations be faced with a crisis). For municipal shelters or those with animal control contracts, check whether some categories of intake, such as owner-surrendered animals, can be temporarily restricted. Even if intake cannot be formally suspended, counsel surrendering owners and finders of stray animals about the current risks, and ask if they can keep the animals for even a few extra days while initial preventive measures are put in place. If a vaccine is available for the outbreak condition, consider vaccinating these animals prior to sending them home with the owner or finder, giving the animal an extra measure of protection should it eventually wind up in the shelter.

***Create a clean break***

Unless the entire shelter operation can be shut down for a quarantine period, it will be necessary to create a clean break between the exposed/at-risk population and newly admitted animals. This is most easily accomplished if an entire distinct building or ward can be emptied. If absolutely necessary, it may be preferable to double up compatible animals with similar exposure histories (e.g., double-up two exposed/at-risk dogs in one run, or combine multiple exposed cats in a group room) so that all at-risk animals may be combined in a single area rather than intermingling unexposed with exposed animals. If it is not possible to create an entire clean ward, some shelters have successfully managed outbreaks by creating a break of several kennels or separate cage banks between exposed and naïve animals. For canine respiratory pathogens, this break must be at least 25 feet in distance. Creating such a break requires very clear visual, and ideally physical, barriers between "clean" and "dirty" areas. This should include large, clear signs, "do not enter" tape across aisle ways, clearly marked separate equipment, and separate clothing for staff entering each area. If sufficient staff is available,

"red" and "green" teams should be designated, and each team should enter only the dirty and clean areas, respectively. Members of the public should only enter "dirty" areas when escorted by staff.

As time passes in an outbreak, if new animals continue to be admitted, and exposed/at-risk animals finish quarantine or are otherwise released, the amount of space needed for "clean" and "dirty" areas will change. If entire clean wards can be opened up for naïve animals one by one, this is ideal. If this is not possible and a break of several kennels has been used, the physical location of the break can be moved to increase the number of runs available for clean dogs. In this way, the number of runs housing clean animals is gradually increased while the number of runs housing exposed animals is gradually decreased while never permitting the two groups to intermix. Of course, runs should be thoroughly cleaned and disinfected prior to being repurposed for clean animal housing.

### *Vaccination and prophylactic treatment of new intakes*

Vaccination of all animals on intake forms the cornerstone of prevention for several diseases that otherwise might lead to serious outbreaks. Intake vaccination becomes even more critical in the face of a known outbreak. While this is particularly true for "vaccine preventable" diseases, vaccination of all animals on intake supports the overall health of the population and thus may even help reduce disease arising from pathogens not contained in the vaccine. Specific recommendations regarding vaccination timing and intervals are given elsewhere in this textbook. In general, during an outbreak vaccines for the disease in question should be started at the youngest possible age, and revaccination of kittens and puppies performed at the shortest safe interval while they remain in the shelter [every 2 weeks with parenteral feline viral rhinotracheitis, calicivirus, panleukopenia (FVRCP) and distemper, adenovirus, parainfluenza, parvovirus (DAPP), respectively]. It is ideal if vaccines can be given prior to admission, for example, by vaccinating animals and returning them to the owner or finder for a few days. If exposed animals have not been vaccinated, it is helpful to vaccinate them as well. While this will not prevent disease from a prior exposure, it will not increase the risk of illness if exposure has already occurred and will increase herd immunity as well as protect individuals should spread continue.

In general, drug treatment of all animals regardless of symptoms should be avoided due to the risk of selecting for drug-resistant pathogens. However, in the case of a few infectious conditions, prophylactic treatment may be useful for animals that must be exposed to a contaminated environment. For example, a single dip with lime sulfur upon intake may reduce risk of dermatophytosis for cats admitted to a ringworm-contaminated facility (B Griffin, Cornell University, 2008, personal communication); kittens and puppies may benefit from prophylactic treatment for coccidia when admitted to a chronically contaminated environment (Daugschies, Mundt et al. 2000); and during outbreaks of *Streptococcus canis* and *zooepidemicus*, antibiotic treatment of all exposed and newly admitted animals has apparently been successful in halting additional disease spread (Tillman and Dodson 1982).

## Documentation

It is always important to maintain complete animal and medical records as a normal course of business in a shelter, but they are especially useful during an outbreak. Keeping clear records can help establish where the outbreak originated, how it spread, when it is over, and assist future planning. Cases or possible cases, test results, time, and spatial pattern of spread should be recorded as described below. Questions to be asked in an outbreak can be categorized as "*what*," "*how many*," "*who*," "*when*," and "*where*."

### *What is causing the observed condition (confirmation of diagnosis and definition of suspect and confirmed cases)*

In a suspected outbreak of serious disease, diagnosis should be confirmed in at least several cases by the accepted gold standard. If no single reliable method of diagnosis is available, multiple criteria should be used for disease confirmation. For instance, in a case of suspected panleukopenia, diagnosis could be made by a combination of symptoms, ELISA test results, results of complete blood counts (CBCs), and in-house necropsy findings, or confirmed by immunohistopathology on necropsy samples. Once diagnosis has been confirmed, a written case definition should be established describing what constitutes a suspect or confirmed case. For instance, a suspect case may have symptoms consistent with the disease, while a confirmed case may have one or more positive test results in addition to symptoms.

### *How many animals are affected*

The number of suspect and confirmed cases should be documented, as well as the method of diagnosis for each. It is also important to document the number of animals exposed. Comparing the number affected to the number exposed can help establish cause. For example, a disease such as canine influenza – for which little to no preexisting

immunity exists in most areas – is likely to affect the majority of the exposed population. If only a small percentage of exposed animals become ill, this makes canine influenza much more likely to be ruled out.

***Who is affected***

Characteristics of affected animals, including age, breed, sex, and vaccination status can help determine which animals are at high risk and can help establish the diagnosis. For example, disease in well-vaccinated adult animals is very unlikely to be caused by parvovirus, panleukopenia, or canine distemper, diseases for which vaccine resistance is rare.

***When did disease develop (how many days since entry into facility)***

The speed of onset of disease may give a hint as to the cause. For example, canine influenza has an incubation period of just a few days, while the incubation period for canine distemper may be as long as several weeks. If signs developed in fewer days than the typical incubation period for the disease, the animal probably contracted the disease in the community and entered the facility already infected. Strict quarantine/cohort admission of incoming animals is indicated in the case of a community-wide outbreak. If signs developed after the typical incubation period, the animal almost certainly contracted the disease within the facility. Reexamination of sanitation, cleaning, and other disease control procedures is indicated in this case.

***How many days since control measures were established***

This question is asked to determine whether initial control measure have been effective. Presumably, control measures are instituted immediately upon recognition of the first case of disease (the index case). Additional cases may develop in animals exposed to the index case prior to establishment of control measures, even if those measures halted subsequent spread. If infection is due to exposure to the index case, signs would be expected to develop within the incubation period for the disease. However, if cases develop after this time has elapsed, and/or in animals that could not have been exposed directly or indirectly to the index case, control has not been effective and stricter measures are required.

***Where did affected animals come from in the community and where were cases housed in the shelter***

Plotting the location of affected animals may be helpful in tracking spread of the disease within the shelter or, if the disease is suspected to originate outside the shelter, affected areas of the community. If disease consistently originates from certain locations within the community, extra precautions should be taken when admitting and housing animals from those areas. Ideally, education, outreach, and low-cost vaccination programs would be developed to target the most common community sources of shelter disease. Preventing disease at the source may ultimately be more cost effective than responding to one outbreak of disease after another.

**Communication**

An outbreak of serious illness can be devastating for a shelter's reputation, causing ripples of damage far beyond the outbreak itself. Fortunately, much of this damage can be averted with a positive and proactive communication plan. In addition, communication can limit spread of disease into adopters' homes and other facilities, avert panic from the public, and even educate the community on how everyone can help prevent such outbreaks in the future (if only by reminding people how they can keep their pets out of the shelter by ensuring current identification). Every multianimal facility needs a planned procedure in the event of a serious outbreak to communicate with staff, clients/adopters, volunteers, board members, the media, and other stakeholders within the community (including local veterinarians). It is rarely too soon to implement a communication plan; rumors often start spreading even as the rest of the outbreak intervention is still in the planning stages. It may be helpful to designate one person to be responsible for each area of communication (e.g., volunteers, staff, adopters, media) rather than take the risk that conflicting messages will be expressed.

It is especially important to contact recent adopters, rescue organizations, transfer shelters, and veterinary clinics (e.g., that perform postadoption exams or surgery) that may have exposed or infected animals in their care. All potentially susceptible animals released from the shelter starting several days before recognition of the index case should be considered at risk. Adopters should be notified of what signs to watch for, whether there is a risk to other pets or people in the home, and what to do if the condition is suspected or diagnosed (e.g., should the animal be brought back to the shelter or taken to a local veterinarian for treatment at the shelter's or adopter's expense). Most shelter software systems make retrieval and contact of adopters fairly straightforward, but if no such system is in place, another plan should be developed to ensure that such records are readily available. E-mail

and phone lists for animal-care organizations in the area are also helpful to have on hand. These lists should include other shelters, rescue groups, veterinary clinics, grooming facilities, boarding kennels, doggy day care centers, and any other facility where the disease could spread. Rapidly releasing accurate information can forestall undue alarm and facilitate rapid recognition and control should the infection spread beyond a single facility. Open communication can also protect and even improve the shelter's reputation, and ensure that community support and trust will continue once the outbreak is resolved.

### *Asking for help*

Asking for help may be the most important aspect of communication in an outbreak, particularly when confronting an outbreak of unknown or rare infectious disease. Outside expertise can add credibility to a shelter's plan of action, and often can add resources such as lower cost diagnostic testing or environmental assessment. Input should ideally be sought from multiple authoritative sources, particularly if mortality is high; drastic measures such as depopulation are contemplated; or an emergent, vaccine-resistant, zoonotic, or foreign pathogen is suspected. Possible resources include university shelter medicine programs, regional veterinary schools or university infectious disease programs, local public health authorities, the state veterinarian and state diagnostic laboratory, the Association of Shelter Veterinarians, and national animal welfare organizations.

## SUMMARY

High-density/high-turnover populations found in shelters and boarding kennels are at risk for outbreaks caused by known and unknown pathogens. Ideally, such outbreaks will be prevented by eliminating risk factors such as overcrowding, stress, lack of vaccination, mixing of species, and overuse of antibiotics. When an outbreak occurs, however, there are still many tools available for control. Efficient diagnosis and isolation of diseased animals; identification and removal of at-risk animals; effective environmental decontamination; protection of newly admitted animals through creation of clean spaces, vaccination and prophylactic treatment; and careful documentation and communication can all greatly mitigate the damage caused by an outbreak of even the worst disease.

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# 4
# Sanitation and Disinfection

*Glenda Dvorak and Christine A. Petersen*

## INTRODUCTION

Sanitation and disinfection are an important part of any infection control plan. When plans are implemented properly, the introduction or spread of pathogenic organisms can, in most cases, be minimized or prevented. While these measures are typically performed at some level in most animal shelters, they are too often conducted using chemicals or methods that are not optimally effective. This creates a false sense of security and can lead to continued dissemination of pathogens despite efforts taken to control them. Whenever there is a disease outbreak, it is a good idea to review sanitation procedures thoroughly, including observation of the actual cleaning process by the staff.

This chapter will overview some of the basic principles behind disinfection, highlighting the importance of disinfectant selection, factors impacting a disinfectant's efficacy, proper cleaning and disinfection techniques, as well as safety concerns for personnel and animals. A discussion of sanitizing and disinfection protocols specific to animal shelters is also included.

## BASIC PRINCIPLES OF SANITATION

While the need for sanitation and disinfection protocols in animal shelters is understood, optimum performance may be limited due to challenges and demands in these settings. Infectious agents can be introduced from a number of sources, including incoming animals, transfer on inanimate objects (fomites) such as carriers, leashes, or bedding, or transfer by personnel (e.g., hands or clothing). Additionally, a high turnover rate of personnel can result in staff members that are untrained in effective sanitation and disinfection procedures.

Before any sanitation and disinfection program is developed and implemented, a basic understanding of the principles behind the methods is needed. An effective sanitation and disinfection program involves three basic principles: (1) selection of an appropriate method, (2) proper use and application, and (3) safety of the personnel and the animals exposed.

### Disinfection methods

Microorganisms vary in their ability to persist in the environment as well as in their susceptibility to disinfection. Therefore, careful selection of a disinfectant method is essential for optimum efficacy. Physical and chemical methods of disinfection may be useful for reducing or inactivating microorganisms in animal shelter settings.

#### *Physical disinfection*

Physical methods of disinfection involve the use of heat, desiccation, ultraviolet light, and radiation. Desiccation or drying can be effective for a number of pathogens; however, some pathogens (e.g., feline calicivirus) may be able to persist in the environment. The application of heat may be as dry heat (flame, baking) or moist heat (autoclave, steam); moist heat is generally more effective and requires less time to disinfect than dry heat. Many vegetative bacteria and viruses are killed by heating at temperature over 70 °C (158 °F) (Quinn and Markey 2001). Some viruses, such as canine parvovirus require higher temperatures for inactivation. Bacterial endospores are also quite thermostable, requiring the use of moist heat at 121 °C (250 °F) for at least 15 minutes for destruction (Quinn and Markey 2001). Direct sunlight or ultraviolet (UV) light can also be effective methods for inactivating a number of microorganisms, such as viruses, mycoplasma, bacteria, and fungi. The placement of UV lamps near the ceiling of shelters may help to reduce airborne infectious particles. Other forms of radiation are less frequently used.

### *Chemical disinfection*

Chemical disinfectant products are registered as "antimicrobial pesticides" and regulated by the U.S. Environmental Protection Agency in accordance with the Federal Insecticide, Fungicide and Rodenticide Act (FIFRA).

An ideal disinfectant is one that has a wide antimicrobial spectrum of action, has efficacy in the presence of organic matter and under a number of environmental conditions (e.g., temperature, pH); has compatibility with a wide range of chemicals (e.g., detergents); and has a high safety threshold, as well as being noncorrosive, nonstaining, and inexpensive. No disinfectant meets all these criteria. Therefore, selection of products must weigh these factors to choose the best disinfectant for a specific use. A complete disinfection program cannot rely on a single product for all purposes.

### Considerations for disinfectant selection

Selecting an appropriate disinfectant requires careful consideration of a number of factors such as the microorganism of concern (if known), characteristics of the disinfectant, environmental influences, the intended use and/or item disinfected, the ease of use, and any safety or hazard issues for personnel and animals. These factors can influence the effectiveness of a disinfection protocol.

Chemical disinfectants are effective for most vegetative bacteria and enveloped viruses. Nonenveloped viruses (e.g., parvoviruses and caliciviruses), fungal spores, mycobacteria, and bacterial endospores are typically more resistant.

Product concentration also influences efficacy. A disinfectant may be "-static" or "-cidal" depending on the concentration used; these are typically specified on the product label. Disinfectants that are "-static" arrest or inhibit the growth of microorganisms, whereas "-cidal" disinfectants inactivate or destroy them. Most disinfectants are more effective at higher concentrations; however, they also typically become more hazardous at increased concentration. Additionally, the use of excessive concentrations when they are not warranted (e.g., routine disinfection) can lead to wasted dollars. Overdilution of a product is equally problematic, as this may render a product ineffective against the target microorganism.

Adequate contact time is essential for all disinfectants because there is a lag period following application of a disinfectant before logarithmic reduction in numbers of viable organisms is initiated. Therefore, ensuring an appropriate contact time can influence whether a pathogen is simply inactivated, killed, or unaffected. Contact times are usually dependent on the product selected and the concentration used; between 10 and 30 minutes are common.

The stability of a product can diminish quickly after preparation or with prolonged storage. The shelf life of a product, both as stock and prepared solutions, should be listed on the label. To maximize stability and shelf life, disinfectants should be stored in a dark, cool location, preferably in stock concentrations, in light-proof containers. Containers should be labeled with the date opened and the expiration time monitored so "outdated" products are not used.

Most disinfectants are inactivated to some extent in the presence of organic material (e.g., feces, blood, secretions, excretions); this is especially true for hypochlorites. One of the most important steps in any sanitation and disinfection protocol is the removal of dirt and debris to ensure optimum efficacy of a disinfectant product. Many disinfectants have limited or no detergent activity for cleaning of the environment, and a separate product is often required for use prior to application of the disinfectant. However, the presence of other chemicals, including detergents, can reduce the efficacy of some disinfectants. Therefore, rinsing between steps is necessary to ensure optimum effectiveness unless products have been specifically tested for efficacy and safety in combination. Equally important is the type of surface being disinfected. While the ideal surface for disinfection is one that is smooth, this is often not the case. Porous, uneven, cracked, or pitted surfaces, especially wooden surfaces and earthen floors, can hide microorganisms and are difficult to disinfect. Some disinfectants (e.g., quaternary ammonium compounds) may interact with minerals (e.g., $Ca^{2+}$, $Mg^{2+}$) in the water ("hard water") or cause corrosion of metallic items. Even temperature can impact efficacy; many disinfectants are less effective at colder temperatures.

Economic considerations are always important. Disinfection is generally a cost-effective means of reducing pathogenic organisms (Dvorak, Petersen et al. 2008). The cost of disinfectant products should always be calculated and compared on a "per gallon" of use (dilution) rather than as the cost of the concentrate. For example, a disinfectant that costs $68.00 per gallon of concentrate will cost $0.27 per diluted gallon (0.5-oz concentrate per gallon of water). Considering that a gallon of diluted disinfectant covers approximately 100–150 square feet (10–15 $m^2$), the cost for disinfecting a 500-square-foot room is $1.35 (Dvorak, Petersen et al. 2008).

Because disinfectants are chemical compounds, there is always some level of risk in their use. Some cause irritations to the skin, mucous membranes, and respiratory tract.

Incorrectly diluted disinfectants, in some cases, can cause severe injury and death even if the same chemicals are very safe when used correctly. Attention to the hazards and safety measures required for use of each product is essential. Hazards may occur directly from the formulation, during dilution or application, as well as residuals in the environment. Always read the product label for the appropriate hazards and necessary precautions that should be taken to ensure the safety of personnel using the product as well as animals potentially exposed.

## DISINFECTANTS COMMONLY USED IN SHELTER SETTINGS

There are several classes of disinfectants that vary in chemical composition and potential effectiveness against microorganisms. Those primarily used in animal shelter settings include quaternary ammonium compounds, hypochlorites, peroxygen compounds, chlorhexidine, and alcohol. A summary of these products is found in Table 4.1. (Note: Specific products may vary in their formulation and efficacy. Always consult the product label for the product's spectrum of antimicrobial activity, intended use, recommended dilution, and necessary exposure times for efficacy.)

### Quaternary ammonium compounds (QACs, quats)

Quaternary ammonium compounds are cationic, surface-active agents commonly used for environmental disinfection. The molecular structure of the chemical contains hydrophobic and hydrophilic regions, which allows it to react with and lyse the cytoplasmic membrane of microorganisms (McDonnell and Russell 1999). Benzalkonium chloride is one of the most widely used members of this group. Quaternary ammonium compounds have a limited antimicrobial spectrum. They are effective against gram-positive bacteria, but have limited efficacy against gram-negative bacteria, viruses, and fungi (Engvall and Sternberg 2004). QACs are not reliably effective against parvoviruses or dermatophytes and are only partially effective against caliciviruses (Hurley 2005; Eleraky, Potgieter et al. 2002; Kennedy et al. 1995). QACs may be sporistatic, but they are not sporicidal or mycobactericidal. The survival and growth of *Pseudomonas* species in QAC solutions has been reported (Quinn and Markey 2001). QACs have the greatest efficacy at neutral or slightly alkaline pH values, but lose their activity at pH values below 3.5 (Quinn and Markey 2001). The activity of these products is greatly reduced in the presence of soaps, anionic detergents, organic matter, and hard water (Engvall and Sternberg 2004; Quinn and Markey 2001). These products are considered stable in storage, nonstaining, and are generally nontoxic and noncorrosive. High concentrations may cause metal corrosion and skin irritation. Incorrect dilution of quaternary ammonium compounds has been associated with severe oral and skin ulcerations, pneumonia, and death in some cases (Adelson

**Table 4.1.** Characteristics of commonly used disinfectants in animal shelter settings.

| | Quaternary Ammonium Compounds (QAC) | Sodium Hypochlorite | Potassium Peroxymonosulfate | Chlorhexidine | Alcohols |
|---|---|---|---|---|---|
| Bacteria | + (gram-negative)<br>± (gram-negative) | + | + | + | + |
| Mycobacteria | ± | + | + | ± | + |
| Bacterial spores | – | ± | ± | – | ± |
| Enveloped viruses | ± | + | + | ± | + |
| Nonenveloped viruses | – | + | + | ± | ± |
| Fungi | ± | + | ± | ± | + |
| Efficacy with organic material | Reduced | Rapidly Reduced | Effective | Reduced | Reduced |
| Efficacy with soap/ detergents | Reduced | Reduced | ? | Reduced | ? |

Note: Product formulations may vary. Always consult the product label for antimicrobial spectrums, application, and hazards.

Source: Greene 2006; Dvorak, Petersen et al. 2008; Quinn and Markey 2001.

+ Effective, ± Variable, – Ineffective, ? Unknown.

and Sunshine 1952; Grier 1967; Serrano 1972; Trapani, Brooks, et al. 1982).

The development of different "generations" of QACs has increased the antimicrobial spectrum, efficacy, and applicability for some products, although in some cases claims of increased efficacy for new generation compounds have not been borne out by research (Eleraky, Potgieter et al. 2002). Ethyl alcohol may potentiate the action of QACs. Some formulations may have detergent properties and may therefore be good for general cleaning purposes.

**Hypochlorites**

Hypochlorites are fast-acting, oxidizing, halogen compounds that work by denaturing proteins (McDonnell and Russell 1999). Sodium hypochlorite is the most common compound used in animal shelters; regular strength household chlorine bleach contains 5.25% sodium hypochlorite in aqueous solution, although more concentrated solutions are available commercially. Hypochlorites have a broad spectrum of activity and are effective against bacteria, fungi and most viruses at low concentrations (2 ppm to 500 ppm available chlorine) (Quinn and Markey 2001). A 1:32 bleach dilution (1562 ppm available chlorine) will inactivate nonenveloped viruses such as parvoviruses and caliciviruses (Scott 1980; Kennedy et al. 1995). Rapid sporicidal action can be obtained around 2500 ppm. Repeated application of 1:10 bleach solutions has been reported as effective against ringworm spores (Moriello, Deboer et al. 2004). These higher concentrations, while effective, can be corrosive and therefore should be used on a limited basis. Table 4.2 summarizes details regarding different bleach dilutions.

Organic material, sunlight, and some metals quickly inactivate hypochlorites, as can exposure to light. Sodium hypochlorite has no detergent properties and surfaces must therefore be precleaned with another product. Open containers of hypochlorite can lose up to 50% of their original concentration within 1 month (Quinn and Markey 2001) so it should be stored for a limited amount of time in light-proof containers. Sodium hypochlorites have optimum activity at a pH close to 5.

Sodium hypochlorite is relatively inexpensive and can be used to disinfect surfaces, equipment, buildings, and vehicles; however, it can be corrosive and damaging to fabrics. While hypochlorites are of low toxicity at effective concentrations, high concentrations are irritating to the mucous membranes, eyes and skin (Greene 2006).

**Table 4.2.** Common concentrations of sodium hypochlorite (bleach) solutions.*

| Sodium Hypochlorite % | Parts per Million (available chlorine) | Bleach to Water Ratio | Bleach Dilution | |
|---|---|---|---|---|
| 0.025% | 250 ppm | 1:200 | 1.5 Tbsp bleach to 1 gallon water | Common household use; sanitizer |
| 0.05% | 500 ppm | 1:100 | 1/4 cup bleach to 1 gallon water | Smooth precleaned surfaces, medical equipment, bedding |
| 0.1% | 1,000 ppm | 1:50 | 1/8 cup bleach to 1 gallon water | Commonly used for nonporous surfaces |
| 0.16% | 1,562.5 ppm | 1:32 | 1/2 cup bleach to 1 gallon water | Commonly used; effective against most shelter pathogens |
| 0.5% | 5,000 ppm | 1:10 | 1.5 cups (12 oz.) bleach to 1 gallon water | Used for porous surfaces such as wood or concrete; caustic; corrosive. This is a very strong solution and should be used on a limited basis. |

*Always use on cleaned surfaces.

Source: Dvorak, Petersen et al. 2008.

Hypochlorites should never be mixed with acids or ammonia because this will result in the release of toxic chlorine gas. Preparation of bleach solutions should always be performed in a well ventilated area.

### Peroxygen-based compounds

Peroxygen compounds are broad spectrum oxidizing agents that denature the proteins and lipids of microorganisms. The most commonly used product in animal shelters is potassium peroxymonosulfate (Virkon-S® or Trifectant®), a peroxygen, organic acid, and surfactant combination. This compound provides some efficacy in the presence of organic matter. Potassium peroxymonosulfate has a wide microbial spectrum of activity and is considered effective against bacteria, nonenveloped viruses (including parvoviruses), and spores (Eleraky, Potgieter et al. 2002). It is not considered to be particularly effective against dermatophytes (Moriello, Deboer et al. 2004). This product can be corrosive at high concentrations. Masks should be worn when preparing and mixing solutions from the powdered form to avoid inhalation of the product. (Disclaimer: The use of trade names does not in any way signify endorsement of a particular product.)

### Chlorhexidine

Chlorhexidine is a widely used biguanide that has applications in antimicrobial soaps, biocidal wound dressings, and surface disinfectants; however, it should not be used as a general purpose environmental disinfection agent due to a limited spectrum of antimicrobial efficacy (Hurley 2005). Chlorhexidine alters the permeability of the cytoplasmic membrane of microorganisms (McDonnell and Russell 1999). Like quaternary ammonium compounds, it is a cationic compound and therefore incompatible with anionic detergents because it forms precipitates with many anion compounds, e.g., phosphates or bicarbonate (Engvall and Sternberg 2004). Chlorhexidine is bactericidal but has variable efficacy on viruses; its activity against enveloped viruses is limited, and it has little activity against nonenveloped viruses. It is not mycobactericidal nor sporicidal and is variably fungicidal (Quinn and Markey 2001; Engvall and Sternberg 2004). The activity of chlorhexidine is optimal in the pH 5–7 range, but is greatly reduced by organic material. In general, the product causes minimal skin irritation; however, frequent use may cause allergic skin reactions (Engvall and Sternberg 2004).

### Alcohols

Alcohols are rapidly acting, broad-spectrum antimicrobial products, most frequently used in hand sanitizers. Alcohols damage microorganisms by denaturing proteins and causing membrane damage and cell lysis (McDonnell and Russell 1999). Ethyl alcohol and isopropyl alcohol are the most widely used compounds. Alcohols are effective against bacteria, including mycobacteria, and fungi; they are not sporocidal. The viricidal activity is variable (Hurley 2005; Engvall and Sternberg 2004; McDonnell and Russell 1999; Quinn and Markey 2001). The antimicrobial activity of alcohols requires the presence of water; therefore, the most effective concentration of ethyl alcohol is in the 60% to 90% range (Quinn and Markey 2001). Alcohols evaporate readily and will not penetrate dried organic matter. Repeated application may be needed; however, damage to rubber and certain plastics may occur after prolonged or repeated contact. Alcohols are inexpensive and relatively nontoxic. Caution should be used with alcohols as they are flammable; storage should be away from heat sources.

## DISINFECTANT LABELS

Regardless of the disinfectant selected, it is essential that the product label be read prior to use. This information is easily overlooked; however, it is a violation of federal law to use a product in a manner inconsistent with its labeling (EPA 2008b). Therefore, strict attention must be given to the proper use of a product with regard to its application, effectiveness, and associated hazards (human, animal, and environment) (EPA 2008c).

The label on a disinfectant identifies its uses and its efficacy against groups of microorganisms. The label claims of limited efficacy, general-purpose or broad spectrum, or hospital or medical, are primarily determined by testing the product against three microorganisms, *Staphylococcus aureus, Salmonella choleraesuis*, and *Pseudomonas aeruginosa* (EPA 1982; Dvorak, Petersen et al. 2008). Table 4.3 shows the label claim that can be used based on its efficacy against these three microorganisms.

Products may claim effectiveness against pathogenic fungi or other microorganisms if efficacy has been proven using standardized testing procedures approved by the Association of Official Analytical Chemists (AOAC) (EPA 1982). Additional information contained on product labels include chemical ingredients, effectiveness of the product under specific conditions (e.g., water hardness, presence of serum) as well as any hazards, safety precautions, and first aid guidance. The label also contains information on its suggested use and dilutions needed. Additionally, suggested application methods and contact times are listed. Figure 4.1 shows a sample product label and highlights some of the important information that is

**Table 4.3.** Testing required to establish a disinfectant label claim.

| Label Claim Listed | Testing of the Product |
|---|---|
| Limited efficacy | Germicidal activity against either gram-positive (*Staphylococcus aureus* testing) or gram-negative (*Salmonella choleraesuis* testing) bacteria |
| General-purpose or broad spectrum | Germicidal activity against both Gram-positive and gram-negative bacteria as tested against *Staphylococcus aureus* and *Salmonella choleraesuis* |
| Hospital or medical claim | Germicidal activity against *Staphylococcus aureus*, *Salmonella choleraesuis*, and *Pseudomonas aeruginosa* (nosocomial bacteria) |

Source: EPA 1982.

found and should be consulted prior to use of any product.

## PROPER USE AND APPLICATION

### Physical cleaning

The removal of grossly visible debris is essential before the application of any disinfectant because organic material can inactivate many disinfectants. Organic materials also serve to physically prevent disinfectants from reaching the microorganisms. Surfaces should be thoroughly cleaned, which may involve sweeping, brushing, and scraping.

### Sanitation/Cleaning

Sanitizing or cleaning helps to reduce the pathogen load and serves to prime the surface for disinfection application. This step alone can remove over 90% of bacteria from surfaces (Quinn and Markey 2001; Engvall and Sternberg 2004). The area or item should be soaked with hot water and detergent. While some disinfectants also have detergent activity and can be used as a sole agent on lightly soiled surfaces, others do not and must be applied to surfaces precleaned with another detergent product. Degreasers are strong detergents and may be needed to remove any oily debris that has accumulated. In larger areas, low-pressure (90–120 psi) garden hose sprayers or other built-in delivery systems may improve the application of the washing solution. Caution should be taken if high-pressure spraying is used; this method can aerosolize microorganisms and enhance spread of contaminants. When cleaning, all personnel should wear protective clothing (e.g., gloves and smocks). In situations involving a known or suspected zoonotic disease, enhanced personal protective equipment (e.g., face masks or goggles, protective gowns, shoe covers, etc.) should be used. Cleaning should proceed from the cleanest areas in a given area to the dirtiest, and from the highest level (ceiling) to the lowest (floor). Particular attention should be paid to vents, corners and floor drains. These areas can serve as reservoirs for pathogens and should be cleaned and disinfected last. All washed items should be rinsed thoroughly since many disinfectants (e.g., quaternary ammonium compounds) are inactivated by detergents, while others will be inactivated by remaining organic debris. Optimally, the washed items or areas should be dried or allowed to dry completely before disinfection application. However, this is frequently impractical in shelters and does not appear to be critical in most cases.

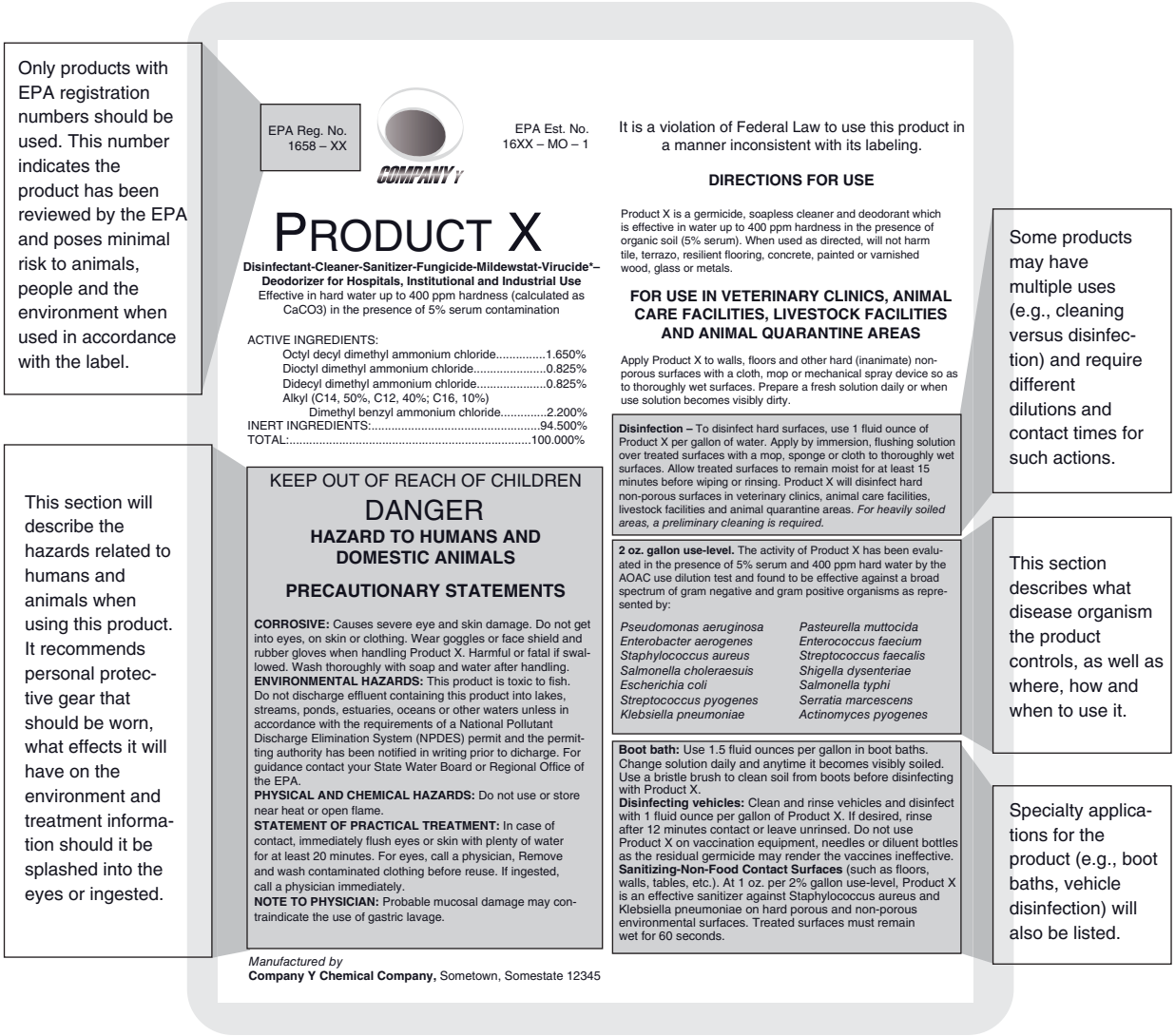
### Disinfection

As previously discussed, proper disinfectant selection is based on the microorganisms suspected, environmental factors (e.g., pH) and safety issues. Always read the entire product label and follow dilution and application instructions to ensure that the safest, most effective concentration is appropriately applied. Contact times are essential yet often overlooked; recommended contact times can be found on the product label. While time constraints in shelter settings may limit the ability to ensure an appropriate contact time, consideration of the potential consequences, particularly for a highly infectious disease, should be weighed. Even if the ideal contact time cannot be routinely achieved, additional contact time should be used following a known contamination with a serious, durable pathogen such as parvovirus; in the face of an outbreak of unknown cause; or in any area from which all organic debris can not be removed (e.g., unsealed, cracked concrete). Once the disinfection procedure is completed (i.e., contact time elapsed), disinfected areas and items should be rinsed thoroughly unless the disinfectant used is labeled otherwise (e.g., products that are left on for residual antimicrobial effect). All areas must be allowed to dry before animals are returned; they can be squeegeed or otherwise physically dried as necessary to achieve this

## DISINFECTANT PRODUCT LABEL

Understanding the information on a disinfectant product label is essential for effective disease organism removal and the safety of those handling the product. Always read the product label before use. It is a violation of federal law to use a product in a manner inconsistent with its labeling. In order to increase awareness of what a product label contains, this handout will provide you with a step-by-step guide of a disinfectant label.

Only products with EPA registration numbers should be used. This number indicates the product has been reviewed by the EPA and poses minimal risk to animals, people and the environment when used in accordance with the label.




This section will describe the hazards related to humans and animals when using this product. It recommends personal protective gear that should be worn, what effects it will have on the environment and treatment information should it be splashed into the eyes or ingested.

Some products may have multiple uses (e.g., cleaning versus disinfection) and require different dilutions and contact times for such actions.

This section describes what disease organism the product controls, as well as where, how and when to use it.

Specialty applications for the product (e.g., boot baths, vehicle disinfection) will also be listed.



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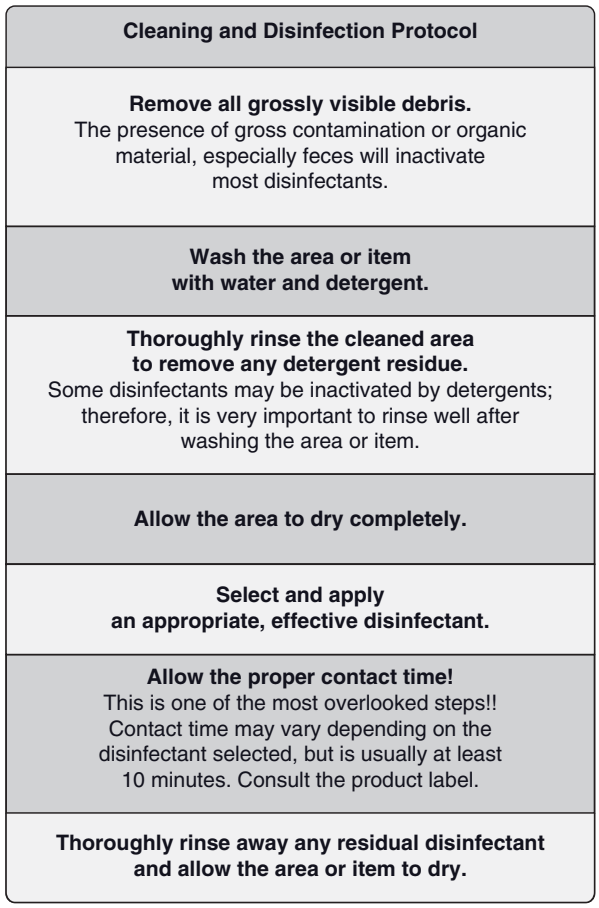
**Figure 4.1.** Sample disinfectant product label.




Used with permission from the Center for Food Security and Public Health, Iowa State University, College of Veterinary Medicine.

**Figure 4.2.** Sample cleaning and disinfection protocol for posting.

purpose. Drying is a critical final step in the disinfection process; as noted earlier, desiccation is an effective physical means of disinfection for many pathogens. Figure 4.2 outlines the necessary steps for an effective disinfection protocol.

### Evaluation

Periodic evaluation of environmental contamination of the shelter is helpful in verifying whether microorganisms are being eliminated. Environmental samples may be obtained by wiping or swabbing the surface to be tested with moistened sterile swabs, or sterile gauze wipes. Commercially available culture plates such as RODAC™ (Replicate Organism Detection and Counting) (Merck) or Petrifilm™ (3M) plates can then be inoculated and incubated for microbial assessment. Plates suitable for testing for a variety of specific bacteria, yeasts, or molds are also available. If sampling demonstrates growth of significant organisms, each step of the disinfection action plan should be evaluated. If large numbers of organisms are recovered from a supposedly sanitary surface (even if those organisms are nonpathogenic), this is an indication that insufficient disinfection has taken place. Environmental culture of this type can be a dramatic tool to demonstrate cleaning deficiencies to staff and veterinarians.

In some cases, specific culture methods are available for testing for particular organisms of concern. This is particularly valuable for control of ringworm spores, which can be difficult to inactivate through chemical disinfection alone. See Chapter 16 on dermatophytosis for more information on environmental culture specifically for this purpose.

Polymerase chain reaction (PCR) testing has been used to evaluate environmental contamination and track disease spread in the human hospital setting (Green, Wright et al. 1998; Gallimore, Taylor et al. 2005; Gallimore, Taylor et al. 2008). PCR is increasingly readily available and offers a method to detect environmental contamination with viruses that cannot be readily cultured. Quantitative reverse transcriptase-polymerase chain reaction (RT-PCR) may even indicate relative levels of contamination. The reliability of this method has not been evaluated in shelters, but it may be preferable to blindly reopening an area to immunologically naïve animals or, alternately, keeping an area closed for prolonged periods (which may result in overcrowding or strain the use of resources in other areas of the shelter). While recovery of an organism such as parvovirus on PCR testing does not necessarily mean the virus is still viable and infectious, it may indicate insufficient decontamination has been performed. Although negative results on environmental PCR do not guarantee the area has been completely decontaminated, the sensitivity of this testing method is such that risk is likely lower in an area from which the pathogen of concern could not be recovered via PCR testing. Because PCR testing is very sensitive to laboratory and handling errors, if this method is used, samples should be submitted to a reputable laboratory, and all instructions for handling followed very carefully.

Factors that can lead to failure of a disinfection program are listed in Table 4.4.

**Table 4.4.** Factors affecting/failure of disinfection program.

| |
|---|
| Improper disinfectant selection |
| Improper disinfectant concentration |
| Inadequate contact time |
| Failure or improper removal of organic material |
| Inactivation by other chemical compounds (e.g., quats and biguanides by residual soaps and detergents or synthetic material or plastics) |
| Improper application |
| Failure to allow areas to dry thoroughly after application |

## EDUCATION AND TRAINING OF PERSONNEL

The proper implementation of any disinfection program will require regular staff training. This is especially important in shelters with high personnel turnover. Training should address proper cleaning and disinfection procedures and highlight why these procedures are important. Allowing input and feedback from staff can aid in compliance and will help identify areas of concern. Disinfection policies and protocols should be provided in a written form and placed in an easily accessible location for all staff. This should include information on which disinfectants to use and for what particular purposes; how they are formulated (diluted); the proper application, including the contact time required; as well as any safety issues or hazards with a particular product. Each chemical disinfectant has a material safety data sheet (MSDS) listing its stability, hazards, personal protection needed, as well as first aid information; these materials should be included. Designation of a specific staff member for the oversight and coordination of the shelter's sanitation and disinfection policy will help with implementation and consistency. Signs placed throughout the shelter can help remind personnel of the importance of following proper disinfection procedures.

## SAFETY OF PERSONNEL AND ANIMALS

Most disinfectants have some level of hazard associated with their use. Some can cause irritation to the eyes, skin, or respiratory tract of both humans and animals. As noted previously, some can cause serious injury, illness, or death when incorrectly used. Shelter staff must be trained in the proper storage, mixing, and application of all products they use. Personal protective equipment (PPE), such as gloves, masks, and eye protection, should be worn when mixing or applying disinfectants. Spills of concentrated product should be immediately and thoroughly cleaned and rinsed.

## SHELTER-SPECIFIC CLEANING PROTOCOLS

Cleaning and disinfection serves as a major barrier against spread of infectious disease in animal shelters. The procedures are time consuming, and if done incorrectly can be ineffective in preventing disease, or even worse, enhance disease spread. Although it is not likely that any shelter will be able to maintain perfectly sanitized animal areas, it is important to strive to achieve the best cleaning and disinfection possible while limiting fomite spread of disease and stress to the animals. All of the practices suggested here will aid in these goals, but each shelter should recognize its own limitations; for instance, if there is insufficient space to keep a dedicated carrier in each cat cage, the technique should be adapted to achieve the best effect.

### Daily versus outbreak protocols

During routine shelter operation, there are particular areas that should receive the most focused cleaning and disinfection. These areas can be identified by the status of the animals that will be coming in contact with the area. Areas or surfaces that will be in contact with incoming animals require stringent cleaning between each animal, as these animals have not yet received intake exams or vaccinations. These areas would include animal transport vehicles, examination surfaces, and the clothing of intake staff. Another area that requires focused cleaning would be any animal housing area that has recently been vacated. Special care should be taken in areas that house kittens, puppies, or sick animals. High-contact surfaces should also receive special attention, including "get acquainted rooms," exercise areas, and for human health as well as reduction of fomite transmission, door knobs and telephones. Stringent daily cleaning is also required in sick animal wards, particularly for those with animals that are ill with pathogens of particular environmental concern, including parvovirus or ringworm spores.

Due to the challenges of infection control at animal shelters, outbreaks of disease do occur. During these times it is particularly important to follow exact cleaning and infection control protocols. In addition, there are some other procedures that may be implemented during these times to isolate and limit the outbreak. (See Chapter 3 on outbreaks for more information about disinfection in the face of an outbreak.) These additional procedures may include the use of shoe covers or boots dedicated to each room, which should be removed when exiting. Disposable gloves should be worn at all times and discarded after cleaning each cage. If a feline disease is suspected or confirmed, cats should not be removed for cage cleaning;

instead, in-residence or spot cleaning should be utilized as described in the cages section below. Fomite spread should be minimized by using a gloved hand to fill food bowls when necessary, and water bowls should be exchanged for a new clean full bowl, prepared in a clean area away from animal housing. The use of disposable food dishes is preferable, especially during an outbreak.

**Footbaths**

The use of footbaths in animal shelter settings may be useful in reducing pathogen loads on footwear, although their value in reducing overall disease spread is questionable. In one study performed in a veterinary teaching hospital, the number of bacteria cultured from boot surfaces was reduced by the use of potassium peroxymonosulfate footbaths, but not by footbaths containing quaternary ammonium compounds (Morley, Morris et al. 2005). However, in a follow-up study, it was found that the number of microorganisms cultured from environmental surfaces was not decreased by use of footbaths containing either type of disinfectant (Stockton, Morley et al. 2006). This suggests that footbaths may form an inadequate barrier against spread of serious disease, and their benefit under routine circumstances may not justify the time and cost associated with correct use and maintenance.

If used, footbaths must contain an effective product, be adequately maintained and correctly used. Incorrect use will be ineffective at best and may even serve to spread disease by serving as a central, wet, contaminated area in which every staff member repeatedly steps. Any gross debris should be removed from footwear prior to using the footbath. An appropriate disinfectant should be selected based on the pathogen of concern and the applicability of the product for such a situation. Disinfectants (e.g., potassium peroxymonosulfate) that have good activity in the presence of organic material should be used, especially when removal of gross debris is difficult and contamination is anticipated, (e.g., after cleaning dog runs). Disinfectant solutions should be changed frequently. In heavy traffic areas, the solution should be changed daily or as soon as gross contamination of the footbath is visible. In situations where there is limited use, a less frequent interval may be sufficient. Footbaths outside of isolation areas should be changed daily. Just as for surface disinfection, contact time is essential for footbaths; brief immersion will not be effective. Typically a 1-minute contact time up to the top of the shoe treads will be sufficient; however, consult the product label for appropriate measures.

In general if footwear precautions are considered necessary, dedicated boots or shoe covers are preferred over footbaths. Dedicated boots or shoe covers are particularly important in areas housing kittens or puppies, or in areas possibly contaminated with durable, highly contagious pathogens such as parvovirus, calicivirus, and ringworm.

**Cages**

Space is one of the most beneficial attributes to utilize when cleaning cages at an animal shelter. If double-sided runs or cages are available, animals should be moved to the other side during cleaning to prevent fomite spread of disease by the person cleaning the cages. Except in dire emergencies, the temptation to place animals on both sides of a double-sided cage should be resisted. In instances where single cages are the only option, spot or in-residence cleaning should be performed for cats. A plastic apron that can be easily cleaned and disinfected should be worn by the cleaning staff. This apron should ideally be lightly wiped with disinfectant between each cage to prevent fomite spread via clothes; if this is not possible routinely, the apron should at least be disinfected after cage cleaning of sick cats and between each area of the shelter. Alternately, a change of clothing can be utilized between areas. There should be a carrier, large paper bag, cardboard box, or other hiding area for the cat to use while the cage is being cleaned. Whenever possible, only one cat or two kittens should be housed per cage to allow in-cage cleaning. Small group housing for cats, where adequate space is available and preplacement testing is appropriately managed, can also be a viable option to allow in-residence cleaning. A few carriers should be available for litters of kittens or cats that must be removed from their cage to clean heavily soiled cages. These carriers should be dedicated to each cat or litter of kittens for their use only for the duration of their stay, and be thoroughly cleaned and disinfected prior to reuse by another animal.

**Floors**

One of the most important principles to remember when cleaning floors is not to contribute to airborne disease by creating an aerosol of either contaminant pathogens or irritating disinfectants through overly vigorous cleaning. Avoid vigorous sweeping when animals are present. Use of dust mops, electrostatic cleaners or damp mops assures that the particulate matter remains on the floor. Save high-pressure cleaning or power washing for areas and times when no animals are present. A mask should be worn during use of high-pressure cleaning to prevent inhalation of disinfectants or zoonotic pathogens by staff. Cleaning with mops and buckets is best restricted for use in areas of

the shelter where animals are not routinely housed. If a mop and bucket must be used in an animal area, double-sided buckets should be used, dedicated to one area only, and mop heads must be disinfected and replaced routinely.

### Office space, foster homes, and outdoor areas

The commonality of these three spaces is that it will be difficult to completely disinfect any of them. The best way to prevent contamination of these areas is to limit pathogen entry via quarantine, diagnostic testing, and prophylactic treatment and vaccination of all animals before they enter one of these areas. If such areas do become contaminated, vigorous, repeated physical cleaning to mechanically remove contamination may be sufficient in some cases. Particularly in areas where ultraviolet light exposure is possible (e.g., outdoor "get-acquainted" areas), restricting animal access to the area for some time may also be helpful; the amount of time will vary from a few days, for less durable pathogens such as canine influenza or feline herpesvirus, to months or longer for hardier pathogens such as unenveloped viruses. Simply holding an area closed will not work for contamination with extremely durable pathogens such as panleukopenia, parvovirus, or ringworm spores. In the unfortunate event that one of these durable pathogens does contaminate one of these hard to clean areas, any means of mechanical removal, e.g., vacuuming or removing a layer of soil in outside areas to reduce pathogen load will be beneficial. Steam cleaning may also be of value. Any contaminated toys, plastic food dishes, or cardboard crates should be discarded. As noted earlier, where possible, environmental culture to evaluate success of decontamination is helpful, and preferable to simply closing off an area for prolonged periods.

### Dishes, toys, and litter pans

These three items should be cleaned and disinfected separately in the order listed to prevent pathogen spread. Stainless steel or disposable dishes and disposable litter pans should be used if possible. A commercial dishwasher is preferable to manual cleaning to completely disinfect items due to the advantages of higher temperatures and mechanical cleaning. When cleaned by hand, items must be washed prior to disinfection, rinsed and allowed to dry thoroughly before reuse.

### Vehicles

Any vehicles used for transporting animals or contaminated equipment have the potential to also become contaminated and further spread disease. Vehicles should be cleaned and disinfected using the same disinfection steps previously described. Primary cleaning should be done first to remove as much dirt and organic debris as possible. Cages or holding areas within vehicles must be thoroughly cleaned and disinfected between each animal use, and the vehicle should be cleaned from top to bottom at least daily and promptly after animals have been transported. An appropriate disinfectant should be applied with a low-pressure sprayer, allowed the proper contact time, rinsed, and the space dried thoroughly before another animal is transported. Vehicles should be stocked with a disinfectant spray effective against parvovirus and relatively active in the face of organic matter (e.g., potassium peroxymonosulfate) for use in the field when full cleaning and disinfection cannot be performed.

### Laundry

Hot water, detergent, and a half cup of bleach per standard household washer load should be used at all times for cleaning laundry. Laundry should be completely dried either in a dryer or in direct sunlight. Washers or dryers should be not be overloaded; if they are, clumps of organic material will not have sufficient contact time with bleach, hot water, and detergent and can retain infectious agents. Overloaded dryers are much more likely to produce damp laundry that is ripe for fungal or bacterial growth. Presorting and separating clothing, especially clothing of personnel working in isolation areas, is a good idea to reduce some of the potential for further fomite transmission.

## CONCLUSION

Properly implemented sanitation and disinfection protocols can serve to minimize the risk of infectious disease introduction and spread in animal shelter settings. This involves the selection of an appropriate cleaning and disinfection product and method; implementing the appropriate steps, including use of the optimal contact time; and ensuring the health and safety of personnel and the animals residing in the shelter.

## INTERNET RESOURCES

Disinfection 101. Center for Food Security and Public Health.
http://www.cfsph.iastate.edu/BRM/resources/Disinfectants/Disinfection101Feb2005.pdf.

Cleaning and disinfecting in shelters information sheet. UC Davis Koret Shelter Medicine Program.
http://www.sheltermedicine.com/portal/is_cleaning.shtml#top3.

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# 5
# Canine and Feline Vaccinations and Immunology

*Laurie J. Larson, Sandra Newbury, and Ronald D. Schultz*

## INTRODUCTION

Vaccination is an essential component of preventative health management programs for animal shelters. Effective vaccination programs, in combination with husbandry practices that minimize stress and reduce the risk of exposure to pathogens, help individual animals stay healthy or reduce the severity of clinical disease. This chapter will cover aspects of immunity as they relate to individuals as well as populations of animals within the shelter, and will address special concerns regarding immunity of juvenile animals. Specific vaccines for dogs and cats will be discussed in the context of vaccination programs designed for the shelter environment. The use of serology for evaluation of immunity will be described. Finally, diagnostic tests that may be affected by vaccination will be covered.

## VACCINATIONS AND IMMUNITY

### Importance of immunity and vaccination

Many of the significant, potentially deadly viral diseases such as canine distemper (CDV), canine parvovirus (CPV-2), and feline panleukopenia (parvovirus) (FPV) are "vaccine preventable" if animals are effectively immunized prior to exposure (Green and Schultz 2006). Vaccination is critically important for all animals entering animal shelters. In a shelter setting where susceptibility to these diseases is common and opportunities for exposure often occur at the time of admission or very soon after, vaccines form one part of a foundation for prevention. Vaccination cannot be relied on alone to protect all animals from illness. Diseases that are not vaccine-preventable, like the canine respiratory disease complex (kennel cough) and feline respiratory disease complex (upper respiratory infection) will commonly occur and can be very severe, even when all animals are vaccinated (Schultz and Conklin 1998; Schultz 1998, 1999). Nevertheless, vaccination provides a helpful adjunct to management even for these diseases by reducing the severity and frequency of clinical signs.

### Community immunity

Currently, in the United States, where probably as many, if not more, dogs and cats are vaccinated than anywhere else in the world, the authors estimate that only 50% of all puppies receive distemper (CDV), parvovirus (CPV-2), adenovirus (CAV-2), and rabies (core) vaccines, and less than 25% of kittens receive the panleukopenia (FPV), calicivirus (FCV), herpes virus (FHV-1), and rabies (core) vaccines. Most communities need to develop programs to vaccinate a much larger percentage of both dogs and cats with core vaccines. When dogs and cats receive only one dose of the modified live virus (MLV) core vaccines after 16 weeks of age, a majority of them would be immune for life to all the core diseases except rabies. However, even with rabies, they would be much more likely to be protected for at least a few years (e.g., 3 years) than if they were never vaccinated. An increase in the percentage of vaccinated animals would have a profound effect on "herd immunity" and provide much better protection for all the animal species susceptible to these core diseases. It would also enhance public health by providing protection from rabies.

Shelter vaccination clinics are one very important way to immunize more animals in the population than are currently being vaccinated. In general, nonvaccinated animals are not veterinary clinic patients. Pet owners who are not

frequent clients at veterinary clinics are often willing to have their animals vaccinated once they understand how important and long lasting a one-time-only vaccination with the core vaccines is for protecting their dogs and cats. In many cases, participation in community vaccination clinics may even increase the human–animal bond or the perception of the animal's value to the owner, which could make it more likely the pet would receive veterinary care in the future.

### Immune status of animals entering shelters

Animals entering shelters are either (a) immunologically naïve and susceptible to infection and development of disease if exposed to pathogens; (b) already immune as a result of natural immunization (e.g., recovery from infection or disease) or previous vaccination; or (c) already infected, either showing clinical signs or possibly incubating disease and/or shedding the infectious organisms to other susceptible animals. A very large percentage of animals are immunologically naïve for the vaccine-preventable diseases upon entry into shelters. In serologic surveys of dogs entering shelters nationwide, the authors found that approximately 50% (±20%) of dogs are immunologically naïve (antibody negative) for CDV, and about 30% (±15%) of dogs are immunologically naïve for CPV-2 (Schultz, Larson, Newbury 2007). In more limited surveys of cats entering shelters, the authors found approximately 50% of cats are naïve for FPV, whereas over 75% of the cats entering shelters have antibodies to FCV and FHV-1, many as a result of natural infection and some as a result of previous vaccination (Schultz, Larson, Newbury 2007). It is clear that many of the cats developed the FCV/FHV-1 antibody as a result of natural infection because they did not have the FPV antibody. If they had been vaccinated, one would expect them to have developed antibody responses against all three viruses.

## VACCINE CHARACTERISTICS: EFFICACY, ONSET, AND DURATION OF IMMUNITY FOR MODIFIED LIVE, KILLED, AND OTHER VACCINE TYPES

### Vaccine efficacy

Vaccines can never be expected to produce more effective or longer-lasting protective immunity than that resulting from natural exposure to infection (whether or not virulent disease develops). In general, for viral diseases in which exposure and recovery from infection confer lifelong immunity, such as CDV, CPV-2, and FPV, corresponding vaccine products will have a similar effect on the immune system. For diseases that do not result in long-lived or complete immunity (e.g., *Bordetella bronchiseptica*, feline herpesvirus) or cross-protection for varying strains (e.g., feline calicivirus), the corresponding vaccines will likely confer similarly limited immunity at best (Schultz 1999).

The most effective vaccines are those used to prevent CDV, CPV-2, and the CAV-2 that prevents CAV-1 (infectious canine hepatitis) in the dog, and the FPV vaccine that prevents panleukopenia in the cat. These vaccines completely prevent infection and clinical disease when administered under optimal circumstances, e.g., before exposure and in accordance with the manufacturer's instructions.

In contrast, vaccination cannot entirely prevent feline respiratory disease complex (FRDC). This syndrome results from an interaction of environmental factors, stress, and multiple infectious agents, including some bacterial pathogens and mycoplasma that are not included in vaccines. In addition, as noted above, the natural immune response against these pathogens is limited. Finally, cats often arrive at shelters already infected with one or more pathogens associated with FRDC, including herpesvirus and calicivirus.

Similarly, vaccines designed to aid in the prevention of canine respiratory disease complex (CRDC) cannot prevent this multifactorial disease. Vaccines, together with good management practices, including attention to husbandry and the environment, should help by reducing the severity or duration of illness in some but not all animals.

### Onset to immunity for modified live versus killed vaccines

Because many animals entering shelters are susceptible to the "core" viral diseases and the risk of exposure is so high, rapid onset of immunity is essential to maintain health for each individual animal and to establish a sufficient level of immunity within the group so that outbreaks can be avoided. Parenterally administered, MLV "core" vaccines provide rapid immunity against CDV, CPV-2, and FPV with a single dose in the absence of maternally derived antibodies (MDAs). With CDV vaccines, immunity develops within hours after vaccination with MLV and recombinant viral vectored CDV vaccines (Schroeder, Bordt et al. 1967; Larson and Schultz 2006). Immunity against CPV-2 was verified in 98% to 99% of dogs without MDA that were challenged experimentally within 3 days after one dose of MLV vaccine (Schultz 2006). In another earlier study, immunity to FPV for cats was demonstrated when cats were exposed almost immediately after MLV parenteral vaccination. In this case, the exposure dose was lower because challenge was through the introduction of

cats that had just been vaccinated into a contaminated environment rather than through experimental challenge by injection. This type of exposure more likely mimics a shelter setting (Brun, Chappuis et al. 1979; Carmichael, Joubert et al. 1983).

Killed viral vaccines for CDV, CPV-2, and FPV should not generally be used in the shelter because it takes a significantly longer period of time for protective immunity to develop than it does for the MLV vaccines. Most killed vaccines, including those for canine parvovirus and feline panleukopenia, require a minimum of two doses for a protective immune response to develop. An initial dose is administered, which primes the immune system, followed in 2 to 4 weeks by the second dose, which provides immunity. In general, protection induced by the killed vaccine does not develop until at least a week or longer after the second dose is administered. In addition, with most killed vaccines, if the second dose is not given within a maximum of 6 weeks after the first dose, it is often necessary to begin the series again because the priming effect may be lost and the second dose will not immunize. All subsequent doses of killed vaccines should provide a boost to the immune response. Rabies virus vaccines, which are killed, are an exception to the requirement for two doses within a 6-week interval, and most animals are provided protection with a single injection. However, it is strongly recommended, and usually required by law, that all animals receive a second dose of rabies vaccine 1 year after the first vaccination.

### Intranasal modified live vaccines

Intranasal vaccines, frequently used as an aid in the prevention of "kennel cough" or CRDC in dogs and "upper respiratory infection" or FRDC in cats, are all modified live products that may provide local immunity in a shorter period of time than parenteral vaccines. Because they are administered at the mucosal surface, maternal antibody interference is not encountered, and these vaccines may be effective at an early age in puppies and kittens. This expectation of effectiveness at an early age from intranasal vaccination does not include immunity for panleukopenia. Parenteral vaccines for panleukopenia are recommended. (Please see specific information on vaccination to immunize against feline panleukopenia in the following sections.)

The "kennel cough" vaccines with modified live *Bordetella bronchiseptica* and canine parainfluenza (CPI), with or without canine adenovirus-2, will stimulate nonspecific immunity within hours after administration, due primarily to the adjuvant effect of *B. bronchiseptica*. Bacteria like *Bordetella* often cause a "shower of cytokines" to be released from cells in the respiratory tract. One of the cytokines released would be the type I interferons (IFN) such as alpha and beta IFN. Interferons can restrict the replication of certain viruses, providing immediate, nonspecific protection against viruses that contribute to CRDC. Specific humoral and cellular immunity in the respiratory tract will develop in 3 to 7 days to provide local immunity of the upper respiratory tract. That is why the intranasal products are recommended for protection against respiratory pathogens, especially in immunologically naïve animals. Animals that have already been naturally immunized as a result of infection with the organisms causing CRDC and FRDC, which would likely be common among adult animals entering a shelter, should develop an anamnestic (secondary) response in a short period of time after administration of an intranasal or a parenteral vaccine. That is probably why it was difficult, if not impossible, for the authors to demonstrate a difference in the protection afforded incoming shelter animals receiving either a parenteral (either whole cell killed or antigen extract) versus intranasal CRDC vaccine or MLV parenteral versus intranasal FRDC vaccines. In those studies, we were unable to show a difference in the development or severity of disease irrespective of type of vaccine used (Newbury, Page et al. 2007).

### Duration of immunity

Once immunity is established, duration of immunity is not a critical consideration for most shelters, as it far exceeds the average length of shelter stay. The canine core (CDV, CPV-2, and CAV-2) and feline core (FPV, FCV, and FHV-1) MLV vaccines provide years of protection after one or two vaccine doses in an animal over 16 weeks of age or after completing the initial kitten or puppy series at 16 weeks of age or older (Abdelmagid, Larson et al. 2004; Schultz 2006; Scott and Geisinger 1999; Mouzin, Lorenzen et al. 2004a, 2004b).

## VACCINATION PROTOCOLS FOR SHELTERS

### Core vaccines for shelter cats and dogs

There are many vaccines available for use in cats and dogs (Richards, Elston et al. 2006; Paul, Carmichael et al. 2006). However, of all the vaccines available, there are only a few that are considered important enough that they should be administered to every dog and cat as they enter the shelter environment. The vaccines that every cat or dog should receive are often referred to as the "core vaccines." Every cat entering the shelter should be vaccinated against

feline parvovirus (panleukopenia) (FPV), feline calicivirus (FCV), and feline herpesvirus type 1 (FHV-1). Every dog should be vaccinated against canine distemper (CDV), canine parvovirus type 2 (CPV-2), canine adenovirus type 2 (CAV-2), canine parainfluenza (CPI) and *Bordetella bronchiseptica*.

Often the vaccines required to prevent or reduce severity of disease caused by viruses will be found together in combination products (e.g., DHPP, DA2PP, FVRCP, which refers to D=CDV, H and A2=CAV-2, P=CPV-2, P=CPI, FVR=FHV-1, C=FCV, P=FPV). The canine *Bordetella bronchiseptica* vaccine will be found alone as a killed parenteral product or as a modified live intranasal product alone or in combination with MLV CPI with or without MLV CAV-2. Each component of the core vaccines for shelter animals is described in greater detail later in this chapter and listed in Table 5.2 at the end of the chapter.

### Addition of noncore components to core vaccines

Because of the type of immune response induced by MLV vaccines for the core viruses and the need for a rapid onset of immunity in the face of almost certain exposure, use of products that contain any other vaccine components that may cause the immune system to develop a less effective response to the core pathogens should be avoided. Although a discussion of basic immunology is beyond the scope of this chapter, there are certain cell types and components of the immune system that should be stimulated at the time of vaccination in order to provide the most rapid onset and most effective long-term immunity. Combination vaccine products used to prevent or reduce the severity of disease in shelters should contain only MLV core vaccines. Rabies vaccines are generally monovalent products and thus are not mixed with other core vaccines. "Core combination vaccines" for shelter animals should not routinely contain agents such as *Chlamydophila felis*, feline *Bordetella bronchiseptica*, *Leptospira* serovars, canine coronavirus, Lyme vaccine, etc. Short-term use of a noncore vaccine in the face of diagnostic confirmation of disease may be warranted for documented outbreaks such as feline *Bordetella* or *Chlamydophila*. When it is found beneficial or necessary to use noncore vaccines, they should be given separately (at a different time or site in the animal if possible.) Vaccines should never be combined by the end user in ways not intended by the vaccine manufacturer.

### Timing of vaccination: vaccination on entry is essential

The demonstrably high level of susceptibility in dogs and cats to viral pathogens that is likely to be present in animal shelters highlights and confirms the critical need for prompt protection provided by vaccines. Vaccination on intake for animals entering animal shelters has been recommended in the feline vaccination guidelines of the American Association of Feline Practitioners (AAFP) and the canine vaccination guidelines of the American Animal Hospital Association (AAHA) and should be considered the standard of care for shelters (Richards, Elston et al. 2006; Paul, Carmichael et al. 2006). Timing is extremely important because hours can make a difference in determining whether a vaccine will or will not provide immunity in susceptible (naïve) animals. Vaccination prior to exposure is the goal.

Vaccination of the immune animal provides no benefit, while vaccination of susceptible animals will be the most important lifesaving step that can be taken. Vaccination of the already infected animal may not help but it will not cause the disease to become worse. Since, most likely, no confirmed vaccination history is available for shelter animals, vaccination of all animals helps create a safety net to protect each individual and promotes good herd immunity (protection of the population) as well. Specific details regarding revaccination for juveniles and adults are given below and in the sections on specific core pathogens.

### Special considerations for vaccination

#### *Vaccination of puppies and kittens*

Juvenile animals (less than approximately 4 months of age) cannot be protected by vaccination as reliably as adults can. At a very early age (e.g., less than 2 to 4 weeks of age), modified live vaccines cannot be safely used due to animals' undeveloped immune systems. From 4 to approximately 16 weeks of age, maternal antibody interference may prevent effective immunization. In general, puppies and kittens in shelters should be vaccinated starting at 4 to 6 weeks of age with the core parenteral MLV vaccines, and as early as 2 weeks of age with intranasal respiratory vaccines labeled for this use. Juvenile animals should be revaccinated with core parenteral vaccines every 2 weeks while in the shelter, until at least 16 weeks of age. Additionally, juvenile animals should be protected from exposure to pathogens by physical separation throughout their shelter stay. The rationale behind these recommendations and other details regarding immunization and protection of puppies and kittens are described in greater detail in the section on juvenile animals. Specific strategies or concerns, where applicable, are described in each core vaccine section.

### *Vaccination of sick or injured animals*

Every animal over 4 to 5 weeks of age should be vaccinated prior to or upon arrival to a shelter regardless of their health status at the time of arrival. Vaccines are unlikely to cause harm, and exposure to virulent virus is likely in the shelter environment. If animals are so ill that vaccination is considered unsafe, these animals should not remain in the shelter environment.

For animals that arrive ill, it is possible, though not likely, that the animal will be unable to mount an immunizing response. It is unlikely that the vaccine will adversely affect the animal, while there is a good chance that much-needed protection will be provided. As an extra measure of safety, these animals may be revaccinated after recovery (and no less than 2 weeks after the previous vaccine).

### *Vaccination of pregnant and nursing animals*

If a pregnant animal arrives at a shelter, the risks and benefits of vaccination must be carefully weighed. Vaccine viruses may present risks to fetuses, but in most cases the risk from a virulent virus is greater as animals enter the shelter. While vaccinating the dam (if she has not been previously immunized) may present a risk to the unborn puppies or kittens, the risk to the unvaccinated dam when she enters a shelter environment, followed by almost certain exposure, could be very high. In efforts to protect the fetuses from the adverse effects of vaccination, the mother and the puppies or kittens could all be lost to disease.

Legal status may be a consideration in deciding to vaccinate a pregnant animal. The risks must be weighed against the benefits. When impounding pregnant animals as part of a legal case, every attempt should be made to obtain permission to vaccinate or to obtain vaccination records to clarify risk for the mother. Even when animals have an uncertain legal status, an argument could be made that, if shelter admission is unavoidable, vaccinating the mother with unknown vaccination history is a reasonable course of action.

Checking antibody levels in pregnant animals would be one way of evaluating risk prior to vaccination (see the serological risk assessment section in this chapter for more details). Pregnant dogs that have the antibody will not be infected with the vaccine virus; thus the embryos/fetuses will not be affected. However, in the case of a combination product, one of the antigens (e.g., CAV-2) for which titers cannot be readily evaluated may infect the embryos/fetuses and cause absorption or abortion.

Whenever a combination product is used, both the benefits and the potential risks or adverse consequences of the other vaccines in the combination, as well as the overall immediate risk from the specific virulent virus in the shelter, must always be considered. This is especially true during pregnancy. If pregnant animals are not vaccinated, every effort must be made to physically protect them from exposure by careful isolation or ideally placing them in off-site housing. Pregnant animals for whom a spay or abortion is planned should always be vaccinated immediately on intake.

Nursing animals should receive core vaccines as usual. Although this will not provide any protection to the offspring, it will not harm the offspring and will confer protection to the mother.

## VACCINE HANDLING, ADMINISTRATION, AND ADVERSE REACTIONS

### Care and handling of vaccines

Most of the core vaccines used in shelters should be MLV vaccines. The only way these vaccines can immunize is when the live vaccine virus or bacteria infect the animal; thus, MLV vaccines are referred to as infectious vaccines. In contrast, the killed (K) vaccines do not infect and are known as noninfectious vaccines. Because MLV vaccines must remain infectious, handling the vaccines to maintain their infectivity is a critical part of the vaccination program. MLV vaccines should always be stored prior to use at refrigeration temperatures (e.g., 33 °F to 35 °F or 1 °C to 3 °C). For long-term storage, they should remain lyophilized (dried cake), not reconstituted with diluents. Never freeze an MLV vaccine prior to or after it is reconstituted with the sterile diluent. Once the vaccine is reconstituted, it should only remain at refrigerator temperatures, ideally for no more than 4 days. If the ambient (room) temperatures are at 70 °F (21 °C) to above 80 °F (26 °C), the vaccines should not be used after remaining 2 to 4 hours at those temperatures. Ideally, vaccines should be reconstituted and used within the first hours; thus single-dose vials are recommended because there is a risk of contamination with bacteria that can grow at refrigerator temperatures with multidose vials. Modified live vaccines should, whenever possible, only be reconstituted with the sterile diluent supplied with the vaccine. If the diluent contains an unneeded or undesirable component (e.g., leptospira), an alternate sterile diluent (e.g., water or saline) can be substituted for the diluent supplied with the vaccine.

Killed vaccines are more stable than MLV vaccines and can be kept in the refrigerator as a liquid (almost all killed vaccines are sold as liquids, rather than lyophilized, as are MLV vaccines) for the shelf life of the product. However,

killed vaccines should also be used within 4 to 6 hours after they have been removed from the refrigerator, especially when ambient temperatures are above 80°F (26°C). One-dose vaccine vials are again more ideal because multiple dose vials can become contaminated.

Killed vaccines should never be mixed with MLV vaccines unless they are part of the commercial combination product because preservatives that are present in some killed vaccines can inactivate the MLV vaccine. The mixing of vaccines of any type in the syringe should be avoided. Neither MLV nor KV vaccines should be used beyond the expiration date of the product.

### Vaccination site guidelines for cats

If possible, AAFP site guidelines should be followed for administering vaccines to cats. These site guidelines help to track potential causes of vaccine-associated sarcomas as well as offering some better treatment options, through the possibility of tumor removal, to individual animals that may develop these invasive tumors. FVRCP should be given in the right forelimb, rabies in the right hind limb, and FeLV in the left hind limb. Injection in the scapular region is no longer recommended because the removal of an invasive tumor from this site can rarely be accomplished. If these guidelines cannot always be strictly followed, the benefit of providing a parenteral vaccination at any acceptable location subcutaneously far outweighs the risk of sarcoma development.

### Adverse reactions

All vaccines have the potential to cause adverse reactions that range from mild (e.g., stiffness, lethargy) to severe (e.g., tumors, anaphylaxis, autoimmunity, death). The MLV core vaccines recommended for shelter animals are among the least likely to cause adverse reactions, whereas the killed adjuvanted vaccines are among the most reactogenic. Furthermore, considering the significant number of animals in shelters that are susceptible to significant disease and death caused by CDV, CPV-2, and FPV, under no circumstance would the risk for an adverse vaccine reaction ever outweigh or negate the benefit of vaccination with the core vaccines. Therefore, every animal entering a shelter should be vaccinated with the core vaccines prior to or at time of entry. If an animal is thought to be so severely immunosuppressed that it should not receive a MLV vaccine, then it would be best to avoid shelter entry where it will likely be exposed to more virulent wild-type agents. If shelter entry and housing are unavoidable, then vaccination most likely carries less risk than admission with no vaccination. Although adverse reactions are rare when using only the core vaccine products, veterinarians should provide the shelter staff that will administer vaccine products with specific training and written protocols for each species and how to respond should an adverse reaction occur. Adverse reactions should be carefully documented as part of the animal's permanent medical record and adopters should be made aware that the reaction occurred.

## CORE VACCINES FOR SHELTER DOGS AND CATS

The following sections address each component of the core vaccines individually to describe the expected onset, duration, and efficacy of immunity.

### The canine shelter core vaccines

#### *Canine distemper virus vaccine*

Immunity to CDV has been demonstrated to develop almost immediately after a single vaccination with an MLV or recombinant product if not blocked by MDAs and has been shown to protect the animal from severe clinical signs of CDV, including neurologic disease and death. However, when animals are exposed to CDV within the first few days following vaccination, it is possible they may become infected, with mild or no clinical signs, and may shed virus into the environment. These milder infections may also be immunosuppressive, and the infected dogs can show clinical signs consistent with CRDC, including pneumonia. Even though significant benefit and protection from challenge has been demonstrated as early as minutes to hours postvaccination, ideally animals would be vaccinated 2 to 3 days prior to exposure in order to completely prevent infection and transmission of virus (Appel 1987, 1999; Larson and Schultz 2006).

When transmission of CDV is a significant problem in shelters already vaccinating at admission, puppies that cannot be effectively immunized on intake because of MDAs will likely develop clinical signs that progress to neurologic disease or death. Adults under these circumstances may be primarily affected with mild to severe respiratory disease, but they too can progress to severe neurologic disease. Puppies under 5 months of age must be protected from exposure throughout their stay in shelters by physical separation and careful handling, especially when outbreaks are occurring.

Immunity to CDV can persist for up to the lifetime of the dog; thus dogs need not be revaccinated more often than every 3 years after the completion of the puppy series at 16 weeks of age or older.

The canarypox vectored recombinant vaccine provides immunity that is equivalent to the modified live viral vaccines and is safer. It can be used in very young puppies as well as in ferrets, wildlife, and exotic species that are susceptible to infection with virulent CDV (e.g., foxes, wolves, coyotes, pandas, large cats, etc.) The recombinant CDV (rCDV) vaccine has an advantage in puppies with MDAs because it will immunize them up to 4 weeks earlier than the MLV CDV vaccines. The monovalent rCDV vaccine is made for ferrets and is called PureVax Ferret CDV. Very young puppies at high risk of infection with CDV can be administered the monovalent product, not a combination product, starting as early as 2 weeks of age. Only 0.3–0.5 ml of the 1 ml PureVax Ferret CDV is required, thus up to three doses per 1 ml vial can be obtained. This product should be given every 2 weeks until a combination product with rCDV and MLV CPV-2 plus other viruses (e.g., CAV-2 and CPI) can be started at 5 to 6 weeks of age.

In older dogs, the MLV and rCDV vaccines will perform similarly (Hageny, Haase et al. 2004; Reed, von Messling et al. 2003), both being highly effective when dogs are vaccinated at intake or prior to infection (Larson and Schultz 2006; Schroeder, Bordt et al. 1967). Canine distemper vaccines are among the most effective vaccines in any species. Vaccinated dogs that have developed detectable antibodies will resist reinfections and disease even when placed into a shelter with a severe CDV outbreak (Larson, Hageny et al. 2006).

### *Canine parvovirus type 2 vaccine*

In the absence of MDAs, immunity to canine parvovirus that lasts for up to the lifetime of the dog can be demonstrated 3 or more days after a single MLV vaccination (Carmichael, Joubert et al. 1983). However, if young dogs are exposed to the virus, either before or within the 3- to 5-day period just after vaccination, they are likely to become infected and develop fulminant clinical disease. Older susceptible dogs are less likely to develop severe disease when compared to dogs less than 1 year of age. Because the environmental persistence of CPV-2 makes exposure likely, it is essential to protect all dogs from fomite transmission or exposure to parvo-contaminated environments during this early period of time when immunity is developing.

All puppies under 16 weeks of age should be considered susceptible regardless of the number of vaccines received, even though it is likely some are effectively protected by vaccination or from MDAs. There is no early protection induced by the parvoviral vaccine prior to the development of immunity. Parvoviral immunity is either complete or nonexistent, unlike early partial immunity induced by CDV vaccines. Adult dogs that are immunologically naïve to CPV-2 may become infected and shed virus without showing signs of disease. The virulent virus that is shed can infect young susceptible dogs and cause severe disease and death.

As with CDV, CPV-2 vaccines provide lifelong immunity, and thus dogs need not be revaccinated more often than every 3 years after the completion of the puppy series at 16 weeks of age or older and revaccination 1 year later.

Current CPV-2 vaccines from the major manufacturers (Ft. Dodge, Intervet, Merial, Pfizer, Schering Plough) have been demonstrated by the author's laboratory to induce protective immunity for all current field types of canine parvovirus (CPV 2a, 2b, and 2c) found clinically (Larson and Schultz 2008, 1997). CPV-2c has only recently been introduced (2005–2006) to the U.S., probably from Europe, as it was detected there in 2001 (Truyen 2006; Buonavoglia, Martella et al. 2001; Martella, Cavalli et al. 2004). No vaccine-resistant variants have been found (Larson, Quesada et al. 2007).

#### *Vaccination of puppies for canine parvovirus*

Some minor but significant differences remain among the current CPV-2 vaccines with regard to their ability to immunize puppies with MDAs at or less than 16 weeks of age. Although the differences cannot be easily demonstrated, field observations by the authors, together with experimental studies, suggest that there are a few CPV-2 vaccines that may be more effective for puppies in a shelter or commercial colony where CPV-2 is causing a significant disease problem.

A CPV-2 product not made by one of the major veterinary biological manufacturers that has performed very well in high-risk kennels or colonies is Neopar. This product is made by a company in Tennessee called Neotech (information listed at the end of the chapter). This vaccine is well recognized and has been used by dog breeders for many years. In comparative studies of CPV-2 vaccines by the authors, this product continues to be among the most effective in immunizing puppies at an earlier age relative to many other vaccines (Larson and Schultz 1997.)

When a monovalent product such as Neopar is used, another vaccine must be given in addition to ensure protection for the other core diseases. When this or any other vaccination protocol is used, staff education, training, and careful attention to compliance is essential. Shelters should

consider carefully the ability of their staff to follow through on any vaccine protocol that adds complication to the basic core vaccines on intake recommendations. Special programs for puppies and kittens need not be used for adult dogs and cats.

When both CDV and CPV-2 outbreaks are concurrent, the monovalent canarypox (from Merial) and the monovalent Progard CPV-2 (from Intervet) or Neopar (from Neotech) can be given to all puppies starting at 4 weeks and repeated every 2 weeks up to at least 10 to 12 weeks of age. After that, a combination core vaccine product that contains CDV, CPV-2, CAV-2 (with or without CPI) should be given at 2-week intervals up to or beyond 16 weeks of age. This vaccination protocol will provide the earliest and best vaccine protection against CDV and CPV-2. Even with this vaccination protocol, some puppies may continue to be affected and even die from CDV and/or CPV-2 because these pathogens, especially parvovirus, are commonly present in most shelter environments.

### *Canine adenovirus type 2 vaccine*

CAV-1 virus (infectious canine hepatitis) is a core vaccine in shelter dogs. Immunity can be demonstrated as early as 7 days after vaccination when the dog is challenged with the CAV-1 virus (infectious canine hepatitis.) It probably takes a similar amount of time (i.e., 7 days) for immunity to develop and to protect the dog from respiratory disease caused by CAV-2. CAV-2 contributes to CRDC in the dog and alone can cause pneumonia (Greene and Schultz 2006). The duration of immunity (DOI) against CAV-1 is a lifetime, but the DOI for protection from CAV-2, one of the many factors that cause CRDC, is approximately 3 years (Schultz 2006). If significant CRDC is a problem in a shelter, particularly if CAV-2 is found on diagnostic samples, a combination intranasal CRDC vaccine that includes CAV-2 in addition to the core parenteral combination viral vaccine may be a helpful adjunct to control the problem.

### *Canine parainfluenza virus vaccine*

Canine parainfluenza (CPI) virus is a core vaccine in shelter dogs. The CPI vaccine should be given intranasally to provide effective immunity from this virus that contributes to CRDC. The duration of immunity is 3 years for CPI. CPI is often part of the intranasal CRDC vaccines that contain *Bordetella bronchiseptica* with or without CAV-2 (see below). The combination intranasal vaccines must be given at least annually because the duration of immunity for the *Bordetella bronchiseptica* component is 1 year or less.

### **Bordetella bronchiseptica *vaccine***

*Bordetella bronchiseptica* is considered a core vaccine for dogs entering shelters, whereas it is not a core vaccine for cats. Both intranasal and parenteral vaccines are available for the dog, while an intranasal only is available for the cat. For use in shelters, MLV intranasal vaccines are recommended that include *Bordetella bronchiseptica* alone or in combination with CPI, with or without CAV-2. All currently available intranasal products are modified live.

The feline monovalent intranasal *Bordetella bronchiseptica* vaccine should not be given to the dog, just as the canine intranasal *Bordetella* vaccine should not be given to the cat; these vaccines have only been tested for efficacy and safety in the respective species.

There is a cellular antigen extract of killed *Bordetella bronchiseptica* monovalent injectable vaccine available for the dog. This injectable canine product should not be used in the cat because it has not been tested for efficacy or safety in felines.

Caution must be taken regarding *Bordetella bronchiseptica* vaccines. Never give the parenteral product intranasally because it will not provide specific immunity to *Bordetella*. More importantly, intranasal products containing MLV *Bordetella* must not be administered parenterally because they can cause a severe local reaction or, rarely, death due to severe acute hepatic failure. If an intranasal *Bordetella* vaccine is accidentally given by injection, it should be considered a medical emergency. The injection site will often be painful and swollen due to a local inflammatory reaction. The ASPCA Poison Control Center recommends the following response: injectable gentamicin sulfate, at a standard dose of 2–4 mg/kg q 6–8 hours, should be diluted in 10–30 ml of saline (depending on the size of the dog) and injected into the affected area. An oral antibiotic, such as doxycycline, trimethoprim sulfa, or tetracycline should also be started immediately. Most animals have only injection site swelling and pain, but some animals have been reported to develop injection site abscesses or even hepatic necrosis. Animals should be closely monitored for vomiting, diarrhea, or inappetance. If liver disease develops, hospitalization and intravenous (IV) fluids along with other supportive care may be required. If liver damage does occur, liver enzyme abnormalities can continue for several months. In some instances, dogs have died.

Intranasal canine respiratory vaccines are MLV products that are administered at the mucous membrane where there will be no interference from MDAs; therefore, these vaccines can be given at an early age (i.e., 4 to 8 weeks),

with no revaccination required. Package inserts often recommend revaccination of pups 2 to 4 weeks after the initial intranasal vaccination because it may be difficult to administer the vaccine into the puppy's nose. A second dose may help to provide protection for those puppies ineffectively immunized because of vaccine delivery issues, but it is not required immunologically. Most puppies housed in shelters would likely have been naturally exposed to the pathogens the intranasal products protect against after 2 to 4 weeks, so revaccination would not be beneficial. Intranasal products can be given to adult dogs once at intake and need not be repeated.

In privately owned animals, revaccination may be necessary as often as every 9 months to a year, as immunity to the *Bordetella bronchiseptica* wanes. In a shelter setting where natural exposure to *Bordetella* is very common, it is likely that immunity will persist for at least the average or standard length of stay for most animals. Animals with minimal exposure to newly arriving dogs, such as dogs in quarantine or legal holding, may benefit from revaccination with intranasal vaccines annually or every nine months.

The killed parenteral *Bordetella bronchiseptica* product, when used, requires the administration of two doses 2 to 4 weeks apart. As with other killed products, the interval between those doses should not exceed 6 weeks (Appel and Bemis 1978).

Recently published research showed the intranasal products to be significantly more effective in reducing clinical signs than the parenteral product postchallenge in a research setting (Davis, Jayappa et al. 2007). In fact, that study showed that dogs in the group vaccinated with the injectable product developed no immunity; their response to challenge was similar to the dogs that received placebo (saline).

## The feline shelter core vaccines

### *Feline panleukopenia virus vaccine*

Similar to the canine parvovirus vaccines, the feline panleukopenia (parvovirus) vaccine provides rapid and long-lasting immunity. Protective benefits of vaccination for susceptible kittens have been demonstrated immediately after vaccination for FPV in one study (Brun, Chappuis et al. 1979). Susceptible kittens vaccinated with a parenteral MLV FPV vaccine and immediately introduced into a contaminated environment developed no clinical signs of disease, while kittens not vaccinated became severely affected. These results most likely represent delayed infection because the authors have demonstrated that kittens challenged experimentally by the intranasal/oral route must be vaccinated at least 3 days prior to challenge for protection to occur (Schultz, unpublished). These FPV results are similar to vaccination and challenge infection with the closely related CPV-2 in dogs (Schultz 2000; Larson and Schultz 1997). As is the case with canine parvovirus, kittens are at risk for FPV infection while in the shelter and should be vaccinated beginning no earlier than 4 weeks of age, then revaccinated every 2 weeks (not more often) up to 16 weeks of age. The last dose of vaccine must be given at 16 weeks of age or older. Cats vaccinated with the last dose after 16 weeks of age and revaccinated again 1 year later need not be revaccinated more often than every 3 years.

The authors do not recommend either killed or intranasally administered MLV FPV vaccines in the shelter environment as they are not as effective at immunizing the cat as are the parenteral (e.g., subcutaneous or intramuscular) MLV vaccines. Although all these vaccines have been demonstrated to eventually provide good immunity against FPV, the onset to protection when the killed vaccine is used may not be sufficiently rapid to prevent outbreaks in a shelter setting. It was found that the intranasal vaccine does not immunize as high a percentage of cats, especially those with MDAs (Schultz 2009). There may be inadequate amounts of vaccine virus reaching susceptible cells for virus replication when the vaccine is given intranasally. MLV vaccines must infect and replicate in the animal to induce immunity.

CPV-2 can cause a panleukopenialike disease in cats, but MLV parenteral FPV vaccination of cats will prevent infection with both FPV and CPV-2 (Truyen, Evermann et al. 1996; Olsen, Larson, Schultz 1998).

### *Feline calicivirus vaccines*

Immunity develops as early as 7 days after FCV vaccination, and the duration of immunity is at least 3 years, but this immunity is never complete in providing protection from infection or disease, especially in high risk situations like shelters. Immunity is always limited as there are many different strains and/or variants of calicivirus. Unlike protection from FPV, which prevents infection, FCV vaccine does not prevent infection, but it is to be hoped that it will prevent or reduce the severity of disease. Unfortunately, there are an increasing number of FCV strains against which vaccination provides limited protection (vaccine-resistant strains). The same tendency to mutate, which results in the many different clinical manifestations of FCV, also means that vaccine resistant strains are constantly emerging, and most current FCV vaccines contain strains that have not been updated in years.

Although new vaccine strategies such as polyvalent vaccines are under investigation, currently it is prudent to assume that even vaccinated cats will be susceptible to infection and potentially severe respiratory disease from some strains of calicivirus, especially in the shelter environment. Shelters must put special management procedures in place to help reduce the severity of FRDC because vaccination alone will not prevent it. In addition, owners with pet cats should take careful isolation precautions to protect them when they adopt or provide foster care for cats from shelters with signs of upper respiratory infection (URI). This is particularly true in any outbreak in which otherwise healthy, vaccinated adult cats have been affected.

Recently, a product has become available for vaccinating cats against development of a disease called virulent systemic feline calicivirus (VSFCV). This product is a killed vaccine; thus it is unlikely to provide benefit in the shelter setting because of the need for multiple doses and delayed time to onset of immunity. In addition, VSFCV is a disease that has arisen in unconnected locations due to isolated mutations of different strains of respiratory caliciviruses. In all outbreaks where VSFCV has been confirmed to date, the pathogen has been a different strain or mutation that has developed, rather than the result of spread from one geographic region to another. The VSFCV vaccine contains a single strain of VSFCV. Because of the variation among strains and the limited likelihood for cross- protection, there is no reason to believe that the single VSFCV strain contained in the vaccine would be protective for other novel mutations that may arise in shelters where cats are infected with multiple strains of FCV. In addition, the other components (FPV, FVR, and FCV) of the combination product with VSFCV vaccine are also killed vaccines. Therefore, this product would not satisfy the need for rapid onset of immunity, especially for feline panleukopenia virus. If a shelter's administrators decide to use the VSFCV vaccine in combination with FPV, they should also use an MLV FPV to prevent panleukopenia, a very important and common disease that will cause disease and mortality in a high percentage of susceptible cats. VSFCV is a disease that to date has been rarely confirmed (Camero, Cavalli et al. 2004).

### *Feline herpesvirus type 1 vaccines*

Feline viral rhinotracheitis (FVR) is another formerly common name for herpesvirus infection in cats. Immunity to FHV-1 develops as early as 7 days postvaccination, and the duration of immunity is at least 3 years. Immunity is never complete, though, as all vaccinated animals remain susceptible to infection with field virus. When this occurs, some cats may show clinical signs, and virtually all develop latent infections. This is not surprising because even following natural FHV-1 infection, previously infected cats can become reinfected when exposed to the challenge virus. Cats that have been vaccinated, however, are more likely to be protected from severe disease than unvaccinated animals (Scott and Geisinger 1999; Lappin, Sebring et al. 2006).

When cats latently infected with FHV-1 become stressed, the latent virulent virus can be reactivated and shed to naïve as well as vaccinated animals. Reactivation and shedding of FHV-1 in latently infected cats may cause recrudescence of disease in stressed animals regardless of vaccine status. Shedding of FHV-1 creates a serious risk in unvaccinated kittens and cats in the same environment.

### *Intranasal combination products for cats*

Intranasal combination vaccines are available that contain FCV and FHV-1 (with or without FPV). These products are used often in pet cats as well as in shelter cats. These vaccines have the advantage of providing local immunity in a shorter period of time than the MLV parenteral products when given to naïve cats and kittens. They also stimulate immunity at an earlier age in kittens with MDAs against FCV and FHV-1. These intranasal vaccines have no advantage with regard to FPV. As recommended in the FPV section, both young and adult cats in shelters should also receive a parenteral MLV FPV, even when the three-way intranasal product is used. Although the intranasal route of administration is theoretically optimal for FCV and FHV-1 vaccine viruses because it provides better local cellular and humoral immunity, use of the MLV FCV/FVH-1/FPV parenteral vaccine alone has been shown to be as effective as a combination of both MLV parenteral and intranasal vaccines for protection against respiratory disease in a shelter setting (Newbury, Page et al. 2007).

## Rabies virus vaccines for dogs and cats

Rabies virus vaccine is not considered a core vaccine for shelter animals. Rabies vaccination is recommended at intake for cats and dogs in long-stay facilities and for those in short-stay facilities prior to or shortly after adoption. Immunity induced by the killed, adjuvanted rabies vaccines, can develop as early as 2 to 3 weeks after vaccination. Challenge studies have shown immunity to persist for a minimum of 3 years with most vaccines and up to 4 years with one feline vaccine. Although core vaccines should not be administered at intervals of less than 2 weeks, it is

acceptable to give the rabies vaccine at the time of adoption (or availability of a veterinarian when required), even if the animal was vaccinated on entry with the core vaccines less than 2 weeks previously.

Regional regulations vary, but where permitted, vaccines should be administered by authorized staff under direct or indirect supervision of a veterinarian, per local law.

Only killed rabies vaccines are available for dogs in the United States. A combination of adjuvant and high immunogenicity of rabies glycoprotein G makes this product highly immunogenic. In addition to killed rabies vaccines for cats, a 1-year recombinant viral vectored feline rabies vaccine is available. This recombinant rabies product is not effective in dogs and should not be used in this species.

The best products to use in shelters are either a 1- or 3-year rabies vaccine. The cost is likely to be similar for either vaccine. Animals without a history of previous rabies vaccination must legally be revaccinated within 1 year in most communities regardless of whether a 1- or 3-year product was used initially. Animals must then be revaccinated once every 3 years, or as often as required by the state or municipality where the animal is living. However, if the dog or cat is not revaccinated within 1 year after the first dose of rabies vaccine, there may be increased duration of immunity if a 3-year product is used, as compared to certain 1-year products. Because increased duration of immunity would benefit the individual animal and the entire community, and many dogs are not revaccinated after they leave the shelter, the 3-year product is preferred. This vaccine strategy requires education and training for staff so they clearly communicate to adopters the legal need for revaccination in one year rather than 3 years. The 3-year product is as safe or safer than the 1-year product.

The 4-year product is acceptable for cats, as is the nonadjuvanted 1-year recombinant feline rabies vaccine. Just as in dogs, for cats, any initial vaccination, without documented vaccination history will most often require revaccination within 1 year no matter which product is used. There is a product available for cats that combines the core vaccine products with a rabies vaccine component. This product can be given as early as 8 weeks of age but should not be used at regular revaccination intervals of 2 weeks since the rabies component should not be given with that frequency.

The age at which first vaccination must be administered and required revaccination intervals are determined by local or state regulations. When a rabies product is labeled as a 1-year product, it should be readministered within 1 year regardless of state law.

Rabies vaccination documentation is also commonly subject to local legislation. In most cases, the vaccination record must contain the serial and lot numbers of rabies vaccines. Many regions require a veterinarian's signature and most require a veterinarian to be present or actually administering the vaccine.

Although local regulations and vaccine manufacturer's recommendations vary, ideally all animals should receive at least two doses of rabies vaccine, with the interval between doses being not less than 3 weeks and not more than 1 year. This is in accordance with most local ordinances that require an animal to be revaccinated either at 1 year of age or within 1 year of the initial vaccination. This protocol will allow subsequent revaccination at 3 or more years to provide excellent protection. Vaccination for any animal with no previous appropriately documented rabies vaccination history should be considered an initial vaccination. To date, there have been very few animals that were not protected and that developed rabies after they had been vaccinated twice. However, a larger number of animals that received only one dose of vaccine have contracted rabies. Also, there are a significant number of dogs that fail to develop adequate antibody titers during the 1-year period after their first vaccine and only after the second dose are antibodies detected. Antibodies are critically important to provide protection from the rabies virus.

## OPTIONAL VACCINES FOR THE CAT OR DOG IN A SHELTER

Giving vaccines in addition to the core vaccines may compromise the immune response to the core pathogens. Therefore, the justification for use of additional vaccines should be carefully considered. In long-stay shelters, the most current AAHA shelter guidelines for dogs and AAFP shelter guidelines for cats should be helpful in deciding when to use optional, noncore products. Vaccine recommendations for cats and dogs in shelter environments were first included in the 2006 edition of the *Canine and Feline Vaccination Guidelines*, and these guidelines are updated yearly or as needed.

### Feline leukemia virus (FeLV) vaccines

One optional vaccine that could be considered for use in shelters is the FeLV vaccine. This is particularly important if the kittens may remain in a group-housing shelter for a prolonged period, where the risk of FeLV exposure exists even if cats are tested on intake (because some early cases

may be missed). In such circumstances, vaccination is beneficial for kittens, but only when FeLV diagnostic testing is done. FeLV negative kittens or those born to FeLV negative queens should be vaccinated twice: once as early as 8 to 9 weeks and again 3 to 4 weeks later with a vaccine from a recognized vaccine manufacturer. FeLV revaccination must be done at an interval of 3 to 4 weeks (as specified) in order for FeLV vaccines to be effective. The age at the time of last vaccination is not a crucial consideration as for other vaccines when attempting to overcome MDAs. Instead, with the FeLV vaccine, the second dose or revaccination must occur not longer than 4 weeks following the initial vaccination. Exposure to a FeLV viremic cat before or during vaccination and up to at least 2 weeks after the second dose is likely to lead to persistent viremia, but after that time, protection should be greater than 90% effective. Revaccination at 1 year of age or 1 year after the last vaccination would be recommended if the cat remains in a high-risk environment. Revaccinations should not be given more often than every 3 years. A single dose of the FeLV vaccines provides no protection; therefore unless two doses can be given 3 to 4 weeks apart, FeLV vaccines should not be used.

### Feline immunodeficiency virus (FIV) vaccines

FIV vaccination is not recommended for shelter cats. The immune response to this vaccine is indistinguishable from the antibody response to natural infection with current diagnostic tests. (Please see the section on diagnostic testing.) This vaccine requires a minimum of three doses with an interval of 2 to 4 weeks between them. When this program is followed, cats may have up to 70% protection from some strains (clades) of FIV, but have little to no protection from other strains. Considering that most cats, including those in shelters, are at low risk of infection with FIV, the need for multiple doses, a long onset to immunity that is only partial, and interference with diagnostic testing, this vaccine is not recommended for shelter cats.

### *Bordetella bronchiseptica* and *C. felis* vaccines

*Bordetella bronchiseptica* and *C. felis* vaccines are not recommended for most shelter cats. However, these vaccines may be helpful under limited circumstances in shelters experiencing severe FRDC. Indications for use include when these pathogens have been specifically identified by laboratory testing as contributing or suspect factors in outbreaks of disease, or these vaccines can be shown to reduce the severity and/or duration of disease when vaccinated and nonvaccinated groups of cats are compared. More evidence is needed in this area before these vaccines can be generally recommended.

### Other noncore vaccines

*Giardia* and feline infectious peritonitis (FIP) vaccines are generally not recommended for any cats by the AAFP guidelines. However, as with the *Bordetella* and *C. felis* products, if a benefit can be shown using these vaccines in a particular shelter, through controlled studies, that information should be published. Until more information is available, these vaccines are not recommended.

Use of canine coronavirus, *Giardia, Porphyromonas* spp. (peridontal), and rattlesnake vaccines is not recommended for most shelter dogs. Four-way leptospira and Lyme vaccines are listed in the AAHA Guidelines as optional vaccines for pet dogs at high risk, but not generally recommended for shelter dogs.

## JUVENILE ANIMALS

### Maternal antibody interference with vaccination

Puppies and kittens in the shelter environment pose a special problem when compared with adult animals with regard to disease prevention through vaccination. This is especially true for canine distemper virus (CDV), canine parvovirus (CPV-2), and feline panleukopenia (FPV).

When juvenile animals receive colostrum through nursing in the first 3 days of life, they acquire varying levels of maternally derived antibodies (MDAs). The amount of maternal antibody received is variable and depends on many factors including litter size, frequency of early nursing, and maternal antibody titer. The antibody will have a half-life (50% of it will decay) approximately every 2 weeks (8 to 13 days).

Juvenile animals that received MDAs have a "window of vulnerability," also referred to as the "window of susceptibility," that develops with declining levels of these antibodies. A virulent virus is better able to overcome MDA protection than a vaccine virus. Levels of MDAs may fall low enough to allow infection with a virulent virus, while at the same time remaining too high to allow effective immunization from vaccination. It is this differential between the onset of susceptibility to virulent virus and the ability of vaccine virus to overcome MDAs in order to immunize that creates the window of susceptibility. The "window" is the period of time or age of the animal when the MDA in the puppies' or kittens' serum fails to provide protection from infection with the wild-type (virulent) virus, while MDAs still block active pro-

tective immunity from developing when the animal receives the vaccine.

With some of the original (pre-1997) CPV-2 vaccines, the window of susceptibility persisted as long as 12 weeks in individual animals. It was possible with some of the "old generation" CPV-2 vaccines to show that puppies born to a dam with a very high level of the CPV-2 antibody could not be actively immunized until 20 to 22 weeks of age, while the MDA only provided protection from infection against the virulent virus up to 10 to 12 weeks of age (Larson and Schultz 1997). That meant that even when the puppy vaccination was started at 4 to 6 weeks of age and continued every 2 to 3 weeks until 16 to 18 weeks of age, those puppies with very high MDAs never developed an immune response from the initial vaccination series because the last dose of vaccines had to be given at 20 to 22 weeks of age. After 1997, the less effective vaccines were either taken off the market or replaced by more effective vaccines (Larson and Schultz 1997).

With the new generation of MLV CPV-2 and FPV vaccines, the window of susceptibility for each species seldom exceeds 2 to 4 weeks. Because it is rarely known when that 2- to 4-week period will occur, this smaller window reduces infection overall but does not diminish the need to sequester juvenile animals from potential exposure to virulent virus during the entire 16-week (or, rarely, longer) period when the 2-week window may have opened. While puppies and kittens may still be affected by viral disease during their initial juvenile vaccination series, when the last dose of CPV-2 or FPV vaccine is given at 16 weeks in shelter puppies or kittens respectively, few if any will have MDAs remaining at levels that can block the development of an immune response to current parvovirus vaccines.

Although not recommended, killed vaccines (except rabies vaccines), if used, can also be blocked by MDAs. If the first dose is blocked, then the second dose will not immunize and provide protective immunity. It will only prime the immune response and a third dose would be required to immunize. In fact, if the second dose is also blocked by MDAs, then it will require a fourth dose to provide protection, as the third dose is the priming dose and the fourth is the immunizing one; thus it takes weeks or more than a month to immunize the animal. This is what the authors found with a commercial killed CPV-2 vaccine that is no longer available (Schultz and Conklin 1998). The same would likely apply to killed FPV vaccines.

### *Variation in maternal antibody levels*

As noted previously, a high percentage of animals presenting to shelters have no history of vaccination or maternal exposure to CDV, CPV, or FPV, and thus will have no maternal antibodies to transmit to their offspring. For many puppies and kittens presenting to shelters, therefore, it is likely that passive immunity for CPV, FPV, and CDV either has waned or was not present on initial presentation. In that case, the first MLV vaccine that is administered should effectively immunize them, regardless of age. A single dose of a modified live vaccine, in the absence of MDAs or when MDAs are low enough not to block vaccination, is sufficient to induce complete immunity against these three pathogens.

Even for puppies and kittens that did receive MDAs, exactly how much is received and when MDAs will fall in each individual is variable. Even within a litter of puppies or kittens, individual antibody levels (titers) can be different enough that some animals will become susceptible to infection earlier due to lower levels of MDAs than others. MDAs can prolong infection within a litter. For example, part of the litter can become infected and die while the other puppies are protected by MDAs for another 2 weeks or more because of their higher level of MDAs. These puppies may become infected later and could even die if they are not properly immunized prior to infection, as MDAs high enough to prevent illness will also have prevented earlier immunization.

Maternal antibodies will also decline at different rates against different antigens. Immune responses to different vaccines (e.g., CDV, CPV-2) in the combination product, therefore, will generally occur at different ages as the puppy or kitten will rarely have levels of antibodies to all viruses that reach low enough levels to allow immunization simultaneously. However, MDA levels to all components of the core vaccines should be at low enough levels in the great majority of juveniles by 16 weeks of age to permit effective immunization. Because it is never obvious which puppies or kittens have MDAs at levels sufficient to interfere with vaccination and which do not, the full series of juvenile vaccinations is recommended for all young animals.

### Risk of vaccine use in very young animals

While protection from CDV can be safely accomplished using a monovalent canarypox vectored recombinant vaccine to actively immunize puppies as early as 2 weeks of age, modified live canine and feline vaccines during the first 2 weeks after birth should not be administered. Prior to 2 weeks of age, the immune system is unlikely to mount an effective immunizing response to many vaccines, and the vaccine virus can cause disease and death at this early age (Schultz, Appel, Carmichael 1977).

Studies performed many years ago by author Schultz demonstrated that the modified live canine viruses can rapidly enter the brains of young (6 to 7 days old), colostrum-deprived puppies, or puppies receiving colostrum that did not have antibody to the viruses (Schultz, Appel, Carmichael 1977). Similar studies have not been performed in orphaned, colostrum-deprived kittens, but one would assume that a similar infection of the brain could occur with modified live FPV, FCV, and/or FHV-1 vaccine viruses if vaccinated at an early age (<2 weeks).

Both puppies and kittens have limited thermoregulatory control during at least the first 7 or more days of life. Thermoregulation may not be fully functional until after 2 weeks of age in some pups and kittens. Body temperatures of these neonates rarely if ever reach temperatures that are adequate for the immune system to function optimally. This leaves puppies and kittens without a well-functioning, active immune system for at least 1 week and often up to 2 weeks or more of age. Thus, MLV vaccines would not be safe to administer, and killed vaccines may not be immunogenic; therefore, neither should be given. Vaccination cannot protect against the many potential pathogens that may be covered by passively acquired MDA (Schultz, Appel, Carmichael 1977; Schultz and Conklin 1998; Schultz 1998; Green and Schultz 2006).

**Other issues with vaccinating juvenile animals**

Since the only antibody that blocks active immunity is IgG absorbed from the intestine into the puppy or kitten's blood during the first 3 days after birth, it doesn't matter how long the puppy or kitten is allowed to nurse after that age, nor will juveniles derive any protection from vaccines administered to nursing mothers (although nursing mothers should still be vaccinated for their own protection). Therefore, young animals can be readily vaccinated prior to weaning, provided they have no MDAs to block vaccination.

Vaccinating pups when MDAs are present will not increase their level of risk by causing MDAs to decline more rapidly while responding to the vaccine virus. Vaccination should not be delayed in an effort to conserve MDAs.

**Vaccine schedule for shelter puppies and kittens**

Multiple doses of core vaccines should be given every 2 weeks to kittens and puppies starting at 4 to 6 weeks of age and ending at 16 weeks to ensure that at least one dose will be given at the age when levels of MDAs in the animal no longer block the immune response to the vaccine. Vaccines are given every 2 weeks in an effort to immunize as soon as possible after interference from MDAs can be overcome. Vaccinating at 2-week intervals helps to keep the window of susceptibility as narrow as possible. Under no circumstance should the vaccines be given more often than a 2-week interval because they will not be as effective when given more often. Too-frequent vaccination also increases an animal's risk of adverse reactions, such as hypersensitivity or allergy to vaccines.

**Physical protection of juvenile animals**

Since it is not possible to know which puppies or kittens received MDAs, when the window of susceptibility will open, nor which puppies and kittens will be effectively immunized by vaccines given prior to 4 months of age, it remains crucial to put management practices in place that protect juveniles from exposure to the infectious agents, especially potentially deadly viruses such as CDV, CPV-2, and FPV. In many cases, the best way to protect puppies and kittens from disease is to move them out of the shelter to other low-risk locations such as clean, low-traffic foster homes or well-separated facilities within the shelter (including separate equipment, supplies, and protective clothing for staff and volunteers). Foster care is often preferable to isolation within the shelter to provide both protection from disease and optimal socialization for animals too young to be made available for adoption. Puppies and kittens can then be raised and vaccinated in a disease-free environment until they are ready for adoption. This minimizes the length of the in-shelter stay, thereby reducing the risk of exposure; however, since this is often not possible, puppies and kittens raised in the shelter environment should be vaccinated every 2 weeks until 16 or more weeks of age, as described above.

**Colostrum replacement for orphans**

Orphaned neonatal pups and kittens presenting to shelters may have missed the opportunity to nurse and acquire passive immunity through MDAs. While passive immunity can be problematic because it is likely to interfere with efforts to immunize through vaccination, MDAs do provide essential protection against many pathogens. Failure of passive transfer puts kittens and puppies at very high risk of acquiring a broad range of infectious diseases, especially during the first 4 weeks after birth and often minor pathogens will cause disease and death (Levy, Crawford et al. 2001).

The best form of immunity in orphaned puppies or kittens is passive immunity similar to what they would normally receive in the colostrum from their mothers

during the first few days after birth. Passive immunity is important not just for the viral diseases discussed in the core vaccines sections, but also to protect juvenile animals from bacterial infections that may lead to sepsis. It is likely that failure of the passive transfer of antibodies is responsible for much of the neonatal mortality seen in orphaned puppies and kittens. Failure occurs when the puppy or kitten either gets no or little colostrum during the first few days of life, or it is unable to absorb the colostral antibody via its intestinal tract.

The intestinal tract of the newborn kitten or puppy can actively transport the IgG antibodies from colostrum to their blood for up to 3 days after birth, but the absorption ceases after colostral feeding and adequate levels of IgG are absorbed. This is the MDA that was discussed earlier in the chapter. When kittens or puppies do not get colostrum during the first few days (e.g., pups or kittens are separated, a mother will not allow animals to suckle, or the mother has no milk or dies at parturition), "artificial colostrum" can be made and administered to correct this failure of passive antibody transfer. While fostering orphaned kittens to lactating queens or pups to lactating bitches may have benefits, queens and bitches in midlactation or even earlier do not have sufficient antibodies in their milk to correct this failure of passive transfer. Moreover, replacement colostrum must be provided within 72 hours after birth in order to be absorbed.

To provide antibodies to colostrum-deprived juveniles, serum from the mother or other adult animals can be collected, preferably from the same environment where the pups or kittens will be housed, to be used as a source of replacement antibodies. Serum should only be obtained from healthy adult animals that have been well immunized. Adult cats must be FeLV and FIV negative. A donor base of known, healthy animals, free from infectious disease, could be established, but this should be approached with clear guidelines and veterinary care and supervision. A pool of potential donors, volunteered by their owners, can be recruited from home settings and screened in advance. Providing free health screening may be an incentive for participation. Veterinary health checks should be performed at least at yearly intervals on all donor animals. After collection, allow the blood to clot, separate the serum and pool it if an insufficient quantity of serum cannot be obtained from a single donor. Serum can be frozen (at –20°C) for later use. Immune canine serum can also be purchased commercially.

For oral administration, add 1 volume of serum (e.g., 10 ml) to an equal volume (10 ml) of milk replacer (e.g., Esbilac) and feed the artificial colostrum to the kittens or puppies for the first 3 days of life. The artificial colostrum will provide some protection through passive immunity.

Significant benefits have been demonstrated by administering serum to colostrum-deprived kittens parenterally, either by intraperitoneal (IP) or, preferably, subcutaneous injection (SQ) (Levy, Crawford et al. 2001). The SQ route would be the route of choice for most shelter personnel, as IP injection is more difficult and possibly dangerous for those not familiar with the procedure. Administering antibodies by injection, when compared to oral administration, extends the length of time that passive transfer can be accomplished because the transfer is not dependent on gut absorption. In the study by Levy, Carmichael et al. (2001), the serum was administered to kittens in three doses of 5 ml each: one dose at birth, one at 12 hours, and another 24 hours later. However, subcutaneous administration of immune serum could take place at any age because, unlike oral administration, it is not dependent on gut absorption. This parenteral administration resulted in serum antibody concentrations that were equivalent to kittens that nursed continuously with the queen present. Similar procedures could be used for orphaned pups where 5 to 10 ml are given, depending on the size of the puppy, every 12 to 18 hours, with a total of three to five doses to obtain levels of antibodies that will provide temporary protection (up to 2 to 4 weeks.) Vaccination should proceed as usual when the puppy or kitten reaches the appropriate age (e.g., 4 to 6 weeks in shelter environments).

## USE OF HYPERIMMUNE SERUM FOR DISEASE PREVENTION

Hyperimmune serum has been found to effectively prevent infection in immunologically naïve dogs exposed to CDV, CPV-2, CAV-1, and canine herpesvirus (CHV-1). In naïve cats, hyperimmune serum has prevented infection with FPV. Hyperimmune serum is given prior to or at time of exposure and can be administered subcutaneously (serum) or intravenously (plasma). Use of hyperimmune serum has also been advocated for recently exposed animals prior to the development of symptoms. While this may be beneficial, use of serum obtained from vaccinated animals in the environment, rather than commercially prepared hyperimmune serum, is not known to be effective. Due to the cost of immune serum or plasma and the difficulty in obtaining it commercially, the practice of passive immunization is rarely used or recommended today (Greene and Schultz 2006). If exposure has possibly already happened, as is often the case in shelter animals, animals should be vaccinated immediately with a MLV vaccine if this has not already been done. In the case of CDV, CPV-2, and FPV,

this will provide immunity in 3 days or less. Though it will not prevent infection due to exposure prior to vaccination, it will not harm animals that have already been exposed, and may prevent illness from future exposures. Passive immunization, either in the natural form of maternal antibody in colostrum, or artificially injected or fed antibodies, is of greatest importance in the newborn puppy or kitten.

## SUMMARY OF RECOMMENDED VACCINE PROGRAMS IN SHELTERS

The best vaccines for dogs in shelters will contain a combination MLV CDV or rCDV, MLV CPV-2, and MLV CAV-2, with or without MLV CPI, given subcutaneously or intramuscularly. The preferred product for CRDC will contain MLV *B. bronchiseptica* and CPI with or without CAV-2, given intranasally.

The best vaccines for cats in shelters will contain a combination of MLV FPV, FCV, and FHV-1 that is given subcutaneously or intramuscularly. Alternatively, the intranasal MLV FCV/FHV-1 vaccine can be given along with a monovalent MLV FPV parenteral vaccine.

Vaccination with these products for all dogs and cats immediately on intake is essential. Puppies and kittens should ideally be at least 4 weeks of age. Under no circumstances should a pup or kitten receive MLV vaccines at less than 2 weeks of age. Repeat administration of parenteral products at 2-week intervals is recommended for puppies and kittens until they reach 16 weeks of age in order to narrow the time during which they are susceptible to disease as maternal antibody levels decline. The intranasal FCV/FHV-1 vaccine may be repeated at 3- to 4-week intervals in kittens.

Vaccination with a 3-year rabies product before or shortly after adoption is recommended for cats and dogs, although in most cases revaccination will be required within 1 year. (Please see the section on rabies vaccine above.)

## RISK ASSESSMENT AND EVALUATION OF SEROLOGIC IMMUNITY FOR CANINE DISTEMPER, CANINE PARVOVIRUS, AND FELINE PANLEUKOPENIA

In recent years, pet owners and veterinarians have become increasingly cautious about the possibility of "overvaccinating" pet animals. In response, measurement of antibody titer levels has gained popularity to evaluate protection against certain diseases for which antibody levels correlate well with immunity (Tizard and Ni 1998). In those pets for whom protective levels are documented, revaccination is generally considered unnecessary. Although not designed or evaluated for risk assessment of recently exposed animals, measurement of titer levels also has application in this population.

The following description of a systematic risk assessment process, based on evaluation for serologic immunity, can be used to evaluate individual animal risk after possible exposure to canine distemper, canine parvovirus, or feline panleukopenia. Because antibody levels closely correlate to protection for these three particular diseases, it can be assumed that healthy dogs and cats (no clinical signs of illness) with protective titer levels are very unlikely to become infected or ill, even if exposed. Some animals with no clinical signs and titers may actually be subclinically infected but will never develop obvious clinical disease. While these animals may shed virus, they have not posed problems clinically when using this risk evaluation system to resolve outbreaks.

While assigning risk groups never gives an absolute guarantee of whether a particular animal will become infected, defining the level of risk for individual animals and subgroups can substantially help to guide decisions. Serologic risk assessment can be used to minimize the amount of euthanasia and other drastic or costly measures taken while still effectively controlling an outbreak. Establishing risk categories for exposed animals also limits the number of animals subject to quarantine, isolation, or special rescue. Because some animals may have strong demonstrable immunity, it is possible to assign these animals to a low-risk group and direct any special precautionary measures only at higher risk animals. Attempting to conserve resources by avoiding diagnostic or titer testing may lead to even greater resource expenditures and euthanasia later. Serologic risk assessment should be used in the context of overall risk assessment and outbreak response, as described in Chapter 3.

### Options for antibody titer testing

Antibody testing may be performed by sending serum samples to a validated diagnostic laboratory or by using an in-house test kit. Diagnostic laboratories will most commonly return quantitative information, while in-house tests give only qualitative (positive or negative) results. All tests need to initially be validated by a laboratory using challenge testing so that cutoff points for risk categories can be determined through the numerical values.

There is currently one test kit available for in-house titer evaluation (TiterCheck™, from Synbiotics, San Diego, CA). These kits have been validated to challenge testing. The TiterCheck™ kit is a well-style kit designed to be used to test for CDV or CPV antibodies in canine serum.

Research by the authors suggests that the CPV test wells can be used to test for feline antibodies to FPV as well, but sensitivity and specificity may not be equivalent. The TiterCheck™ kits have been validated (for canine viruses) so that a positive result is indicative of a titer level that was protective from challenge. Other similar tests may soon be on the market.

At the time of this writing, TiterCheck™ costs approximately $11.00/animal (not including staff time) when all 14 sample wells are run simultaneously, making it a reasonable tool for outbreak response in many shelters. The test gives the most accurate information when run by technicians experienced with running similar well-type tests. In the authors' experience, the washing step is among the most critical. False positives are more likely when washing is insufficient. Even though false positives may occur, clinically, the test and associated risk category designations have been useful tools for shelters responding to outbreaks. If staff do not have sufficient training or time to carry out the test, a validated commercial laboratory is the preferred choice for serologic evaluation. In many cases, however, the lengthier turnaround time for receiving test results may make use of a commercial lab impractical, especially when dealing with an outbreak. Regardless of whether an in-house test or commercial laboratory is used, the same principles of interpretation apply.

**Initial evaluation for clinical signs**

Serology for risk assessment can only be interpreted in animals that are completely free of clinical signs of the illness in question at the time of testing. Positive titers in animals that have any signs of illness may reflect an active immune response to infection rather than a preexisting protective titer level. Results must also be interpreted with caution in animals recently recovered from illness. In these animals, positive titers may reflect an immune response to recent infection. While these animals are unlikely to develop severe disease from the condition in the future, they may still be shedding and therefore pose an infectious risk to others. This is particularly a concern for conditions with potentially prolonged postrecovery shedding, such as canine distemper.

The initial evaluation for illness is critically important. In the face of an outbreak, all dogs showing clinical signs even suggestive of distemper, such as nasal or ocular discharge, respiratory disease, anorexia, or unexplained gastrointestinal disease or, for the parvoviruses, dogs or cats with vomiting, diarrhea, lethargy, or inappetance, must be considered high risk. Evaluation must include close observation through daily monitoring sheets or direct observation of fecal quality and output, appetite, and attitude as well as other clinical signs. If clinical signs go unrecognized, when risk assessment is attempted, an infected animal may be improperly identified as having immunity.

**Interpretation of positive titer results in adult dogs and cats**

Dogs and cats with no clinical signs that test antibody positive on the TiterCheck™ kit or are above the protective cutoff for samples sent to a diagnostic laboratory can be assigned to a low-risk category. Because those animals have the antibody and no clinical signs, it is most likely that their antibody is a reflection of immunity and not infection. Dogs and cats in this low-risk category for CPV, FPV, and CDV are unlikely to become infected or develop clinical signs of disease. The long incubation period for CDV makes it somewhat more likely than for the parvoviruses that titers may rise faster than clinical signs in response to infection, making low-risk dogs (positive titers) for CDV slightly more of a risk than when categorizing low risk for CPV. However, when using this system to manage several outbreaks, this theoretically increased risk has not caused a problem clinically.

Animals categorized as low risk based on positive titers may remain in the general population and be adopted with relative safety. It is advisable to make potential adopters aware that there was an outbreak and that the animals were potentially exposed in the shelter, while explaining the testing and risk categorization that has been done. *Low risk* does not mean *no risk*; there is always some risk associated with acquiring a new pet from a multianimal background such as a shelter or pet store. This strategy has been used successfully in managing several shelter outbreaks, to the authors' knowledge.

**Interpretation of negative titer results in adult dogs and cats**

In the face of an outbreak, dogs and cats that have no clinical signs and negative test results on the TiterCheck™ kits or are below the protective cutoff for samples sent to a validated diagnostic laboratory, must be considered at high risk of becoming infected because they were likely to have been susceptible at the time of exposure. Not all titer-negative animals will become ill, particularly if they were vaccinated on intake or before. However, these animals are at relatively high risk of breaking with disease any time within the incubation period. These animals should be removed from the general shelter population immediately. Detailed information regarding management

of high-risk animals is available in the specific chapters for each disease and in Chapter 3 on outbreak management.

**Interpretation of titer results in juvenile animals**

For puppies and kittens under 5 months of age, it is impossible to differentiate actively produced antibody immunity from passive, maternally derived immunity. Titers resulting from active immunity reflect not only the presence of circulating antibodies but also suggest the presence of associated memory cells, while titers resulting from passively acquired antibodies would represent only those antibodies in circulation. Memory cells, as part of active immunity, increase immune response in the face of a challenge. Passively acquired antibody titers suggest no such reinforcements and so it is possible that a higher measurable antibody titer may be needed for protection from challenge. Also, if antibodies are passively acquired (MDAs), they are constantly on the wane so that an animal that was protected at the time of testing may lose that protection within a very short period of time.

Ideally, a higher bar for titer level would be set for juveniles to suggest low risk. As described above, TiterCheck™ in-house tests are qualitative tests designed to give only a positive or negative result based on a titer level that was shown to be protective for adult dogs with active immunity. Quantitative titer testing for puppies or kittens may be a better determinant of risk because a higher cutoff point can be used. However, puppies and kittens (less than 16 weeks of age) with positive antibody titers on the qualitative TiterCheck™ kit will most likely have high enough levels of antibodies to protect them from challenge. In most cases, it is probably safe and simplest to assign puppies and kittens with no clinical signs and a qualitatively positive result on the TiterCheck™ antibody test to the low-risk group.

It should be understood, however, that the assignment of juvenile animals to a low-risk group does not reflect the same level of certainty as for an adult because it may be based on MDA titers rather than active immunity. In addition, documented "low-risk" status may change rapidly as maternal antibodies wane. Juvenile animals with positive titers have been assigned to an indeterminate risk category in Table 5.1 below for this reason. Puppies and kittens with positive titers should be moved through the shelter system as quickly as possible.

Prolonged waiting time for results and variations between types of testing and cutoff points used by each lab often make outside laboratory testing impractical. While quantitative antibody titer levels are ideal for risk evaluation in puppies and kittens, use of the TiterCheck™ kit is still most often preferable to either waiting for lab results, blindly assigning risk categories, or treating all puppies as equally high risk after exposure.

**Table 5.1.** Risk factor determination.

| High Risk | Indeterminate Risk | Low Risk |
|---|---|---|
| No antibody on titer testing, regardless of age | Puppies and kittens < 5 months of age, with antibody present | Animals > 5 months of age, with antibody |
| Exposed, with no vaccination history | | Known vaccination at >16 weeks of age |
| Clinical signs present | No clinical signs | No clinical signs |

## VACCINE EFFECTS ON DIAGNOSTIC TESTING

**FeLV and FIV vaccine effects on testing**

FeLV and FIV alone or in combination are probably the most commonly performed diagnostic tests in shelters. These tests have both high sensitivity and specificity. FeLV tests detect viral antigen and when positive, demonstrate virus in the blood or other secretions depending on the sample tested. Vaccination with FeLV vaccines will not affect test results (Goldkamp, Levy et al. 2008; Richards 2003).

In contrast, the FIV test detects antibodies. Since antibodies are produced by vaccination, as well as from infection with virulent virus, it is not possible to differentiate vaccinated animals from infected animals with any test available at the time of this writing. An enzyme-linked immunosorbent assay (ELISA) test has been evaluated that appears to successfully distinguish vaccinated from infected cats. This ELISA is not yet commercially available, but further testing is in progress (Levy, Crawford et al. 2008).

**Effect of vaccination on testing for CPV-2 and FPV using parvovirus fecal antigen ELISA test**

A test for detection of CPV-2 antigen in feces of dogs suspected of having CPV-2 disease is very helpful in making a diagnosis. This test can also be used for cats

when testing for feline panleukopenia virus (FPV) in cats. The two viruses are antigenically similar and the antibody used to detect the CPV-2 virus will react with FPV antigens (Larson, Quesada et al. 2007).

Several recent studies from the authors' laboratory as well as by others have examined the likelihood of positive FPV and CPV-2 tests following vaccination and found true positives from vaccination to be extremely rare. There was some variation across all the commercially available tests, with the Idexx™ tests giving the fewest positive tests after vaccination.

In a study by the authors' laboratory, more than 600 recently vaccinated dogs were tested for fecal parvovirus antigen using the Idexx Snap test. None of those dogs had a positive test. The Witness™ test detected CPV-2 in less than 1% of the samples. Similar results were found with cats. Over 600 cats were tested postvaccination, with only one positive on the Idexx™ test. That cat died after vaccination with FPV, and it was believed to be a nonresponder to FPV (Larson, Quesada et al. 2007).

A similar study by others found that, as in the authors' study, of 64 vaccinated, 10-week-old specific-pathogen-free (SPF) kittens, only one kitten of the 64 total tested positive (weakly) with the Idexx Snap test postvaccination (Patterson, Reese et al. 2007). More frequent positive results were found using other test brands in this study.

This is important information for shelters because many shelters are currently following recommendations to vaccinate all animals on intake. If a positive or weak positive test in an infected animal is mistakenly identified as a false positive test because of recent vaccination, an opportunity may be missed to interrupt the cycle of transmission, and needed care and intervention may be delayed because it is believed the animal does not have virulent parvovirus. While it is known that vaccinated animals are, in fact, likely to shed vaccine virus postvaccination, the level of virus shed is below the range that would be detected as positive on most of the fecal antigen tests. Even when more sensitive methods of viral detection such as hemagglutination (HA) or viral isolation (VI) are used, only a small percentage of animals will have detectable levels of virus in their feces postvaccination. Therefore, a positive test with antigen detection tests such as hemagglutination or ELISA is strongly indicative of virulent viral infection, irrespective of recent vaccination with CPV-2 or FPV.

In contrast, if polymerase chain reaction (PCR) is used to detect CPV-2 or FPV in feces, then many fecal samples from vaccinated animals are positive due to the sensitivity of the assay. Unfortunately, there is no convenient way to determine whether the virus is vaccine or virulent virus. Therefore, negative results on the PCR test for parvovirus are meaningful, but positive results obtained from fecal samples of animals vaccinated during the previous 2 weeks may result from either vaccination or true infection.

### Canine distemper vaccine effects on testing

CDV vaccine virus may be detectable by all common methods of antigen detection including PCR, virus isolation, fluorescent antibody (FA), and immunohistochemistry (IHC) (Appel 1987.) Vaccine virus may interfere with diagnostic testing for up to 2 weeks after vaccination with a MLV vaccine because the MLV vaccine replicates in a variety of cell types and is present in leukocytes throughout the body. How long vaccine viruses may persist in various tissues is individual-animal dependent, but would not be expected to be detectable beyond 2 weeks. Interference with testing and false positives would not occur with some tests (virus isolation, FA, IHC) when the canarypox vectored rCDV product is used and is unlikely to occur with PCR testing. The rCDV vaccine does not contain infectious CDV (Noon, Rogul et al. 1980).

Vaccination could also easily interfere with paired antibody titer testing used as a diagnostic tool for CDV and/or CPV-2 infection. It would be expected that a dog's antibody titer would rise significantly in the 3-week period following vaccination with CDV or CPV-2 vaccines.

### Feline herpesvirus/feline calicivirus vaccine effects on testing

Feline herpesvirus and feline calicivirus may be shed for a 2-week period from cats that have recently been vaccinated with an MLV intranasal vaccine. The first 3 to 7 days are the most common for viral shedding postvaccination. Shedding would interfere with both viral isolation and PCR, giving positive results. Field strain viruses cannot be easily differentiated from vaccine viruses in most cases; although reverse transcriptase-polymerase chain reaction (RT-PCR) can distinguish vaccine from field strain FCV, this test is not commercially available (Lappin, Sebring et al. 2006).

### *Bordetella*/CAV-2/CPI (intranasal vaccine) effects on testing

All currently available intranasal *Bordetella* vaccines are MLV, thus they can be shed in detectable quantities, generally for not more than 2 weeks postvaccination. During this shedding period, vaccine pathogens could give false positives when testing with PCR or culture.

**Canine Lyme vaccine effects on testing**

There is a rapid test (4Dx, Idexx Laboratory) available for use in the shelter to identify dogs that are likely to be infected or that may have previously been infected with *Borrelia burgdorferi*. Positive tests for *Borrelia* are often an impediment to transfer, transport, or adoption because it can be unclear how to interpret the positive result. Many positive dogs are not in need of any treatment. Dogs that have been previously vaccinated may also be positive on the screening test; therefore, it is sometimes necessary to perform a laboratory-based quantitative test to identify the infected from the vaccinated dogs. A positive test would suggest that animal is infected and should possibly be treated with antibiotics, especially if it is showing clinical signs, such as arthritis. This test also detects the heartworm antigen and antibodies to *Ehrlichia canis* and *Anaplasma phagocytophilum*.

**Antibody testing for diagnosis of canine distemper, canine parvovirus, and feline panleukopenia**

Antibody testing for CDV, CPV, and FPV has been discussed in both the context of risk assessment and vaccination of pregnant animals. (Please also see sections on risk assessment and vaccination of pregnant animals.) In these cases, antibody titers are used as a means of assessing immunity to infection or previous vaccination history. Using antibody titers for CDV, CPV, and FPV as tools to help diagnose current infection is, in general, not recommended in shelters because, ideally, shelters will be vaccinating on intake with MLV vaccines. It would be expected after receiving an MLV vaccine that antibody titers would climb. Little differentiation could be made between vaccine response and infection when looking at paired titers over time.

## SUMMARY

Core vaccination of all dogs and cats upon entry is essential to maintaining a healthy shelter population. Along with other good management practices, a well-implemented core vaccination program should protect most animals from the most severe, life-threatening diseases found in shelters and reduce clinical signs for others. Susceptible animals respond very quickly to vaccination with core vaccines like CDV, CPV-2, and FPV; they develop immune responses that are protective within hours in some cases to just a few days in others. Vaccines are powerful tools but alone cannot be expected to resolve every disease problem in shelters. Practices must be put in place to

**Table 5.2.** Basic core vaccination recommendations for animal shelters.

| Species/Age Group | Recommended Core Vaccines | Timing for First Vaccination | Revaccination |
|---|---|---|---|
| Adult dogs | MLV DHPP/DA2PP or recombinant CDV combination core vaccine (rCDV+CPV2+ CAV-2+/– CPI) | Prior to or on intake | 2 or more weeks after initial vaccination or after adoption (1 dose is immunizing) |
| Puppies (starting at 4–6 weeks up to 16 weeks of age) | MLV parenteral recombinant viral vectored CDV DHPP/DA2PP CDV, CPV-2, CAV-2 with or without CPI | On intake or when they reach 4–6 weeks of age | Every 2 weeks until at least 16 weeks of age |
| All dogs and puppies starting as early as 4 weeks | IN CRDC vaccine, *B. bronchiseptica*, CPI with or without CAV-2 | On intake | Single dose adequate for adults and puppies |
| Adult cats | MLV parenteral FVRCP, feline panleukopenia, FHV-1, and FCV | On intake | 2 or more weeks after initial vaccination or after adoption |
| Kittens (starting at 4–6 weeks of age) | MLV parenteral FVRC, feline panleukopenia, FHV-1 and FCV | On intake or when they reach 4 weeks of age | Every 2 weeks until at least 16 weeks of age |

reduce the risk of exposure and the infectious dose of pathogens for susceptible animals. Because so many animals have not been effectively immunized prior to shelter presentation, every animal, except those that arrive with a documented history of vaccination, should be considered susceptible at admission. Juvenile animals present a special challenge for shelters and must be presumed to be susceptible until they are over the age of 16 weeks due to unknown levels of maternal antibodies that can block vaccination, but may or may not prevent disease.

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# 6
# Pharmacology

*Virginia R. Fajt*

## INTRODUCTION

One of the roles of the shelter veterinarian is to make good judgments about pharmacological approaches to infectious disease management. Simply using the therapeutic agent that is most effective may not be the best strategy for making decisions about pharmacotherapeutics in a shelter. For example, selecting the most effective drug may be too expensive for a nonprofit organization or may result in the reduction of clinical signs but no decrease in disease spread. Therefore, the shelter veterinarian must also consider economic, logistical, and philosophical constraints on drug selection and dosing. In a shelter, rather than asking the single question – is the drug effective? – the veterinarian must ask a twofold set of questions:

1. What drug or drugs are likely to be effective if used properly? Is therapeutic intervention likely to improve the clinical outcome for the animal(s)? What are the requirements for proper use?
2. What constraints might there be on using the most effective drug properly, and how can the veterinarian address them?

The first step is how to determine which drugs are the most effective to use for a particular condition. Finding the most effective drugs requires examining the evidence, which may come from the literature, drug approval data, clinical experience, and data from the shelter in question. This examination requires skills that may not be in every veterinarian's toolkit since the profession is only recently beginning to move away from expert-based decision making into evidence-based care. The skills of searching for and appraising the evidence are outlined in this section. In addition, background information is presented for the critical appraisal of the evidence, in particular for antimicrobial therapy selection, as are some examples of evaluating the evidence for other anti-infectives and ancillary therapies. Finally, there is a brief discussion of the follow-up necessary to assess the adequacy of the evidence-based care.

The second part of the twofold question about the constraints on making the best therapeutic decision must be addressed. The shelter veterinarian must examine the evidence for efficacy through various lenses. Economic factors are most obvious, such as actual drug cost, cost of labor to deliver drugs to patients, and effect of therapy on holding times for animals. Regulations regarding drug handling will always be an issue in shelter settings where a licensed veterinarian may not always be on the premises. Public health issues such as the development of antimicrobial resistance may constrain antimicrobial use. Finally, and sometimes most importantly, as shelters usually operate in the public eye in some manner, the public's perception of how animals are treated and handled must play a role in the selection of therapeutics.

## WHAT DRUG IS LIKELY TO BE EFFECTIVE, AND HOW SHOULD IT BE USED TO MAXIMIZE EFFICACY?

### Principles of evidence-based veterinary medicine

Historically, veterinarians have used expert opinion and textbook resources to guide their drug selection. The increased pace of medical research, the ease of access to research findings, and the increased legal pressure on medical professionals require a shift from the reliance on experts to using the best evidence available at the time of the decision.

Evidence-based veterinary medicine (EBVM) has been defined as "the use of current best evidence in making clinical decisions" (Cockcroft and Holmes 2003) or "the integration of best research evidence with clinical expertise and owner/manager values" (Larson and Fajt 2009). The thrust of evidence-based veterinary medicine is "confidence in the scientific methodology that has developed over the centuries to enable us to distinguish what is likely to be true from what is likely to be false" (Cockcroft and Holmes 2003).

Some argue that evidence-based veterinary medicine eschews personal experience and expert opinion. In fact, the ideal practice of evidence-based veterinary medicine uses ALL the available evidence but gives more value to certain kinds of evidence than to others. The veterinary oath that inspires veterinarians also obligates them to provide treatments for which there is good evidence of efficacy. The issue, of course, is what is good evidence?

Table 6.1 provides the classical hierarchy described in the human evidence-based medicine literature, as relates to therapy, from best to worst.

Evidence higher on the list is stronger because of reduction of bias, stronger evidence for causation, and so on. This hierarchy is a good starting point for making decisions about the quality of evidence available, but the ultimate decision must be made by practitioners with the patients in front of them.

So how does one practice evidence-based veterinary medicine? How does one incorporate the principles into every day practice? The basic steps are described below. More information may also be found at the Center for Evidence-Based Medicine Web site (www.cebm.net), and at the Web site of the newly chartered Evidence-Based Veterinary Medical Association (www.ebvma.org), as well as in various publications (Cockcroft and Holmes 2003; Kochevar and Fajt 2006).

There are four basic steps: (1) ask a clinical question related to the question of what drug is effective; (2) search for evidence to answer the question; (3) appraise the evidence for validity and applicability; and (4) apply the information to the patient(s).

1. Ask a focused clinical question.

   The focused clinical question is the beginning of the process, and the steps that follow hinge on creating good clinical questions. A reasonable clinical question allows the practitioner to focus the search for evidence on sources that will provide the best evidence. The focused clinical question also prevents the search for evidence from deteriorating into a "just in case" search and resulting in wasted time and effort. Particularly, the busy shelter veterinarian would want to create focused clinical questions to make the most efficient use of time and resources.

   There are four main elements of a good focused clinical question: patient, intervention, comparison, and outcome (PICO) (Cockcroft and Holmes 2003). Creating a clinical question that includes all of these elements will provide the practitioner with the best chance of finding relevant evidence.

**Table 6.1.** Hierarchy of levels of evidence for therapeutic interventions.

| Level | Type of Information | Notes |
|---|---|---|
| 1a | Systematic reviews of randomized control trials | |
| 1b | Individual randomized control trials | |
| 1c | All or none | Met when all patients died before the treatment became available, but some now survive on it; or when some patients died before the treatment became available, but none now die on it. |
| 2a | Systematic reviews of cohort studies | |
| 2b | Individual cohort studies | |
| 3a | Systematic reviews of case-control studies | |
| 3b | Individual case-control studies | |
| 4 | Case series | |
| 5 | Expert opinion without explicit critical appraisal, or based on physiology, bench research, or "first principles" | |

Source: Adapted with permission from the Center for Evidence-Based Medicine (www.cebm.net).

*Patient*: What patient or patient group is of concern? Is it animals of a particular breed or age? What is the primary problem to be dealt with? To what population does the animal (or animals) belong?

*Intervention*: As this discussion refers to therapy, the main interventions of interest are in therapeutics. What drug or drug combination should be used?

*Comparison*: What would happen if the intervention was not performed? In many cases, the comparison may be between a new drug and nothing. In other cases, the comparison may be between a standard protocol and something new. Either way, defining exactly what the comparison is will be useful when searching for evidence.

*Outcome*: What is the intended or desired outcome of therapy? Is it a complete cure of the disease being treated? Is it reduced costs of treatment? Perhaps the interest is in decreasing animal days in isolation. Whatever the desired outcome, putting it in the clinical question will permit a targeted search for the best evidence to solve the current problem.

Some examples of focused clinical questions related to practice of shelter medicine might include: In cats undergoing spay or neuter procedures, are multiple doses of oral meloxicam safe? Does treatment with an antimicrobial shorten the course of upper respiratory infections in cats in shelters? Which antimicrobial is most likely to be effective and at what dose? Is compounded itraconazole safe and effective in the treatment of dermatophytosis in multiple cats to eliminate the potential for spread to new animals?

2. Find the best evidence to answer the clinical question.

The next step in the practice of evidence-based veterinary medicine is to locate the best evidence to answer the clinical question. The burgeoning of electronically available resources has greatly enhanced our ability to search for evidence. It is becoming easier for practitioners even in the far reaches of the world to access electronic databases and full-text research articles. Many veterinary libraries will grant access to electronic resources to practitioners for minimal cost. Free online access to Medline is available through PubMed at http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=PubMed.

Systematic reviews are prominent in the human medical literature and are just beginning to appear in the veterinary literature. Systematic reviews differ from standard review articles in that the protocol for searching is identified as are the methods of inclusion and exclusion of articles. In the systematic review, the quality of the evidence is generally categorized explicitly, and the final recommendations are generally well defined.

Also prominent in the human medical literature are databases of critically appraised topics (CATs). These are short summaries of the evidence for a particular clinical question. These are starting to be incorporated into veterinary medical education (Hardin and Robertson 2006). An excellent project for a specialty association such as the shelter medicine group would be the development of CATs for access by members.

Other sources of evidence include Centre for Agricultural Bioscience (CAB) abstracts (available through many libraries), the Consultant Diagnostic Support System offered by Cornell University, the Veterinary Information Network (www.vin.org), the International Veterinary Information Service (www.ivis.org), as well as abstracts from continuing education meetings.

Note that evidence from nonshelter settings may not be applicable nor require critical evaluation for their applicability, which is the next step to be discussed. For example, a food additive might be useful in a clinical trial, but problems with feed intake in a stressed animal in a shelter might render this treatment ineffective. Similarly, treatment of a single animal with a communicable disease becomes problematic when a contaminated environment is the source of the infection.

The use of clinical experience for evidence can be very useful, particularly in the area of shelter medicine where there are few published studies using shelter populations and shelter conditions. However, clinical experience should be gained from the use of appropriate record keeping and not from the assuredly unscientific method of personnel's memory of cases and outcomes. Record keeping to evaluate treatment outcomes is common practice in food animal industries. By tracking treatment used against outcome, retrospective analyses can be done to determine the success of those treatments. If a recovery rate of 80% was expected, but with the new treatment, only 50% of the animals appeared to recover, an examination should be undertaken to determine if it was the drug itself or if there was some other reason for the reduced treatment success (timing of therapy, concurrent disease, stress levels, etc.). An educational model of a treatment tracking program is available by searching the Web site at www.sheltermedicine.com. This program can be used to perform simple treatment trials to compare

drugs, if treatments are assigned randomly and if case definitions are consistent across patients.

The key to using any of these resources is to critically appraise the evidence for its strength and lack of bias, which is the next step in the process. In general, any appraisal should answer the overall questions: is the evidence valid, is it important, and is it applicable to your patient(s)?

3. Critically appraise the evidence.
   The next step in practicing evidence-based veterinary medicine is to critically appraise the evidence uncovered in step 2. Worksheets have been created to assist in this process (see www.cebm.net/worksheet_therapy.asp), and the process begins with answering the questions in Table 6.2.

   This step combines an appraisal of the quality of the data (including such aspects as randomization procedures and case definitions) with an appraisal of its applicability to the practice population. First, are the data good? Second, is the patient population similar enough or is the desired clinical outcome similar enough to apply it to the practice? Desired clinical outcome includes not only resolution of an infectious condition but also optimal use of practice resources. For example, if a treatment is highly successful but requires the use of funds that then become unavailable for disease prevention or education, it may not be applicable to the shelter practice.
4. Apply the evidence to practice.
   This step is essentially making the final decision. Was there sufficient valid, important, and applicable evidence to utilize the therapy in the practice? Does the evidence support current practices? This step should not be done cavalierly; new findings discussed at continuing education meetings provide directions for thinking about making changes, but should be critically

**Table 6.2.** Step 3: Critically appraising the evidence. Questions to answer when reviewing evidence to answer a clinical question.

| |
|---|
| Was the assignment of patients to treatments randomized? |
| Was the randomization concealed? |
| Were all patients who entered the trial accounted for at its conclusion? |
| Were they analyzed in the groups to which they were assigned? |
| Were the patients and clinicians kept "blind" to which treatment was being received? |
| Aside from the experimental treatment, were the groups treated equally? |
| Were the groups similar at the start of the trial? |
| Are the valid results of this randomized trial important? |
| This requires a comparison of usual rate at which the disorder occurs with the experimental event rate, in order to calculate relative and absolute risk reduction. |
| Usual (control) event rate (%) = CER |
| Experimental event rate (%) = EER |
| Relative risk reduction = (CER-EER)/CER |
| Absolute risk reduction (ARR) = CER-EER |
| Number needed to treat* = 1/ARR |
| Can one apply this valid, important evidence about a treatment in caring for the patient? Is the patient so different from those in the trial that its results cannot help? How great would the potential benefit of therapy actually be for your individual patient? |
| This can be assessed by dividing the NNT as calculated above by the risk of the outcome of the patient. For example, if the patient has the same risk as those in the trial, then the number needed to treat for the patient is the same as in the trial. However, if the patient has a lower risk of the outcome, then the number needed to treat for a patient like this one will be higher. |
| Are the patient's values and preferences satisfied by the regiment and its consequences? |

*Number of animals needed to treat in order to avoid one negative outcome.

Source: Adapted with permission from the Center for Evidence-Based Medicine (www.cebm.net).

evaluated in the context of patient values, shelter values, community values and expectations, shelter resources, and other constraints.

Consider a hypothetical nutritional supplement that reduces the shedding of dermatophytes. If the costs of the supplement (including drug and labor costs) were $5000/year to treat all cats, but the costs of remodeling the cat room to reduce cat-to-cat transmission were $8000, does that make sense for the shelter? What if the supplement were only 75% effective in reducing transmission? What if the adopter population included a high percentage of immunocompromised individuals? Simply evaluating the efficacy of the treatment does not adequately address all the issues related to therapy.

***Examples of utilizing EBVM skills***

Presented below are examples of simplified versions of the four basic steps of EBVM practice, with clinical questions currently of interest to veterinarians working in shelters.

*Example 1: Lysine supplementation in cats for upper respiratory infections*

1. Create a clinical question.
   Using the PICO format discussed above, one question might be: Does oral lysine supplementation in cat food reduce the clinical signs of viral upper respiratory infections in cats in shelter settings?
   P = the patients are cats in shelters
   I = the intervention is oral lysine in cat food
   C = the comparison is no supplementation
   O = the outcome desired is reduced clinical signs
2. Search for the evidence.
   Using the key words generated by the question, a PubMed search was performed. As this area of research is relatively new, a relatively broad search was performed ("lysine," "cats," "respiratory OR virus"). After eliminating the articles with no relevance, there were four papers related to the topic, three of which demonstrated effects of lysine.
3. Appraise the evidence
   One paper described research (Maggs, Collins et al. 2000) that was performed in vitro and demonstrated a reduction in herpes viral replication; this paper might be categorized as Level 5 evidence: supports an affirmative answer to the clinical question but is not definitive. The next two papers (Stiles, Townsend et al. 2002; Maggs, Nasisse, Kass 2003) presented data from induced infection of cats with feline herpes virus; Maggs and coworkers did not demonstrate a difference from the control in the number of eyes affected by conjunctivitis, but Stiles and coworkers demonstrated a reduction in severity of conjunctivitis with lysine supplementation via oral bolus. These papers might be considered Level 1 evidence, since they were randomized and placebo-controlled. However, the fact that infection was induced rather than naturally occurring might reduce one's confidence in the support for the original clinical question. The last paper (Maggs, Sykes et al. 2007) attempted to mimic more completely a shelter or large cattery setting, with supplementation of feed rather than bolused lysine, and the respiratory disease was naturally occurring. However, no difference was detected among the treatment and control groups, although this was partially attributed to fighting within a treatment group. This study provides Level 1 evidence but does not support an affirmative answer to the original question.
4. Apply the evidence to practice.
   The evidence found in one resource, PubMed, appears to lend some support for the supplementation of lysine to reduce clinical signs of upper respiratory disease in cats, but if a grading system were used to assess the cumulative evidence, then one might choose to assign a grade of C to the evidence supporting the supplementation of lysine in cats in shelters (see Table 6.1).

In a shelter setting, the evidence must be applied to a population of animals rather than to an individually owned animal. In the single animal in a household, reduced clinical signs may be very desirable. However, if a shelter euthanizes cats for upper respiratory disease, the outcome for the shelter will not be a decrease in euthanasia, since the lysine supplementation appears only to reduce clinical signs rather than decrease the frequency of disease. The answer to this clinical question is not helpful, so the question needs to be re-asked, with the outcome being elimination of the disease rather than just reduction in clinical signs.

This exercise is not meant to discourage veterinarians from supplementing with lysine (or any other currently acceptable medical practice), but rather to encourage the clinician to make decisions with knowledge of the likelihood of success with the chosen therapy, and the ability to explain and justify the results, whether positive or negative.

*Example 2: Heartworm,* Wolbachia*, and tetracycline*

1. Ask a clinical question.
   Does doxycycline (or other tetracyclines) decrease the worm burden in heartworm infected dogs?
2. Search for the evidence.
   In PubMed, using the keywords *Wolbachia* and tetracycline or doxycycline and narrowing the search with *Dirofilaria*, a number of articles describing the positive effects of doxycycline in vitro and in human filarial disease can be found.
3. Appraise the evidence.
   A number of articles described the symbiotic nature of *Wolbachia* with *Dirofilaria* as well as the possible pathogenesis of *Wolbachia*'s contribution to heartworm disease. For example, an immune response to *Wolbachia* has been found in dogs infected with *Dirofilaria immitis* (Kramer, Simon et al. 2005). Tetracycline has also been shown to inhibit L3 to L4 molting (Smith and Rajan 2000). Evidence from treatment of dogs infected with heartworms is scarce, however. One paper describes the effect of tetracycline therapy on microfilaremic dogs, in which six treated animals did not have significantly different microfilaremia from control dogs (Bandi, McCall et al. 1999), although embryo development in adult worms was blocked. Clearly, this is a burgeoning area of research, but the evidence supporting the clinical use of tetracycline to decrease the heartworm burden in dogs is limited.
4. Apply the evidence to practice.
   Randomized control trials of this therapeutic intervention could potentially be carried out in shelter settings, but evidence for the wholesale recommendation of tetracyclines for dogs with heartworm infection remains in the experimental stages.

## Outcomes assessment: how to know if the interventions worked

Did changing from one therapy to another really improve the financial picture, or does it change some other parameter such as number of animals euthanized or number of adoptions? Did treating all cats with lysine in the food actually decrease the incidence or severity of upper respiratory disease compared to last year? The goal for interventions should be made clear, as should the metrics that are tracked to monitor the intervention. A change in severity of disease may be important for a shelter that does not euthanize symptomatic animals. On the other hand, shelters that do euthanize symptomatic animals will only benefit from interventions that reduce incidence of disease, rather than severity. Benefits to society or to adopters may occur with either intervention, but the goals of the shelter are likely to be more diverse than simply pleasing adopters. Did changing the medical records system increase the number of animals that are treated properly? The only way to assess the outcomes of the interventions is to have the paper or computer records to verify. Clinical impressions and anecdotes provide ideas for further assessment, but they are biased in so many ways as to be wholly unreliable for supporting decision making.

Reliable record systems are numerous. Whether self-created or bought, computerized or paper, they all have their advantages and disadvantages. Whichever system is chosen, it must be used to be effective and supportive of decision making. The advantages of having the evidence in the form of records to justify decisions may be invaluable when it comes to convincing a board of directors or the general public of the merits or shortcomings of a therapeutic intervention.

In addition to having a record-keeping system, there must be treatment protocols and established practices for record keeping. Consistency in treatment choices leads to the consistent ability to evaluate the success of therapeutic interventions.

## General principles of treatment of infectious diseases

### *Background information for reviewing the evidence that guides selection and regimen design for antimicrobial therapy*

Selecting an antimicrobial and a regimen that will be efficacious has become an increasingly complicated venture. The factors below have made the design of antimicrobial regimens increasingly more complex, requiring more than just an entry in a formulary to adequately describe:

1. Improved knowledge of bacterial species and pathogenesis
2. More sophisticated diagnostic data available from laboratories performing antimicrobial susceptibility testing
3. Improved knowledge of the most effective regimens for antimicrobial therapy
4. Accumulation of pharmacokinetic data
5. Continuing expansion of the antimicrobial arsenal, at least in terms of new drugs within old classes of compounds
6. Changes in and spread of genetic material encoding antimicrobial resistance

The following information is provided as background for this process, suggesting the considerations required

prior to the choice of an antimicrobial and its regimen. The steps are outlined and then described more fully in the next section.

***Steps to successful therapeutic selection***

A conceptualization of the ideal sequence for successful antimicrobial therapy selection is pictured in Figure 6.1. The *first step* to successful therapeutic selection is to know (or have solid evidence) that there is a bacterial infection present and that reducing the growth of the bacteria or eliminating the infection will result in improvement of clinical signs or will prevent other medical sequelae.

The *second step* is to consider which antimicrobial might successfully be used.

The *third step* is to determine what concentration of antimicrobial is required to inhibit bacterial growth. This is the essence of antimicrobial susceptibility testing and requires the clinician to consider more than just the "susceptible" designation received from a clinical laboratory.

The *fourth step* is to determine what dose of the antimicrobial might be required to achieve the above-determined concentration at the site of infection. In other words, what are the pharmacokinetics of the antimicrobial? In addition, antimicrobial drugs have differing pharmacodynamics, meaning that the best presentation of drug to bacteria differs with the drug group. For example, some drugs require long periods above the minimal inhibitory concentration (MIC) of the bacteria, whereas other can go below the MIC for a large percentage of the dosing interval, as long as there is an initial high concentration.

The *fifth step*, in an ideal world and not depicted in the figure, would be to have best-quality research evidence in the form of randomized control trials of effective use of the dose and regimen determined in the previous step, with the bacterial disease of interest in the species of interest, and in the clinical setting of interest (acknowledging that treating individual cases of bacterial disease may be quite different from outbreaks of bacterial disease in populations).

*Confirming the presence of bacterial disease*

The first step is not the purview of this discussion; background knowledge of disease processes as well as clinical experience will determine this step.

*Selecting an antimicrobial*

This step actually requires information from the next steps, but general considerations for antimicrobial selection can be made. For example, based on which bacteria are expected to be present and the expected spectrum of various antimicrobial groups, a drug group or groups might be ruled out or ruled in as possibilities. Table 6.3 contains some generalizations about the spectrum of activity of the major groups of antimicrobials. One way to determine when a particular drug group is likely to be ineffective is to look at the "holes" in each list. For

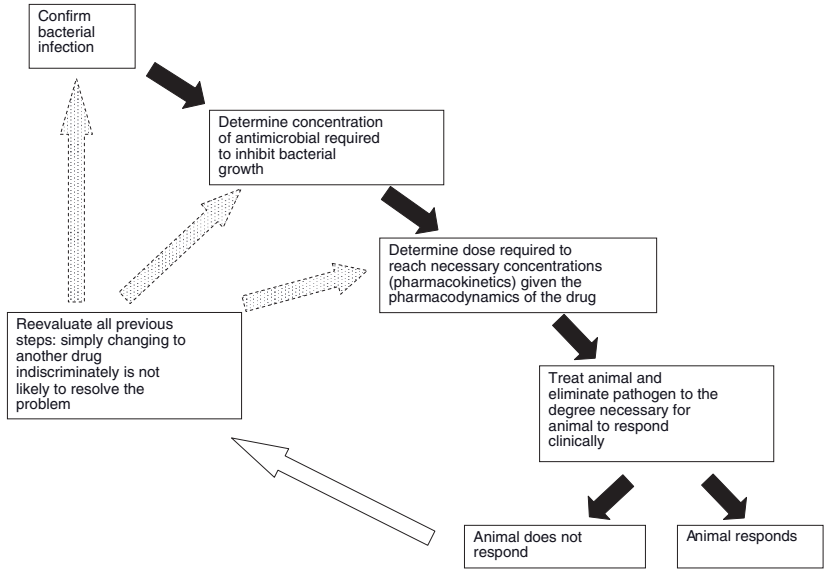


**Figure 6.1.** Idealized flow chart for making therapeutic decisions about antimicrobial therapy.

**Table 6.3.** Generalized spectra of antimicrobial drugs.[a]

**Gram-Positive Organisms**

| Aerobes | Obligate anaerobes |
|---|---|
| Penicillins | Penicillins |
| Aminopenicillins | Aminopenicillins |
| Penicillinase-resistant | |
| Carbapenems | Carbapenems |
| Amoxicillin-clavulanate | Amoxicillin-clavulanate |
| Group 1 cephalosporins | Group 1 cephalosporins |
| Group 2 cephalosporins | Group 2 cephalosporins |
| (Group 3 cephalosporins) | Group 3 cephalosporins |
| Group 4 cephalosporins (exc. *Staph. aureus*) | Group 4 cephalosporins |
| Group 5 cephalosporins (exc. *Staph. aureus*) | Group 5 cephalosporins |
| Vancomycin | Vancomycin |
| Lincosamides | Lincosamides |
| Macrolides | Macrolides |
| Chloramphenicol | Chloramphenicol |
| Florfenicol | |
| Fluoroquinolones | |
| Potentiated sulfonamides | |
| Tetracyclines | (Tetracyclines) |
| | Metronidazole |

**Gram-Negative Organisms**

| Respiratory and Fastidious Pathogens | Enterobacteriaceae | Pseudomonas | Obligate Anaerobes | Others (not all drugs listed) |
|---|---|---|---|---|
| Aminoglycosides | Aminoglycosides | Aminoglycosides | | |
| (Penicillins) | | | Penicillins | |
| Aminopenicillins | | | Aminopenicillins | Aminopenicillins |
| | | Antipseudomonal | | |
| | Beta-lact. resist. | | | |
| Carbapenems | Carbapenems | Carbapenems | Carbapenems | |
| Amoxicillin-clav. | (Amoxicillin-clav.) | | Amoxicillin-clav. | |
| | (Ticarcillin-clav.) | | | |
| | Group 3 ceph. | | Group 3 ceph. | |
| Group 4 ceph. | Group 4 ceph. | (Group 4 ceph.) | (Group 4 ceph.) | |
| Group 5 ceph. | Group 5 ceph. | | (Group 5 ceph.) | |
| | | Group 6 ceph. | | |
| | | Group 7 ceph. | | |
| Macrolides | | | (Macrolides) | Macrolides |
| Chloramphenicol | Chloramphenicol | Chloramphenicol | Chloramphenicol | |
| Florfenicol | | | | |
| Fluoroquinolones | Fluoroquinolones | Fluoroquinolones | | Fluoroquinolones |
| Potentiated sulfas | Potentiated sulfas | | | Potentiated sulfas |
| Tetracyclines | (Tetracyclines) | | (Tetracyclines) | Tetracyclines |
| | Polymyxins | | | |
| | | | Metronidazole | |
| | | | Lincosamides | |

**Table 6.3.** *Continued*

| | |
|---|---|
| **Spirochetes** | Aminopenicillins, tetracyclines, macrolides |
| **Mycoplasma** | Tetracyclines, (lincosamides), (macrolides), fluoroquinolones |

**Penicillin drug group examples**
Penicillins
Penicillin G, penicillin V
Aminopenicillins
Amoxicillin, ampicillin
Penicillinase-resistant penicillins
Oxacillin, methicillin, cloxacillin, dicloxacillin, nafcillin
Antipseudomonal penicillins (carboxypenicillins and ureidopenicillins)
Carbenicillin, piperacillin, ticarcillin
Beta-lactamase resistant penicillins
Temocillin

**Cephaloporins drug group examples**
Group 1 (1st generation, parenteral)
Cephalothin, cefazolin, cephapirin
Group 2 (1st generation, oral)
Cefadroxil, cephalexin
Group 3 (2nd generation, both)
Cefotetan, cefoxitin, cefuroxime
Group 4 (3rd generation, parenteral)
Cefotaxime, ceftizoxime, ceftriaxone, ceftiofur
Group 5 (3rd generation, oral)
Cefixime, cefpodoxime
Group 6 (3rd generation, parenteral)
Ceftazidime
Group 7 (4th generation)
Cefepime, cefquinome

[a] Gray areas indicate relative lack of efficacy of a drug group. Parentheses indicate variable susceptibility.

example, metronidazole is not usually considered effective against aerobes, and lincosamides are generally not considered effective against gram-negative aerobes. Table 6.4 outlines the gram-staining characteristics and oxygen requirements of some of the major veterinary bacterial pathogens.

These categorizations are not absolute. There are organisms within each grouping that may be resistant to the specific drugs within a class, and the changes in resistance patterns worldwide will eventually render some of these generalizations too inaccurate for empirical antimicrobial selection. In addition, some of the drug groups are very general and include drugs with very different spectra. One would not want to look at Table 6.3 and say, for example, that since tetracyclines and beta-lactams are in all four quadrants, the drugs in both groups could be considered equivalent. Individual drugs vary considerably, thus assigning equivalence to doxycycline and amoxicillin-clavulanate would be risky indeed. Specific, potentially successful drug–pathogen combinations can be more accurately determined with antimicrobial susceptibility testing, as discussed in the next step.

### *Antimicrobial susceptibility testing*

#### WHEN SHOULD SUSCEPTIBILITY TESTING BE PERFORMED?

Information on the concentration of antimicrobial required to inhibit growth of bacterial organisms has been available in some form for decades. Given the changes in susceptibility patterns of some bacteria, the most current data should be utilized whenever possible to make antimicrobial and dosing decisions. In some clinical settings, this may take the form of submitting a sample to a diagnostic

**Table 6.4.** Gram staining and oxygen requirement of major veterinary bacterial pathogens.

| | Aerobes | Facultative Anaerobes | Obligate Anaerobes |
|---|---|---|---|
| **Gram positive** | *Dermatophilus*<br>*Mycobacterium*<br>*Nocardia*<br>*Rhodococcus*<br>*Rickettsia* | *Actinomyces*<br>*Arcanobacterium pyogenes*<br>*Corynebacterium*<br>*Enterococcus*<br>*Erysipelothrix rhusiopathiae*<br>*Listeria monocytogenes*<br>*Staphylococcus*<br>*Streptococcus* | *Clostridium* spp.<br>*Actinobaculum suis* |
| **Gram negative** | *Anaplasma marginale*<br>*Bordetella*<br>*Borrelia burgdorferi (microaerophilic)*<br>*Brucella*<br>*Campylobacter (microaerophilic)*<br>*Chlamydia*<br>*Chlamydophila*<br>*Ehrlichia*<br>*Lawsonia intracellularis*<br>*Leptospira*<br>*Moraxella bovis*<br>*Pseudomonas* | *E. coli*<br>*Proteus*<br>*Salmonella*<br>*Actinobacillus*<br>*Haemophilus gallinarum*<br>*Haemophilus parasuis*<br>*Histophilus somni*<br>*Klebsiella*<br>*Mannheimia haemolytica*<br>*Nicoletella*<br>*Pasteurella multocida* | *Bacteroides*<br>*Dichelobacter*<br>*Fusobacterium*<br>*Brachyspira* |
| No gram staining | *Mycoplasma* spp. | | |

laboratory to determine the inhibitory ability of antimicrobials for the actual isolate from the animal being treated. In other settings, particularly in settings where (1) populations of animals are being treated, and (2) economic constraints may be significant, culture and susceptibility testing might be performed on a certain percentage of animals, might be performed in the case of refractory infections, or might not be performed at all. Testing is recommended specifically in shelters during outbreaks of disease caused by pathogens with unpredictable susceptibility patterns (e.g., *Bordetella*), by pathogens causing high mortality, and by pathogens with zoonotic potential (e.g., *Salmonella*). Testing is also recommended when a therapy that has been used successfully in the past is not working as expected.

While cost is often cited as a reason for skipping testing, shelter veterinarians should consider the cost of drugs and labor associated with therapy that might not be effective; paying on the front end might save money on ineffective treatments and prevent prolonged shelter stays and longer times to adoption.

When susceptibility testing is not performed, for example, in individual cases of bacterial infections, published susceptibility data may be used (see the example of *Bordetella bronchiseptica* susceptibility reported in the literature in Table 6.5), or a practitioner may request historical data from the local diagnostic laboratory or veterinary teaching hospital microbiology laboratory. It is the author's opinion that government-run diagnostic laboratories have an obligation to provide data of this nature to their clientele, but obtaining this information may be easier said than done.

### WHAT INFORMATION IS OBTAINED FROM SUSCEPTIBILITY TESTING?

The purpose of susceptibility testing is to use an in vitro method to make a prediction about clinical success. The major methods of susceptibility testing include the classic Kirby-Bauer disk diffusion method and the broth dilution method (Walker 2000). While these methods will not be described in detail here, the busy practitioner is reminded that such testing is not a black box or a magic trick but rather a standardized method of determining how much drug it takes to inhibit growth of an organism under specific conditions. Diagnostic laboratory personnel do not have any special knowledge of infections that allow them to predict clinical susceptibility but rather rely on published cutoff values, much like making a value judgment

**Table 6.5.** Synopsis of selected published antimicrobial susceptibility information on *Bordetella bronchiseptica*.*

| Organism | Drug | Species | Site of Infection | $MIC_{50}$[d] | $MIC_{90}$[d] | S | I | R | Reference |
|---|---|---|---|---|---|---|---|---|---|
| *Bordetella bronchiseptica* | Amikacin | Canine and Feline | Respiratory[b] | | | 19/22 | | 6/22 | Foley, Rand et al. 2002 |
| *Bordetella bronchiseptica* | Amoxicillin-clavulanate | Canine | Unknown[a] | | | 8/9 | | | Authier, Paquette et al. 2006 |
| *Bordetella bronchiseptica* | | Feline | Unknown[a] | | | 4/4 | | | Authier, Paquette et al. 2006 |
| *Bordetella bronchiseptica* | | Canine | Respiratory[b] | 0.75 | 1.5 | | | 0/78 | Speakman, Dawson et al. 2000 |
| *Bordetella bronchiseptica* | | Canine and Feline | Respiratory[b] | | | 13/22 | | 9/22 | Foley, Rand et al. 2002 |
| *Bordetella bronchiseptica* | | Mostly feline | Respiratory[b] | 4 | 32 | | | 14.5%/152 | Speakman, Binns et al. 1997 |
| *Bordetella bronchiseptica* | Ampicillin | Canine | Unknown[a] | | | 10/24 | | | Authier, Paquette et al. 2006 |
| *Bordetella bronchiseptica* | | Feline | Unknown[a] | | | 0/7 | | | Authier, Paquette et al. 2006 |
| *Bordetella bronchiseptica* | | Canine | Respiratory[b] | 2 | 12 | | | 19.2%/78 | Speakman, Dawson et al. 2000 |
| *Bordetella bronchiseptica* | | Canine and Feline | Respiratory[b] | | | 1/22 | | 21/22 | Foley, Rand et al. 2002 |
| *Bordetella bronchiseptica* | | Mostly feline | Respiratory[b] | 32 | >32 | | | 90.1%/152 | Speakman, Binns et al. 1997 |
| *Bordetella bronchiseptica* | Cephalosporins | Canine and Feline | Respiratory[b] | | | | | 22/22 | Foley, Rand et al. 2002 |
| *Bordetella bronchiseptica* | Cephalothin | Canine | Unknown[a] | | | 18/24 | | | Authier, Paquette et al. 2006 |
| *Bordetella bronchiseptica* | | Feline | Unknown[a] | | | 5/7 | | | Authier, Paquette et al. 2006 |
| *Bordetella bronchiseptica* | Chloramphenicol | Canine and Feline | Respiratory[b] | | | 22/22 | | | Foley, Rand et al. 2002 |
| *Bordetella bronchiseptica* | Clindamycin | Canine | Unknown[a] | | | 0/9 | | | Authier, Paquette et al. 2006 |
| *Bordetella bronchiseptica* | | Feline | Unknown[a] | | | 0/4 | | | Authier, Paquette et al. 2006 |
| *Bordetella bronchiseptica* | Doxycycline | Canine | Respiratory[b] | 0.19 | 0.75 | | | 0/78 | Speakman, Dawson et al. 2000 |
| *Bordetella bronchiseptica* | | Mostly feline | Respiratory[b] | 0.5 | 2 | | | 2%/152 | Speakman, Binns et al. 1997 |

**Table 6.5.** *Continued*

| Organism | Drug | Species | Site of Infection | $MIC_{50}$[d] | $MIC_{90}$[d] | S | I | R | Reference |
|---|---|---|---|---|---|---|---|---|---|
| *Bordetella bronchiseptica* | Enrofloxacin | Canine | Unknown[a] | | | 23/23 | | | Authier, Paquette et al. 2006 |
| *Bordetella bronchiseptica* | | Canine | Respiratory[b] | 0.5 | 1 | | | 0/78 | Speakman, Dawson et al. 2000 |
| *Bordetella bronchiseptica* | | Canine and Feline | Respiratory[b] | | | 22/22 | | | Foley, Rand et al. 2002 |
| *Bordetella bronchiseptica* | | Feline | Unknown[a] | | | 6/6 | | | Authier, Paquette et al. 2006 |
| *Bordetella bronchiseptica* | | Mostly feline | Respiratory[b] | 1 | 2 | | | 7.2%/152 | Speakman, Binns et al. 1997 |
| *Bordetella bronchiseptica* | Erythromycin | Canine | Unknown[a] | | | 5/12 | | | Authier, Paquette et al. 2006 |
| *Bordetella bronchiseptica* | | Feline | Unknown[a] | | | 1/3 | | | Authier, Paquette et al. 2006 |
| *Bordetella bronchiseptica* | Gentamicin | Canine | Unknown[a] | | | 23/24 | | | Authier, Paquette et al. 2006 |
| *Bordetella bronchiseptica* | | Feline | Unknown[a] | | | 7/7 | | | Authier, Paquette et al. 2006 |
| *Bordetella bronchiseptica* | | Canine and Feline | Respiratory[b] | | | 19/22 | | 3/22 | Foley, Rand et al. 2002 |
| *Bordetella bronchiseptica* | Orbifloxacin | Canine | Unknown[a] | | | 9/9 | | | Authier, Paquette et al. 2006 |
| *Bordetella bronchiseptica* | | Feline | Unknown[a] | | | 2/4 | | | Authier, Paquette et al. 2006 |
| *Bordetella bronchiseptica* | Penicillin | Canine | Unknown[a] | | | 0/13 | | | Authier, Paquette et al. 2006 |
| *Bordetella bronchiseptica* | | Feline | Unknown[a] | | | 3/5 | | | Authier, Paquette et al. 2006 |
| *Bordetella bronchiseptica* | Sulfadiazine | Canine | Respiratory[b] | 1.5 | >256 | | | 19.2%/78 | Speakman, Dawson et al. 2000 |
| *Bordetella bronchiseptica* | | Mostly feline | Respiratory[b] | 8 | >128 | | | 7.2%/152 | Speakman, Binns et al. 1997 |
| *Bordetella bronchiseptica* | Tetracycline | Canine | Unknown[a] | | | 22/24 | | | Authier, Paquette et al. 2006 |
| *Bordetella bronchiseptica* | | Feline | Unknown[a] | | | 7/7 | | | Authier, Paquette et al. 2006 |
| *Bordetella bronchiseptica* | | Canine | Respiratory[b] | 0.75 | 1.5 | | | 0/78 | Speakman, Dawson et al. 2000 |
| *Bordetella bronchiseptica* | | Canine and Feline | Respiratory[b] | | | 22/22 | | | Foley, Rand et al. 2002 |
| *Bordetella bronchiseptica* | | Mostly feline | Respiratory[b] | 2 | 2 | | | 1.2%/152 | Speakman, Binns et al. 1997 |

| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| *Bordetella bronchiseptica* | Ticarcillin-clavulanate | Canine and Feline | Respiratory[b] | | | 18/22 | 4/22 | Foley, Rand et al. 2002 |
| *Bordetella bronchiseptica* | Trimethoprim | Canine | Respiratory[b] | 2 | >32 | | 26.9%[h]/78 | Speakman, Dawson et al. 2000 |
| *Bordetella bronchiseptica* | | Mostly feline | Respiratory[b] | 64 | 500 | | 29.6%[h]/152 | Speakman, Binns et al. 1997 |
| *Bordetella bronchiseptica* | Trimethoprim-sulfadiazine | Canine | Unknown[a] | | | 12/24 | | Authier, Paquette et al. 2006 |
| *Bordetella bronchiseptica* | | Feline | Unknown[a] | | | 4/4 | | Authier, Paquette et al. 2006 |
| *Bordetella bronchiseptica* | Trimethoprim-sulfamethoxazole | Canine and Feline | Respiratory[b] | | | 22/22 | | Foley, Rand et al. 2002 |

*The susceptibility to several antimicrobials, listed alphabetically, is reported here. As an example, review the entries for enrofloxacin. Five sets of data are reported, with the majority of isolates demonstrating susceptibility to enrofloxacin. Some of the studies measured actual MICs, whereas others used breakpoints of some sort (see footnotes for breakpoints used). When CLSI guidelines are used, the breakpoints reported in Table 6.6 can be used to estimate the MICs of the organisms.

The method of testing is indicated by superscript under "Site of Infection." Unless noted, the testing is assumed to be in compliance with the CLSI guidelines for susceptibility testing of bacterial isolates from animals. The denominator in each column is the total number of isolates tested or the percent of isolates, and the numerator is the number of isolates tested.

[a] Kirby-Bauer method.

[b] Broth dilution method.

[c] Includes susceptible and intermediately susceptible.

[d] μg/ml (number of isolates).

[e] Etest method.

[f] Susceptibility breakpoints used in this paper were: ampicillin ≤64 μg/ml, amoxicillin-clavulanate ≤64/32 μg/ml, chloramphenicol ≤64 μg/ml, cephalexin ≤128 μg/ml, tetracycline ≤64 μg/ml, and trimethoprim-sulfamethoxazole ≤16/304 μg/ml.

[g] Susceptibility breakpoints used in this paper were: very susceptible ≤0.06 μg/ml, less susceptible 0.12–1 μg/ml, intermediate and resistance ≥2 μg/ml; therefore, very susceptible and less susceptible were combined for the "S" category by this author, and intermediate and resistant are reported as "R."

[h] Breakpoint of 500 μg/ml, which is not based on CLSI standards.

on a cholesterol level in a human patient: the level that is called "unhealthy" versus "healthy" is based on correlation of levels with other unhealthy events.

The correlation between in vitro inhibitory data and in vivo clinical response is not usually 100% and is often much less, something that should be kept in mind when using susceptibility testing results from clinical cases. In vitro testing conditions do not (and cannot) precisely mimic local conditions during a bacterial infection, so this is one major source of difference between in vitro and in vivo activity. Other reasons for failure of in vitro growth inhibition to predict clinical response include, but are not limited to:

1. Ability of the drug to penetrate to the site of infection
2. Inactivation of drug at the site of infection (or conditions not conducive to action, such as anaerobic conditions and aminoglycosides)
3. Importance of the organism to the disease process (just because it was cultured does not mean it is a significant participant)
4. Timing of antimicrobial administration (for some infections, once the pathogenic processes are in place, elimination of the organism will not speed up the healing)

The criteria for correlating a given inhibitory concentration and clinical success are termed "breakpoints." The theory behind the development of breakpoints is to establish a cutoff value of inhibitory concentration such that if a pathogen requires more than that cutoff to inhibit in vitro growth it is highly unlikely that the pathogen growth will be inhibited in vivo by that antimicrobial, and treatment with it will not result in clinical cures.

Breakpoints have been established and are updated on a continual basis by the Clinical and Laboratory Standards Institute (CLSI) Veterinary Antimicrobial Susceptibility Testing Subcommittee (VAST). The CLSI is a global, nonprofit, standards-developing organization that promotes the development and use of voluntary consensus standards and guidelines within the health-care community. One of the publications put together by this subcommittee, and updated on a regular basis, is known as M31 (CLSI 2002). The committee outlines the standards for performing susceptibility testing, including the breakpoints to use for each drug or representative drug. Breakpoints are ideally determined using a complicated process of evaluating several layers of data, including pharmacokinetics of the antimicrobial in the species of animal, pharmacodynamics of the antimicrobial, MICs of populations of pathogens isolated from clinical cases, and results from clinical trials of the antimicrobial. An excerpt of the most recent version of the M31 is presented in Table 6.6. This is not a complete list of drugs for which there are breakpoints, but includes the drugs that would be most commonly used in shelter medical cases.

**Table 6.6.** Minimum inhibitory concentration (MIC) breakpoints for drugs likely to be used to treat canine and feline pathogens in shelter settings.*

| | MIC Breakpoint (μg/ml) | | | |
|---|---|---|---|---|
| Antimicrobial Agent | S | I | F | R |
| Amikacin | ≤16 | 32 | | ≥64 |
| Amoxicillin-clavulanic acid | | | | |
| Staphylococci | ≤4/2 | | | ≥8/4 |
| Other organisms | ≤8/4 | | | ≥32/16 |
| Ampicillin | | | | |
| Enterobacteriaciae | ≤8 | 16 | | ≥32 |
| Staphylococci | ≤0.25 | | | ≥0.5 |
| Enterococci | ≤8 | | | ≥16 |
| Streptococci (not *S. pneumoniae*) | ≤0.25 | 0.5–4 | | ≥8 |
| *Listeria* spp. | ≤2 | | | |
| Cefazolin | ≤8 | 16 | | ≥32 |
| Ceftiofur | | | | |
| Bovine (Respiratory Disease) *Mannheimia haemolytica* | ≤2 | 4 | | ≥8 |

**Table 6.6.** *Continued*

| Antimicrobial Agent | MIC Breakpoint (μg/ml) S | I | F | R |
|---|---|---|---|---|
| *Pasteurella multocida* | | | | |
| *Histophilus somni* | | | | |
| Swine (Respiratory Disease) | ≤2 | 4 | | ≥8 |
| *Actinobacillus pleuropneumoniae* | | | | |
| *Pasteurella multocida* | | | | |
| *Salmonella choleraesuis* | ≤0.25 | | | |
| Equine (Respiratory Disease) | | | | |
| Streptococcus equi subsp. zooepidemicus | | | | |
| Cephalothin | ≤8 | 16 | | ≥32 |
| Chloramphenicol | | | | |
| Organisms other than streptococci | ≤8 | 16 | | ≥32 |
| *S. pneumoniae* | ≤4 | | | ≥8 |
| Streptococci (not *S. pneumoniae*) | ≤4 | 8 | | ≥16 |
| Clindamycin | | | | |
| Dogs (skin, soft tissue infections) | ≤0.5 | 1–2 | | ≥4 |
| *Staphylococcus* spp. | | | | |
| Difloxacin | | | | |
| Dogs (dermal, UTI) | ≤0.5 | 1–2 | | ≥4 |
| Enterobacteriaceae | | | | |
| *Staphylococcus* spp. | | | | |
| Other organisms | | | | |
| Enrofloxacin | | | | |
| Cats (dermal) | ≤0.5 | | 1–2 | ≥4 |
| Dogs (dermal, respiratory, UTI) | ≤0.5 | | 1–2 | ≥4 |
| Enterobacteriaceae | | | | |
| *Staphylococcus* spp. | | | | |
| Other susceptible organisms | | | | |
| Erythromycin | | | | |
| *Enterococcus* spp. | ≤0.5 | 1–4 | | ≥8 |
| *Staphylococcus* spp. | ≤0.5 | 1–4 | | ≥8 |
| Streptococci | ≤0.25 | 0.5 | | ≥1 |
| Gentamicin | ≤4 | 8 | | ≥16 |
| Gentamicin | | | | |
| Dogs | ≤2 | 4 | | ≥8 |
| Enterobacteriaceae | | | | |
| *Pseudomonas aeruginosa* | | | | |
| Equine | ≤2 | 4 | | ≥8 |
| Enterobacteriaceae | | | | |
| *Pseudomonas aeruginosa* | | | | |
| *Actinobacillus* spp. | | | | |
| Marbofloxacin | | | | |
| Cats (dermal) | ≤1 | 2 | | ≥4 |
| Dogs (dermal, UTI) | ≤1 | 2 | | ≥4 |
| Enterobacteriaceae | | | | |

**Table 6.6.** *Continued*

| Antimicrobial Agent | MIC Breakpoint (μg/ml) S | I | F | R |
|---|---|---|---|---|
| *Staphylococcus* spp. | | | | |
| Other organisms | | | | |
| Orbifloxacin | | | | |
| Cats (dermal) | ≤1 | | 2–4 | ≥8 |
| Dogs (dermal, UTI) | ≤1 | | 2–4 | ≥8 |
| Enterobacteriaceae | | | | |
| *Staphylococcus* spp. | | | | |
| Other susceptible organisms | | | | |
| Penicillin | | | | |
| Staphylococci | ≤0.12 | | | ≥0.25 |
| Enterococci | ≤8 | | | ≥16 |
| *S. pneumoniae* | ≤0.06 | | | |
| Streptococci (not *S. pneumoniae*) | | | | |
| viridans group | ≤0.12 | | | ≥4 |
| beta-hemolytic group | ≤0.12 | | | |
| *Listeria* spp. | ≤2 | | | |
| Rifampin | | | | |
| Organisms other than streptococci | ≤1 | 2 | | ≥4 |
| *Streptococcus pneumoniae* | ≤1 | 2 | | ≥4 |
| Sulfisoxazole | ≤256 | | | ≥512 |
| Tetracycline | | | | |
| Organisms other than streptococci | ≤4 | 8 | | ≥16 |
| *Streptococcus pneumoniae* | ≤2 | 4 | | ≥8 |
| Trimethoprim-sulfamethoxazole | | | | |
| Organisms other Streptococci | ≤2/38 | | | ≥4/76 |
| *Streptococcus pneumoniae* | ≤0.5/9.5 | 1/19–2/38 | | ≥4/76 |

*Breakpoints categorize bacterial isolates as susceptible (S), intermediately susceptible (I), or resistant (R). The "F" category is similar to intermediately resistant and is used only for those agents which have flexible dosage labels. Shaded rows are breakpoints extrapolated from human medicine.

Source: Reprinted with permission from the Clinical and Laboratory Standards Institute. Performance Standards for Antimicrobial Disk and Dilution Susceptibility Tests for Bacteria Isolated from Animals (M31-A2). CLSI, 940 West Valley Road, Site 1400, Wayne, PA 19087, USA, www.clsi.org. Readers should refer to the most current edition of M31 for updates to breakpoints.

It is important to note that these breakpoints are valid for a given animal species, disease, pathogen, drug, and regimen (dose, route, duration, frequency). While the dose is not always noted in the breakpoint table, one should not assume that all doses could be used appropriately for any pathogen. The other important note is that many of the breakpoints have actually been extrapolated from human medicine. Therefore, while they represent an approximation of a reasonable breakpoint, they were developed using human pharmacokinetic data and human pathogen population data. In other words, when a user gets a report from a laboratory that states a particular pathogen is "susceptible," this is not a guarantee of efficacy but rather an estimate of a prediction.

Users should be aware that not all drugs used clinically are tested separately; some of the drugs tested are class representatives. Susceptibility in one drug is assumed to represent susceptibility to all drugs:

- Ampicillin: also tests for amoxicillin
- Tetracycline: also tests for doxycycline
- Cephalothin: representative for first-generation cephalosporins
- Clindamycin: also tests for lincomycin
- Sulfasoxazole: representative for sulfonamides
- Trimethoprim-sulfamethoxazole: representative for all trimethoprim-sulfa combinations

There are organisms that do in fact respond differently to different drugs within a class, but they are the exception rather than the rule. For example, a small percentage of isolates will exhibit in vitro susceptibility to doxycycline but will be resistant to tetracycline. Whether this correlates to clinical response is unknown, since the breakpoints used for both drugs are based on current human pharmacokinetics.

### *Dose selection: pharmacokinetics and pharmacodynamics*

Does the busy practitioner really have to determine doses for each case? Isn't that the purpose of a formulary? Those are reasonable questions, and while it is believed that not everyone will be designing dose regimens for antimicrobials, this section on dose selection is included to highlight important considerations that the practitioner should critically evaluate when confronted with data from a published article or a pharmaceutical representative.

#### PHARMACOKINETICS: WHERE IS THE DRUG AND FOR HOW LONG?

Because a basic tenet of pharmacology is that the dose given is proportional to the concentration of drug in the body, if the concentration of antimicrobial required to inhibit the growth of a pathogen is known, the dose required to achieve that concentration can usually be determined. This may not always be a simple calculation, but the science of pharmacokinetics attempts to mathematically model drug concentrations over time so that predictions can be made.

Pharmacokinetic data are often presented as individual factoids, e.g., the half-life of drug X is 4 hours. The long version of this statement would likely read as follows:

1. A small number of healthy animals were studied. Applicability to diseased patients is assumed but often not demonstrated.
2. Serum concentrations of the drug were measured at several discrete intervals over time, and the rate of elimination was calculated for each individual animal. If serum concentration is proportional to tissue concentrations at the site of infection, this parameter is useful; if not, more information may be needed.
3. The average rate of elimination was calculated. As this is an average, it does not capture the variability inherent in all pharmacokinetic data.

The point of this long version is to demonstrate that elimination half-lives or any other pharmacokinetic parameter should not be interpreted as a single data point but rather as estimates of values that generally represent the average animal.

Other pharmacokinetic data whose value is often misunderstood are "tissue concentrations." These data are often gathered to assess the degree to which a drug might penetrate to areas of infection. It is dogma that more lipid-soluble drugs move into cells more easily, but this is not an absolute, as drugs do not enter cells only by diffusion through the cell wall. They can also enter via pores or via active or facilitated transport. Other potential barriers to drug entry into parts of the body include physiological barriers such as the blood-brain barrier.

The veterinarian's interpretation of the importance of knowing tissue concentrations should be tempered by an understanding of how tissue concentrations are determined. It should be understood that:

1. Collection of samples from a particular area may be difficult; taking bone samples to measure bone penetration is not straightforward.
2. Antimicrobial drugs may bind to a particular tissue and be detected, but may not, in fact, be available or active in inhibiting the growth of bacteria. For example, tetracyclines bind to bone and may be measured in high concentrations there, but bound tetracyclines are not active.
3. In order to measure the concentration of antimicrobial, the tissue is macerated first. A drug that is water-soluble and does not enter cells then becomes underrepresented in terms of concentration in the areas where it actually is (outside cells). A drug that is lipid-soluble and enters cells more readily is overrepresented in cells, but the infection may still be extracellular and might not be inhibited by the antimicrobial concentration present there.

#### PHARMACODYNAMICS: HOW DOES THE DRUG WORK, AND WHAT DOES TIME DEPENDENT MEAN?

In addition to knowing or being able to predict the concentration of antimicrobial at the site of infection,

experimental evidence suggests that the relationship between concentration and efficacy is more complicated than simply being above the inhibitory concentration of the bacterial pathogen. This is often described as the pharmacodynamics of the antimicrobial, and current knowledge suggests there are two major categories of antimicrobials: those that are most effective when drug concentrations stay above an inhibitory concentration for a certain percentage of the dose interval (time dependent) and those that are most effective when drug concentrations exceed the in vitro inhibitory concentration by a certain proportion and do not need to remain above the MIC for a long period of time (concentration dependent or peak dependent). These categories have been shown to be generally true according to the antimicrobial group, as depicted in Table 6.7.

These categorizations should bring into question the dosing frequency required, in particular for time-dependent drugs. A beta-lactam with a short half-life is unlikely to maintain adequate serum concentrations to inhibit growth unless it is either given relatively frequently or if the MIC of the organism is very low. Pharmacokinetic analysis of five dogs given oral cephalexin and cefadroxil (30 mg/kg for both) suggested that drug concentrations remain above 1 µg/ml for a mean of approximately 29 hours when administered without food and 16 hours with food (Campbell and Rosin 1998). This would suggest once-a-day therapy would be acceptable for pathogens with low MICs. Looking at Table 6.6, note that the susceptible breakpoint for cefazolin is ≤8 µg/ml; therefore, knowledge of actual MIC rather than breakpoint MIC would be necessary to accurately predict clinical success.

Doxycycline is another antimicrobial that may have time-dependent pharmacodynamics, although this has not been definitively shown experimentally. Based on one study in dogs and cats treated with 5 mg/kg orally with food administered twice a day, serum concentrations at 4 hours after dosing averaged approximately 3 µg/ml, suggesting that twice a day dosing might be useful for pathogens with low MICs (Wilson, Morris et al. 2006). In this same study, relatively high urine concentrations were obtained 4 hours after administration (52–54 µg/ml in cats and dogs) suggesting treatment of urinary tract infections with higher MICs may be successful.

In studies in which once-a-day dosing of doxycycline was shown to be effective (Owen, Sturgess et al. 2003), it might be deduced that either the organism had a very low MIC, there was a prolonged postantibiotic effect, or growth inhibition was not required for the entire dosing interval for animals to overcome infection. For the practicing veterinarian making a treatment decision, the recommendation should be to use clinical trial data whenever possible, unless the actual MIC of an organism is available and can be compared with pharmacokinetic data. (As a side note, some summary pharmacokinetic data are available in publications such as *Target: The Antimicrobial Reference Guide to Effective Treatment*, published by North American Compendiums.)

It might be concluded that using so-called peak-dependent (sometimes called concentration-dependent) drugs would be advantageous in shelters since compliance with thrice or even twice daily dosing may be suboptimal. However, as demonstrated in the previous paragraph, information is needed not only about drug pharmacokinetics but pathogen information as well in order to draw reasonable conclusions.

**Table 6.7.** Pharmacodynamic parameters predicting clinical efficacy by antimicrobial drug group.

| Drug Group | Pharmacodynamic Parameter |
|---|---|
| Beta-lactams | Time > MIC = at least 50% of dosing interval |
| Tetracyclines<br>Phenicols<br>Macrolides | Time > MIC = close to 100% of dosing interval |
| Fluoroquinolones | $AUC_{24}$:MIC = 100–250 |
| Aminoglycosides | $C_{max}$ : MIC = 8–10 |

Source: Andes and Craig 2002.

## ANTIMICROBIAL RESISTANCE AND PRUDENT USE GUIDELINES FOR DOGS AND CATS

### Clinical and public health importance of resistance

The increasing prevalence of antimicrobial resistance in clinical bacterial isolates from animals and humans worldwide demands that all health professionals be concerned. In addition, there is escalating concern regarding selection for resistant commensals when animals or people are treated with antimicrobials. Therefore, veterinarians should consider the potential to select for resistance in pathogens as well as in normal flora or other pathogens in the animals they treat. Bacteria are highly capable of passing genetic material within their species as well as among other species. The proximity with which humans and companion animals reside suggests that this

transfer of mechanisms of resistance on genetic material can become problematic.

The call for veterinarians and their allied health personnel is to use antimicrobial drugs prudently, i.e., in a manner that maximizes therapeutic efficacy while minimizing the selection for resistance. It is expected that the first goal, maximizing efficacy, contributes toward accomplishing the second goal of minimizing resistance selection. In this section, some background information on resistance is given, and then the efforts within the veterinary profession to encourage prudent use are discussed.

**Antimicrobial resistance**

Resistance can be innate or acquired. Innate resistance is a characteristic of an organism that makes it inherently resistant to a particular antimicrobial. For example, anaerobes are innately resistant to aminoglycosides because there is no transport system in the organism. Acquired resistance can occur through a mutation or through transfer of genetic material from one organism to another. In the first case, mutations occur frequently when organisms replicate. These mistakes in replication of genetic material may result in the creation of a protein that is protective for the organism, i.e., resistant to the antimicrobial. The mutation might result in an enzyme that destroys the antimicrobial, or it might change the conformation of the ribosome to which the antimicrobial would normally attach. This change allows this mutated organism to survive when the others are inhibited by the antimicrobial. It then grows and replicates and may potentially continue to cause disease.

There are some types of resistance that are "inducible," meaning that they are present in the bacterial cell but not turned on. When exposed to an antimicrobial, however, the mechanism is activated (e.g., an enzyme begins to be produced) that confers resistance.

Reports continue to be published of individual resistant organisms, such as methicillin resistant *Staphylococcus aureus* (MRSA) (Rich 2005; Morris, Rook et al. 2006; Strommenger, Kehrenberg et al. 2006). However, trends toward increasing resistance have not been reported for all pathogens. Reports from diagnostic laboratories may be useful to the practitioner in making decisions about antimicrobial use, although a centralized system of data organization has yet to be assembled for all veterinary pathogens, particularly for companion animals.

Typically, the bacteria in one arena, such as animals, humans, or soil are considered to be separate and unique to it, but this is unlikely to be the case. It is therefore not unreasonable to think that selection for resistance in one arena (human medicine) would affect another arena (veterinary medicine), or vice versa. It is a tenet of antimicrobial use that it selects for resistance. Once resistant organisms have been selected for, the question is: will they remain in the population or are they less fit in some way to survive for long periods of time? These questions are still not fully answered, and are likely to be different depending on the mechanism of resistance and the location of the natural reservoir of bacteria, among other things.

**Reducing selection for resistant organisms**

Prudent use guidelines suggest that one important way to reduce the selection for resistance is to use antimicrobials appropriately (right dose, frequency, duration) and only when necessary.

The first means of reducing the selection for resistance is by drug selection. The antimicrobial with the narrowest spectrum that still includes the target pathogen is most desirable; this will limit the selection of resistant nontarget organisms, such as commensals on the skin or in the gut. These commensals (or even pathogens that are not yet causing disease in the patient being treated) can then share their genetic material containing mechanisms of resistance with other bacteria in the individual animal, with other animals, or the people with which it has contact.

The second means of reducing the selection for resistance is by appropriate drug dosing. Data are not available for all drug–pathogen combinations, but there are some data to suggest dosing that reduces the selection for resistance for certain drug groups. The mutant prevention concentration (MPC) was defined recently as the concentration that inhibits the growth of mutant organisms, i.e., those with stepwise mutations leading to resistance. It is typically measured using a higher number of organisms than used in MIC testing. In reported experiments so far, the MPC has been higher than the MIC, but the magnitude of the difference varies among drug–bug combinations and even within drug groups. The clinical significance of MPC measurement in veterinary medicine has yet to be determined, but research will likely continue in this area.

The American Veterinary Medical Association has developed guiding principles of prudent antimicrobial use (American Veterinary Medical Association 2006) that have been used by species-specific veterinary groups to develop more detailed guidelines. Prudent use is antimicrobial therapy that optimizes therapeutic efficacy while minimizing the potential selection for resistant organisms.

Major principles of prudent use include emphasizing preventative strategies for control of infectious disease, using narrow-spectrum antimicrobials whenever possible, using culture and antimicrobial susceptibility testing to aid the selection of appropriate antimicrobials, and using antimicrobials only when indicated and for only as long as needed to attain the desired clinical response. The question of how long to treat infections has not been as completely addressed as other aspects of antimicrobial therapy, so this principle of prudent use can be problematic. The main point of this recommendation is to avoid long-term treatment of unresponsive infections, in which therapy is merely resulting in exposure of other bacteria to selection pressure rather than having any effect on the infection itself. One final principle of prudent use is that accurate records of antimicrobial use and outcome of therapy are recommended. (Details of these principles can be viewed at the AVMA Web site, www.avma.org.)

Following the publication of these general principles, the American Association of Feline Practitioners and the American Animal Hospital Association have developed more detailed principles for prudent antimicrobial use. They are also available on the AVMA Web site.

## WHAT CONSTRAINTS MIGHT THERE BE ON USING THE MOST EFFECTIVE DRUG PROPERLY AND HOW CAN THE VETERINARIAN ADDRESS THEM?

As discussed at the beginning of the chapter, shelter veterinarians make pharmacotherapeutic decisions on the basis of efficacy alongside the economic, logistical, and philosophical constraints associated with working with shelters. Typical constraints on drug selection and use relate to financial factors, personnel issues, legalities and regulations related to drug selection and use, public perception in the community of shelter animals and their handling, and public health issues such as the development of antimicrobial resistance.

Profit is not the motive in the shelter setting, but cost reduction is usually a factor. Motivation can originate from the desire to adequately serve the needs of the shelter population or to serve the needs of more animals than currently served for the same cost. Other motives include protecting animal welfare and controlling disease.

Many of these issues cannot be addressed by this author. Issues surrounding antimicrobial resistance have been discussed above. Legal issues are touched on below, but the practitioner is reminded to review state veterinary and pharmacy Practice Acts and local ordinances related to drug selection, use, and storage prior to implementing changes.

### Drug regulations

#### *Extralabel drug use: the Animal Medicine Drug Use Clarification Act of 1994 (AMDUCA)*

AMDUCA (and the regulations promulgated from it in 1997) codified the ability of veterinarians to legally utilize drugs in an extralabel fashion, i.e., in a manner not on the label such as in a different species, at a different dose, for a different duration or frequency, or for a different indication (U.S. Food and Drug Administration 1996). While it seems that many of the provisions apply more often to extralabel use in food-producing animals, there are a number of requirements for extralabel use that apply to all species.

Extralabel use must be in the context of a veterinarian–client–patient relationship. Extralabel use by a lay person is not permitted except under the supervision of a licensed veterinarian. (This means that lay persons may not initiate extralabel use.) Extralabel drugs must be dispensed with a label containing the name and address of the prescribing veterinarian, established name of the drug, directions for use, and any cautionary statements. Finally, records will be maintained on individual animals that provide the condition treated, species of animal, dosage, duration of treatment, and number of animals treated. These records must be maintained for 2 years and must be made available to the FDA if requested. The implications of the labeling requirement in a shelter may vary from state to state, depending on the status of the animals in the shelter. The author's interpretation is that if the animals are owned by the shelter, a complete label as just described might not be necessary for use within the shelter. However, prudent pharmacy practice dictates the use of relatively complete labels for the purpose of minimizing medication errors and maximizing animal health and human safety. So even if animals are owned by the shelter, it would still be judicious to label medications completely.

#### *Initiation of drug administration*

The initiation of drug administration in the shelter can be problematic, particular in smaller or more rural settings where a veterinarian is not on-site full time. State-by-state regulations will not be iterated here, but practitioners should make themselves familiar with their state veterinary and pharmacy Practice Act to determine the latitude

allowed and supervision required of personnel administering drugs to patients in a shelter.

Controlled substances fall into a different category, as those regulations generally are initiated at the federal level. However, there are some states that have more stringent regulations than the federal Controlled Substances Act, so the practitioner should become familiar with those rules, which may be in the state Practice Act, or they may have their own Act.

### *Compounding/extemporaneous formulations*

The use of extemporaneous formulations, i.e., compounding, has a long history in veterinary medicine, as drugs are often approved for limited numbers of species and indications. In addition, given that there is a large variation in weight among breeds, particularly within the canine and feline species, doses can very considerably in volume or size. Therefore, veterinarians should be cognizant of current regulations regarding compounding. There are two main types of compounding, which are viewed in quite different ways by regulatory agencies: (1) manipulating an approved animal or human drug in a manner not stated on the label, such as reconstituting at a different concentration, or mixing with a flavoring agent; and (2) making a drug from so-called bulk drug (raw ingredients), such as purchasing raw ivermectin and creating a product.

The first type of compounding has some protection under AMDUCA, provided a valid veterinarian–client–patient relationship exists and there is no approved product in its available dosage form and concentration that could be used in an extralabel manner. This Act does not, however, allow for the second type of compounding, either from unapproved drugs (e.g., drugs approved in other countries but not in the U.S.) or from bulk drugs.

As of this writing, the U.S. Food and Drug Administration Center for Veterinary Medicine has in place a Compliance Policy Guide (U.S. Food and Drug Administration Center for Veterinary Medicine 2003), which outlines their policy on the acceptability of compounding. Some of the boundaries for veterinarians who perform their own compounding include using good compounding practices (e.g., in an appropriate environment), being knowledgeable about the stability and potency of compounded products, compounding for individual patients rather than in anticipation of future need, and not advertising or giving fanciful names to compounded products. Compounding pharmacies for veterinary medicine are not immune to regulation either, and of late, they have come under scrutiny legally as well as ethically. The AVMA has considerable information on how to select a compounding pharmacy and how to comply

**Table 6.8.** Selected references on compounding.

Rita K. Jew, Robert J. Mullen, and Winson Soo-Hoo, *Extemporaneous Formulations*, The Children's Hospital of Philadelphia, American Society of Health-System Pharmacists, Bethesda, Maryland.

Milap C. Nahata, Vinita B. Pai, and Thomas F. Hipple, *Pediatric Drug Formulations*, 5th edition. Cincinnati: Harvey Whitney Books Company.

Lawrence A. Trissel, *Trissel's Stability of Compounded Formulations*, 3rd edition. Washington, D.C.: American Pharmacists Association Publications.

**Table 6.9.** Extemporaneous formulations.

| Drug | Desired Concentrations | Formulation | Duration of Stability | Evidence for Stability |
|---|---|---|---|---|
| Carprofen | 1.25 mg/ml<br>2.5 mg/ml<br>5.0 mg/ml | 25 mg tablets of Rimadyl (crushed 100 times) mix 1:1 with a 1:1 mixture of Ora-Plus and Ora-Sweet, then diluted to desired concentrations<br>OR<br>25 mg tablets of Rimadyl (crushed 100 times) with 1% methylcellulose gel, then diluted to desired concentrations | 21 days refrigerated | Hawkins et al. 2006 |
| Meloxicam | 0.25 mg/ml<br>0.5 mg/ml | 1.5 mg/ml Metacam in deionized water* or in 1% methylcellulose gel | 28 days refrigerated | Hawkins et al. 2006 |

* Distilled water can be substituted for deionized water, according to the authors.

with the *Compliance Policy Guide*, all of which is available on their Web site (www.avma.org).

For those veterinarians who consider compounding under certain circumstances, for example, when financial conditions do not permit the use of labeled product, due consideration should be given both to proper compounding (or selection of a good compounding pharmacy) and to the liability should an adverse event occur. Products made from bulk drugs do not undergo the same manufacturing requirements as approved commercial drugs do, and there will always be issues of potency and safety (there is no warranty or guarantee as to how much actual drug is present in the bulk product). The author is aware of compounded itraconazole products made from bulk drug that contained considerably lower concentrations of active drug than was on the label. Purchasing one's own bulk drug is fraught with the same problems and must be advised against. If compounding is being considered, it should be remembered that pharmacists are specifically trained in compounding practices. Their expertise should be consulted to avoid the production of impotent or dangerous products. In addition, there are multiple published resources with stability data for compounded formulations of many drugs (see Table 6.8). Many of these are available in medical libraries, at veterinary teaching hospitals, or even local human hospitals or pharmacies. Table 6.9 contains the published stability information on a couple of compounded formulations that might be used in shelter medicine.

Finally, state Veterinary Practice Acts as well as Pharmacy Practice Acts should be reviewed for locally acceptable or unacceptable practices when it comes to compounding.

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# 7
# Necropsy Techniques

*Patricia A. Pesavento*

## INTRODUCTION: WHY AND WHEN SHOULD A NECROPSY BE PERFORMED?

The loss of an animal is always discouraging, but it does provide an opportunity to gain valuable insight on diseases, treatment, and husbandry practices. One of the most important things a shelter can do to better manage disease is to obtain as much information as possible from any animal that dies. Consider, for example, the situation faced by the shelter given below:

> *Linda is a technician at Metro City All-Paws Rescue. She has noticed that, over the last month, the mortality rate in the feral cat room seems quite high. She checks the records and confirms that, in the past month, 8 out of 40 cats have died. In the previous month, five cats had died. Averaging over the year prior, the monthly mortality was one death per approximately 40 cats total. After consulting with the team, they recognize that many of the recent deaths have been associated with both upper respiratory (URI) signs and skin abscesses. Limited diagnostics had been performed on affected cats, and both herpesvirus and calicivirus were found by oropharyngeal swab samples.*

In the case of contagious disease or herd husbandry problems, a necropsy performed on sentinel cases could potentially save the lives of dozens of animals. In our example above, premortem diagnostic tests had been performed on some of the animals that had died, but the agents detected were common in the shelter environment and were therefore not convincingly the cause of death. Moreover, it was unclear to the shelter staff whether the URI or the abscesses were related to the animals' deaths, to each other, or just coincidental findings. An unexplained increase in mortality is one of the most compelling reasons for a shelter to perform a necropsy. Following is a partial list of other reasons, with specific attention to those significant to a shelter:

1. When there is unexplained death, or deaths, in the population
2. When there is the possibility that contagious disease could affect other shelter animals (which includes limiting future losses)
3. When zoonoses are suspected (when contagious disease from an animal could affect human workers or visitors)
4. To evaluate effects of treatment, especially when a new treatment is involved or if a reaction to a drug or disinfectant is suspected
5. To document the accuracy of a diagnosis
6. To document a legal case (e.g., suspected poisoning, suspected abuse)
7. To enhance discussion of health maintenance programs with animal shelter specialists

The estimated population size of shelter animals is 6 million to 25 million, the variation arising from the types of shelters included in the estimate. This number is roughly equivalent to the number of dairy cows in the United States and Canada, which is approximately 9 million (MacDonald, O'Donoghue et al. 2007). Like the dairy industry, shelters are intensive housing situations where transmission, exposure, and susceptibility to infectious disease are heightened. Necropsy is commonly used in large animal herd health to track infectious disease; hundreds of clinicians and pathologists are singly devoted to perform large animal diagnostics in the U.S. and Canada, and much of the diagnostic work is state and/or federally funded. In contrast, few states support necropsy or diagnostics of nonprivately owned, small, companion animals. In shelters, there is a

need for more methodical scrutiny for emerging diseases, infectious diseases, and zoonoses. Multiple studies in both the human and veterinary literature have found necropsy to be the most accurate method for collecting effective diagnostic samples, assessing diagnostic accuracy, and predicting disease emergence. The purpose of this chapter is to provide practical guidelines and list resources available for performing necropsies and for collecting, storing, and shipping samples for diagnostic testing.

For ideal infectious disease surveillance an accredited pathologist would examine all deaths at a given shelter. This is not an option for most shelters. Full necropsy services at state diagnostic laboratories or at veterinary schools are variably available and at variable cost for small animals. In contrast, performing a necropsy at a shelter and storing samples (for possible future examination) is relatively inexpensive and both biopsy services ("necropsy in a bottle") and microbiology services are readily available. Shelter personnel need to be trained to perform necropsies and properly sample cadavers as part of the overall healthcare plan for assessment and maintenance of the continued health of their shelter population.

## WHY SAMPLE TISSUES AT NECROPSY?

Outcome from infectious illness is directly proportional to time to pathogen identification.

Sample collection is one of the most important reasons for a shelter to perform a necropsy (see Figure 7.1). Samples collected at necropsy can be used for culture, cytology (impression smears), polymerase chain reaction (PCR), serology, histological analyses, and other tests. For example, nasal or oropharyngeal swabs from live, affected animals with clinical signs of pneumonia may reveal significant, coincident, commensal, or opportunistic viral or bacterial pathogens. In contrast, if a dog in an outbreak is euthanized or dies with severe respiratory disease, microbiological or molecular detection and identification of pathogens taken directly from a lung tissue sample can narrow or pinpoint etiology with great precision. Distinguishing the key pathogens in an outbreak of disease is very important to a shelter: sensitivity studies on significant isolated bacteria, for example, would help in treatment plans for other dogs in the shelter.

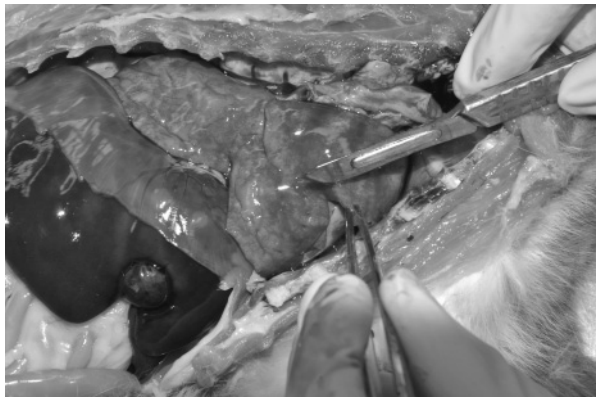

**Figure 7.1.** The prosector takes a sample of lung. Samples taken for microbiological analysis (culture or PCR) should be taken first during a necropsy. Use a sterile scalpel blade or scissors to take a section, and/or use a sterile swab to sample.

Necropsy has its limitations, and necropsy findings can be inconclusive as to the actual cause of death. Some conditions are simply not characterized by lesions that can be detected either grossly or microscopically. However, as a method to rule in or out infectious (contagious) versus other causes of death (toxin, neoplasia, trauma, heat stroke), the necropsy is extremely accurate. It is the intention of this chapter to put clinicians in a confident position to collect samples correctly so that the best material is available for analysis and diagnosis.

## THE NECROPSY

### General considerations

To complete an effective necropsy, specific and consistent protocol (procedure, sampling, documentation) should be followed. The optimal time to perform a necropsy is as soon as possible after the animal's death. Depending on environmental conditions, changes in tissues occur in minutes after an animal has expired. Since these changes may obscure the true cause of death in an animal, it is important, for an accurate diagnosis, to take appropriate tissue samples for culture and/or microscopic examination in a timely fashion.

While a complete necropsy is optimal for disease surveillance or in most forensic cases, it is a substantial time commitment. Any animal that dies should be examined to the best of one's time and ability; however, a necropsy performed specifically for the purpose of sample collection can be much shorter (collecting gastrointestinal samples in a dog with diarrhea to rule in or out parvovirus, for example). Here are a few important considerations before performing a necropsy:

1. Zoonoses: Be aware that animals in the shelter may have a disease that is transmissible to humans (zoonosis), and even more likely, a disease transmissible to

other animals. The situation postmortem is no different from when the animal was alive; however, exposure to some agents is higher when a necropsy is performed [bloodborne pathogens (e.g., anthrax, rabies), some fecal pathogens]. The necropsy should be performed in a quiet, isolated, well-aerated space. Precautions should be taken consistently (protective clothing, gloves, mask) during a necropsy, and any unfixed tissues should be placed in leak-proof containers or disposed of as medical waste according to the protocols specified by the state or institution.

2. Handling cadavers: If the necropsy cannot be carried out immediately, store cadavers in a refrigerator (+2 °C to +4 °C) as soon as possible after death, until the necropsy can be performed. Freeze a cadaver only if absolutely necessary, since histological interpretation is compromised by "ice artifact" (crystallization of tissues). The cadaver can be frozen if there is no one available to perform the necropsy for an extended period of time. It is important to be aware that while still present in tissue some microbes will not be viable after freezing.
3. Euthanasia: Euthanasia policy and strategy is widely variable among shelters. It is important to work within the established guidelines of a shelter. Consider an outbreak situation with a high rate of mortality, for example. If a shelter has a "no kill" policy, necropsy examination would be limited to animals that have died or been euthanized as a result of terminal disease. In those shelters that do euthanize animals, it may be beneficial to perform a necropsy on a more recently affected or moribund animal. It is important to select an animal that is showing clinical signs of the disease and one that represents other animals in the group who are affected with similar signs. Be attendant to the clinical history (including duration) and to any therapy. If an animal has received recent antibiotics, for example, there is substantial risk that a causative bacteria would fail to be cultured. The method of euthanasia should always be documented. There are both gross and histologic sequelae to any form of euthanasia, and it is important to understand whether a lesion is "real" or simply related to the method of euthanasia. For example, intra-abdominal administration of pentobarbital can result in puncture trauma, a layer of chemically induced necrosis on the surfaces of abdominal organs, or in perimortem intra-abdominal hemorrhage (see Figure 7.2).

Intravenous injection can cause trauma and hemorrhage in the region overlying the vein used for the injection. The method of euthanasia should avoid, as much as possible, obfuscation of the disease process. For example, because euthanasia solution is caustic, intra-abdominal administration of euthanasia solution is not the best route of administration if an animal has enteric (gastrointestinal) disease.

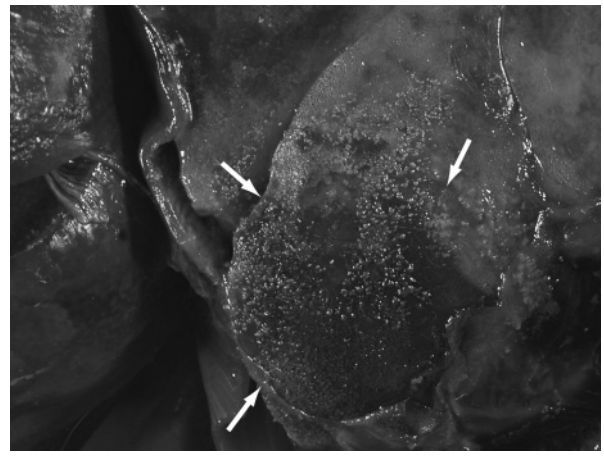

**Figure 7.2.** Euthanasia can cause artifactual changes to tissues. Here the granular, dull texture of the region of lung defined by the arrows is caused by intrathoracic contact with beuthanol during an intracardiac euthanasia.

## Documentation

### *Written data*

Premortem information: Historical and clinical information are equally as important in your investigation as transcribing observations at the necropsy. Premortem information includes clinical signs, date of intake, and onset of illness, location held in shelter, and treatments received. Especially in a shelter, this information is necessary to identify patterns of susceptibility to disease over time, whether geographical, age related, treatment associated, time of year, etc. This information is also essential to interpret the necropsy and histological lesions, and/or to compare future or past cases. Premortem and historical information can be written on a separate form or can be included on the necropsy form itself.

Necropsy results: There are several well-organized necropsy templates available (see below, resources), and a shelter should have copies of one of these on hand. Which directions, form, and/or template is used is not important; they are designed to remind the prosector (person doing

the dissection) to be methodical, thorough, and consistent. Try to be as objective as possible in reporting observations; specifically, describe abnormalities without presuming cause (without adding interpretation). For example, if the liver appears large, the organ should be weighed or, if there is no scale, describe how this interpretation was made: "The edges of the liver lobes were rounded and the caudal aspect of the liver extended to . . . ." The features (shape, position, color, consistency) should also be noted if the liver is abnormal. In this same example, the objective gross diagnosis is hepatomegaly, or large liver (a suspicion of cause can be noted, but recognized as such). Interpretation of organ size based on weight relies on its comparison (ratio) with the body weight of the animal.

Documentation of normal and abnormal findings is not only important for interpretation of individual lesions but also necessary for the health of the shelter: shelters that have cases that appear before the state board or media will be scrutinized for their management of an outbreak. If an organ or system was not examined, this should also be noted (for example, if only the abdominal cavity and gastrointestinal system were examined, there should be a note on the report saying that the thoracic cavity was not examined).

***Photographic data***

Visual data can have great importance in the communication of necropsy findings, and with digital hegemony, most shelters own or have access to a digital camera. Photographic data is complementary to the written description of a lesion and can be even more persuasive than a written report in the legal documentation of findings. However, a photograph should never be substituted for a written record. The combination of words and pictures is vital for communication, and two-dimensional photographs can only rarely fully represent the texture, cut surface, depth, and extent of any single lesion or systemic process.

## STEPS IN PERFORMING A NECROPSY

A list of the instruments and equipment needed to perform a necropsy can be found below.

### The necropsy, materials needed

Not all of the listed tools will be needed to perform each necropsy, but this is a good starting list of the things that should be on hand for any given situation. Maintaining a devoted "necropsy kit" can save time.

1. Camera
2. Notebook or pathology form
3. Protective clothing
   - Gloves (latex, nitrile, or rubber)
   - Boots
   - Mask (to cover mouth and nose)
   - Eyewear or goggles
4. Instruments
   - Sharp knife (and/or scalpel)
   - Knife sharpener
   - Scissors
   - Forceps
   - Small shears
   - Ruler
5. Collection gear
   - Specimen container (plastic) with tight-fitting lid for fixed samples (plastic tubs, Rubbermaid, specimen cups, Tupperware type)
   - 10% buffered formalin (for fixed specimens/histology)
   - Plastic bags with closure (whirl-pack, zip-lock) for unfixed samples(fresh or frozen)
   - Tags (to identify specimens)
   - Collection vials (can be used for urine, blood, joint fluid, etc.)
6. Transport/shipping containers
   - Ice packs
   - Heavy-duty bags or leak-proof containers
   - Packing material (preferably absorptive)
7. Disinfecting/cleaning materials

### General information

Remember that while there is no single correct method to perform a necropsy, consistency is important. If a cadaver is opened in the same way for each necropsy, one is more likely to recognize abnormalities of any sort, e.g., size, position, color. Even in the case where the animal's disease appears to be limited to, for example, the respiratory system, the author recommends that the animal's body be opened in the same way so that both body cavities are examined visually. Respiratory distress can arise from abnormalities in organs not present within the thoracic cavity, and concurrent diseases, if present, can be very important to disease progression. The most common example of this that is seen in shelters is immunosuppression (caused by, for example, certain viral diseases, like parvovirus), predisposing an animal to a "secondary" infection, such as bacterial pneumonia.

Step-by-step instructions on how to perform a necropsy are available from a number of books and Web-based sources. Five sources are listed below. While not all of these protocols specifically use dogs and cats as models,

the general approach to a necropsy is similar in all domestic species. The fourth listed resource by Severidt et al., for example, although specifically addressing cattle, has an excellent section on sample handling and submission. The fifth listed resource by Sinclair et al. is a reference for forensic-style necropsies. The purpose, style, and documentation of a forensic necropsy differ from the necropsy described in this chapter, whose aim is to establish the cause of common or emerging infectious shelter disease.

**Resources for performing a complete necropsy:**

1. The Armed Forces Institute of Pathology, Department of Veterinary Pathology www.afip.org/vetpath/ddpdf/dd1626.pdf#search=%22necropsy%20tissue%20checklist%22 (or search AFIP, veterinary pathology, Form 1626). This site provides a form (DD Form 1626) maintained by the Armed Forces Institute for Pathology (AFIP), Division of Veterinary Pathology. It is a comprehensive, 12-page document with sections for data and interpretation (pp. 1–2), gross necropsy findings (pp. 3–8) and a detailed necropsy protocol (pp. 9–12). Included (p. 7) is a tissue checklist to record tissues collected during the necropsy.
2. *The Necropsy Book*, 3rd edition by Drs. John M. King, David C. Dodd, and Lois Roth. This guide is available for purchase at the CL Davis Foundation publications site (www.afip.org/CLDavis/Pub_on_demand.html). It is widely used by veterinary schools to teach basic necropsy techniques to veterinary students and is an inexpensive manual that contains an organ-based approach to a necropsy, including many drawings. The information on patterns of lesions is particularly useful for making the best decisions, at the gross necropsy, for sample collection.
3. *Necropsy of Wild Animals*, by Linda Munson DVM, Ph.D. This is a PDF document available on the Web, composed by Munson and maintained by the University of California's Wildlife Health Services (www.vetmed.ucdavis.edu/whc/pdfs/necropsy.pdf#search=%22munson%20necropsy%20wildlife%22). It is an excellent reference for the steps in a complete necropsy, including drawings, and the "models" are felines and canids. The site includes a comprehensive tissue checklist for collection of samples during a necropsy.
4. *Dairy Cattle Necropsy Manual* by Severidt, Madden, Mason, Garry, and Gould. This is a Web-based set of directions, with color photographs, for necropsy of a ruminant. It is available from Colorado State at www.cvmbs.colostate.edu/ilm/proinfo/necropsy/notes/INDEX.HTML. The color pictures and video clips are very useful, and it has a well-thought-out discussion of considerations for sample shipping and herd health problems that are very relevant to those seen in the shelter.
5. *Forensic Investigation of Animal Cruelty: A Guide for Veterinary and Law Enforcement Professionals*, by Leslie Sinclair, Melinda Merck, and Randall Lockwood. This book is a valuable resource for shelter personnel who are confronted with potential animal cruelty cases. Included are examples that well illustrate the problems, pitfalls, and best approaches to individual cases and a number of important topics. For detailed guidelines regarding forensic necropsies, *Veterinary Forensics* by Melinda Merck is also recommended.

## Opening the animal for analysis and sampling

It is important to think about the samples that should be collected prior to the necropsy and to have the materials at hand that are necessary for collection. Samples destined for microbiology or other infectious disease diagnostics should be taken first, with sterile instruments if possible, and with minimal handling. If a sample needs to be refrigerated or frozen, do so as soon as possible after collection. While many premortem tests can be performed postmortem, tissues collected postmortem, if collected properly, can be more accurate for establishing cause of disease: For example, a culture of lung tissue to diagnose a bacterial cause of pneumonia is more accurate than a culture from an oropharyngeal swab, which would additionally contain a number of potential commensal bacteria.

### *Necropsy analysis and sampling, a beginning*

1. Place the carcass on its left side.
2. Assess the general condition. Determine the nutritional state of the animal. This can be done using a body condition scoring system, but should also include looking for external (subcutaneous) and internal fat stores. In most animals, stores of fat surrounding the kidney and the heart are the longest retained, so these should be specifically examined if emaciation is suspected. Note the muscle mass of the animal.
3. Oral exam. Note the condition of the teeth; look for masses or ulcers on the lingual, buccal, and/or gingival mucosa.
4. Cut the skin along the ventral midline from the chin to the tail.
5. Reflect the right limbs by cutting through the muscles to the hip and shoulder joints. Reflect the skin to the level of the backbone (see Figure 7.3).

**Figure 7.3.** Prepare to open the animal by reflecting the skin. A cut along the thin, black solid line will reveal the abdominal cavity; continue the incision across the pelvic region and along the ventral midline. Open the thoracic cavity by cutting the ribs along the dotted line to the thoracic inlet and finish the opening by cutting each rib just dorsal to the vertebrae.

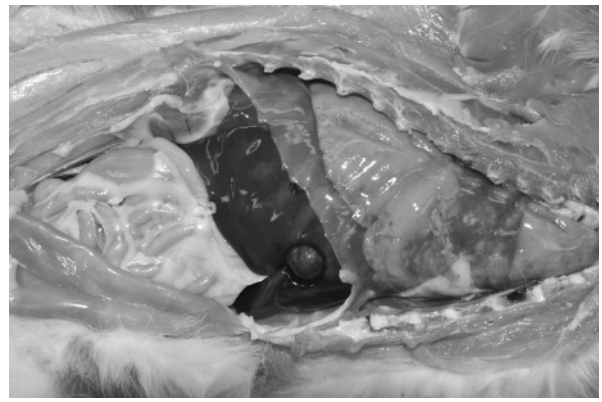

**Figure 7.4.** A properly opened body ready for diagnostic sampling.

6. Open the two body cavities (abdomen, chest):
   a. Open the abdominal cavity by cutting through the body wall musculature along the caudal border of the ribcage, and extend the cut to the pelvic region. Open the right side of the chest cavity by cutting the ribs along the sternum and adjacent to the backbone (see Figure 7.3).
   b. Record any abnormal locations or sizes of organs.
   c. Record the quantity, color, and contents of any fluids in the body cavities.
   d. Note the amount and quality of food in the digestive tract.
   e. If samples of organs are to be taken for culture or microbe analysis of any type, do so early, before they have been removed and handled. A description of the best samples to take for common shelter problems is provided in the next section.
7. For samples destined for histopathology, use a sharp knife or scalpel, hold tissues at the edges only, and quickly place in formalin. If a complete necropsy is desired (if there is a sudden death, for example), samples should be taken from all listed organs (refer to the tissue checklist), including normal and abnormal regions. Samples that include both abnormal areas and surrounding normal areas are best. Do not scrape the surfaces of tissues. Histopathology samples from any organ should be no thicker than 1 cm so that formalin penetration of the tissue is adequate, but take multiple samples so that they represent the range of lesions (see Figure 7.4).
8. Specific tissues to sample in the case of gastrointestinal or respiratory disease are listed separately below. For shipping, if the appropriate ratio for fixation has been used (10 formalin:1 tissue), and there has been an appropriate time of fixation, some formalin can be removed once the specimen is fixed. Waste formalin is considered a hazardous waste and must be handled following current state and federal regulations, as well as U.S. Environmental Protection Agency guidelines. This is important when multiple samples are collected since OSHA and Transportation Safety Regulations limit the size and quantity of formalin containers that can be shipped. Proper fixation depends on sample size and the density of the tissue. For properly cut samples of most visceral organs, 24 hours is usually sufficient. For shipping samples, use an FAA-approved leak-proof container, place it in a ziplock plastic bag, and then in a second outer bag that contains the clinical history and request. Remaining samples can be placed and stored in a large plastic container of formalin in case additional samples are needed.
9. Examine organ systems in a methodical manner, which can be guided by any one of the resource sites listed in the previous section. Have a tissue checklist on hand.

***Tissue checklist for necropsy***

Preserve the following tissues in 10% buffered formalin at a ratio of 1 part tissue to 10 parts formalin. Tissues should be no thicker than 1 cm.

1. Liver: sections from each lobe, including the gall bladder
2. Kidney: sections should extend from cortex to medulla and be collected from each kidney (see Figure 7.5)
3. Stomach: sections from fundus (body) and pylorus
4. GI Tract:
   a. Oral/pharyngeal mucosa and tonsil, plus any areas with erosions or ulcerations
   b. Tongue: cross section near tip including both mucosal surfaces

   **Segmental (up to 5 cm long) sections of:**
   c. Esophagus
   d. Small intestines: duodenum, jejunum, ileum
   e. Large intestines: cecum, colon
5. Spleen
6. Pancreas
7. Adrenal gland
8. Heart: longitudinal sections including atrium, ventricle, and valves from both left and right sides.
9. Lung: regional samples including cranioventral, caudodordsal, and hilar with major bronchus included
10. Lymph nodes: possibilities include iliac, mesenteric, hilar, mandibular, and retropharyngeal
11. Thymus: if young animal

**Other possible tissue sections to consider (case dependent):**

12. Skin: any affected regions
13. Brain: if there are neurologic signs, the entire brain should be submitted cut longitudinally along midline
14. Reproductive tract: the entire uterus and ovaries with longitudinal cuts into lumen of uterine horns, or both testes (transversely cut) with epididymis
15. Salivary gland
16. Trachea
17. Nasal turbinates
18. Thyroid/parathyroids: leave intact
19. Urinary bladder, ureters, urethra: cross section of bladder and 2-cm sections of ureter and urethra
20. Eye: intact
21. Spinal cord (if neurologic disease): sections from cervical, thoracic, and lumbar cord
22. Diaphragm, skeletal muscle: cross section of thigh muscles
23. Bone marrow: opened rib or longitudinally sectioned one-half femur; marrow must be exposed for proper fixation

## THE DIAGNOSTIC SHELTER NECROPSY

Consider the following case history:

*There is an outbreak of diarrhea, with a concurrent increase in mortality, in cats and kittens in a large municipal shelter. Several cats and kittens have been found dead within the past few weeks. The bodies were disposed of and the cages cleaned thoroughly but even with isolation procedures in place, the number of affected animals appears to be increasing. The shelter manager and part-time veterinarian at the shelter are very concerned. They both suspect that the virus feline panleukopenia is the culprit. Animals are vaccinated at intake and*

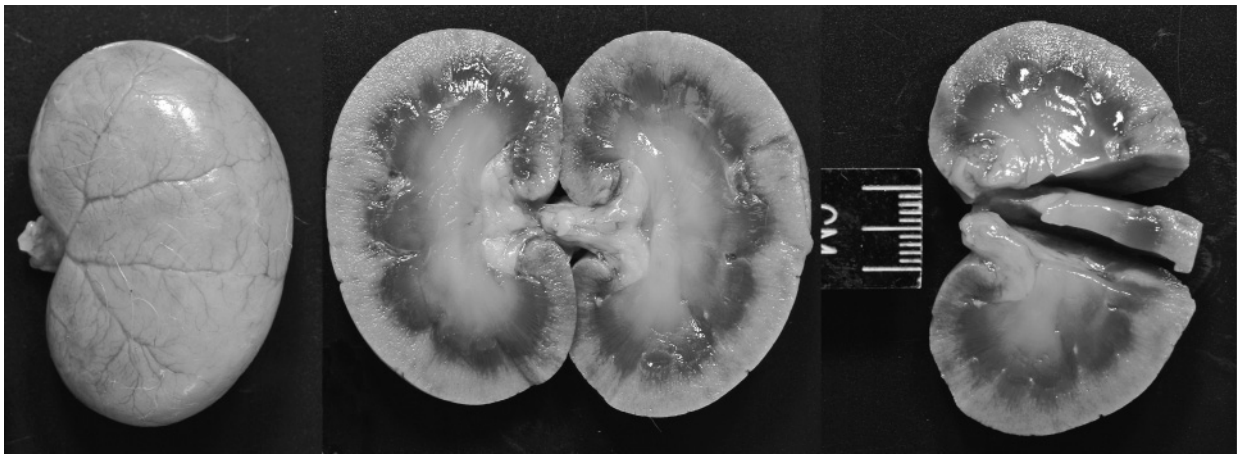

**Figure 7.5.** Sections to be submitted for histological analysis need to be thin enough to properly fix in formalin. In this example, the (a) kidney has been cut along a (b) mid-sagittal plane. (c) A properly cut section is pictured for fixation in 10% buffered formalin.

*every 3 weeks during their stay, but the disease presentation seems more aggressive than they have seen in the past, and several older cats have been affected. A fecal antigen test was performed on two affected animals, but the result was negative for viral antigen on the first and weakly positive on the second animal. Although apparently well yesterday, a cat and a 3-month-old kitten were found dead at morning rounds. They believe both animals are part of this outbreak, although diarrhea was only seen in the cat's and not the kitten's cage. What is the best way for staff to establish the cause of gastrointestinal disease in their feline population?*

This scenario is not at all uncommon in shelters. If accurate (sensitive and specific) premortem tests are available and results are consistent in affected animals, a cause for increased morbidity and mortality is comfortably assigned. However, there are many reasons why a shelter might seek additional information on a disease (less sensitive test, unusual presentation for a disease, unusual behavior of disease in a population, nonresponsive to treatment for that disease). In this case, although feces from one cat tested positive for the presence of feline panleukopenia virus, the disease seemed to be occurring in the face of vaccination and isolation and was occurring in animals less commonly associated with the suspected disease (older animals).

Staff are understandably very busy and need to efficiently diagnose the problem. What should they do? The tests have been somewhat equivocal and doing full necropsies on each of these animals seems like it would be very time consuming; moreover, they are not sure whether the gross exam will be helpful since they are not exactly sure what they are seeing.

Just as a complete physical exam is needed to establish a clinical picture of a sick animal, a complete necropsy would be needed in each case of death to establish a definitive cause and to identify systemic problems that might have contributed to the death or disease of an individual animal. However, in a shelter (herd) situation, it is sometimes practical, sufficient, and time efficient to ask a more specific (limited) question about disease or death of an animal.

Gastrointestinal and respiratory diseases, in particular, are frequent problems in a shelter. To ask a more limited question of a necropsy means that the necropsy itself can be simplified. Necropsy samples can be the best samples to definitively diagnose a cause of disease, and proper necropsy sampling in a sentinel case or an infectious outbreak will save other animals.

**Sampling a carcass, general considerations**

The success of infectious disease diagnosis depends largely on the quality of the specimen and the conditions under which the specimen is transported and stored before it is processed in the laboratory. It would be naive to generalize; depending on the suspected agent and the test, the optimum sample and optimum conditions for stabilization during transport are variable. For example, if a bacterial agent is suspected, freezing the specimen could compromise future culture; however, DNA would remain intact and a PCR test relying on extracted bacterial DNA would be fine. Some viruses, on the other hand, can withstand freezing, especially if samples are stored in the proper media. There are specific transport media that stabilize viruses and prevent bacterial overgrowth. What this means, of course, is that if the cause of disease is completely open, and multiple tests are going to be performed, multiple types of samples are necessary. Collection is simpler if a certain agent is highly suspect, or if a single agent needs to be ruled in or out.

Because gastrointestinal disease and respiratory disease are the most common infectious diseases associated with morbidity and mortality in the shelter environment, the following section is devoted to the sampling of a cadaver in these types of outbreaks.

**Necropsy and sampling for gastrointestinal disease**

The following sample collection would be a good starting point for sampling any enteric disease (diarrhea and/or vomiting) of unknown origin in both dogs and cats. While causes for diarrhea can be remote from the gastrointestinal system (heat shock, for example), most contagious (infectious) or toxin-associated GI disease results from direct attack on the gastrointestinal system. Moreover, distribution of lesions (grossly) is very helpful in determining cause of disease.

1. Feces: If abundant, collection can be made from the distal colon. Even if scant, feces can be scraped from the colonic mucosa. Postmortem feces are useful samples for multiple tests, including fecal antigen test (parvoviruses, see below), for direct smear/fecal flotation/parasite analysis, or for viral analysis by direct electron microscopy (DEM) or viral culture. Only specific diagnostic laboratories or veterinary schools would offer the latter tests (DEM, viral culture). DEM is a fast and specific test for visualizing most enteric viruses, including parvovirus, coronavirus, and rotavirus. If collecting formalin-fixed tissue, collect tissue from an undisturbed (unsampled) region of the colon (mucosa is fragile and will slough easily with handling).
2. Formalin-fixed tissues: Histological samples should be taken in all cases, no matter what supplementary diag-

nostic tests you choose. Histology can be pathognomonic (definitive), it can direct you to possible causes, or it will confirm or refute the results of other diagnostic tests. A general list for sampling an animal with enteric disease is found below. In nearly all cases, these samples would be sufficient to diagnose or exclude common shelter enteric pathogens. In cases where the agent or cause is unexpected, these samples would establish whether an enteric disease is inflammatory, infectious (contagious), toxic, or neoplastic.

**Tissue checklist for gastrointestinal disease**
Tissues should be no thicker than 1 cm. Tissues should be placed immediately in 10% buffered formalin at a ratio of 1 part tissue to 10 parts formalin.

a. Duodenum: two (up to 5-cm long) segments.
b. Pancreas: 1-cm section, can be left attached to the duodenum.
c. Jejunum (proximal, mid, distal): at least three (up to 5-cm-long) segments.
d. Ileo-ceco-colic junction: These regions can be sampled individually, or this region can be taken in its entirety. If the latter is chosen, open the sample enough that formalin can perfuse the mucosa throughout the section. Do not scrape or touch the mucosa while handling (see Figures 7.6 and 7.7).
e. Colon (distal): one sample (proximal is included in sample "d" above).
f. Liver: up to 1-cm-wide sections (from all distinct lobes, including gall bladder)
g. Mesenteric lymph node
h. Any regions you perceive are abnormal or different.

3. Microbiology: screening for bacterial or fungal organisms of significance can be done on feces, small intestinal contents, or a combination of both. Be aware that antibiotic therapy can skew or prevent culture of many bacteria. Any premortem therapy should be noted in the submission form and on the necropsy report. Culture for significant enteric bacteria often requires selective media or selective conditions (enrichment or anaerobic conditions). Feces can be collected in any number of different sterile or clean containers, including bags, urine cups, or tubes. If feces are submitted, specify on the request that *significant* enteric organisms (such as *Salmonella*, *Clostridia*, and *Campylobacter*) are of concern. Culture results need to be correlated with histological findings; *Clostridia*, for example, can be cultured from normal intestines and *Salmonella*, although always significant for herd health and zoonotic reasons, can be shed asymptomatically in cats and dogs. Be aware also that so-called commensal (usually nonpathogenic) organisms can become virulent (e.g., some strains of *E. coli*). Diagnosis in these cases would require a combination of histological and microbiological results, or specialized microbiological analysis. Specimens destined for culture should be transported

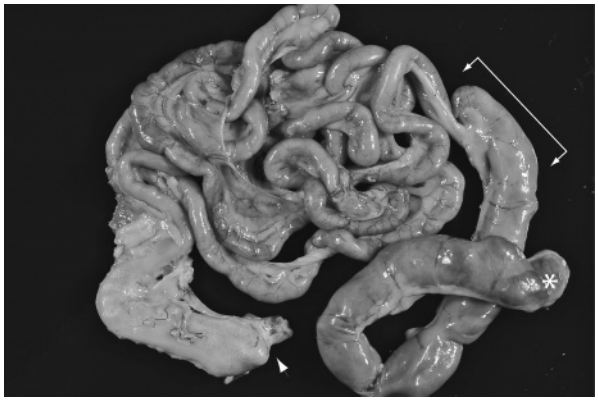

**Figure 7.6.** The intestines, extending from the gastroesophageal junction (arrowhead) to the distal colon (asterisk) have been removed. In the case of gastrointestinal disease (or for any complete necropsy) the ileo-ceco-colic junction (bracketed by arrows) is one of the important sections for submission.

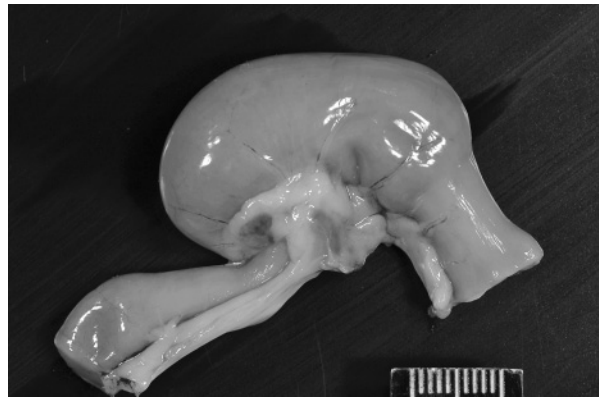

**Figure 7.7.** The ileo-ceco-colic junction is pictured. The intestine can be opened along a sagittal plane for greater penetration of the formalin fixative.

and processed as soon as possible. Delays of over 48 hours are undesirable. If processing is delayed, refrigeration is preferable to storage at ambient temperature; freezing will kill many types of bacteria (see adjunct diagnostics).

4. Molecular diagnostics: Detection and characterization of pathogenic organisms increasingly relies on DNA or RNA amplification techniques (PCR). These samples need to be taken early in the postmortem, using sterile techniques, and from tissue that has been minimally manipulated. DNA or RNA from the infectious agent will degrade at rates dependent on time, environmental factors (temperature, pH) and the organism itself. Ideally, samples from affected organs are fresh or fresh/frozen for molecular analysis. PCR from fixed or paraffin-embedded tissues is laboratory dependent. Most diagnostic laboratories or veterinary schools can offer guidance and a list of possible tests, the preferred or potentially useful tissue samples, and the preferred method of shipment. Whole blood (e.g., heart blood) or highly vascularized tissues (spleen, liver, lung) are reliable sources for circulating infectious agents (septicimia, viremia, or hemoparasites). Individual PCR tests and enteric PCR "panels" are available in many commercial laboratories and veterinary schools. For enteric disease, feces are usually the sample of choice for DNA retrieval, but individual laboratories vary and should be consulted directly. There are important considerations for whether and when to use PCR for diagnostic analysis. First, PCR is highly sensitive. This is a powerful argument for the usefulness of the test, but also the basis for caution. False positives can occur as the result of sample contamination (environment, handler) or recent vaccination. All results should be considered in the context of clinical information, including disease, treatment, and vaccination history. For accurate assessment of causation, PCR results should be correlated by histopathological analysis of formalin-fixed tissue**.** For example, if *Salmonella* spp. is detected by PCR, the correlative lesion of *Salmonella* associated gastrointestinal disease is an acute and necrotizing enteritis. It is true that if many cases in a single outbreak are evaluated by a single test, correlation and causation can be established by epidemiology (e.g., only and all cases of enteric disease are positive for *Salmonella*). However, this can be both unfeasible (depending on the incidence of disease) and expensive. Using histopathology correlated with PCR (or a number of other diagnostic tests) can establish causation in an individual animal. Second, while PCR is an excellent way to rule out known causes of disease, most diagnostic PCR assays are not designed to detect newly emergent disease. This is another reason to include histological analysis of tissues in the diagnostic plan: By ruling out common diseases, a newly emergent cause for disease can be more quickly identified. Remember, the most difficult emergent diseases to recognize and identify are those that mimic known diseases. For retrospective analyses, DNA can also be extracted from tissue embedded in paraffin; however, this is offered by a more limited number of laboratories.
5. Toxicology: It is best to contact a toxicology laboratory, state laboratory, and/or a poison control center such as the ASPCA (www.aspca.org/apcc) for guidance. The appropriate sample for analysis is dependent on the type of toxin, among other variables. In the case of gastrointestinal illness, source (food) and stomach contents should be saved. For heavy metal analysis, samples of liver and kidney should be collected, placed in separate plastic bags, and frozen until submitted. If a toxin is suspected, but unknown, perform a necropsy, and in addition to histological samples, freeze the liver, kidney, fat, stomach contents, and muscle.
6. Serology: Serodiagnostic tests are tests performed on serum or plasma to detect either the presence of antibodies to a particular pathogen or the presence of circulating antigens from the pathogen itself. Both of these types of tests can be performed postmortem, on serum obtained from a pooled blood source (heart, major veins). The significance of the result should be considered before this particular technique is used; few tests are validated for postmortem serum. Nonetheless, a positive titer is generally considered significant. In a shelter situation, this type of testing could be used to determine whether individuals in the population have ever been exposed to a particular disease-causing agent or in population health monitoring.

***Parvovirus (CPV, feline panleukopenia virus)***

In the shelter, the most common causes of intestinal disease associated with mortality are the canine and feline parvoviruses. Suspicion and caution for this disease, therefore, is high; however, no clinical or gross finding is specific to parvoviral enteritis. This is a good reason to perform a necropsy on a dog or cat that is either suspicious for parvovirus or even known to be infected with it.

1. Establishing cause:
   a. Tissues for histology: Necropsy with histology can confirm the presence of parvovirus and would be

important in ruling out parvovirus during an investigation of an unusual outbreak of GI disease. Acute cases of parvovirus are nearly pathognomonic by histological analysis, and chronic (historic) cases can also be detected by a pathologist; the architecture of the small intestine is not restored to normal for 2 to 3 weeks postinfection.

b. Other tests: In dogs, although the parvovirus antigen tests on feces are highly sensitive during viral shedding in the early stages of infection, these peak viral titers are brief and occur at the time of, or prior to, the onset of clinical signs (Greene 2006). Subsequent viral shedding is known to fluctuate, and if the fecal antigen test is performed late after infection, virus in feces may be undetected. Testing of nearby recently exposed animals is warranted, and in an animal that has died, feces should be retested at the time of necropsy with fecal material collected from pooled segments of the lower intestine (duodenum, jejunum, and colon). Numerous cases of dogs or cats have been seen whose feces were negative 1 to 2 days prior to death and submitted for evaluation of "nonparvoviral diarrhea." These same animals were often positive by fecal antigen test at the time of necropsy, and in these cases there was concurrent histologic confirmation of parvoviral disease to establish etiology.

   The usefulness of the antigen test in cats is less well established. It is generally considered (K. Hurley, personal communication) to be less sensitive, but whether this is a repercussion of a lower viral titer or virus specific characteristics is unclear. Tissue and fecal samples from dogs or cats collected at the time of necropsy are also useful for PCR amplification of virus from feces or tissue. There is a higher sensitivity by using the PCR on infected tissues as compared with fecal antigen retrieval (Decaro and Elia 2005). In addition, many laboratories offer additional diagnostic methods on tissue samples such as immunofluorescence or immunohistochemistry.

2. Unusual presentation:
   The progression of any disease can vary greatly among affected animals. Among the factors that can alter the "normal" course of disease are coinfections, viral dose and virulence, and/or the animal's age, breed, and clinical presentation. Unusually "hot" forms of parvovirus have been documented, and verbal reports of "vaccine resistant" or unusual strains are more frequent. The most common form of canine parvovirus in the U.S. is strain 2b. Recently, parvovirus strains 2a (and 2c) have been identified in the U.S., and several of these cases are reportedly "unusual" (either age-affected, occurring in a vaccinated animal, or recalcitrant to aggressive therapy). Whether or not there are strains that can manifest with unique clinical progression is unknown, and information on vaccine resistance or altered test sensitivity is incomplete.
3. Concurrent disease(s):
   Parvoviral disease, even when suspected or confirmed clinically, may be exacerbated by concurrent infections with bacteria, *Giardia*, hookworms, or other enteric viruses such as coronavirus. Samples should be gathered that can potentially rule concurrent disease either in or out.

*Gross findings of parvoviral disease*

The gross findings of parvoviral disease, although caused by a similar virus, manifest somewhat differently in the dog and cat. It would be unlikely that a puppy or adult dog would die suddenly of parvovirus in the absence of dehydration, diarrhea, and other well-documented clinical signs. On the other hand, kittens can die peracutely of panleukopenia, with no preceding signs noted. On necropsy, dogs commonly have segmental to diffuse subserosal hemorrhage (reddening) that predominantly affects the small intestine (see Figure 7.8).

The small intestine can be flaccid and/or dilated. There will be scant ingesta within the intestinal system and no formed feces within the colon. On section of the small intestine, the mucosa is segmentally to multifocally

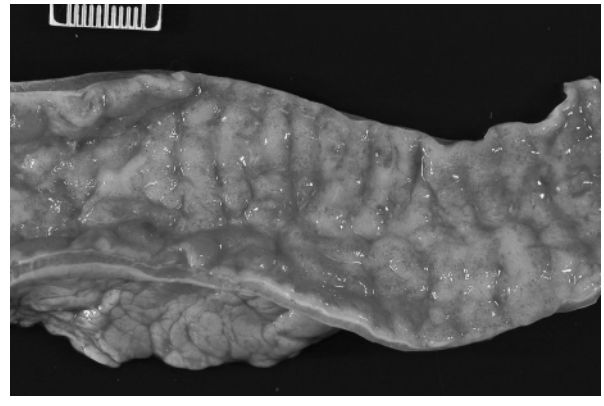

**Figure 7.8.** Canine parvovirus (CPV). The intestines are segmentally thick, edematous, and hemorrhagic, and the mucosal surface (pictured here) is dull and felt-like.

discolored tan to dark red (necrosis, congestion, hemorrhage). Peyer's patches, which are more concentrated in the distal small intestine and ileum, are (or can be) dark red (lympholysis).

In cats, the findings can be similar but are usually subtle. The small intestine is flaccid or dilated, but not always reddened, and the gastrointestinal contents, although typically watery or scarce, do not always contain blood. In both dogs and cats, the mesenteric lymph nodes are enlarged, congested and wet (edematous). Because the effect of panleukopenia on bone marrow and primary lymphoid tissues is quite predictable in the feline form of the disease, it is a good idea to include these tissues when performing a necropsy on either a dog or a cat.

**Respiratory disease, general**

The following collection would be a good starting point for sampling any respiratory disease of unknown origin in dogs or cats. While causes for respiratory distress can be remote from the respiratory system, most contagious (infectious) pneumonias or upper respiratory infections result from direct attack on the respiratory tissues. Gross lesions of the lung are difficult to interpret. This is, in no small part, because there are often perimortem lung changes, and such variability makes a baseline interpretation of "normal" very difficult. Histological samples are of paramount importance when trying to discern factors contributing to lung disease. In cats in particular, analyzing the upper respiratory tract as well as the lung is important; many common infections of the upper respiratory tract can contribute to fulminant respiratory disease, and severe URI is often interpreted as pneumonia (infection of the lower respiratory system).

1. Microbiology: In respiratory disease, depending on the lesions and clinical course, bacterial cultures can be taken from the nasal cavity, frontal sinus (swab immediately after opening), and/or lung. In general, because URI is so common in kittens and cats in a shelter, cultures should be taken from both the nasal cavity/sinus and the lungs. In dogs or cats with a clinical course clearly associated with the lower respiratory tract (pneumonia), lung tissue should be submitted. Accurate culture results require sterile technique. During a necropsy, these should be the first specimens taken, and the tissue should be minimally or not manipulated. This can be achieved by using sterile instruments and/or a swab stick or by placing a piece of tissue directly into a sterile container. Be sure to alert the microbiology laboratory that the specimen was taken at the time of necropsy. Antibiotic therapy can skew or prevent culture of many bacteria. Any premortem therapy should be noted in the submission form and on the necropsy report.
2. Molecular diagnostics: Fresh or fresh/frozen lung or upper respiratory tissue samples are necessary to diagnose agents contributing to pneumonia (former) or URI. These samples need to be taken early in the postmortem stage, using sterile technique, and from tissue minimally manipulated. DNA or RNA from the infectious agent will degrade at rates dependent on time, environmental factors (temperature, pH), and the organism itself. Ideally, samples from affected organs are fresh or fresh/frozen for molecular analysis. PCR from fixed or paraffin-embedded tissues is laboratory dependent. Most diagnostic laboratories or veterinary schools can offer guidance and a list of possible tests, the preferred or potentially useful tissue samples, and the preferred method of shipment.
3. Formalin-fixed tissues: Histological samples should be taken in all cases no matter what supplementary diagnostic tests are chosen. Histology can be pathognomonic (definitive), it can direct you to possible causes, or it will confirm or refute the results of other diagnostic tests. The following is a general list for sampling an animal with respiratory disease. In nearly all cases, these samples would be sufficient to diagnose or exclude common shelter respiratory pathogens.

***Tissue checklist for respiratory disease***

Tissues should be no thicker than 1 cm. Tissues should be placed immediately in 10% buffered formalin at a ratio of 1 part tissue to 10 parts formalin.

a. Nasal conchae, sinus
b. Trachea, one to two cartilage rings
c. Lung, multiple samples, including cranioventral portions of the cranial lobe(s), the caudal and dorsal regions of the caudal lobes, and hilar region including major bronchus
d. Hilar lymph nodes, and/or lymph nodes from the thoracic inlet
e. Heart, longitudinal sections including atrium, ventricle, and valves from both left and right sides

***Common respiratory diseases in the shelter***

*Canine distemper virus (CDV)*

Clinical impression is rarely sufficient to differentiate canine distemper from other causes of infectious canine respiratory disease. Premortem testing options are limited;

serological tests are limited by viral immunosuppression and interference due to maternal or vaccine-induced antibodies, fluorescent antibody (FA) testing (cells from conjunctiva, blood, respiratory tract epithelium, or urinary bladder) is very specific but has low sensitivity. Another premortem test is PCR (urine sediment, epithelial swabs, bronchoalveolar lavage (BAL), buffy coat preps, and cerebrospinal fluid (CSF); however, PCR may also detect vaccine virus in recently vaccinated animals. If an animal dies with suspect distemper or if presentation of the disease is unusual and confirmation is necessary, distemper can be identified reliably on necropsy samples and histopathology by a qualified pathologist.

Gross findings: If the lungs are involved, canine distemper virus will be disseminated (affecting all lobes). In most cases, oculonasal discharges are thick and mucopurulent. The lungs, generally, can be edematous or consolidated (interstitial pneumonia). Look for thick, foamy to mucopurulent hemorrhagic exudates in the airways. Secondary (bacterial) infection is common, both because of viral damage to the airways and because of lymphoid depletion. Therefore, a cranioventral distribution of lung consolidation (bronchopneumonia) does not rule out distemper. Lymphoreticular tissues are characteristically involved and are the primary site for viral replication. There can be enlargement of the tonsils and/or atrophy of the thymus. Hyperkeratosis ("hardpad disease") of the nose and/or footpads is sporadically present. There are no gross lesions of the central nervous system (CNS), even when nervous signs are uniquely present. The heart should always be examined, opened, and sampled when investigating respiratory outbreaks; right heart failure (e.g., heartworm) often poses clinically as respiratory distress.

Histopathology: In addition to the list above for general respiratory disease, histopathologic samples are useful in diagnosis of CDV include brain and bladder. Samples submitted for histology and paraffin-embedded are also used for immunohistochemistry, which is one of the definitive methods of identifying CDV-induced respiratory and/or neurologic disease.

Molecular diagnostics: PCR can be used to detect virus in lung, CSF, feces, or urine. False positives are possible within 1 to 3 weeks of vaccination. Consult with the diagnostic laboratory regarding testing details.

*Canine infectious respiratory disease complex ("kennel cough," multiple agents)*

Kennel cough is caused by a combination of both viral and bacterial agents. The range of morbidity and mortality can be attributed to a number of problems, including husbandry, but in any case, knowing the spectrum of infectious agents that are contributing to the disease is helpful in identifying problems, developing isolation procedures, and ongoing therapy. While many laboratories offer tests for common agents of kennel cough, new bacterial and virus agents have recently been identified. Confirmation of specific causative agent(s), whether novel or typical, requires a combination of histology, microbiology, and (for the viral component) PCR or virus isolation. Histology (including PCR or immunohistochemistry) is also necessary to rule in or out viruses as contributory or causative in an outbreak of respiratory disease.

Gross findings: The gross lesions of kennel cough complex typically reflect aerogenous introduction of bacteria into the pulmonary tissues. The lungs are congested and consolidated, most consistently within the cranial and ventral portions of the cranial lobes. There can be pleural mottling that may involve multiple lobes. Depending upon whether a viral component is acute or chronic, the bronchopneumonia could be superimposed on a more diffuse pattern of lung involvement (interstitial pneumonia). Whenever examining the thoracic cavity, look for excessive pericardial and thoracic fluid production (normal is less than 5 ml in both cavities), with or without pericarditis and pleuritis.

Histological, microbiological (lung), and molecular diagnostic (lung) samples should be taken according to the general respiratory disease protocol above.

*Canine influenza (CIV)*

It can be difficult to determine the role of this virus in a clinical event, as with most viral diseases. Reliable diagnosis of CIV-associated disease by serology requires both acute and convalescent serum samples. Virus detection by PCR in respiratory secretions from acutely ill or recently exposed animals is possible, but false negatives are not uncommon. The Becton-Dickinson Flu-A ELISA test may also be used on nasal secretions from acutely affected animals. While the mortality rate of canine influenza is, to date, fairly low (5% to 8%), if an animal does die or is euthanized with respiratory disease, the most accurate test for the virus is a PCR test of respiratory tissue. This, combined with histological features of viral-induced pneumonia, would be the "gold standard" for confirmation of the presence and effect of the virus. In several identified cases of CIV, there was a concurrent and severe bacterial pneumonia, so samples for culture and antibiotic sensitivity should be concurrently submitted.

Gross findings: Influenza virus will be hematogenously disseminated (affecting all lobes). The lungs can be hemorrhagic or consolidated (interstitial pneumonia). Again, lungs are among the most difficult of organs in which to detect gross changes; histological analysis is of paramount importance in evaluating the sequelae of the virus and/or coinfections in the lungs. Follow the tissue collection protocol that was elaborated for respiratory disease sample collection.

PCR: Fresh, or fresh/frozen respiratory tissue is always best, but RNA extracted from paraffin-embedded tissues has been used to detect virus. Laboratories that offer this type of testing are limited. The following will accept samples by courier; specific instructions are listed below.

California:

www.vetmed.ucdavis.edu/vme/taqmanservice/diag_home.html

New York:

www.diaglab.vet.cornell.edu/issues/civ.asp

U.S.:

http://www.idexx.com/animalhealth/laboratory/realpcr/tests

*Feline upper respiratory infection (feline URI)*

Feline URI is typically multifactorial and, as with kennel cough, recognition of the contributory infectious agents can be very helpful in organizing a response. Moreover, unusual agents or unusually virulent agents have plagued some shelters. The most commonly recognized agents involved in infections limited to the upper respiratory tract are feline calicivirus (FCV), feline herpesvirus (FHV1), *Mycoplasma*, *Chlamydia*, and occasionally *B. bronchiseptica*. Other bacterial organisms such as *Streptococcus canis* have also and more recently been described in outbreak situations (Pesavento, Bannasch et al. 2007). Nasal swabs can be performed postmortem, and sampling in an outbreak of severe URI should include the histological samples described in the general section on respiratory disease. Many diagnostic laboratories now offer PCR panels for the most common organisms associated with feline URI. Nonetheless, presence of the pathogen does not always imply causation, and concurrent culture and histology can be very helpful in identifying cause. Gross assessment of URI cannot distinguish among even the most common agents involved in URI; however, it is helpful to note the character of the nasal conchae and lungs, and whether or what type of fluid is present within the sinuses.

## OTHER SHELTER NECROPSIES

### Necropsy on a previously healthy animal found dead

***Acute death***

Common causes of acute death, with special attention to possible shelter situations or submissions are anaphylaxis, physical trauma (with neurologic or hemorrhagic consequences), intestinal malpositions (volvulus, intussusception), cardiomyopathy, electrocution (lightning or chewing on electric cords), gunshot, drowning, septicemia, heat stroke, dehydration, or ingestion of toxins or poisons (plant or synthetic, including disinfectants). Note that the most common cause of acute death in incompletely vaccinated shelter cats is panleukopenia. While some of these conditions may be obvious on gross necropsy (physical trauma, intestinal malpositions, gunshot, cardiomyopathy), in others histopathology is useful (e.g., some toxins, septicemia), while still others are unlikely to have either gross or histological lesions (e.g., anaphylaxis, dehydration, electrocution, some toxins, heat stroke). Even in this latter subset, a gross necropsy effectively rules out most possible causes of disease. In all cases, diagnosis requires a good history to arrive at the definitive diagnosis.

***Feline infectious peritonitis (FIP)***

There is no single, predictable target organ for feline infectious peritonitis (FIP). The virus widely (systemically) disseminates in macrophages, and the clinical outcome is dependent on both the host immunity and the specific organ affected. Histopathology on biopsy or necropsy specimens remains the gold standard for diagnosis. A definitive diagnosis is particularly important if littermates of an affected kitten remain in the shelter, as these may be at increased risk of FIP themselves if a littermate succumbed to the disease. Many of the premortem tests, and especially a cumulative amount of information, can be highly suggestive of the disease. If an animal dies or is euthanized with suspect FIP, a necropsy with histology would be diagnostic.

Gross findings: In the effusive form, there will be fluid within either or both the thoracic and abdominal cavities. The fluid is high in protein and may vary from slightly viscous to gelatinous in character. The surfaces of the viscera are covered with tiny (1–5 mm) friable, pale tan to white plaques (fibrin) that can give the surfaces a granular appearance (see Figure 7.9).

In the noneffusive (chronic) form, there will be nodules (granulomas) of variable size present in one or multiple organs. These can vary in color from off white to light tan,

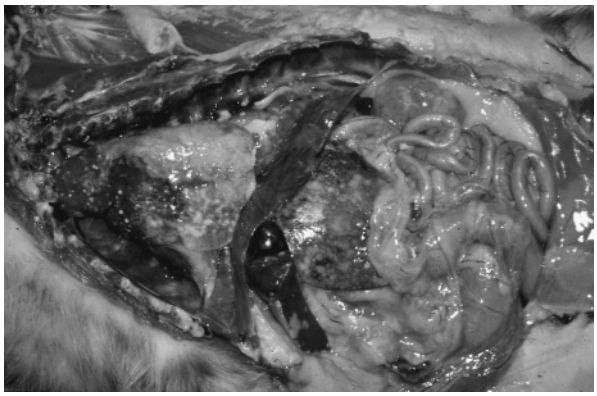

**Figure 7.9.** Feline infectious peritonitis (FIP) virus (feline coronavirus). In the effusive form of FIP, along with intracavitary fluid, the surfaces of abdominal and thoracic viscera are covered with small (1–2 mm) to coalescing pale tan plaques.

in texture from slightly firm to soft. The nodules are typically associated with capsular or serosal vessels, although when abundant, this can be difficult to distinguish. Within organs, the granulomas can be scattered throughout the parenchyma. Lymph nodes are often enlarged.

Formalin-fixed tissues: Samples should be taken from affected organs (in the case of the noneffusive form, this would be any viscera with detectable granulomas). In the case of the effusive form, multiple samples should be taken from affected viscera (liver, GI, lung). If the clinical presentation is limited to the nervous system, and FIP is suspected, it is imperative to submit brain tissue. Rarely, however, are brain lesions uniquely present.

## CONCLUSIONS

It is impossible to provide necropsy guidelines for every infectious disease encountered in shelter animals; therefore, a few characteristic diseases were selected. It is hoped that the information in this chapter will enable the shelter diagnostician to work more closely with pathologists and microbiologists to develop good shelter surveillance programs.

This chapter should aid veterinarians in collecting samples so that the pathologist and the diagnostic laboratory can analyze and diagnose problems more accurately. Necropsy has multiple potential roles in shelter animal health: it is a method to detect disease, to establish cause of death, and to assess diagnostic suitability in a single animal, and is a source of knowledge to apply to future cases.

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# Section 2
# Respiratory Diseases

# 8
# Feline Upper Respiratory Disease

*Janet M. Scarlett*

## INTRODUCTION

Upper respiratory tract disease (URTD) is a common and vexing problem for veterinarians managing the health of cats in animal shelters. The agents that cause URTD are common, highly infectious, and well adapted to cause disease, particularly in highly vulnerable shelter populations. Vaccines are available for the agents that most commonly cause disease, but they uniformly fail to prevent infection and often only lessen the severity of respiratory signs, rather than prevent them. People and other fomites (objects contaminated with respiratory secretions) facilitate URTD transmission, making control of respiratory disease very difficult. The goal of URTD management is to minimize its occurrence, as the nature of the agents and shelter populations preclude complete prevention.

## AGENT CHARACTERISTICS AND EPIDEMIOLOGY

### Agents

Feline herpesvirus-1 [formerly feline rhinotracheitis virus (FVR)] and feline calicivirus (FCV) are the most common causes of URTD in cats (August 1984; Ford 1993; Gaskell, Dawson et al. 2006). Bacterial agents contributing to feline URTD include *Bordetella bronchiseptica*, *Chlamydophila felis*, and *Mycoplasma* species (Gaskell, Dawson et al. 2006).

The role of herpesvirus and calicivirus as primary respiratory pathogens is well established. Feline herpesvirus-1 (FHV-1) is an alpha herpesvirus of cats with only one serotype occurring worldwide in domestic cats (Gaskell and Willoughby 1999). Different isolates exist, but they vary little in their antigenic composition or in the signs that they produce (Gaskell, Dawson et al. 2007).

Feline calicivirus (FCV) is a member of the virus family *Caliciviridae*. As an RNA virus (dependent on the error-prone replication associated with RNA-dependent RNA polymerases), there is one genogroup (genotype I) in the U.S., but many strains and isolates. Apart from one other Japanese genotype (genotype II), strains do not appear to vary by geographic region (Ossiboff, Sheh et al. 2007). The plasticity of the FCV genome enhances the adaptability of the virus, while at the same time complicating the development of vaccines that are protective against all strains. Furthermore, this plasticity has resulted in strains of varying virulence, ranging from those causing inapparent infections to those causing virulent systemic feline calicivirus disease (VS-FCV) (Pedersen et al. 2000; Hurley, Pesavento et al. 2004; Hurley and Sykes 2003), also called virulent systemic disease (VSD) in Great Britain (Radford, Coyne et al. 2007) and previously called hemorrhagic-like fever (Pedersen et al. 2000).

The virulent strains have caused outbreaks that are particularly troubling for shelters, not because they are common, but because they apparently arise preferentially in rescue shelters and spread from shelter animals to those in veterinary offices and in the homes of staff. These strains have been genetically distinct from common field strains of FCV and from each other (Rong, Slade et al. 2006; Abd-Eldaim, Potgeiter et al. 2005), suggesting that the VS-FCV isolates have arisen independently in each outbreak (Ossiboff, Sheh et al. 2007). Current vaccines (as of the middle of 2008) have failed to provide protection against some virulent strains.

Some researchers have hypothesized that hypervirulent strains arise in rescue shelters because caliciviruses are replicating at high rates in these populations in hosts with high levels of non-neutralizing immunity. These rapidly replicating strains theoretically lead to shedding of high concentrations of virus and high transmission rates. Cats in these populations are thought to simultaneously heighten their immune response and may themselves not display signs. However, when infected cats are introduced into feline populations with no previous exposure to these strains (e.g., veterinary hospitals, households), the rapidly replicating viruses spread quickly, overwhelm immune defenses, and produce VS-FCV (Radford, Coyne et al. 2007). Mysteriously, these strains have not persisted beyond 2 to 3 months, probably because they have produced high mortality, control measures have been implemented quickly, or the virus continued to mutate to less lethal forms (Hurley and Sykes 2003). Fortunately, fewer than 10 of these outbreaks have been reported to date (Hurley and Sykes 2003; Coyne, Jones et al. 2006; Hurley, Pesavento et al. 2004; Pedersen et al. 2000; Schorr-Evans, Poland et al. 2003).

*Chlamydophila felis* [formerly *Chlamydia psittaci (var felis*)] was once believed to routinely cause a broad spectrum of respiratory signs but is now recognized primarily as a cause of conjunctivitis in cats (Hoover and Kahn 1987; Wills, Gruffydd-Jones et al. 1984; Shewen, Povey et al. 1980). Rarely, infected cats display systemic signs (TerWee, Sabara et al. 1998).

*Bordetella bronchiseptica* acts as a primary pathogen under laboratory conditions (Coutts et al. 1996; Jacobs, Chalmers et al. 1993; Elliot 1991), and in light of its ability to paralyze the mucociliary apparatus, some researchers regard this organism as a primary pathogen in the field as well (Lappin 1999). Recovering this organism alone from cats with respiratory disease in the field lends further credence to its ability to act as a primary pathogen there as well (Welsh 1996; Binns, Dawson et al. 1999; Willoughby, Dawson et al. 1991).

*Mycoplasma* species can be cultured and *Mycoplasma* spp. DNA can be recovered by polymerase chain reaction (PCR) from the nasal cavity or pharynx of cats with or without clinical signs of disease (Blackmore, Hill et al. 1971; Tan, Lim et al. 1977). They are not found in the lungs of healthy cats, but have been recovered from cats with lower respiratory tract disease (Randolph, Moise et al. 1993). They are believed to be opportunistic invaders primarily, but in some cases of lower respiratory tract disease they may act as primary pathogens (Chandlers and Lappin 2002). Other secondary bacterial invaders include *Staphylococcus* spp., *Pasteurella multocida, Streptococcus* spp., and *E. coli*.

**Host range and zoonotic potential**

Feline herpesvirus-1 infects domestic cats and several other members of the *Felidae* (Gaskell, Dawson et al. 2007; Evermann, Laurenson et al. 1993; Spencer and Morkel 1993), as does the feline calicivirus (Gaskell, Dawson et al. 2006). These agents have no known zoonotic potential. *Chlamydophila felis* infects cats and has been definitively linked to infection in at least one immunocompromised person with chronic conjunctivitis (Browning 2004). A seroprevalence survey of small animal veterinarians in Japan revealed that 8.8% had antibodies to *Chlamydia psittaci* Fe/Pn1 of feline origin, but no data were provided regarding clinical illness (Yan, Fukushi et al. 2000). *B. bronchiseptica* causes respiratory disease in dogs, cats, rabbits, horses, laboratory rodents, pigs, and in rare cases, humans (Datz 2003). More than 35 cases of *B. bronchiseptica* have been documented in immunocompromised people, underscoring that a low zoonotic risk exists (Dworkin, Sullivan et al. 1999). In addition, at least one case of pertussis-like illness has been reported in a boy whose face was sprayed with an intransal *B. bronchiseptica*/parainfluenza vaccine while holding his dog for vaccination (Berkelman 2003).

**Distribution**

Many reviews suggest that approximately 80% of all cases of feline URTD are caused by FCV and FHV, with each agent contributing about equally to disease (Gaskell and Wardley 1977; Ford 1993; Gaskell and Dawson 1998). Most studies of the frequency of respiratory agents in cats are based on detection of virus shedding at one point in time (prevalence studies) among client-owned cats.

Among clinically affected cats, prevalence rates of calicivirus (based on virus isolation) have ranged from approximately 10% to 33% (Harbour, Howard et al. 1991; Binns, Dawson et al. 2000) as compared to 11% to 39% for the herpesvirus (Sykes, Anderson et al. 1999; Binns, Dawson et al. 2000). Among cats without signs, the ratio of recovery of calicivirus to herpesvirus has been generally higher. Shedding rates of calicivirus of 8% to 41% among nonclinically affected cats and 0.4% to 1.75% for herpesvirus have been reported (Wardley and Povey 1974; Coutts et al. 1994; Harbour, Howard et al. 1991). A recent report involving 152 cats from 22 Swedish catteries found prevalence rates as low as 2.6% for calicivirus and 0% for herpesvirus in apparently healthy resident cats (Holst, Berndtsson et al. 2005). Since calicivirus shedding is of

longer duration than that of herpesvirus on average, recovering calicivirus more frequently may not indicate a higher relative incidence of this virus.

Comparing the prevalence of infection with these agents across studies is complicated by differences in the tests used to recover and identify the agents (e.g., viral isolation, PCR), at what point in the course of disease the cats were sampled, where samples were obtained (e.g., oropharynx, conjunctival sac), and the nature of the populations sampled (e.g., pet cats, rescue or purebred catteries). Some researchers believe that widespread vaccination has reduced the frequency of herpesvirus-infected cats shedding virus, but not the proportion shedding calicivirus (Harbour, Howard et al. 1991; Baulch-Brown, Love et al. 1997). The degree to which these prevalence estimates apply to animal shelters in the U.S. is unclear, but calicivirus recovery exceeded that of herpesvirus in a recent study of cats in seven of eight animal shelters in California (Bannasch and Foley 2005). A much higher prevalence of FHV-1 positive cats was identified in two Colorado shelters (85.2%) than had been reported previously (Veir, Ruch-Gallie et al. 2004).

Studies of the incidence of infection with each respiratory agent are needed to accurately assess the risk to cats of developing these infections in shelters. Such data would assist veterinarians in targeting their preventive measures. Pedersen et al. (2004) conducted a prevalence study of herpesvirus and calicivirus infections at several points in time in two shelters in California that indirectly provide information on the relative incidence of infections due to these agents. These authors found that 4.3% and 10.5% of cats were shedding herpesvirus and calicivirus, respectively, at entry into the study shelters. One week later, these shedding rates had increased more than tenfold for herpesvirus (to 51.7%) and more modestly to 16.7% for calicivirus. Although the number of samples studied declined considerably by the second week, 40% of cats were still shedding FHV-1 at 2 weeks, and 20% were shedding calicivirus. Unfortunately, the clinical status of these cats was not provided, but the estimated incidence of infection was approximately 45% to 47% for herpesvirus and about 6% for calicivirus during the first week in these shelters (Pedersen et al. 2004). Incidence estimates based on clinical cases (without regard to causative agent) suggest that up to 40% of cats develop URTD signs in the first week in shelters and an even higher proportion develop signs during the second week (Edinboro, Janowitz et al. 1999; Dinnage, Scarlett, Richards 2008). It seems likely that the incidence and prevalence of infection with respiratory agents varies by shelter, related to the community incidence of these agents, the season, virulence of strains (particularly of calicivirus), management, and other factors, but this remains to be documented.

The frequency of other agents in shelters is also unclear for reasons similar to those described above. The prevalence of recovery of *Bordetella bronchiseptica* using oropharyngeal or nasal swabs from cats varies considerably across shelters. In the U.K. prevalence estimates ranged from 0% to 19.5% among cats from rescue catteries (Binns, Dawson et al. 1999; McArdle, Dawson et al. 1994). In the U.S. a study of four shelters in southern Louisiana found 3.1% of cats were culture positive (Hoskins, Williams et al. 1998), and in a shelter in Colorado, 4.9% of cats with signs of acute respiratory disease were culture positive (Veir et al. 2004). Unfortunately, in the Louisiana study, prevalence estimates were calculated by lumping cats from all rescue catteries or shelters together, which obscured the variability of prevalence among the shelters studied. Similarly, the variability of *B. bronchiseptica* recovery among shelters within the same region and across regions is unknown.

Studies of seroprevalence of antibodies against *Bordetella* suggest that infections are common during the lifetime of cats. Seroprevalence estimates were as high as 83% among rescue cats in the U.K. (McArdle, Dawson et al. 1994), but appeared to be lower (24.1%) in four U.S. shelters (Hoskins, Williams et al. 1998). Anecdotally, some shelters in the U.S. report endemic *Bordetella* associated with URTD, while others do not. Factors (e.g., strain differences, presence of other agents, management) that influence the persistence of *Bordetella* in shelters are poorly understood.

Evidence strongly suggests that cats and dogs infect each other with *B. bronchiseptica* (Binns, Speakman et al. 1998; Dawson, Jones et al. 2000; Foley, Rand et al. 2002). Molecular typing of *Bordetella* isolates from dogs and cats using pulsed-field gel electrophoresis (PFGE) supports the hypothesis that transmission between these species is likely to occur. Dawson, Jones et al. (2000) reported that the PFGE patterns of *Bordetella* isolates were more similar among dogs and cats living together, than from two cats (or two dogs) living separately. Foley, Rand et al. (2002), examining isolates from dogs and cats from two U.S. shelters, reported similar PFGE and antibiotic resistance patterns from affected dogs and cats. Using a different methodology, Binns and coworkers (1998) found that living in a household with dogs with respiratory disease was a risk factor for infection of cats with *Bordetella.* Estimates from surveys in the U.S. suggest that *C. felis* infections may account for 5% to 10% of feline respiratory

disease (Gaskell and Dawson 1998). Prevalence of *C. felis* infections based on PCR or culture among laboratory and privately owned cats with conjunctivitis ranged from 13% to 34%, depending on country of residence, origin of cats (e.g., shelter, cattery), and the assay used (Wills, Gruffydd-Jones et al. 1984; Wills, Howard et al. 1988; Gruffydd-Jones, Jones et al. 1995; Rampazzo, Appino et al. 2003; Sykes, Anderson et al. 1999). Using PCR, Italian researchers found prevalence estimates in three colonies of stray cats to range from 13.9% to 27.3% (DiFrancesco, Carelle et al. 2003). The organism has been isolated from 4% and 6% of clinically normal cats as well (from rectal and conjunctival swabs, respectively) (Greene 2006a). Cai, Fukushi et al. (2002) demonstrated that prevalence estimates were higher using PCR than bacterial culture in Japan, but what proportion of PCR-positive cats are capable of transmitting agent is unknown. Colonies of cats with endemic *C. felis* infections have been identified, suggesting that shelters (particularly those housing cats long term) are at risk. *Chlamydophila felis* infections occur worldwide and do not have known geographic or environmental predilections (Ramsey 2000).

Mycoplasma organisms have been recovered from the oropharynx of cats from throughout the world. Recovery rates of these organisms from the upper respiratory tract ranged from 39% to over 80% of clinically healthy cats, with no apparent geographic predilection (Tan, Lim et al. 1977; Randolph, Moise et al. 1993; Blackmore, Hill et al. 1971). One study in a Colorado shelter reported recovering *Mycoplasma* spp., from 60.7% (37 of 61) of cats with respiratory signs. The infected cats were all co-infected with other organisms (Veir et al. 2004).

Trends in prevalence over time are difficult to assess accurately for the reasons described above. Seasonal fluctuations depend on geographic location, usually coinciding with fluctuations in the numbers of susceptible kittens and the times when cats are most likely to be outside and interacting with other cats. Two studies provide some insight into long-term trends. Evaluating submissions of samples to a diagnostic service in the U.K. from 1980 to 1989, Harbour, Howard et al. (1991) failed to demonstrate significant trends in viral recovery rates among cats with clinical signs in that decade. Also, in 1992, another study of clinically healthy cats attending cat shows in the U.K. demonstrated that the recovery rates of calicivirus and herpesvirus were not significantly different compared to those of a similar survey conducted before the introduction of widespread vaccination (Coutts, Dawson et al. 1994). These data suggest no effect of vaccination on the relative frequency of calici and herpesvirus infections over time.

## CLINICAL SIGNS

Although some clinical signs may be more commonly associated with one pathogen than another, diagnosis of the causative agent cannot be made based on clinical signs alone (Figure 8.1). Sneezing and nasal and ocular discharges are associated with FCV, FHV-1 and *B. bronchiseptica* infections (Gaskell, Dawson et al. 2007; Radford, Coyne et al. 2007). The incubation period of feline upper respiratory infections is usually 1 to 6 days for the viral pathogens and may be longer for primary bacterial infections.

Oral ulceration (primarily on the tongue, as well as on other areas of the mouth, lips or nose) is commonly associated with FCV infection but can occur with herpesvirus infection as well. Lameness and skin lesions also occur in some FCV-infected cats (presumably reflecting differences among strains in tissue tropism), and the virus has been implicated in the etiology of lymphoplasmacytic gingivitis stomatitis (LPGS) complex (Knowles, Gaskell et al. 1989; Lommer and Verstraete 2003).

Mortality in outbreaks caused by VS-FCV strains has ranged from 33% to 50% (Hurley and Sykes 2003). Cats infected with the hypervirulent strains have signs indicat-

**Figure 8.1.** Cat in early stages of a herpesvirus infection. The causal agents in cats with upper respiratory tract infections cannot be reliably diagnosed on the basis of clinical signs alone.

ing widespread lesions, including typical URTD signs, fever, anorexia, subcutaneous edema (often of limbs and face), and ulceration of the mouth and skin (especially on the paw pads, pinnae, and nares) (Hurley, Pesavento et al. 2004; Hurley and Sykes 2003). At necropsy, affected cats may have bronchointerstitial pneumonia, and liver, spleen, and pancreatic necrosis (Pesavento, MacLachlan et al. 2004). With the exception of hypervirulent strains of FCV, herpesvirus infections generally cause more severe disease than calicivirus, especially in young kittens where mortality may be high. Early signs of herpesvirus include fever, depression, inappetance, and sneezing followed by serous nasal and ocular discharges. Other signs may include drooling, oral ulceration (rarely), viral pneumonia, and neurologic signs (Gaskell, Dawson et al. 2007). FHV-1 commonly causes acute, mild ocular disease, but may lead to more chronic manifestations such as conjunctivitis, keratoconjunctivitis sicca, eosinophilic keratitis, stromal keratitis, symblepharon, and corneal sequestrum. Similarly, with the development of diagnostic PCR, herpetic dermatitis has been diagnosed in cats (Hargis, Ginn et al. 1999a, 199b). FHV-1 can also lead to osteolytic changes in the nasal turbinate bones and may be involved in the etiology of chronic rhinosinusitis in cats (Radford, Coyne et al. 2007).

Signs of infection with *B. bronchiseptica* may include oculonasal discharges, sneezing, conjunctivitis, submandibular lymphadenopathy, fever, and lethargy. Coughing may also occur, but coughing in cats is much less common than in similarly infected dogs. Subclinical infections are common (Bemis 1992). Disease is generally more severe in kittens, sometimes producing pneumonia and death (Datz 2003; Gaskell, Dawson et al. 2006). The virulence among *Bordetella* strains varies (Speakman, Dawson et al. 1999), potentially explaining the wide variability among shelters reporting this organism as a significant problem.

*C. felis* is principally associated with conjunctivitis, usually involving one eye, but both eyes can be affected. Clinical signs can include conjunctival hyperemia, blepharospasm, chemosis, and serous to mucopurulent ocular discharge. Experimentally, and possibly in shelters, high dose exposure can elicit systemic signs such as fever, depression, nasal discharge, lameness, and stunted growth (TerWee, Sabara et al. 1998).

In cats already compromised by infection with other respiratory agents, *Mycoplasma* spps. produce lower respiratory tract disease including pneumonia, bronchopneumonia, and pyothorax (Foster, Barrs et al. 1998; Slavik and Beasley 1992). There is mounting evidence that *Mycoplasma* spps. may be primary feline respiratory pathogens as well (Chandler and Lappin 2002; Foster, Barrs et al. 1998).

Although cats recovering from respiratory infections may be immune to the agent causing the initial disease for several months to years following infection, reinfections with these agents are not uncommon. All of the respiratory agents can cause subclinical infection.

## THERAPY

Treating upper respiratory tract infections in shelter cats differs from that of owned animals. Shelter cats are more likely to be exposed to respiratory agents such as *Bordetella bronchiseptica* and *Chlamydophila felis* and a variety of secondary bacterial infections (by virtue of the concentration of these bacteria in shelter environments). Shelter cats are often highly stressed, compromising their ability to resist infection from exogenous agents and overgrowth of endogenous bacterial flora.

Respiratory infections are generally treated empirically without culturing and antibiotic sensitivity testing. Since the majority of respiratory infections are viral in origin, and in light of the increasing concern regarding the development of antibiotic resistant bacteria, antimicrobial therapy should be reserved for cats with clear evidence of secondary bacterial infection (e.g., purulent ocular or nasal discharges). In lieu of treating every mildly affected cat with respiratory signs with antibiotics, measures designed to reduce the risk of secondary bacterial infections should be adopted. These include insuring good air quality in areas where sick cats are housed; adequate hydration to promote normal functioning of the mucociliary apparatus; reducing stress in the isolation ward; thorough cleaning; and minimizing fomite transmission.

Broad-spectrum antibiotics with efficacy against anaerobes are recommended for bacterial infections secondary to normal flora overgrowth (Lappin 2003). Empirically, shelter veterinarians report better response to treatment of cats (with evidence of bacterial infections) when therapy is started with doxycycline (5–10 mg/kg q 12 h PO). This response to doxycycline probably reflects the higher frequency of *Bordetella* and *Chlamydophila* infections in shelter cats and the higher likelihood of secondary infections with *Mycoplasma* spps. normally resident in the upper respiratory tracts of cats (against which doxycycline is usually effective). Doxycycline is also relatively inexpensive and can be administered once daily. Caution should be exercised when administering doxycycline tablets, however, because of the risk of esophagitis and esophageal strictures. Doxycycline can be easily compounded in liquid form and treatment should be continued

for a minimum of 10 days, regardless of remission of signs. Other antibiotics useful in treatment of URTD include amoxicillin-clavulanic acid (15 mg/kg orally every 12 hours) and first-generation cephalosporins (Lappin 2003).

Veterinarians may encounter cats in shelters with chronic rhinitis thought to be secondary to osteochondritis caused by herpesvirus infections. Affected cats often respond to treatment with clindamycin because of its efficacy against anaerobic and gram positive bacteria and its ability to penetrate cartilage and bone. In shelters that have the resources to treat these cats, they should be treated for a minimum of 4 to 6 weeks or until the respiratory signs have been absent for 2 weeks (Lappin 2003). Overall, supportive therapies similar to those used in owned cats should be administered to affected cats to improve the comfort of the cats, address dehydration, and stimulate appetite.

*Chlamydophila felis* and *Mycoplasma* spps. are frequently isolated from cats with conjunctivitis and topical tetracycline ointment is recommended for use three to four times daily in infected cats. Alternatively, once-daily oral doxycycline treatment is also effective and may be a more practical choice in some shelters where frequent treatment is not an option. Treatment may need to be continued for 3 to 6 weeks to resolve *Chlamydophila* infection completely. If the duration of treatment is insufficient, signs and shedding that initially resolve may be followed by recurrence once treatment is discontinued.

Herpesvirus-associated ocular disease can manifest with multiple presentations as described earlier in the chapter. Affected eyes must be monitored daily as the disease can progress quickly. Most cases respond to treatment with topical antibiotic ointments that lubricate the eye and treat secondary bacterial infection. Drugs of choice include ointments containing tetracycline or erythromycin, which are also effective against *Chlamydophila*. The duration of therapy will depend on the course of the disease. For cats with herpetic keratitis, the minimum effective treatment regimen includes topical antiviral products and antibiotics. The purpose of the antibiotic is to prevent the viral corneal lesions from developing secondary bacterial infections that can lead to severe, sight-threatening sequelae. NeoPolyBact or erythromycin ointment are recommended (both cost less than $10 a tube), two to three times daily. If tubes are shared between cats, care should be taken to avoid contaminating the tube's tip, as this is an excellent way to spread FHV.

Several approaches are clinically effective and relatively cost effective at this time (sadly, most other antiviral options remain expensive or require very frequent administration). Selection of the approach to use will depend on the shelter and its resources. One option is to use idoxuridine. This is an older medication with good anti-FHV activity. It has to be compounded, so veterinarians must shop around for the best price. The real drawback to idoxuridine is that to be effective it must be administered at least four times daily.

The second antiviral option is cidofovir 0.5% solution. Anecdotally, cidofovir has worked in shelters with good success. This antiviral has good anti-FHV activity and only needs to be administered twice daily to be highly effective. The medication also has to be compounded and has limited availability. It is about double the cost of idoxuridine, but the lower frequency of administration makes the bottle last much longer.

Empirically, some shelter veterinarians report good response from an antiviral solution of betadine diluted 1:30 with sterile saline, administered one drop in the affected eye twice daily. Treatment with antivirals and antibiotics is continued ideally until the cornea is fluorescein negative, or alternatively for 2 weeks.

In order to effectively manage cases of severe lower respiratory infections or in the face of outbreaks of respiratory disease, culture and antimicrobial susceptibility testing is warranted. Conjunctival and oropharyngeal samples can be useful for isolating upper respiratory pathogens; diagnostic samples for lower respiratory disease should be obtained via bronchoalveolar lavage (or upon necropsy if affected cats die or are euthanized).

## MODES OF TRANSMISSION

URTD agents are highly infectious and are transmitted principally in ocular, nasal, and oral secretions (Gaskell and Dawson 1998; Povey and Johnson 1970; Gaskell and Willoughby 1999). The tidal volume of cats is thought to be too small for efficient aerosol transmission (Wardley and Povey 1977; Gaskell and Povey 1982), with the exception of sneezing cats that may propel viral-bearing macrodroplets up to 4 feet (Povey and Johnson 1970). Droplet transmission is probably important in shelters with group housing, where cats can sneeze in close proximity to one another, and in shelters with facing cage banks less than 4 feet apart. The primary modes of URTD transmission in shelters are by fomites or direct cat-to-cat transmission.

Calicivirus can survive up to 28 days at room temperature in the environment even in a dried state (Doultree, Druce et al. 1999). Contaminated fomites are probably the most important means of FCV spread in shelters with individual cat housing. Recent research suggests that FCV

survives for a variable amount of time on different surfaces, but can remain viable on unlikely surfaces such as telephone buttons and computer keyboards for hours after contamination (Clay, Maherchandani et al. 2006). Although herpesvirus-1 is more fragile outside the body, surviving only 18 hours at 15°C in a damp environment and up to 12 hours in a dry environment (Povey and Johnson 1970; Povey 1979), frequent handling of infected cats and ineffective cleaning and disinfection undoubtedly facilitate herpesvirus spread by fomites as well. *Chlamydophila* organisms have relatively poor survival outside the host, but *Bordetella* organisms may survive outside of the body in low-nutrient fluids (Porter, Parton et al. 1991). These agents are transmitted by direct cat-to-cat contact and indirectly, by fomites (Speakman et al. 1999). *Chlamydophila felis* is also shed from the reproductive tract and young kittens can be infected during parturition (Pedersen 1988). Conjunctivitis caused by *C. felis* can persist or recur, and shedding can continue for several months following apparent recovery unless effective antibiotic therapy of adequate duration is administered (Gaskell 1992).

Since the agent responsible for URTD in cats in shelters cannot be reliably determined on the basis of clinical signs alone, cats with ocular or nasal discharges (serous or mucopurulent), sneezing, or nasal congestion are considered to have URTD. They, as efficient shedders of the largest quantity of agent, must be separated from healthy cats.

The carrier state for these agents is well established (August 1984; Gaskell and Dawson 1998; Povey and Johnson 1970; Wardley and Povey 1976). Cats with herpesvirus, calicivirus, *Bordetella bronchiseptica*, and *Chlamydophila felis* infections shed agent (and are infectious) at multiple stages of infection, including during the incubation period, while displaying clinical signs (most efficiently), and following recovery from clinical disease. Each of these agents can also infect and be shed by cats who never display clinical signs. The periods and amount of shedding, however, vary by agent and stage of infection.

Shedding of the herpesvirus begins as early as 24 hours postinfection and usually continues for 1 to 3 weeks. FHV-1 DNA can be detected for beyond 3 weeks, but whether cats are shedding infectious virus at this stage is unknown (Gaskell, Dawson et al. 2007). Following recovery from the initial infection, 80% to 100% of cats become latent carriers; they remain infected but do not shed virus. Kittens may become latently infected following exposure to the queen, even in the presence of maternal antibodies, ensuring transmission of the virus to subsequent generations. The primary site of latency is the trigeminal ganglia (Gaskell, Dawson et al. 2007). Following stress (e.g., being brought to a shelter, parturition, rehousing within the shelter), however, approximately 45% of cats in one study began reshedding virus 4 to 11 days (mean 7.2 days) poststress and continued to shed for 1 to 13 days (mean 6.5 days) (Gaskell and Povey 1977). The proportion of infected cats whose infection becomes patent again following a stressful event may be even higher in shelters. As described earlier, Pedersen, Sato et al. (2004) reported a tenfold increase in the percentage of cats shedding herpesvirus within the first 7 days of entrance into two shelters in California.

Infectious calicivirus also appears in respiratory secretions about 24 hours following infection (Knowles and Gaskell 1991) and shedding continues well after clinical recovery (August 1984). One study found most cats still shedding virus 30 days postinfection, and 50% continued to shed at 75 days postinfection (Wardley and Povey 1976). A few cats remain lifelong shedders. Some studies suggest that the duration of shedding may vary among different FCV strains. Regardless of the strain, the persistence of shedding is presumably not related to stress as is true for FHV-1 (August 1984).

One study of kittens infected with *B. bronchiseptica* documented bacteria in the oropharynx as many as 19 weeks following infection. Whether the concentrations of organism present were sufficient for transmission to other cats was not determined. Parturition precipitated shedding in one of two pregnant queens, but the offspring were not infected (Coutts, Dawson et al. 1996).

Similarly, *C. felis* organisms can persist in the conjunctiva for 2 months or longer in naturally and experimentally infected cats, and the organism has been recovered from 4% to 6% of clinically normal cats (Terwee et al. 1998). The transmission risk these cats pose to others is unknown. It is not known whether *Chlamydophila* infections remain latent, being reactivated when cats are stressed, or whether some infected cats are persistently infected with slowly replicating organisms (Wills and Gaskell 1994).

Regardless of the causative agent, it is not practical or necessary to routinely identify subclinical shedders in shelters. In light of the prolonged shedding period of calicivirus, recommendations to isolate recently recovered cats from healthy cats in purebred catteries have been made (Knowles and Gaskell 1991). Similar recommendations in most shelters are impractical as the pressures for cage space are too great and the period of shedding among cats is too variable. Fortunately, they do not shed virus as efficiently as cats with signs. Therefore, most shelters live

with the ambiguity of the subclinical carrier state and attempt to minimize transmission through good cleaning and disinfection, isolation of clinical cases, and other management strategies described in the next section. Additional caution may, however, be warranted when dealing with unusually virulent viral strains, such as virulent systemic feline calicivirus. In cases where severe or fatal disease has been documented, especially in otherwise healthy, vaccinated cats, caution should be exercised when reintroducing recently recovered cats into a vulnerable population or adoptive home. Fatal disease has been transmitted by recently infected, subclinically affected cats with virulent FCV.

### Risk factors for URTD

Feline URTD is ubiquitous in cat populations and those housed in groups (such as in shelters) are at highest risk of URTD (August 1984; Knowles and Gaskell 1991; Binns, Dawson et al. 2000; Welsh 1996; Helps, Lait et al. 2005). The length of time spent in the shelter appears to be a significant risk factor for the development of URTD, based on the results of two studies and anecdotal reports. The risk of contracting URTD rose significantly after spending about 5 days in the shelter and increased between 5% and 13% daily thereafter in these studies (Edinboro, Janowitz et al. 1999; Dinnage et al.). While the incidence of the various agents probably varies by shelter, there is no known geographic pattern to their occurrence. At a population level, the common upper respiratory agents cause more frequent and severe disease in kittens, young cats, and rescue catteries (August 1984; Ford 1993; Binns, Dawson et al. 2000). Several epidemiologic studies of URTD have suggested other risk factors as well. Aged cats (11 years and older) were significantly more likely to develop URTD (compared to cats 7 to 11 months of age) in a cohort study of cats in a northeastern U.S. shelter) (Dinnage and Scarlett 2000). Increasing age, residence in a rescue cattery, and less than excellent hygiene increased risk of *B. bronchiseptica* infection in European catteries (Helps, Lait et al. 2005). In a similar study of risk factors associated with *B. bronchiseptica* infection in rescue catteries in the U.K., only the presence of respiratory signs in dogs was significantly associated with *Bordetella* infections in cats (Binns, Dawson et al. 1999). In studies of risk factors for *C. felis* infections, males, the Birman breed (Wills, Howard et al. 1988), and young age (Rampazzo, Appino et al. 2003) were associated with significantly higher risk. Other important risk factors include stress and increasing numbers of cats in shelters (Binns, Dawson et al. 1999; Helps, Lait et al. 2005; Speakman et al. 1999; Pedersen 1991).

## DIAGNOSIS

Shelters rarely use diagnostic tests to verify URTD or to identify the exact agent(s) causing disease in their cats. In the face of outbreaks (where the frequency or severity of disease is truly in excess of what is usually observed) further diagnostic work-ups are justified to help guide treatment and prevention strategies. For example, the identification of cats having signs compatible with virulent calicivirus infection, and subsequent confirmation with diagnostic testing, could avert transmission to other animals with the institution of appropriate preventive and control measures.

Before collecting and submitting samples for diagnosis, the diagnostic laboratory should be consulted. Conjunctival and oropharyngeal swabs are the most commonly collected samples for culture of respiratory agents. Samples for viral isolation should be placed in viral transport media for transport to a diagnostic laboratory. Samples for chlamydial culture should be placed in a chlamydial transport media (e.g., 0.2 m sucrose and 0.02 m phosphate), and those to be cultured for *B. bronchiseptica* should be placed in charcoal Amies transport medium before transport to the laboratory (Greene 2006a). Samples from bronchoalveolar lavage should be collected for isolation of *Bordetella* organisms, especially from cats with evidence of lower respiratory disease. Depending on the purpose of testing, other diagnostic techniques can also be used (e.g., PCR). Caution must be exercised when interpreting PCR results, particularly when attempting to diagnose the cause of current respiratory signs. Subclinical carriers of respiratory pathogens are common, and a positive PCR result does not necessarily imply a cause and effect relationship (see Chapter 7 regarding necropsy).

## DISEASE CONTROL AND PREVENTION

Elimination of upper respiratory tract infections in cats in animal shelters is virtually impossible because of carrier states, the agents' high infectivity, their ease of transmission (especially on fomites), the inability of vaccination to prevent infection and shedding, and susceptibility of cats to reinfection. Nonetheless, management practices can substantially reduce the frequency and severity of disease. Since the biology of the feline respiratory agents presents so many challenges, minimizing the occurrence of these agents requires the use of a broad range of control measures. To provide a framework for discussing each of these measures, the discussion is divided (somewhat arbitrarily)

into six sections on the basis of how each approach contributes to a reduction in clinical disease. Recommendations within sections sometimes overlap.

### Minimize agent concentration in the environment

#### *Avoid overcrowding*

One of the most serious threats to the health of cats in many shelters today is overcrowding. Housing more animals in a facility than can be cared for properly increases stress for both animals and care providers, decreases the effectiveness of sanitation, and increases agent load in the environment (Lawler 1998; August 1990; Hurley 2004). Crowding is a risk factor for high rates of respiratory infections in cats (Binns, Dawson et al. 1999; Pedersen 1991; Speakman et al. 1999) and in other species (Barr 2003; Brogden, Lehmkuhl et al. 1998). The number of cats that can be adequately cared for in a shelter will depend on numerous factors, including facility design and size, the type of housing, air quality and ventilation, number of staff, and the effectiveness of the cleaning and disinfection program. Shelters experiencing high rates of respiratory disease probably have too many cats to insure proper care.

#### *Cleaning and disinfection*

Since respiratory agents survive for variable periods of time outside of the host's body and because fomites are so important to the transmission of URTD, effective cleaning and disinfection protocols are *essential* to minimize URTD occurrence (Greene 2006b; Gilman 2004; Boothe 1998; Lawler 1989). Of the five respiratory agents described above, the calicivirus, a nonenveloped virus, is the most difficult to eliminate from shelter surfaces and fomites (Kennedy, Mellon et al. 1995; Scott 1980; Eleraky, Potgieter et al. 2002). Regardless of the agent or the product chosen, however, disinfection must be preceded by thorough cleaning and removal of organic matter; this is a vital step that should not be overlooked as organic matter inactivates most disinfectants (Gilman 2004; Boothe 1998; Lawler 1989; Anon. 1997). Nasal and ocular discharges frequently contaminate cage surfaces (including difficult-to-clean cage doors), requiring staff first to scrub these surfaces with hot water and detergents before rinsing and disinfecting (Figure 8.2). After rinsing again, the use of 5% sodium hypochlorite (bleach) at a 1:32 dilution (1 part bleach to 32 parts water or ½ cup of bleach per gallon of water) will effectively kill calicivirus and other respiratory agents in the environment when allowed to sit on the surface for at least 10 minutes. Higher concentrations are *not* necessary to kill calicivirus effectively, and they are irritating to the respiratory tract of animals and humans, potentially enhancing susceptibility to respiratory infections. Therefore, higher concentrations should *not* be used routinely in shelters (except in the face of ringworm outbreaks or during periodic "deep" cleaning when animals are temporarily removed from the environment). Veterinarians should insist that directions for making bleach solutions be posted near the mixing area to insure that staff prepares the concentration correctly each day. Storing the bleach out of the sunlight and in its original or a darkened or opaque container is essential to insure that the concentration (when mixed) remains sufficient to kill calicivirus and other respiratory agents. Following disinfection, the bleach solution should be rinsed off and the surface should be dried before returning the animal to the cage. (Boothe 1998; Lawler 1989).

**Figure 8.2.** Cat above had just sneezed on the bars of the cage. Cats with upper respiratory signs frequently contaminate their cages with mucopurulent discharges that must be scrubbed to remove the organic matter before disinfection.

While quaternary ammonium disinfectants are effective against the other respiratory agents, they do not reliably inactivate calicivirus. FCV has been widely used as a surrogate for human noroviruses (also in the family of *Caliciviridae*) for evaluation of disinfectants. At least one report of a new quaternary ammonium product effective against FCV has been published (Jimenez and Chiang 2006). Until there is additional independent testing, however, only products of known efficacy should be used. The effectiveness of quaternary ammonium disinfectants against herpesvirus and bacterial agents is reduced by the

presence of soap, hard water and low pH (Boothe 1998; Lawler 1989).

Potassium peroxymonosulfate (Trifectant® or Virkon S®), while more expensive than bleach, is also effective against calicivirus and is less corrosive, less irritating to the respiratory tract, works better in the face of organic matter, and can be applied to carpeted surfaces (Gilman 2004). Bleach or potassium peroxymonosulfate must be a component of the disinfection protocol, but these need not be used daily. Some shelters use strategies such as alternating these compounds with a quaternary ammonium product to reduce the corrosiveness of bleach to the environment and to reduce the cost of disinfection if they are using Trifectant® (Gilman 2004). Whatever strategy is adopted, veterinarians should monitor disinfectant effectiveness in minimizing URTD in their shelter by monitoring disease rates before and after changes in protocols.

Since fomite transmission of feline respiratory agents in shelters is so important, water and food dishes, toys, and other equipment in contact with cats must be washed and disinfected between animals. Similarly, people's smocks, pens, and clipboards are also important fomites, and should remain in their designated areas or be washed and disinfected before movement between areas. Hot and cold water should ideally be available in each housing area. As is true for the control of all infectious diseases, different people and equipment should be used to clean areas of potentially exposed, sick, and healthy animals. In shelters where staff must work in more than one area, washable aprons or smocks designated for each area are ideal. If that is not possible, then cleaning should proceed first from areas housing high-risk residents (e.g., kittens) to, last, those that are already sick. Often overlooked, meet-and-greet areas should be cleaned and disinfected as often as possible during busy adoption hours.

For shelters with individual cat cages, numerous approaches to cleaning have been recommended (Gilman 2004; EPA 1997). No research has documented the superiority of one method over another, although methods that avoid or minimize handling of the cats (thereby reducing stress and possible agent transmission by the handlers) are theoretically desirable. It has been documented that moving cats from one cage to another is sufficient to reactivate herpesvirus shedding in a substantial proportion of latently infected cats (Gaskell and Povey 1977; Maggs and Nasisse et al. 2003). Therefore, in individual cat cages, if the cage remains clean, then scooping the litter box and adding fresh water and food daily may be preferable to handling (and stressing) each cat during cleaning every day. Similarly, if cats are housed in cages with more than one compartment, the cat may be shepherded into one compartment while the other section is cleaned, avoiding the stress and potential exposure to contaminated handlers.

### *Hand disinfectants*

Since people handle cats that shed respiratory agents, frequent hand washing or sanitizing is essential. By removing or diluting bacteria and viral agents from the hands, people are less likely to transmit agents from cat to cat. Alcohol-based (70% alcohol is recommended) hand disinfectants are generally effective against vegetative bacteria and enveloped viruses (Rotter 2001), but not nonenveloped viruses. Their effectiveness is contingent on sufficient contact time, and since they evaporate quickly, multiple applications may be necessary. In recent tests using FCV as a surrogate for human noroviruses, Gehrke et al. (2004) found isopropanol to be more effective at reducing FCV concentrations on finger tips than ethanol. Since there is strong interest in finding products effective against human noroviruses (closely related to FCV), other hand disinfectant products are being developed that may work well against FCV (as well as the other respiratory agents) (Kramer, Galabov et al. 2006). Since it is often not practical for staff, volunteers, or the public to thoroughly wash their hands after handling individual cats, requiring the use of hand sanitizers between cats may be more feasible (despite their questionable efficacy against calicivirus). Thorough hand washing or frequent changes of gloves should be used in the face of suspected or documented outbreaks of calicivirus.

Gilman (2004) wrote, "While there are modern and effective disinfectants and cleaning tools, it is the animal care staff's attention to detail that will make a critical difference in the health of shelter animals." Staff *must* be educated to the importance of adherence to these cleaning/disinfection protocols and motivated to implement them. They may not understand disease etiology and transmission and therefore not understand the importance of their activities in spreading or limiting the spread of URTD. Veterinarians should insure that a shelter's sanitation protocols are available in written form and incorporated into new and continuing staff and volunteer training sessions. In addition, despite good training programs, resourceful staff can devise short cuts or forget the importance of certain procedures. Since effective sanitation is so important to good URTD management, veterinarians should periodically observe staff cleaning and address departures from protocol through appropriate means.

### *Ventilation*

Veterinarians need not be ventilation experts to assist shelters in improving ventilation in their facilities. Although aerosolization of respiratory agents is unlikely to be a primary means of transmission, good ventilation helps optimize the humidity level and reduce particulates and ammonia fumes that increase risk of URTD (Johnson 2004). Good ventilation probably also reduces the risk of secondary bacterial infections. Veterinarians can counsel shelters on the importance of regular cleaning of grills and ventilation ducts, and regular cleaning and replacement of air filters to ensure that hair and other debris do not impede air flow. Simple procedures such as holding a piece of paper to an intake register can indicate whether, and with what force, air is moving. Veterinarians can also recommend turning on fans following cleaning to promote rapid drying, which in turn reduces the humidity and retards the survival of pathogens and the growth of mold in the environment (Gilman 2004). Fans should be placed to ensure that the flow of air does not fall directly on the animals.

In shelters where URTD rates are high, veterinarians should consult with heating, ventilation, and air conditioning (HVAC) experts to insure that the HVAC system is functioning optimally (Johnson 2004). HVAC specialists, many of whom are familiar with guidelines to optimize ventilation for humans, may not be familiar with comparable guidelines for animal facilities. In order to consult effectively, veterinarians should understand what is ideal from a disease control standpoint. Unlike facilities that house humans, animal facilities ideally require 10 to 12 complete air changes per hour, rather than recycling air within the facility (Griesemer, Berman et al. 1978; Sinclair 1997). It is likely that relevant air quality is at the level of an individual cat's nose; therefore, cages enclosed on three sides may impede air flow and create less than ideal air quality for individual cats, even in the face of good air circulation within the surrounding environment. Traditionally, separate ventilation has been recommended, particularly for cat isolation rooms in shelters (August 1990). Since it is unlikely that aerosolization of feline respiratory agents is an important mode of transmission, investing in expensive separately ventilated isolation rooms may not be cost-effective. A possible exception may be in shelters with endemic kennel cough and documented *Bordetella* infections in their cats, but there is no documentation of aerosol transmission between the dogs and cats in shelters. More studies are needed.

Temperatures in the shelter should range from approximately 65°F to 75°F (the lower end of the range for adults and the upper end for kittens) (Sinclair 1997). Microenvironments with temperature extremes (such as in cages below windows in the winter) may exist in the shelter and may put some cats at high risk of URTD if not corrected. Constant intake of fresh air and the exhausting of circulated air are ideal, but outside air often requires heating or cooling for animal and human comfort. In order to minimize expense, ventilation systems should ideally allow regulation of the recirculation ratio, increasing the proportion of outside air during respiratory disease outbreaks and decreasing it when rates are low. Relative humidity levels of between 30% and 79% are desirable, although optimal humidity levels are probably closer to 35% to 45%.

When veterinarians have the luxury of consulting about cage purchases, cages that enable air flow (e.g., open fronts with back vents or two open sides) provide superior air flow to those enclosed on three sides. Cages with shelves or connecting portals can minimize stressful handling during cleaning, as discussed previously.

### *HEPA filters, ultraviolet light, and ozone generators*

Human health-care and research facilities often utilize ultraviolet light and HEPA (high-efficiency particulate air) filter units to reduce microbe concentrations in their environments. Stand-alone HEPA filter units are generally impractical to operate in animal facilities because expensive filters must be replaced frequently after becoming clogged with animal fur and dander (Johnson 2004). When they are installed properly in central systems behind filters designed to remove hair and larger particles, they can remove all but micron-sized particles. It is essential that HEPA filters be installed by experts who understand their limitations and placement and can advise shelters on their maintenance (Johnson 2004).

Ultraviolet light disinfection works by disrupting cellular DNA, but the UV rays must strike the microorganisms. Ultraviolet light units are used in hospitals and research laboratories to kill microbes on surfaces and in air streams, but they have many limitations. When used for surface disinfection, cleaning must precede use of UV light to remove organic matter, and animals and people must be removed before disinfection, as UV light is injurious to skin and eyes. The consistency of the surface being disinfected is critical, and areas shaded from the UV light are not disinfected (such that other means must still be employed to disinfect these surfaces) (Andersen et al. 2006). UV disinfection lights can also be placed in ventilation systems to disinfect air streams. Because aerosol transmission of feline respiratory agents is unlikely to play a major role in URTD transmission, UV light disinfection

of air streams has a history of variable success (Kowalski and Bahnfleth 2000), and UV light does nothing to remove particulate matter and other respiratory irritants from the air, these devices seem ill advised in shelters at the present time.

Ozone generators produce ozone, which is a respiratory irritant (EPA 2008). Ozone can compromise the body's ability to resist respiratory infections and worsen chronic respiratory diseases such as asthma; therefore, ozone generators are not recommended for use in shelters.

The relative impact of either HEPA filters or UV light disinfection units on feline respiratory disease rates in shelters is unknown. It seems likely that good traditional cleaning and disinfecting protocols using traditional approaches, coupled with improvements to staff training, stress reduction, efforts to reduce fomite transmission, and appropriate vaccination protocols will do more to reduce URTD rates than the installation of HEPA filters and ultraviolet light disinfection units. The most powerful method of improving air quality is probably source reduction, e.g., by prevention of crowding and improvement in cleaning in cat housing areas, such that fewer airborne contaminants are created (EPA 1990).

## Enhancing host resistance

### *Reduce stress*

Any source of stress (e.g., emotional, physical, environmental) can potentially reduce immune function (including responsiveness to vaccination) and increase shelter cats' susceptibility to development of URTD or prolong their recovery (Miller 2004; Greene 2006c). As discussed previously, stress (e.g., entering a shelter) is a documented trigger for the recrudescence of herpesvirus shedding and disease (Gaskell and Povey 1977; Pedersen, Sato et al. 2004). Therefore, a consistent high plane of nutrition (appropriate for age and physiologic status), environment enrichment, appropriate handling, a comfortable environment (e.g., away from loud noises, barking dogs), and other stress-reducing strategies in the shelter such as turning off the lights at night are essential to an effective URTD management program (Reid, Goldman et al. 2004; Griffin and Hume 2006; Case and Fahey 2004; Lawler 1998).

Not as widely discussed as a risk factor for URTD is stress among the staff. High staff stress almost assuredly contributes to higher risk of URTD in cats, probably through several avenues. High stress in staff, depending on its origin, may result in rough handling of cats or poor attention to details in the preventive medicine protocols. Good management of staff and volunteers in shelters is essential to effective URTD control programs.

### *Vaccination*

Reliance on vaccination alone will not effectively reduce URTD occurrence in shelters. The respiratory vaccines do not prevent infection, shedding of agent, or carrier states following infection (Gaskell, Dawson et al. 2007). Rather, these vaccines are designed to lessen the severity of disease. All cats (and if financially prohibitive, only cats identified as adoptable, long-term holding, and legal cases) should be vaccinated at or before entry to the shelter with a modified live vaccine for FCV and FHV-1. These are core shelter vaccines according to American Association of Feline Practitioners (AAFP) guidelines (Richards, Elston et al. 2006). Since rapid onset of protection among cats is the goal, killed vaccines are not recommended for most shelters (Richards, Elston et al. 2006). As with other infectious agents in that environment, achieving a rapid immune response assures maximum protection for cats in the shelter. In the United States, shelters must choose between intranasal (IN) or parenteral modified live virus (MLV) vaccines for FCV and FHV-1. Compared with parenteral MLV vaccines, IN vaccines can be used in the face of maternal antibodies in young kittens and have the advantage of inducing mucosal immunity where respiratory agents enter the body, thereby offering more rapid immunity compared to their parenteral counterparts (Knowles and Gaskell 1991; Greene 2006c; Ford 2004). Of course, shelter personnel must have the expertise to administer IN vaccines appropriately. A recent study of a commercial IN vaccine for FHV-1, FCV, and panleukopenia demonstrated a significant reduction of respiratory disease scores after challenge with FHV-1 among cats vaccinated 4 and 6 days before challenge compared to controls (Lappin, Sebring et al. 2006). Also, where it is not possible to foster kittens outside of the shelter, kittens as young as 3 weeks of age may receive IN vaccine for respiratory viruses. Although not stated on the label and not evaluated scientifically, one 0.5 ml IN dose may be divided among two or three kittens (3 to 5 weeks old) to provide early protection (Ford 2004). Cats receiving IN vaccines may develop transient, mild clinical signs within 4 to 6 days of administration. In shelters euthanizing cats for signs of URTD, allowances must be made for mild URTD signs developing during this interval. In shelters not using IN vaccines, 6-week-old kittens vaccinated parenterally with MLV vaccination will develop significantly higher antibody titers than their unvaccinated littermates (Dawson, Jones et al. 2000). If kittens over 6 weeks of age remain in the shelter for more than two weeks, they should be revaccinated at 2-week intervals until they are 16 weeks of age. In sanctuaries where cats may be in residence for

years, the AAFP report recommends that cats be vaccinated against FCV and FHV-1 using the schedule of every 3 years used for pet cats, although research is needed to confirm this recommendation. For optimal protection against panleukopenia, parenteral vaccine administration is recommended. Use of an IN vaccine should be considered an adjunct rather than replacement for a parenteral modified live vaccine with or without herpes and calicivirus components. (Please consult Chapter 5 on vaccinations and immunology for further information.)

The high genomic plasticity of FCV enables the virus to respond to environmental selection pressures and complicates the development of vaccines that protect equally against all isolates. The frequency distribution of FCV field isolates has changed since the development of most vaccines marketed today (Harbour, Howard et al. 1991). Current vaccines are predominantly based on one strain (either FCV 255 or FCV-F9) (Poulet, Brunet et al. 2005). While these strains still circulate, current vaccines often do not provide protection against a growing number of new isolates (Dawson, McArdle et al. 1993). Vaccine failures have been attributed to infection with FCV strains antigenically distinct from vaccine strains (Harbour, Howard et al. 1991; Dawson, McArdle et al. 1993), and vaccinated cats have not been protected against virus isolates causing virulent systemic disease (Hurley, Pesavento et al. 2004; Pedersen, Elliot et al. 2000). The development of a new generation of FCV vaccines that are effective against a broader spectrum of FCV isolates is an active area of current research. At least one vaccine is available in Europe that is effective against two FCV strains (Poulet, Brunet et al. 2005; Radford, Dawson et al. 2006), and a manufacturer in the U.S. has recently introduced a vaccine against one strain causing virulent systemic (VS) disease. Since isolates associated with outbreaks of VS-FCV have been unique and unlike either the current vaccine strains or each other, it seems highly unlikely that the new VS-FCV vaccine will provide protection against future VS-FCV outbreaks.

*Bordetella bronchiseptica* and *Chlamydophila felis* vaccines are not core vaccines for cats in shelters (Richards, Elston et al. 2006). These bacterins, like the URTD viral vaccines, do not prevent infection or shedding of agents (Wills, Gruffydd-Jones et al. 1987). Their use may be warranted in the face of outbreaks where these organisms have been identified, or in shelters with endemic infections caused by these agents. When used, IN vaccination for *B. bronchiseptica* induces a nonspecific immunity that protects temporarily against other respiratory pathogens (Schultz 2003). When necessary, kittens may be vaccinated as early as 4 weeks of age for *B. bronchiseptica* and at 9 weeks of age for *C. felis* (Richards, Elston et al. 2006). Anecdotally, some shelters experiencing *B. bronchiseptica* outbreaks in their cats report significant declines in clinical signs and in kitten mortality after the introduction of *B. bronchiseptica* vaccine. On the other hand, Schultz and Ford report that in their experience this has not been true (Schultz 2003; Ford 2004).

The recommendations offered above are made based largely on principles of immunology and studies conducted outside of animal shelters. Studies of the efficacy of vaccination in shelters are few in number. A vaccine trial in a California shelter involving 57 cats found that the combination of an MLV intranasal and killed parenteral vaccination protocol reduced respiratory signs approximately 66% compared with parenteral vaccine alone, suggesting that concurrent vaccination with parenteral and IN vaccines is superior to either mode of vaccination alone (Edinboro, Janowitz et al. 1999). However, it is not known whether this benefit was associated with superior protection from a modified live vaccine or the route of administration. In an observational (and nonrandomized) study of 701 litters of kittens, 531 kittens, and 2,203 adult cats in a Massachusetts shelter over a 50-week period, IN vaccination reduced signs twofold in litters of kittens and individual kittens compared with unvaccinated kittens during the first 5 days of shelter residence, but not in adults during the same period. Parenteral vaccination with a MLV vaccine, however, appeared to reduce the frequency of URTD approximately 60% in cats with more than 5 days' residence in the shelter compared with cats receiving IN vaccine during the same period (Dinnage et al.). More research is needed in shelters to identify optimal vaccination protocols. Until that time, shelter veterinarians should make their recommendations based on available knowledge and the performance of various protocols in their own shelter.

### *Drug prophylaxis*

L-lysine and interferon have been used by shelters prophylactically in an attempt to reduce the incidence, severity and shedding of virus among cats infected with infectious agent(s). In clinical trials in humans with recurrent clinical lesions due to herpes simplex virus type 1 (HSV-1), the amino acid L-lysine has been shown to reduce the recurrence rate, severity of lesions, and healing time (Griffith, Norins et al. 1978; Griffith, Walsh et al. 1987). L-lysine is thought to inhibit viral replication by competing with arginine, which is essential to herpesvirus replication. In cell culture, lysine has been shown to inhibit

viral replication of FHV-1, presumably using this mechanism (Maggs et al. 2000; Griffith, DeLong et al. 1981). A few trials in cats are emerging. Stiles, Townsend et al. (2002) demonstrated a significant reduction in the severity of signs of FHV-1 associated conjunctivitis in a blinded, randomized trial of eight cats; there were four cats receiving 500 mg of lysine twice daily compared with four cats receiving a lactose placebo. The incidence of disease and frequency of virus isolation were not significantly different between the groups (although the statistical power to find differences between the groups was low).

In a 2003 study (Maggs and Naisse et al. 2003), cats were stressed by a change in housing immediately following randomization to treatment (with 400 mg of oral lysine daily) or placebo. Observations were made for 15 days before all cats were treated with intramuscular methylprednisolone acetate. Observations were then made for an additional 15 days. The number of virus-shedding episodes in the treated group was significantly reduced compared with the placebo group following the change in housing, but not after immunosuppression with prednisolone. Unfortunately, few cats developed clinical signs in either group, so the statistical power to detect differences in incidence of signs or severity of disease was low.

In a subsequent clinical trial, Maggs et al. (2007) evaluated the safety and efficacy of oral lysine supplementation on diminishing the severity of respiratory disease in cats and measured plasma lysine and arginine concentrations. Trial cats were selected from a colony of cats that had recently experienced an outbreak of URTD. Designed to more closely simulate populations in shelters, Maggs et al. found that cats in the supplemented group had significantly more severe signs than those not supplemented. Male cats in the supplemented group also demonstrated more aggressive behavior towards each other than observed in the control cats. Since the arginine concentrations of supplemented cats were reduced in the supplemented group and failed to return to basal concentrations after treatment, Maggs et al. (2007) recommended more research to demonstrate the safety of supplementing with lysine. In light of these results, it seems prudent to avoid the use of lysine until its safety and efficacy has been more extensively evaluated in shelters.

Interferons are cell-derived proteins that inhibit the synthesis, assembly and release of a wide range of DNA and RNA viruses. In vitro human and feline interferons have been shown to have antiviral activity, but in vivo, this activity was apparent only at high doses (Fulton and Burge 1985; Cocker, Howard et al. 1987). In a 1999 study, cats treated with 25 U of natural human interferon alpha early in the course of disease had less severe URTD than control cats. Viral shedding was not reduced (Nasisse, Halenda et al. 1996). More research is also needed to establish the utility of using interferon in shelter cats to reduce the incidence or severity of URTD.

## Minimizing exposure

### *Quarantine*

Preventive medicine principles strongly recommend the use of quarantine to reduce the introduction of infectious agents into populations. The use of quarantine (10 to 14 days) in sanctuaries and some adoption guarantee facilities may be warranted. In light of the strong association between length of time in the shelter and risk of URTD and the necessity of keeping days of residence in the shelter as short as possible (to maximize the numbers of cats saved), however, quarantine is probably counterproductive in most shelters. Apparently healthy cats should be added to the shelter population after being examined, vaccinated, and neutered. The faster these animals can be put on the adoption floor and removed from the facility, the less likely they are to become sick in the shelter. Some cats will develop URTD following adoption, and prospective owners must be warned (preferably verbally and in a handout) that any cat adopted from a shelter may develop an upper respiratory tract infection or "cold" (not unlike their children when introduced to day care). In light of this risk, the handout should describe the signs of URTD, why it cannot be prevented entirely, and caution new owners to isolate the new cat from others in the household for approximately 2 weeks. Adopters should also be counseled to seek veterinary assistance immediately if their cat develops mucopurulent ocular or nasal discharge or systemic signs (e.g., anorexia). See the information sheet on feline upper respiratory infection at www.sheltermedicine.com for an example of a handout for adopters. The vast majority of cats developing URTD in their new home will recover uneventfully with or without treatment.

### *Isolation*

Shelters that euthanize cats with URTD should do so as quickly as possible to prevent transmission of disease from these cats. In shelters that treat respiratory infections, affected cats should be identified and isolated immediately from healthy cats in an isolation room(s). The room should be well ventilated, preferably without the necessity of keeping the doors open. The purpose of an isolation room is to minimize the likelihood of transmission of infectious agents from sick to healthy cats. Isolation is achieved by physically separating sick cats from healthy ones and by

limiting the movement of objects that serve as fomites (including staff) between contaminated areas (housing sick cats) and "clean" areas (housing healthy cats). This is essential to prevent transmission of highly infectious respiratory agents. Isolation in a facility *does not* consist of a separate set of cages on one side of a room or in a hallway. The isolation room should ideally be located at a distance away from healthy, adoptable, and juvenile animals that are most susceptible to disease. Only a few trained people who understand the risks associated with handling cats with URTD should be allowed in the isolation room. The area(s) should be clearly marked as isolation, and the doors(s) should be closed at all times. If ventilation is compromised by closed doors, then the doors can be left open after staff has gone home. The closed doors and signage remind staff that cats with respiratory disease are in residence, and anyone entering the room should wear a smock (that remains in that room). Hands must be washed thoroughly after leaving the room or gloves should be worn and removed prior to exiting, and cleaning and other equipment should be designated for use only in that room. If possible, an exam or treatment table should exist in the isolation room or very close to it in order to eliminate the need to carry sick cats through areas with healthy animals to examine them. Contaminated smocks, stethoscopes, etc., should be kept in the isolation area where no one will forget and mistakenly use them with healthy cats. Shelters that allow open access to the isolation room or that house sick cats in hallways are defeating the purpose of having isolation.

Although cats can continue to shed organisms after clinical signs have disappeared (for variable and often prolonged periods), they should be removed from isolation when fully recovered. It is impractical in most shelters to keep these cats isolated once removed from isolation, and they should be placed for adoption as soon as possible. Some shelters have designated areas or group rooms for recently recovered cats versus those that have never been ill. This may be helpful, as cleaning and care can then proceed from unaffected to recently recovered cats. Staff members sometimes fail to report sick cats promptly or even attempt to "hide" cats with signs, hoping they will be adopted, rather than be euthanized or placed in isolation. Cats with clinical signs of disease are the most efficient transmitters of these highly infectious agents, and leaving them among the healthy cats places those felines in jeopardy of becoming infected as well.

Staff must be educated to understand that timely intervention can reduce animal suffering, prevent worsening of signs, or even prevent deaths in affected kittens. Similarly, staff often wish to allow cats in the isolation ward access to the floor while they are cleaning, arguing that these cats are rarely outside of their cages. The risks associated with this practice have not been documented, but it is known that cats can be coinfected with more than one respiratory agent. Since affected cats are already debilitated, an infection with a second agent is likely to prolong their recovery. Sick cats may benefit from mild exercise and socialization, but this should take place in an area that is well away from the floor surface contaminated by other cats and debris drifting out of cages throughout the day. This area should be cleaned between cats.

#### *Foster care*

One of the most effective means of reducing exposure among kittens and other high risk cats is to utilize a well-designed and managed foster care program (Sinclair 2004). Kittens younger than 8 weeks of age should be placed in foster care as soon as possible. It is ideal if they can avoid entering the shelter or enter only into an area devoid of other cats. It is also ideal if these kittens can be taken directly to off-site adoption sites, thereby bypassing exposure to agents in the shelter. If kittens must be housed in the shelter, they must have an area separate from the adult cats and away from barking dogs.

Kittens returning from foster care at 8 weeks of age are highly susceptible to respiratory infections because of waning maternal immunity. Housing these kittens separately from adult cats and marketing them as quickly as possible is very important. Some shelters similarly place sick cats with prolonged recovery times in foster homes, and these cats often recover shortly after removal from the stressful shelter environment.

### Minimizing transmission

#### *Housing and traffic patterns*

Staff cleaning or handling cats with URTD or dogs with canine respiratory disease complex should avoid handling or walking through areas that house healthy cats, at least until they have changed clothing and thoroughly washed their hands (because *B. bronchiseptica* is probably transmitted between dogs and cats).

Kittens should be housed separately from adult cats, and elderly cats should have quarters separate from younger animals. Ideally, cats should not be exposed to barking dogs or having dogs walked through their residence areas. If single-cat housing is used, double-tiered is superior to triple-tiered caging, as triple-tiered cages are difficult to clean and disinfect. Similarly, it is difficult for staff (or potential adopters) to adequately view these animals.

Cages that face each other should be at least 4 feet apart to prevent droplet transmission of respiratory agents when cats sneeze, and all cages should be free of drafts or other extremes in the microenvironment. Although crowded shelters occasionally place banks of cages in corridors temporarily, this should be reserved for emergency circumstances and should not be done in highly trafficked corridors or areas where dogs may pass closely by the cages.

Studies are under way to compare the URTD rates among cats housed in single cages to those housed communally, but data are not yet available. Anecdotally, in the author's experience, most shelters in the U.S. with experience in housing cats using both approaches believe that their respiratory disease rates are lower among cats in communal housing. Although some studies in the U.K. indicate that stress levels in group-housed cats are higher than in singly housed cats, until comparative studies are published, it is unclear which type of housing is superior in promoting low URTD rates. Since colony housing is becoming more popular, there is an urgent need to scientifically evaluate its impact on URTD in shelters.

Ideally, in all animal areas, human traffic should proceed from the most susceptible animals to those most resistant to disease (Lawler 1998; August 1990). For URTD, then, the public should encounter kittens first, then adults. Like so many situations in shelters, adoption goals may be at odds with what is ideal from a preventive medicine standpoint. Many shelters have potential adopters encounter their adults first to encourage adoption of adults over kittens. They believe that this strategy increases adult cat adoptions, but it has the potential to place kittens at risk.

## DISEASE SURVEILLANCE

Most small animal clinicians have thought little about disease surveillance in populations. Since dogs and cats in the U.S. live predominantly in households with three or fewer animals, small animal veterinarians have little need for disease surveillance. In shelters with multiple animals, multiple staff, and multiple volunteers, however, veterinarians must rely on others to promptly identify and report sick animals. Similarly, they must assess the incidence of disease in their facility, track changes in incidence over time, and evaluate the effects of changes to preventive medicine protocols on the frequency of disease occurrence.

An effective surveillance system requires prompt and accurate disease recognition, rapid and consistent disease reporting, laboratory support (if diagnostic testing is necessary), entry of data into a data capture system, summarization and interpretation of data, and reporting to the appropriate people, including management (Hurley 2004; Osterholm, Hedberg et al. 2000). Failing to have a disease surveillance system to monitor population health is analogous to lacking a stethoscope and thermometer to assess an individual animal's health. Without being able to count cases and calculate disease rates, it is difficult to assess the effectiveness of preventive medicine protocols, identify mild to moderate outbreaks, and monitor progress in reducing disease.

Surveillance programs can range from simple to sophisticated. Ideally, disease rates should be calculated to account for the changing numbers of cats in the shelter (e.g., by season), but just counting the number of cases of URTD can provide a barometer of the incidence of disease over time. After a few years of data collection, the usual seasonal variation in cases will be apparent, and current case numbers can be compared with those observed in previous years to assess significant changes. Regardless of how the cases are tracked, staff must be trained to identify signs of URTD (including those associated with VS-FCV) and motivated to report infected cats promptly to a designated person (e.g., veterinarian, veterinary technician, manager). Staff must understand that leaving clinically ill cats with healthy cats will result in transmission of infections and additional cases, contaminate the environment, and lead to higher incidence rates of URTD. Medical records for affected animals in the shelter are an important component of the surveillance system and enhance the quality of medical care of individual cats as well. Medical records enable caregivers on any given day to view the treatments and progress of each cat. They also can be used to count cases over time.

## STAFF AND VOLUNTEER EDUCATION AND MOTIVATION

Shelter veterinarians must rely on staff and volunteers to implement most of their preventive and control measures. In order to achieve maximum compliance, veterinarians should be involved in developing written protocols, providing explanations as to why they are important, and, where possible, assisting with staff motivation as well. With the support of shelter management, the veterinarian can be a powerful motivator to elicit staff and volunteer compliance.

Since highly infectious respiratory agents contaminate so many areas and items in the shelter, including staff, successful URTD management programs require a team approach. Staff should understand the overall approach to URTD control and the important role they play in the

process. Data regarding the incidence of disease should be shared with them regularly so that they feel a part of the progress made and motivated to continue their efforts.

## ADOPTING A SYSTEMATIC APPROACH TO MANAGEMENT OF URTD

When investigating an outbreak or examining an animal, veterinarians must use a systematic approach to ensure that they do not overlook something of importance. Similarly, it is important to develop a systematic approach to disease control, including a management program for URTD in shelters (Hurley 2004; Radostits 2001). This helps insure that important intervention strategies are not overlooked and that a management plan is created that can be shared with all care providers and managers. Everyone must understand and be responsible for their roles in the overall URTD program.

Since several respiratory agents are involved and their epidemiology is complex, the management program must be multi-faceted in order to reduce transmission of these agents, maximize host resistance, and minimize the amount of contamination in the environment. The systematic approach should involve:

1. A disease surveillance system, including detailed medical records for sick cats
2. Specification of goals, both short and long term
3. An assessment of the total facility from the perspective of how the facility enhances or diminishes the likelihood of upper respiratory disease in cats
4. The identification of impediments to achieving the URTD goals and strategies to overcome them
5. Plans to achieve the goals, both long and short term
6. Plans to evaluate the data from the surveillance system to evaluate whether the goals are being met
7. Mechanisms to report results to everyone who has participated in the URTD program, as well as to the executive director and the board of directors
8. Plans to celebrate and move on to new goals if the old ones have been met; if the goals have not been met, time to reflect on why and to revise the plans (or change the goals) and begin the process again

Perhaps the single-most important facet of this approach is making time to think, plan, and team build, a difficult task in the busy, ever-challenging, and often overwhelming shelter environment. Yet time set aside to plan is probably the first goal to achieve for many shelters. Once implemented, planning will contribute toward fewer crises and facilitate an effective team approach to the many problems that arise every day, as well as create an effective disease management program.

1. *Surveillance system:* A disease surveillance system can be complex or very simple, depending on software and expertise in the shelter. The goal is to keep track of cats that become sick with URTD in the population and track how that number (in relation to population size) changes over time. This is best accomplished with a medical records system that also enhances individual animal care (Reneau and Kinsel 2001). The health management team can then assess whether the incidence of URTD is increasing, decreasing, or remaining constant. Preferably, this count is made in relation to the total number of cats in the shelter (i.e., rates are calculated). However, to begin just by defining what constitutes a case, counting, and tracking the number of cats that become ill can be helpful. Over time, if the total population entering the shelter annually remains fairly constant, the number of cats developing URTD at one point in time (e.g., this July) can be compared to the number the following year (e.g., next July). More sophisticated monitoring with a commercial software package can provide even more detailed information to calculate rates and identify cases by origin (stray or owner surrender), by age, or other characteristics. Once a system is in place, the effect of changes in management on URTD incidence can be monitored.
2. *Setting goals:* Explicit and realistic goals and a time frame to achieve them should be set. For example, a goal might be to write down the disinfecting protocol before the next staff meeting. Alternatively, once it is determined that one out of three cats entering the shelter develops URTD, a goal could be to reduce that to one out of four cats entering the shelter over the coming year. Setting goals provides targets to aim for and motivation to achieve them.
3. *Complete review of the facilities:* The facilities (including ventilation, temperature regulation throughout the shelter, traffic flow) and current management practices that affect URTD should be thoroughly reviewed and discussed. This review usually suggests relatively easy changes to current protocols (or even relatively inexpensive changes to the facilities) that could reduce disease immediately. For example, one shelter, after taking inventory of their physical facilities, realized that their garage had become a disorganized, catch-all area. Animal control vehicles had not been housed in the garage for years. For a small investment, this area

was converted into two cat-holding areas to provide better isolation for kittens returning from foster care.

4. *Explicitly identifying those factors, policies, and concerns that serve as impediments to achieving the goals:* If potential impediments is identified, preemptive strategies can be developed to minimize or eliminate their impact. For example, if there is an insufficient number of staff members to finish cleaning all cat cages before the shelter opens and allowing the disinfectant to work for 10 minutes, then additional staff may need to be added or current staff responsibilities rearranged.
5. *Plans to achieve the goals must be developed:* Plans should be developed to achieve the goals. In some shelters the plans may not look very different from what is already being done. What might look different, for example, is the addition of a review of how the URTD program is progressing and a plan to address any difficulties. In other shelters, plans might include initiating a medical record system. Plans for URTD control should include access to a diagnostic laboratory to which samples can be sent when necessary. Similarly, protocols for collecting and sending commonly required samples for URTD diagnosis should be readily available to shelter staff.
6. *Data analysis and review:* Initially, it might be difficult to accurately assess progress since there are many reasons for changes in the numbers of cats that become sick in shelters such the season of the year, changes in population dynamics (e.g., proportion of kittens), etc. Numbers (or preferably incidence rates) can be graphed, and potential reasons for their fluctuation discussed. Over time, comparisons would be made between URTD rates this year and those of the previous year, between different areas of the shelter (e.g., group housing versus individual cage housing) and so forth.
7. *Feedback provided to staff, volunteers, and board members:* Feedback serves as further incentive to continue implementation of the plan. Shelter staff and volunteers like to feel that their efforts are contributing to the health of the shelter animals. They need feedback to keep them motivated to adhere to prevention protocols. Informing staff that the incidence of URTD is dropping can be a powerful motivator. Similarly, finding rates of URTD incidence that are stable or increasing can trigger discussions of why progress has not been made.
8. *Reassess goals and draft new ones:* If goals are met, there is cause to celebrate and reconfirm efforts to set and meet new goals. If goals are not met, then reasons for not reaching them can be addressed. With a surveillance system, data can be generated to document progress or justify the need for additional resources to expedite progress.

## CONCLUSION

Upper respiratory tract disease in cats is often the most vexing disease problem facing veterinarians in shelters today. Too many otherwise adoptable cats are euthanized for URTD, too many suffer, and too many resources are devoted to treating affected cats that should be used to prevent cats from entering shelters. Respiratory agents cannot be eliminated because of their highly infectious nature, their carrier states, and because vaccination does not prevent infection or shedding. The incidence of URTD, however, can be reduced to a low level if shelters adopt a team approach, follow a well-considered URTD control program, monitor their efforts, and persevere. The shelter veterinarian should be an integral part of this process, working closely with the shelter manager, staff, and volunteers to increase their understanding of and compliance with URTD-reducing protocols. The shelter administration must participate in the process and be willing to invest the resources (staff, time, and money) necessary to implement a high-quality program. The veterinarian must provide leadership regarding the components of a URTD program and work closely with staff and management to plan, execute, and evaluate the program.

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# 9
# Canine Kennel Cough Complex

*Claudia J. Baldwin*

## INTRODUCTION

Minimizing the occurrence of infectious disease outbreaks in densely populated shelter environments that handle transient animals is one of the most challenging situations that veterinarians face. Pathogens that cause canine kennel cough complex (CKCC) (also known as kennel cough, infectious tracheobronchitis, or canine infectious respiratory disease complex) are easily spread in such environments. Animal shelters provide care for transient animals that carry the pathogens common to the larger community. Once they enter shelters, those animals that are infected can quickly expose and infect others, and those who are naïve, underprotected by lack of past exposure or immunizations, or have underlying disease or immunocompromise are at greatest risk of contracting disease.

CKCC is thought to be the most common infectious respiratory disease in dogs. Strategies for prevention rather than treatment are instrumental in minimizing CKCC in the shelter environment. The initial health assessment of dogs on intake is an essential component of the disease control plan. Training of shelter personnel in history taking, observation, and physical examination of the dog should therefore be provided. Incoming dogs with a recent history of sneezing, coughing, or oculonasal discharge, or displaying any of these signs of possible infectious disease, should be isolated until a veterinarian or trained staff member can perform a complete physical examination. Other causes of cough or altered respiratory patterns [e.g., degenerative, allergic, metabolic, neoplastic, other inflammatory or infectious (heartworm or parasitic) disease, or trauma] should be considered. Protocols that require health assessment and vaccination on intake, appropriate housing and segregation of new arrivals, disease surveillance, sanitation and disinfection, and isolation and treatment are the keys to successful management programs. In addition, stress can have a negative impact on the immune response to a pathogen. Methods that reduce stress and barking in dogs may be extremely beneficial in helping to curtail disease transmission (Miller 2004).

CKCC is generally not associated with high mortality, but significant morbidity can occur, and outbreaks in dense populations are common. Occasionally, outbreaks coupled with canine influenza or *Streptococcus zooepidemicus*, or in which canine distemper is a contributing factor may be associated with severe illness, pneumonia, and death in some dogs. Incubation periods, carrier states, shedding postinfection, and immunity following recovery vary with each agent. Clinical signs also vary depending upon the agent or agents involved. The sudden onset of paroxysmal coughing has historically been one of the classic signs of CKCC that would lead one to be concerned with the existence of the disease in the population. Classic paroxysmal coughing is, however, no longer the most common sign of "shelter cough" currently recognized. CKCC more commonly presents as nasal and/or ocular discharge or a moist cough. This change in predominant clinical signs may be due to a different mix of pathogenic agents present (e.g., canine influenza virus, canine respiratory coronavirus), different vaccination practices (e.g., more widespread vaccination against *Bordetella*) or the fact that a mix of pathogenic agents is usually responsible for shelter cough. Diagnostic testing for identification and confirmation of etiologic agents in population outbreaks may be warranted, especially if the clinical course varies or morbidity and mortality exceed expected levels. Treatment often consists of supportive care; specific therapy may be aimed at suspected or confirmed pathogens. The prognosis for recovery is excellent in uncomplicated single agent infections in immunocompetent dogs. However, the prevention and

treatment of respiratory disease complex in shelter animals often presents a more challenging situation.

## EPIDEMIOLOGY/DISEASE COURSE

### Etiologic agents

CKCC can develop when infectious agents disrupt and colonize epithelium of the upper respiratory tract (URT), i.e., nasal cavity, larynx, and trachea, as well as the lower respiratory tract (LRT), i.e., bronchi, alveolar, and pulmonary tissues. There are a number of primary infectious agents that can cause CKCC. These include viral, bacterial, and *Mycoplasma* agents. Single agent disease can occur, but disease associated with multiple agents is also well documented. There are a number of secondary viral and bacterial pathogens that can contribute to and worsen the clinical signs, disease course, treatment, and prognosis. Additionally, some infectious agents that may primarily affect the LRT should be considered as differentials in shelters with outbreaks of respiratory disease (see Table 9.1).

#### *Primary viral pathogens*

*Canine adenovirus (CAV) type 2 (CAV-2)*

Canine adenoviruses (CAVs) are DNA viruses of the *Adenoviridae* family. The adenoviruses are commonly found in dogs with CKCC as sole agents, or in conjunction with bacterial pathogens, such as *Bordetella bronchiseptica* (*B. bronchiseptica*). Canine infectious hepatitis virus type 1 (CAV-1), plays a minor role compared to CAV type 2 (CAV-2), which causes infectious laryngotracheitis. CAV-2 has a broad range of natural terrestrial (e.g., foxes, wolves) and marine mammal hosts. (Buonavoglia and Martella 2007) Following oronasal contact, virus replication of CAV-2 occurs in the epithelium of the URT and LRT. CAVs are reported to cause a mild URT disease that is self-limiting and presents as a cough. CAV-2 infection can result in tonsillitis or extend to infection of type 2 alveolar cells with resultant interstitial pneumonia (Ford 2006). Some dogs may not exhibit overt clinical signs but are still infectious.

**Table 9.1.** Canine kennel cough complex viral and bacterial pathogens.

| Agent | Abbreviation |
|---|---|
| Canine adenovirus–2 | CAV-2 |
| Canine parainfluenza virus | CPiV |
| Canine respiratory coronavirus | CRCoV[a] |
| Canine herpesvirus | CHV[a] |
| Canine distemper virus | CDV |
| Canine influenza virus | CIV[b] |
| *Bordetella bronchiseptica* | *B. bronchiseptica* |
| *Mycoplasma cynos* | *Mycoplasma spp.* |
| *Streptococcus equi* subsp. *zooepidemicus* | *S. zoo*[b] |

[a] Potential pathogens, suspected to be contributory to CKCC.

[b] Emerging pathogens associated with severe disease for which more study is needed.

*Canine parainfluenza virus (CPiV)*

Canine parainfluenza virus (CPiV) is another agent known to cause CKCC. It is regarded by some as the most common pathogen involved in CKCC (Ford 2006), while others report it is found less commonly (Foley and Bannasch 2004). CPiV, which is recognized worldwide, is an enveloped single strand RNA virus of the *Paramyxoviridae* family. Infections with CPiV are typically restricted to the URT because the virus does not replicate in macrophages. Clinical signs of infection with CPiV as a sole infectious agent include a cough of short duration (less than 6 days) with only minimal systemic signs. Conjunctivitis and serous nasal discharge may be seen.

Laryngeal edema is responsible for the high-pitched honking cough characteristic of CPiV. CPiV infection may be self-limiting or may be complicated by invasion of secondary bacterial agents. Facilitation of entry of secondary agents occurs because of viral damage to the epithelium. With the addition of other pathogens, increased morbidity and potential mortality may be seen.

*Canine respiratory corona virus (CRCoV) and canine herpesvirus (CHV) as potential pathogens*

Canine respiratory corona virus (CRCoV) is an RNA virus of the family *Coronaviridae* and is well known as an enteric pathogen in the dog. Canine herpesvirus (CHV) is an alpha-herpes virus associated with the reproductive tract and is a pathogen in puppies. These pathogens have been isolated from coughing dogs but are not considered by many to be primary pathogens in CKCC. CRCoV, a group 2 respiratory pathogen similar to bovine coronavirus (CV) and human CV OC43 but distinct from enteric CV, has been isolated from dogs housed in populations.

In one retrospective study of tissue harvested from dogs with morphologic respiratory disease, 2 of 126 cases were identified with CRCoV by means of immunohistochemical

staining. Virus was detected in the epithelium of the bronchi or large bronchioles. In one dog, canine distemper virus (CDV) antigen was also present (Ellis, McLean et al. 2005). In a longitudinal study performed at a rehoming facility in the United Kingdom (U.K.) with endemic CKCC, CRCoV and CHV, as well as other viral pathogens, were detected by polymerase chain reaction (PCR) on respiratory tissue harvested at necropsy. CRCoV was detected most frequently within the first week of residence and then a decline in prevalence was seen. Other viral pathogens were detected during the second, third, and fourth weeks of residence. Coinfections were recognized, but no CAV-2 pathogens were detected (Erles, Dubovi et al. 2004).

The presence of serum antibodies to CRCoV in canines on entry into the rehoming facility in the U.K. was shown to be 30.1% (Erles, Toomey et al. 2003). Seropositivity to CRCoV in the general canine population in North America (across Canada and the United States) was 54.7% (547/1000); 36% (297/824) of U.K. dogs tested positive (Priestnall, Brownlie et al. 2006). Isolation of the organism has been unsuccessful, precluding further study to clearly determine the pathogenic potential of this virus in the canine population.

CHV is a member of the *Herpesviridae* family. Illness from CHV was first described as a fatal septicemic disease in puppies less than 2 weeks of age; older puppies and adults often show no clinical signs, and the virus can be transmitted in utero, resulting in fetal death. Dogs remain latently infected and excretion of virus can occur for variable periods of time and following stress. CHV has been associated with CKCC although the role that it plays is not clear. In the study cited above of a population of dogs at a rehoming center in the U.K. where CKCC was endemic, detection of CHV by PCR occurred in 12.8% (27/211) and 9.6% (10/104) of tracheal and lung tissues, respectively. CHV was more likely to be detected in dogs with moderate to severe CKCC and more likely to be present during the third or fourth week in residence. The presence of antibodies to CHV was not significantly different between dogs that developed CKCC and those that did not (Erles, Dubovi et al. 2004).

A recent review of canine respiratory viruses cites several studies. In household and colony-bred dogs, the presence of serum antibodies to CHV ranges from 39.3% in the Netherlands to 88% in England. Studies in Italy indicate that prevalence in kenneled dogs is similar (27.9%) and lower in pet dogs (3.1%) (Buonavoglia and Martella 2007). In a study of antibody responses to both CRCoV and CHV in kenneled dog populations, seroconversion did support the presence of these viruses but their role in the pathogenesis in CKCC needs further study (Erles and Brownlie 2005).

### *Secondary viral pathogens*

Canine distemper virus (CDV) and canine influenza virus (CIV) can cause URT signs but may also be associated with LRT signs and severe systemic disease.

#### *Canine distemper virus (CDV)*

CDV is regarded as a secondary pathogen of CKCC. A member of the *Paramyxoviridae* family, CDV has a range of natural hosts (e.g., canine, raccoon, skunk), some of which may be transported in animal control vehicles or admitted to shelters. Infection with CDV can cause systemic disease involving the respiratory, gastrointestinal, and neurologic systems. CDV can cause upper respiratory signs alone and/or bacterial pneumonia without systemic illness and is therefore a reasonable differential for CKCC, particularly if more severe disease is seen in some dogs. It can work synergistically with CPiV and bacterial pathogens, such as *B. bronchiseptica*, to complicate CKCC. This viral agent is covered in more detail in Chapter 10.

#### *Canine influenza virus (CIV)*

An emerging pathogen affecting the dog is canine influenza virus (CIV), an enveloped RNA virus and member of the influenza virus A genus in the family of *Orthomyxoviridae*. It represents an unprecedented interspecies transfer of virus from the equine to the canine. CIV has not been a recognized cause of CKCC but has been identified in populations of greyhounds and in pet dogs. As this is a new pathogen, immunity to CIV is not expected, and all dogs are considered susceptible. In a dense population of dogs, such as is encountered in many shelters, a high percentage of animals would be expected to become infected. The incubation period is approximately 2 to 5 days. Up to 25% of infected dogs may remain asymptomatic and shed the virus. Clinical signs may include initial fever, purulent nasal discharge, and coughing that may last for 2 or more weeks, or a peracute syndrome associated with hemorrhage into the respiratory tract and death. In addition to the trachea, LRT tissue is also affected with inflammation and suppurative bronchopneumonia (Crawford, Dubovi et al. 2005). CIV has also been reported in association with *Streptococcus equi zooepidemicus* (Yoon, Cooper et al. 2005). CIV is covered in more detail in Chapter 11.

***Primary bacterial pathogens***

Bordetella bronchiseptica

*B. bronchiseptica*, a gram-negative aerobic bacterium, is recognized as both a significant primary and secondary agent in CKCC. However, this bacterium can also be isolated from the URT (nasal passage through the pharynx) of normal healthy dogs. Hundreds of isolates of *B. bronchiseptica* with variable pathogenicity and virulence have been harvested from dogs with CKCC. Host distribution and virulence of the organism is variable depending on the isolate (Ford 2006). Following exposure to the pathogen, *B. bronchiseptica* attaches to and replicates on cilia of the respiratory epithelium. A variety of potent toxins are produced that impair phagocyte function and reduce ciliary function, allowing opportunistic organisms to colonize the epithelium. Although this is an extracellular pathogen, it can invade host cells and evade host defenses by several intrinsic mechanisms. A carrier state or persistent infection can then result.

*B. bronchiseptica*, as a single agent, produces rhinitis, mucoid nasal discharge, and cough. The cough may be harsh and severe. It is often complicated by infection with other bacteria and viruses. The presence of CAV and/or CPiV often leads to more severe clinical disease. Concurrent infection with CPiV can result in clinical pneumonia.

In a recent case review of dogs less than 1 year of age with a history of being housed in a community setting and with contagious respiratory tract infection characterized by bronchopneumonia, *B. bronchiseptica* was isolated in 49% (32/65). Dogs infected with *B. bronchiseptica* were more likely to have originated from a pet store (19/31 dogs). Other populations included breeders, shelters, and other sources, with shelter dogs representing only 8% (5/65) of the total dogs included. Dogs with *B. bronchiseptica* were younger and were more severely affected than those with bronchopneumonia from other bacterial agents. Viral pathogen testing was not reported (Radhakrishnan, Drobatz et al. 2007).

Mycoplasma *spp.*

*Mycoplasma* organisms vary from bacteria because of the lack of a cell wall. These microbes are enclosed in a cytoplasmic membrane and can be commonly harvested from the nasopharyngeal and laryngeal mucosa of healthy dogs. The reports of the presence of *Mycoplasma* spp. in the LRT of healthy dogs have been conflicting. When associated with disease, *Mycoplasma* spp. have been found to colonize all respiratory epithelium, with resultant purulent bronchitis and bronchiolitis, and interstitial pneumonia.

In a recent prospective study including a rehoming facility in the U.K. with endemic CKCC, *Mycoplasma cynos* (*M. cynos*) was the only *Mycoplasma* spp. isolated from kennel aerosols. *Mycoplasma* spp. were cultured from tonsillar, tracheal, and bronchial lavage samples and identified by PCR and sequencing. Only *M. cynos* was demonstrated on the ciliated tracheal epithelium and associated with CKCC when found in the LRT. In addition, isolation of *M. cynos* correlated with an increased severity of CKCC, younger age (under 1 year), and in dogs kenneled for a longer period of time (over 1 week). This same population of dogs was known to be infected with *B. bronchiseptica, Streptococcus equi* subsp. *zooepidemicus*, CRCoV, CPiV, and CHV, which emphasizes that CKCC is a complex disease with many pathogens potentially acting synergistically (Chalker, Owen et al. 2004).

Streptococcus equi *subsp*. zooepidemicus

Recently, another emerging pathogen, beta hemolytic *Streptococcus equi* subsp. *zooepidemicus* (*S. zooepidemicus*), has been identified and is being recognized as a significant pathogen in shelter dogs in the U.S. (Pesavento, Hurley et al. 2008). It has been associated with hemorrhagic streptococcal pneumonia in a colony of dogs (Garnett, Eydelloth et al. 1982). An association with CKCC and *S. zooepidemicus* was later reported in the U.K. in a well-established rehoming kennel. *S. zooepidemicus* was more likely to be isolated from dogs with clinical signs compatible with CKCC and from dogs with longer stays in the kennel (Chalker, Brooks et al. 2003).

***Mixed populations***

Mixed populations of viral and bacterial pathogens are commonly seen with CKCC. Other bacterial agents that may be involved include *Pseudomonas*, *Pasteurella* spp., and coliforms. These organisms are considered to be opportunistic, and their presence can contribute to very serious infections of the pulmonary tissue.

**Susceptible species, breed, and age**

Infections with CAV, CHV, and CRCoV are species specific, and no breed or age predilection is known. The dog is the primary susceptible species for CPiV infection, but cats may become subclinically infected and may shed virus. Additionally, at 2 weeks of age, dogs become susceptible to CPiV, making both species and age segregation important to prevent subclinically infected cats from spreading disease to puppies. Development of encephalomyelitis has been associated with a potentially more severe variant of CPiV virus in puppies (Foley and Bannasch

2004). CDV is specific to the dog, ferrets, and wildlife, but is unlikely to infect appropriately vaccinated puppies over 4 months of age. If CDV were contributing to CKCC, some degree of gastrointestinal and/or neurologic disease would be expected in the population; however, this effect may be masked by widespread recent vaccination. CIV, as an emerging pathogen, is likely to infect a high percentage of the population exposed, regardless of age, breed, or vaccination status of the dog.

*B. bronchiseptica* does infect other species, including the domestic cat and humans (human infection is rare), and may cause significant respiratory disease in concert with viral pathogens, especially in kittens. In addition, cross-species transmission has been described. Wildlife and rodents may also harbor this organism. *B. bronchiseptica* infection has recently been associated with younger dogs (Radhakrishnan, Drobatz et al. 2007). *M. cynos* was recently associated with CKCC in dogs less than 1 year of age (Chalker, Owen et al. 2004). *S. zooepidemicus*, well known to infect the LRT in both foals and adult horses and the equine reproductive tract, has no apparent breed or age predilection in the dog (see Table 9.2).

**Zoonotic potential**

CAV has no zoonotic potential although CAV-2 is clinically and genetically similar to the adenoviruses that cause common colds in humans. CPiV transmission to humans has not been described although it is related to simian virus 5, which is thought to infect humans persistently (Foley and Bannasch 2004). CRCoV, a group 2 respiratory pathogen, is similar to human CV OC43 but is not thought to have zoonotic potential. CDV, CHV, and CIV are similarly not thought to have zoonotic potential. *Mycoplasma* spp. are known to infect other species, including humans, but clear transmission has not been documented, and they are not thought to have much zoonotic potential. Humans are known to become infected with *S. zooepidemicus,* but the infection is rare and is associated with contact with horses or consumption of unpasteurized milk products (Kuusi, Lahti et al. 2006). Of the CKCC pathogens, *B. bronchiseptica* is the only agent known to have zoonotic potential, with the immunocompromised and those with respiratory disease at greatest risk (Foley and Bannasch 2004). See Chapter 23 for additional information on zoonosis.

**Table 9.2.** Canine kennel cough complex pathogens.

| Agent | Zoonotic | Modes of Transmission | Incubation Period (days) | Asymptomatic Carrier | Duration of Shedding (days) |
|---|---|---|---|---|---|
| CAV-2[a] | No | Aerosol, direct | 3–6 | No | Up to 14 |
| CPiV[b] | Yes? | Aerosol, direct | 3–10 | No | 8–10 |
| CRCoV[c] | No | Aerosol? direct? | ? | Yes | ? |
| CHV[d] | No | Aerosol? direct, fomites | ? | Yes | ? |
| CDV[e] | No | Aerosol, fecal/oral | 9–14 | No | 90 |
| CIV[f] | No | Aerosol, direct, fomites | 2–5 | Possible | 7–10 |
| *B.b*[g] | Yes | Aerosol, direct, fomites | 2–6 | Yes | 90+ |
| *Mycoplasma*[h] | No | Aerosol? direct | 3–10 | Yes | 90+ |
| *S. zoo*[i] | No | Aerosol, direct? | ? | Yes? | ? |

[a] CAV-2: Canine adenovirus-2 is a well-known pathogen.

[b] CPiV: Canine parainfluenza virus is a well-known pathogen.

[c] CRCoV: Canine respiratory corona virus is not well defined. In one study, CRCoV was detected most frequently in the first week of shelter residence, suggesting a short incubation period, and was detected less frequently by week 3, suggesting a shedding period of up to 2 weeks.

[d] CHV: Canine herpesvirus as a pathogen in CKCC is not well defined and much is unknown. In one study, CHV was detected most frequently during weeks 3–4 of shelter residence, suggesting a longer incubation period.

[e] CDV: Canine distemper virus can occur with CKCC pathogens but more significant disease is expected.

[f] CIV: Canine influenza virus is an emerging pathogen about which much is unknown. Suspects or infected dogs should be kept in an area with separate ventilation and separated by at least 30 feet from the uninfected.

[g] *B. bronchiseptica* can be harvested from the oropharynx of normal dogs.

[h] *Mycoplasma* spp. are part of the normal flora of the oropharynx of dogs.

[i] *Streptococcus equi* subsp. *zooepidemicus* is an emerging pathogen and much is unknown about it.

**Prevalence**

CKCC is considered to be among the most prevalent of infectious respiratory diseases of the dog and is seen primarily in transient populations housed in high density. Animals housed in boarding facilities, commercial kennels, and veterinary facilities are at risk, as are dogs in pet stores and shelters. In general, prevalence in the population is expected to decrease significantly when dogs are housed in smaller, less dense populations, such as private homes.

**Morbidity, mortality, prognosis**

CKCC morbidity in dense populations, such as shelters, can be high and can fluctuate with the time of year because of increased population density, temperature, and humidity. Mortality rates are generally much lower. Both morbidity and mortality can increase when multiple agents are involved. Puppies are at increased risk for severe disease and mortality. CKCC can be seen in the owned pet that has been housed in a transient or densely populated environment as well. Prognosis for recovery from uncomplicated CKCC is good. Prognosis for recovery from complicated CKCC is guarded but improves when diagnostic testing and specific supportive treatment or management can be provided. In shelters unable to provide this level of care, the prognosis may be guarded to poor. Some shelters euthanize animals with CKCC because of the high morbidity and costs associated with isolating and/or treating animals, not because of the severity of disease.

**Mode(s) of transmission and incubation periods**

Incubation periods may be as short as 2 days and as long as 14 days. For some of the pathogens, the incubation period is unknown. Dissemination of disease is promoted with high population density and when carrier animals are mixed with young and naïve dogs that are most susceptible to infection. Direct dog-to-dog transmission is probable when dogs are sharing kennels, when solid walls are not used to separate runs, or when dogs have access to common run areas where they may be exposed to exudates. In addition, some pathogens are spread primarily through aerosolized microdroplets, making the management of crowding and housing a huge factor in the prevention and management of CKCC in shelter environments. Fomites play a critical role in transmission (Petersen, Dvorak et al. 2008). CDV, because of the multisystemic nature of the infection, can also be transmitted through an oral/fecal route.

**Carrier state**

An asymptomatic carrier state for CAV-2, CPiV, CDV, and CRCoV is not thought to occur; however, a CHV carrier state has been documented (Foley and Bannasch 2004). Both *B. bronchiseptica* and *Mycoplasma* spp. can be harvested from the URT of normal dogs and those dogs may serve as carriers. Carrier states of the emerging pathogens CIV and *S. zooepidemicus* are not well defined, but up to 25% of dogs infected with CIV do not exhibit clinical signs and may shed for a brief period after infection (Crawford, Dubovi et al. 2005).

**Shedding**

Most of the viral pathogens are shed for 2 weeks or less postinfection. One exception is CDV, which may be shed for 3 months. Shedding following infection with respiratory CHV and CRCoV is unknown. *B. bronchiseptica* and *Mycoplasma* spp. shedding can persist for 3 months or more following clinical CKCC (Foley and Bannasch 2004; Ford 2006). The length of time for shedding postinfection with *S. zooepidemicus* is unknown. It should not be assumed that dogs with mild clinical disease are not shedding. In fact, shedding of organisms can be high even when clinical signs are not severe (see Table 9.3).

**Clinical Signs**

Because a combination of pathogens is frequently involved in CKCC, it is difficult to attribute individual clinical signs to a given pathogen or vice versa. The most common organisms responsible for CKCC are *B. bronchiseptica* in combination with CPiV or CAV. In general, the summer and fall are the typical seasons to see CKCC. If pathogens are allowed to persist in the population year round, CKCC may result. Typical clinical signs may include conjunctivitis, nasal discharge, and cough in an otherwise healthy dog. This may progress from a soft cough to paroxysms of high-pitched cough, often referred to as “honking” or “goose honking.” Retching frequently follows the cough with either no material visibly expectorated, or a small amount of white frothy fluid. Physical examination may be unremarkable with the exception of tracheal sensitivity upon palpation and resultant coughing. However, caution should be used when interpreting the results of tracheal palpation as a diagnostic tool for CKCC.

A more severe syndrome may occur in dogs with little to no previous natural or vaccine exposure, or when multiple pathogens and environmental factors contribute to disease. Although these dogs may primarily exhibit a cough, there may also be ocular and/or nasal discharge of a serous, mucoid, or mucopurulent character. Involvement of the LRT may follow. Bronchopneumonia may be associated with anorexia, fever, increased respiratory rate

**Table 9.3.** Canine kennel cough complex pathogens.

| Agent | Clinical Signs | Diagnostic Tests | Treatment[a] |
|---|---|---|---|
| CAV-2[b] | Conjunctivitis, cough | PCR | Nursing care |
| CPiV[c] | Conjunctivitis, cough | PCR | Nursing care |
| CRCoV[d] | Cough, nasal discharge? | PCR | Nursing care |
| CHV[e] | Cough, nasal discharge? | PCR | Nursing care |
| CDV[f] | Respiratory, GI, neurologic | PCR, Serology | None |
| CIV[g] | Asymptomatic or fever, cough, purulent nasal discharge or peracute death with pulmonary hemorrhage | PCR, Serology ELISA | Nursing care |
| *B.b*[h] | Cough, mucoid nasal discharge | Culture | Tetracyclines |
| *Mycoplasma*[i] | Conjunctivitis, cough | PCR, Culture | Tetracyclines |
| *S. zoo*[j] | Peracute death with pulmonary hemorrhage | Culture | Penicillins, Cephalexin |

[a] Nursing care: more specific treatment, such as cough suppressants and antibiotics, may be warranted. The use of antibiotics should not be routine, to avoid development of resistant bacteria. However, use should be considered when nasal discharge is purulent.

[b] CAV-2: Canine adenovirus-2: PCR ocular, nasal, oropharynx.

[c] CPiV: Canine parainfluenza virus: PCR ocular, nasal, oropharynx.

[d] CRCoV: Canine respiratory corona virus is not well defined.

[e] CHV: Canine herpesvirus as a pathogen in CKCC is not well defined.

[f] CDV: Canine distemper virus can occur with CKCC pathogens but more significant disease is expected. GI: gastrointestinal. As treatment is usually unsuccessful, euthanasia should be a strong consideration when CDV is confirmed.

[g] CIV: Canine influenza virus is an emerging pathogen.

[h] *B. bronchiseptica* can be harvested from the oropharynx of normal dogs. Specificity of culture increases when tracheal sampling can be done.

[i] *Mycoplasma* spp. are part of the normal flora of the oropharynx of dogs and can be harvested from the trachea as well. PCR for *M. cynos* would be ideal.

[j] *Streptococcus equi* subsp. *zooepidemicus* is an emerging pathogen. Bacterial culture of oropharynx, trachea, or pulmonary tissue is recommended for diagnosis.

and change in respiratory pattern, and increased end-inspiratory (bronchovesicular) sounds on auscultation. This severe presentation may be mistaken for CDV infection.

**Diagnosis**

A presumptive diagnosis of CKCC can be made based on observation of a cough and associated tracheal sensitivity. Incoming dogs should be visually assessed for evidence of oculonasal discharge, sneezing, and cough. Visual daily health assessments should be performed and notations made of any dogs that are inappetent, overly lethargic or depressed, or displaying clinical signs of respiratory disease. When examining animals housed in several different areas of the facility or performing rounds, inspections of animal groups should proceed from healthy populations, to quarantine, and finally to isolation. Dogs with clinical signs should be closely examined by the shelter veterinarian or a trained assistant following inspections of all other groups.

Diagnostic testing is available for all of the pathogens known to be involved in CKCC. When outbreaks occur, the pattern or severity of disease changes, or if zoonotic disease is of concern, testing is indicated. Sampling from the nasal, pharyngeal, and/or tracheal epithelium, and virus isolation or PCR testing for most pathogens can be done. PCR tests for CAV-2, CPiV, CHV, CIV, *B. bronchiseptica*, and *Mycoplasma* spp. are available. Samples should be taken from the deep pharyngeal area, or preferably the trachea, to culture for *B. bronchiseptica*, *Mycoplasma* spp., *S. zooepidemicus*, and other bacterial pathogens; susceptibility to antimicrobials should be

assessed as well. Serum neutralization or hemagglutination inhibition antibody titers might be used to establish exposure but have little clinical application as they could reflect vaccination or natural exposure, except in the case of emerging diseases, such as CIV. For CIV, diagnosis is established by virus isolation, PCR, serology, or Enzyme Linked Immunosorbent Assay (ELISA) for virus antigens. To this author's knowledge, diagnostic tests for CRCoV are not currently commercially available.

False negative results could occur due to either poor sample quality, faulty sample handling, or missing a shedding period. False positive results might occur secondary to vaccination. Sampling of dogs with acute disease and from areas of the respiratory tract apparently affected based on clinical signs is most useful (e.g., deep nasal swabs from dogs with nasal discharge and sneezing). Identification of the pathogens involved provides the opportunity to investigate the potential sources of entry and transmission, evaluate sanitation and disinfection protocols, and reassess vaccination and other health-care protocols. The findings may also facilitate the making of sound management, treatment, and euthanasia decisions. The identification of the pathogens does not rule out contributions of an unidentified agent, however. When severe disease is present or when outbreaks occur, if the opportunity presents itself, the most accurate method to obtain a definitive diagnosis is by means of necropsy. (See Chapter 7 on necropsy techniques.)

**Treatment**

Treatment of CKCC should involve good nursing care in the form of monitoring fluid and food intake, offering a quiet, stress-free environment, utilizing strategies to reduce excitement and barking, and providing adequate ventilation with fresh air if possible. The use of harnesses or "gentle leaders" instead of neck collars that put pressure on the trachea may help as well. Isolation areas for treatment of the affected are ideal so infected dogs are not moved into the main shelter area with the general population.

***Antimicrobial therapy***

As CKCC frequently involves viral pathogens, the use of antimicrobials should be questioned, especially in uncomplicated cases. There is no evidence that prophylactic use of antimicrobials to prevent CKCC is effective, and this strategy should be avoided, as indiscriminate use of antimicrobials may lead to bacterial resistance in a population. The use of antimicrobials could be of benefit in reducing the magnitude of disease and duration of coughing in symptomatic dogs, especially if endemic bacterial disease has been confirmed, the clinical course of the disease worsens, or percent of the population affected increases.

Treatment options for CKCC in a shelter may include amoxicillin, amoxicillin-clavulanate, azithromycin, cephalexin, clindamycin, doxycycline, enrofloxacin, or trimethoprim-sulfonamide (TS). The choice of antimicrobial should be directed by whether or not a primary or secondary bacterial infection is suspected. Generally, oral administration is chosen for cost effectiveness. Antibiotic susceptibility test results from pathogens harvested from a sampling of CKCC dogs can be used as a guide and should be obtained if disease is more severe or widespread than expected or does not respond to initial treatment. Doxycycline is regarded by some as the first line of treatment since other antimicrobials have often been widely used and resistance has developed. Doxycycline is also widely used empirically because it is effective against *Bordetella* and *Mycoplasma*. Additionally, doxycycline is comparatively less costly and can be administered once daily, which may increase compliance, especially when many dogs are under treatment. TS has been regarded as an excellent choice for treatment of *B. bronchiseptica*. However, in a recent retrospective study of community acquired *B. bronchiseptica*, only 9 of 31 isolates were sensitive (Radhakrishnan, Drobatz et al. 2007). *Mycoplasma* spp. are generally sensitive to clindamycin, doxycycline, and enrofloxacin. *S. zooepidemicus*, as a group C streptococcus, would not be expected to be sensitive to doxycycline but rather to penicillin (G and V), cephalosporin (cephalexin), and macrolide (erythromycin) antibiotics (Greene and Prescott 2006). If a mixed secondary bacterial infection is suspected, cephalexin may be a good choice pending culture and susceptibility testing. Duration of treatment recommended may be up to a minimum of 14 days, depending on the antimicrobial and the pathogen when known.

***Antitussive, bronchodilator, and anti-inflammatory therapy***

Antitussive therapy has been thought to be extremely important in interrupting the cough cycle associated with CKCC. However, evidence that over-the-counter antitussive compounds are beneficial is lacking. Narcotic cough suppressants are effective in reducing cough frequency and intensity, but narcotics may also reduce expectoration and compromise ventilation, which is undesirable (Ford 2006). Administration of bronchodilators or anti-inflammatory drugs (e.g., prednisone) may be beneficial in individual patients but are not generally recommended in dogs with CKCC. In addition to these reasons, it is recognized

that administration of medication to large numbers of dogs in a population without suitable precautions (e.g., changing gloves) when going from one sick animal to another could potentially facilitate fomite spread of disease.

***Therapy not recommended***

Antiviral therapy, intranasal vaccination, and the use of expectorants are not recommended to treat CKCC. Antiviral drugs are generally very specific and targeted against specific viruses. No effective antiviral drugs have been developed against the viruses known to be associated with CKCC. In addition, there is no evidence that expectorants or intranasal vaccination as therapy are helpful (Ford 2006).

## PREVENTION AND CONTROL

Facility design can greatly influence prevention and control of infectious disease (Johnson 2004). Separate ventilation systems and exposure to fresh air may be beneficial; however, shelters with indoor/outdoor housing often still encounter problems with CKCC. Runs with solid walls separating dogs, and runs divided by guillotine doors can be very helpful in blocking transmission of disease and facilitating cleaning procedures that minimize fomite transmission. Housing dogs in separate cages or runs is ideal, although housing dogs together that originate from the same household or that are littermates is acceptable for enrichment purposes. It is highly desirable to segregate juveniles from adults, and to house age-matched animals together in the same section because this will reduce stress and minimize transmission to the immunoincompetent or naïve (Miller 2004). When communal housing of dogs is absolutely necessary and not used purposefully for stress reduction or behavior enrichment, cohort housing (all-in/all-out) of dogs that enter the shelter on the same date rather than mixing new dogs with dogs already in residence is critical to control canine respiratory disease. Severe, prolonged outbreaks have been associated with constant remixing of dogs in cohousing situations (Pesavento, Hurley et al. 2008). It should always be borne in mind that crowding must be avoided whenever possible as it only contributes to an increase in disease transmission. A finding in a recent controlled prospective vaccination study was that the strongest predictor for coughing was the number of days spent in the shelter. Each additional day increased the risk of coughing by 3% (Edinboro, Ward, Glickman 2004).

### Quarantine recommendations

Ideally, dogs that enter the shelter should move through in waves, which require smaller kennel rooms that many shelters do not have. So while in principle quarantines would seem to be useful, the effectiveness of quarantines in shelters has not been established because new arrivals are often added to the quarantined population, defeating the purpose: the ability to observe a select group of animals for a defined period of time. It has already been demonstrated that longer stays in shelters result in increased disease transmission. Quarantines may be most useful when animal transfer programs result in several animals arriving at the shelter on the same day so that an all-in/all-out system can be utilized. They can be considerably less useful as a matter of routine or during mild disease outbreaks.

If it is elected to institute a quarantine, CKCC pathogens may incubate for up to 2 weeks before clinical signs of disease are seen, therefore a 2-week quarantine would be necessary. After that time, dogs would move forward toward adoption. Any animal in quarantine that exhibits evidence of respiratory disease should be removed and isolated. Quarantine may need to be restarted following each new potential exposure. Even when disease is endemic, movement of symptomatic dogs to less affected areas should be restricted. Reducing the length of stay of incoming dogs should also be a top priority to decrease the risk of infection.

### Isolation recommendations

Any dog that exhibits clinical signs of CKCC should be isolated without delay. As shedding of the pathogens involved with CKCC may persist for at least 2 weeks and up to 3 or more months, dogs moved to adoption areas may serve as a source of infection. Ideally, dogs that have recovered from CKCC should be housed separately and adopted from a recovery room rather than the main adoption room. At a minimum, they must not be cohoused directly with unaffected dogs. To avoid cross-species transmission of disease and to reduce stress, separate isolation facilities should be available for the different species. Dogs with signs of CKCC who are eating and drinking can be fostered or adopted out as long as the destination home is well managed in regard to preventative health care of the home resident dogs, oral and written instructions for care are supplied, and the adopters are advised of the modest risk of transmission to pet animals and rare zoonotic infection. (See the section on client education.) The risk of transmission to pet animals must be considered greater if otherwise healthy, well-vaccinated dogs in the shelter are affected, as may occur with canine influenza and other emerging pathogens. In these cases, adoption or foster care in homes with no other

dogs or the ability to practice high-level disease control would be advisable.

**Vaccination**

Vaccination is available against some components of CKCC. Typical vaccine components include the primary viral pathogens CPiV, CAV-2, and CDV. Because the shelter environment has the challenge of high population density and high probability of exposure to multiple infectious agents, the risk assessment and protocols recommended are different from those for the owned pet. Guidelines for vaccination of dogs in the shelter environment were published by the American Animal Hospital Association in 2006 (Paul, Carmichael et al. 2006). For the primary respiratory pathogens, modified live virus (MLV) vaccines are recommended because they provide more rapid immunity and one dose may be sufficient in animals over 3 to 4 months of age. They are available in combination with canine parvovirus for parenteral administration. Shelter puppies should be vaccinated beginning at 6 weeks of age and revaccinated at 2-week intervals until 16 weeks of age.

Vaccination should be given immediately upon entry into the shelter, as virtually immediate protection has been documented for some pathogens (e.g., canine distemper); delaying vaccination even for a few hours may increase the risk of infection. Alternatively, CPiV and CAV-2 can be administered via intranasal (IN) vaccination along with avirulent live bacterin for *B. bronchiseptica,* and in pups as young as 2 to 3 weeks of age. Onset of immunity occurs within 3 to 5 days following IN vaccination. In pups vaccinated at less than 6 weeks of age, an additional dose should be given after 6 weeks (Paul, Carmichael et al. 2006); otherwise, one dose is sufficient.

The efficacy of vaccination against the agents involved in CKCC is variable. Vaccination for CDV and CAV-2 offers excellent immunity, while vaccination for other pathogens offers less protection. Vaccination does, however, play a role in controlling CKCC in the shelter environment. In one recent prospective study comparing two IN vaccines for *B. bronchiseptica* and CPiV, one with and one without CAV-2, and using a placebo for a third group, the reported overall incidence of CKCC decreased from 50% to 20% in 1 month. The IN *B. bronchiseptica*–CPiV vaccine and the IN *B. bronchiseptica*–CPiV–CAV–2 vaccine were 20% and 24.4% effective, respectively, in reducing coughing compared to the control placebo group (Edinboro, Ward, and Glickman 2004).

In another recent prospective controlled study, mucosal immune response was assessed in 9- to 10-week-old healthy puppies vaccinated with either an IN avirulent live culture (in combination with MLV CPiV and CAV-2) or a subcutaneous (SQ) antigen extract vaccine of *B. bronchiseptica*. The puppies were then challenged IN with live virulent *B. bronchiseptica.* IN-vaccinated dogs developed higher levels of *B. bronchiseptica*-specific IgA titers in nasal secretions. Mean cough scores, number of days of coughing, and shedding were significantly lower in the IN-vaccinated group compared to the SQ-vaccinated and control groups (Davis, Jayappa et al. 2007).

Immunity following MLV immunization for CDV and CAV-2 lasts several years, while immunity following CPiV and *B. bronchiseptica* is of much shorter duration.

Potential adverse effects of IN vaccination are oculonasal discharge, sneezing and coughing, seen within 3 to 10 days. These signs cannot be readily distinguished from signs of true clinical disease. Other adverse effects are possibly inclusive of local, mild, and systemic effects. A significant reaction can be seen if IN *B. bronchiseptica* is administered SQ. Delivering this virulent organism SQ can result in a local inflammatory reaction, abscessation, and, rarely, hepatic failure and death (Toshach, Jackson, and Dubielzig 1997.) Realization that this has occurred should prompt immediate treatment in the form of local infusion at the injection site of gentamicin (2–4 mg/kg) diluted in 10–30 ml of sterile water. This may be followed by oral administration of doxycycline and careful monitoring and supportive care if needed (Paul, Carmichael et al. 2006).

Vaccines are not thought to have a therapeutic effect on dogs already infected. Vaccination of dogs before or upon entry to the shelter, however, is expected to decrease the overall incidence of disease (Edinboro, Ward, and Glickman 2004).

**Disinfection**

Cleaning, sanitation, and disinfection of the shelter are among the key factors for control of infectious disease. These procedures are most difficult to perform well when population density is high. Protocols for this process should be clear and posted for easy reference. All staff and volunteers should receive initial training, and performance should be assessed regularly. Disinfectants used in the shelter should be diluted to the appropriate concentration, and manufacturers' instructions should be adhered to, which includes allowing sufficient contact time on surfaces that have been properly cleaned to remove organic material. Removal of the disinfectant by rinsing with water is often necessary, depending on the chemical used. Disinfection of transport vehicles, medical, groom-

ing, and other equipment, communal areas, including adoption or acquaintance areas where potential adopters spend time with dogs, and treatment rooms should not be overlooked. In addition, hands should be cleaned between handling of dogs, as pathogens are known to attach to the hair coat and can be transferred via hands from one dog to the next. In addition, transmission on clothing is likely, considering the high degree of contact with clothing in the course of normal handling and treatment of dogs. Strong consideration should be given to wearing disposable gloves and gowns in isolation and treatment areas (Gilman 2004; Dvorak, Petersen et al. 2008; Hurley and Baldwin 2008).

Most of the CKCC pathogens are inactivated by the disinfectants commonly used in shelters (e.g., alcohol, bleach, quaternary ammonium compounds, and potassium peroxymonosulfate). CAV-2 is more resistant but can still be inactivated using a 1:32 dilution of bleach to water, or peroxymonosulfate, with appropriate contact time (usually 10 minutes). It is essential to dry surfaces after rinsing. In a recent shelter investigation in the U.S. that revealed many pathogens contributing to disease and the death of shelter dogs, *S. zooepidemicus* was cultured from standing water following cleaning (Pesavento, Hurley et al. 2008). Environmental sampling of airborne and surface pathogens should be used to assess whether disinfection protocols are effective and being adhered to by staff.

### Euthanasia guidelines

Dogs with CKCC that exhibit severe signs of disease such that they are unable to eat and drink, or show signs compatible with pneumonia, such as anorexia, fever, increased respiratory rate, change in respiratory pattern, and increase in end-inspiratory (bronchovesicular) sounds, should prompt consideration of euthanasia if appropriate supportive care and specific treatment (e.g., antimicrobials) cannot be offered and animal suffering results. These clinical signs could occur prior to or following treatment with appropriate antimicrobials. Consideration for the health of the general population must also be given. In a dense population with endemic or epidemic disease, decreasing the number of dogs in the population through removal for offsite care, or euthanasia of severely affected animals, may allow for changes that lead to the improvement of the health of the overall population. This approach must be coupled with careful review of vaccination, treatment, housing, quarantine, isolation, and environmental control protocols and measures. Conscientious record keeping is essential so that it may be determined which strategies were actually effective in resolving the outbreak.

## CLIENT EDUCATION/IMPLICATIONS FOR FOSTER CARE AND ADOPTION

Attempts to decrease the length of stay, which in turn decreases the chances that dogs will acquire disease from within the shelter, should always be made. The clinical course of the disease may provide an indication of which common pathogens are responsible for the signs of CKCC and whether fostering and adoption can be safely promoted. Identification of pathogens within the shelter, by means of antemortem or postmortem sampling, is also helpful in determining whether dogs can be placed in foster care or adoption. Changes in the magnitude or severity of clinical disease within the shelter, such that CDV, CIV, or *S. zooepidemicus* are suspected, should be reason for concern.

Shelters should strive to have knowledgeable and responsible foster families who can offer a respite to dogs with CKCC. Foster home pets should be current on vaccination. The foster caregiver's veterinarian should be made aware that the caregiver works at a shelter so that an appropriate risk assessment for vaccination can be made. Risk analysis will determine whether foster home pets may require more frequent vaccination because of the possibility of increased exposure to pathogens. Information sheets on CKCC will help prepare the foster home about what to expect and how to care for the dog. Guidelines for when veterinary care is needed should be provided, and the shelter should be alerted when care is needed, whether care is available at the shelter, or if the dog must see a veterinarian from the community. Foster dogs should be free from clinical signs of CKCC for at least 14 days before returning to the shelter or going to an adoptive home. Foster families should also be advised to keep the dog away from dog parks, pet stores, and other canine gathering places until 14 days after clinical recovery.

The education of adoptive families is equally important for the successful placement of shelter dogs in homes. Discussion of CKCC with the client and supplying information sheets is good practice. Information sheets distributed to foster families can be easily adapted for adopters. It should be recommended that dogs be examined by their regular veterinarian within a few days of adoption (www.sheltermedicine.com/portal/is_infectious_tracheobronchitis_canine.shtml#foster 2007).

## CONCLUSION

CKCC presents a significant management problem in shelter environments because it is highly contagious and reduces adoption rates, and because affected animals may require intense medical management. A significant burden

can be placed on finite shelter resources with the increased length of stay, costs for increased time of personnel to care for the sick, and medical costs for drug therapy. Knowledge of etiologic agents, modes of transmission, incubation and organism shedding periods, clinical signs, diagnostic testing availability, and treatment protocols are necessary to properly manage CKCC. Prevention and control, rather than eradication of pathogens, is the goal, beginning with a sound vaccination program, good husbandry, appropriate housing, management procedures designed to reduce stress, prevention of transmission including judicious use of quarantine and isolation measures, and sound sanitation and disinfection protocols. Disease surveillance is also essential. Challenges are present in both open admission shelters that must admit all animals and limited admission shelters that can control the flow of animals. As population density increases, the severity and magnitude of disease may intensify. Strategies to manage density by limiting admission to the shelter, decreasing length of stay through fostering and adoptions, and appropriately treating those animals that can be adequately cared for with the resources available will result in fewer animals being at risk.

For effective implementation of control measures for CKCC, additional characterization and investigation of disease, prevention, and treatment in shelters are needed. Veterinary resources are now available so that observational and experimental (randomized control trial) studies can be initiated in order to apply evidence based medicine to shelter medicine (Schmidt 2007). These and similar resources will help guide veterinary professionals to conduct and evaluate studies, and the results will provide the evidence needed to make sound assessments and develop strategies to minimize disease in shelter environments.

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# 10
# Canine Distemper Virus

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## INTRODUCTION

Canine distemper virus (CDV) causes a highly contagious infection in dogs that once was the species' most common and deadly infectious diseases. Although largely controlled by vaccination in owned pets, distemper remains a significant cause of morbidity and mortality in shelters because of the presence of frequently susceptible dogs and puppies. Infection can be inapparent, mild, or severe, leading to death in up to 50% of the infected animals. Problems with CDV in shelters can remain at low levels for long periods or cause obvious acute outbreaks with high morbidity and mortality.

## AGENT AND EPIDEMIOLOGY

Canine distemper virus is an enveloped RNA virus in the genus *Morbillivirus* in the family *Paramyxoviridae*. The other viruses in the same genus include the closely related measles virus of primates, rinderpest of ruminants and pigs, and the peste des petits ruminants virus found in certain small ruminants. Animals susceptible to CDV that are most likely to be present in shelters or have contact with shelter animals are dogs, ferrets, coyotes, skunks, and raccoons. Many other species are also susceptible to infection. While dogs are the primary host for CDV, it is likely that the raccoon population acts as a reservoir and is responsible for much of the exposure and maintenance of CDV in some communities. A significant source of infection in at least one major CDV outbreak in shelter dogs was found to be infected raccoons. The exposure apparently occurred when both species were collected and placed into animal control vehicles (Hurley 2005). Zoonotic transmission of CDV has not been demonstrated.

There is often confusion with regard to cats because of the disease sometimes referred to as "feline distemper." Feline distemper is caused by feline parvovirus (panleukopenia), which is the ancestral virus of canine parvovirus type 2. CDV does not infect domestic cats nor cause disease in that species; however, it does cause disease in large felids (e.g., lions and tigers) (Ikeda, Nakamura et al. 2001; Spencer 1995).

### Biotypes of CDV

There are a variety of biotypes of CDV, and they have different incubation periods as well as different disease patterns in the animal. The more classic, acute biotype of CDV that was originally isolated and characterized is often referred to as the Snyder Hill strain of virus because it was isolated and characterized at the Veterinary Virus Research Institute (now the James A. Baker Institute for Animal Health) at Cornell University, which is located on Snyder Hill Road, Ithaca, New York. Today, the acute virus biotype Snyder Hill has been replaced by a subacute virus biotype referred to as R252. A very similar, if not identical virus, A75 has also been isolated. These two isolates are of the same or similar biotypes and probably are the more common biotype in the field since the 1980s.

Importantly, although there are multiple biotypes, there is only one serotype (antigenic type) of CDV, and thus the modified live virus (MLV) vaccines made in the late 1950s and early 1960s remain highly effective in limiting infection and preventing disease. Today, in most communities of developed countries such as the United States, where approximately 50% or more dogs are vaccinated (Schultz, unpublished), disease caused by CDV is rarely seen because vaccinated dogs are immune to infection and/or disease. CDV-induced disease remains common in regions where fewer than 25% of dogs are vaccinated and in environments such as shelters where unvaccinated dogs may be densely housed or exposed to infected dogs or wildlife.

### Transmission

CDV may be shed in virtually all body secretions and excretions depending on the stage of infection. Transmission most commonly occurs through inhalation of airborne virus or direct contact between susceptible and actively infected dogs (Appel 1987). Fomite or environmental transmission of CDV is also possible, but the virus does not remain infectious for more than hours to a few days, depending on ambient temperature and other conditions. Fomite and environmental contamination is therefore of less importance for disease transmission than for a hardier virus such as canine parvovirus. Nevertheless, in an environment such as a shelter where infected dogs may be housed in close proximity to susceptible dogs and the virus need only survive for minutes on contaminated fomites, this route of transmission may become significant. Because the virus does not persist long in the environment, mildly affected and recovering animals play an important role in maintaining transmission cycles in shelters.

### Pathogenesis

Virus replication initially occurs in lymphoid tissues when CDV first enters the body (Appel 1987; von Messling Milosevic, Cattaneo 2004). In all likelihood, phagocytic cells transport the virus from the respiratory tract to local lymph nodes or other respiratory lymphatic tissues, where CDV actively replicates in an immunologically naïve dog. Once the virus begins to replicate in the macrophage/monocyte and the T and B lymphocytes, it is rapidly transported to peripheral lymphoid tissues throughout the body, including lymph nodes, spleen, bone marrow, Kupffer cells of the liver, etc. (Appel 1987).

During this early phase of the infection, the animal becomes immunosuppressed with severe T and B lymphocytopenia, interference with macrophage function, as well as other immune function impairment (Krakowka, Olsen et al. 1975; Schobesberger, Summerfield et al. 2005). The authors have also demonstrated suppression of neutrophil function in vitro (Schultz 1978). Immunosuppression can last for weeks, depending on the biotype of CDV infecting the dog. This immunosuppression probably contributes to many of the signs of disease seen in shelters as infected dogs become vulnerable to secondary infections.

### Risk factors for infection

The authors have found that during the past 5 years of evaluating titers from dogs entering shelters throughout the US, approximately 50% (±20%) of dogs are antibody negative for CDV at the time of intake. That means that those dogs have probably never been vaccinated or naturally infected, are susceptible to infection, and have a high probability of becoming infected if exposed. In contrast to canine parvovirus, where adult dogs tend to have at least some age-related defense against the development of severe clinical signs, susceptible dogs in any age group may develop severe clinical signs of CDV. Age offers no specific benefit or protection from development of disease. More obvious clinical signs, higher morbidity, and mortality may be seen more commonly in shelter puppies because young dogs are more likely to be immunologically naïve and are more difficult to immunize effectively. Because of the possibility of maternal antibody interference with vaccination, all puppies under 16 weeks of age must be considered potentially susceptible, regardless of their vaccination history.

## CLINICAL SIGNS AND DISEASE COURSE

### Incubation period, viral shedding, and carrier state

The time until onset of clinical signs, the duration of infection and disease, and the severity of disease is both virus strain and host (dog) dependent, as is the case for many viral infections/diseases (Appel 1987; Summers, Greisen, Appel 1984). The incubation period, in the authors' experience, depending on the strain of virus and the dog, ranges from just less than 2 weeks up to 6 weeks postinfection. Prior to the 1970s, the acute form of CDV was commonly seen in the field. Since the early 1980s, only the subacute form of disease has been reported.

Clinical signs of CDV have frequently been described as biphasic. The earliest sign of infection with CDV would normally be an initial febrile response within a few days to a week after infection. This often goes unrecognized, especially in shelter settings. The initial febrile response often coincides with the onset of a period of immunosuppression that can occur as early as 3 days postinfection and persist for weeks to a month or more. Clinical signs of neurologic disease may develop concurrently with other systemic signs, in the absence of other signs or develop 1 to 3 weeks or even longer after resolution of other systemic signs of illness.

Viral shedding begins by 1 week postinfection, sometimes prior to the development of clinical signs. Viral shedding may continue for up to 16 weeks postinfection, but usually resolves more quickly. Shedding is most common in respiratory secretions, but is possible from all tissues and bodily excretions. There is no carrier state, per se, for CDV. A syndrome known as old dog encephalitis (ODE) has been described. ODE does not result from a chronic infectious carrier state of CDV but rather from

progressive neurologic disease induced initially by CDV. Although there is no true carrier state for distemper, subclinical infections are common, and these dogs may serve as transient carriers while they are infected and shedding virus.

Recovered animals may remain infectious for up to 4 months postrecovery. Therefore, potentially infectious, exposed, or recovered dogs should be kept away for 4 months from puppies and unvaccinated dogs, and from dogs that have been vaccinated in the previous 3 days in either the shelter or the community. Dogs may be tested for viral shedding postrecovery by reverse transcriptase-polymerase chain reaction (RT-PCR) of nasal and conjunctival swabs. PCR testing is probably best performed starting approximately 2 weeks after the resolution of clinical signs. Although unproven, a positive PCR would suggest the animal remains contagious to others, while a negative PCR would suggest the dog is less likely to be infectious. Once recovered from clinical signs, dogs will normally be immunocompetent and can be vaccinated and spayed without additional precautions.

**Clinical signs**

There is significant variation in the clinical signs seen in dogs with CDV infections. It is estimated that 25% to 75% of infected animals will never show clinical signs of disease. Some of these dogs are likely to have immunosuppression and will shed virus, whereas other dogs [depending on the dog and biotype (strain) of virus] will develop severe disease where mortality can exceed 50%. In general, of those dogs that develop clinical signs of distemper, mortality will be about 50% (± 20%). In shelters, additional mortality may occur due to pneumonia and other secondary infections in dogs with CDV-induced immunosuppression.

The earliest recognized clinical signs of CDV infection are often oculonasal discharge and conjunctivitis, followed by anorexia. These signs occur early in the first to third weeks after infection and can be difficult to differentiate from more benign disease, but should be recognized as potentially suggestive of CDV.

These early signs may be followed in the second week or later by vomiting and diarrhea. Gastrointestinal signs may be associated with tenesmus and bloody feces. Intussusception is a risk. Dramatic wasting can occur with or without anorexia. Dehydration and systemic collapse are a significant risk without proper medical support and intervention. As a result of viral infection of the pulmonary tissues, lower respiratory disease may also be seen during this later phase.

Skin disease (pustules) or a measleslike rash (which is very rare) may be seen in a small percentage of infected dogs. Digital and nasal hyperkeratosis have also been well described and are most often associated with varying levels of neurologic disease. Distemper was once known as “hardpad disease,” a reference to the digital hyperkeratosis that is less commonly seen today.

A careful ocular exam is indicated in all cases of suspected distemper because ocular signs are relatively common. The most common ocular signs are crusting, ocular discharge, and conjunctivitis as described above. Dogs may also be seen squinting or blinking their lids. Keratoconjuctivitis sicca (“dry eye”) may result in ulcer formation and perforation of the cornea, as first described by Dr. Henri Carré in 1905 in what may have been one of the earliest descriptions of distemper. Other ocular signs of CDV result from viral effects on the optic nerve and the retina. Lesions that develop on the retina, secondary to degeneration and necrosis, appear as gray-pink densities. Postinfection, these lesions can be identified as hyperreflective areas suggestive of previous infection with CDV. Optic neuritis, sudden blindness and retinal detachment can also occur.

Dogs often appear to recover completely from respiratory or systemic disease, but in a small number of cases, severe neurologic disease develops months later. This delayed neurologic form of disease is due to an immunopathologic destruction of nervous tissue rather than viral-induced damage to the tissues. Dogs with this form of disease will have high levels of CDV antibody in their cerebrospinal fluid (CSF) and a monoclonal IgG protein detectable by immunoelectrophoresis of CSF.

In other cases, dogs will develop neurologic signs in closer proximity to the time of infection. In these cases the neurologic disease results from viral invasion of neurologic tissue rather than an immunopathologic process as described above. When present, the central nervous system (CNS) infection can be primarily white matter or gray matter disease, depending on the biotype of the virus (Pearce-Kelling, Mitchell et al. 1991; Summers, Greisen, Appel 1984). The acute strains are more often associated with gray matter pathology, whereas the subacute strains are more often associated with white matter pathology. Clinically the two forms are indistinguishable. Convulsions are characterized by salivation and chewing movements (petit mal) and seizures that may become more frequent and severe (grand mal). Although mortality can be very high in dogs that develop CNS signs, a few dogs completely recover clinically, whereas others have neurologic signs that persist (e.g., persistent myoclonus).

Other reported signs of CDV infection include enamel hypoplasia as a result of neonatal infection; metaphyseal osteosclerosis; an association with hypertrophic osteodystrophy (HOD), especially in large breed puppies; and various complications of pregnancy related to transplacental infection such as abortion, still birth, and birth of weak puppies.

### *Secondary infections associated with immunosuppression*

As described above, CDV can cause a period of immunosuppression with or without concurrent typical signs of canine distemper. Immunosuppression then most often leads to clinical signs of canine respiratory disease complex (CRDC), commonly referred to as kennel cough. This is a complex disease caused by a variety of bacteria (*Bordetella, Streptococci, Pasteurella*), *Mycoplasma*, and viruses [(canine adenovirus-2, canine parainfluenza virus (CPIV)] as described in detail elsewhere in this text. When present in dogs coinfected by canine distemper, CRDC may cause severe clinical signs, including pneumonia and death. In shelters, respiratory disease from secondary pathogens may appear more quickly than actual pulmonary infection with CDV virus. Immunosuppression may also contribute to other opportunistic infections, most notably salmonellosis, which may present a zoonotic risk and lead to hemorrhagic diarrhea, sepsis, and death in infected dogs.

## DIAGNOSIS OF CANINE DISTEMPER

In the early stages of disease, it is often difficult to diagnose distemper, as the signs may resemble CRDC (kennel cough) or other diseases depending on the system affected. Clinical signs of CDV encompass a wide range of disease symptoms that frequently overlap with other conditions commonly seen in shelters. Oculonasal discharge, upper and lower respiratory disease, gastrointestinal disease such as inappetance, vomiting, and diarrhea are the most common early signs of disease while neurologic disease is the most distinctive late-phase clinical sign. Neurologic disease suggestive of CDV in any individual animal in a shelter setting warrants further investigation. Neurologic disease suggestive of CDV in multiple animals within the population or after adoption, or markedly increased frequency or severity of CRDC is cause for diagnostic evaluation of the group.

Isolation of the wild-type (virulent) virus has always been difficult because the virulent virus does not readily replicate in tissue culture cells – either primary cells or cell lines. Appel found that primary cultures of alveolar macrophages could be used to isolate wild-type virus, but the cells did not grow well; fresh lung tissue was required, and the cells could not be passed (Appel and Jones, 1967; Appel, Pearce-Kelling, Summers 1992). Because of the difficulty of growing CDV in tissue culture, immunofluorescent antibody (IFA) tests were adapted for detection of CDV in tissue sections and in various other sources where cells could easily be obtained (e.g., conjunctival swab, rectal mucosa swab, leukocytes, etc.). IFA tests were used for years prior to the development of other more reliable and sensitive diagnostic methods.

Antemortem tests now also include RT-PCR, immunohistochemistry (IHC), and serologic tests; each has limitations. These assays are used on cells from various sources such as conjunctival, rectal, buccal, mucosal, and vaginal swabs, tracheal washes, cerebral spinal fluid, and buffy coats, as well as tissue biopsy imprints or sections (Saito, Alfieri et al. 2006; Damian, Morales et al. 2005). Serologic tests that measure IgM (early in infection) versus IgG (later in infection) have also been used for diagnosis in live dogs, but have not been found to be very reliable in the field (Blixenkrone-Møller, Pedersen et al. 1991). Because the sensitivity of all available antemortem tests is limited, and shedding may be variable, negative test results, particularly from a single patient, do not completely rule out distemper. Postmortem testing is more reliable, as multiple tissue samples can be tested by RT-PCR, IFA, or IHC. In addition, histologic tissue changes and presence of viral inclusion bodies in cells are diagnostic for CDV (Appel 1987).

### Reverse transcriptase-polymerase chain reaction assay

RT-PCR assay is now commonly used to detect viral nucleic acid in samples from suspect animals. Since CDV is shed in all body secretions/excretions during acute systemic disease, a variety of samples can be tested and would be expected to be positive in infected dogs depending upon the phase of infection. It would also be expected that many of the samples currently tested would be positive in recently vaccinated animals because the MLV vaccine CDV replicates in most of the same cell types as the virulent virus. Although vaccine virus replication is transient and virus is not shed at sufficient levels to infect in-contact naïve animals, the sensitivity of RT-PCR could detect the vaccine virus in certain samples. It is not currently known how long after vaccination the specific animal would remain positive, or how commonly positive results occur after vaccination. It is likely the animal would be positive as soon as 3 to 4 days after vaccination, and viral nucleic

acid could positively be detectable, at least in certain samples (those with leukocytes), up to 2 weeks. The only vaccine that should not be detected would be canarypox vectored recombinant CDV vaccine found in the Recombitek® vaccine.

### Immunohistochemistry and immunofluorescent antibody tests

Immunohistochemistry (IHC), and to a lesser extent today, immunofluorescent antibody (IFA) tests are used primarily on tissue sections after postmortem examination for detection of CDV in situ. Because these assays are designed to detect intact virus, with viral protein associated with the envelope antigens, these techniques have a reduced sensitivity and a shorter period of detection time compared to RT-PCR, which detects viral RNA. They are unlikely to detect CDV from the modified live vaccine for more than a few days, with a peak time of 3 to 7 days after vaccination. This is in contrast to the presence of nucleic acids that are produced at higher levels and detected at higher sensitivity with PCR. Because CDV is widespread in tissue in infected dogs, IHC or IFA tests of tissue sections are sensitive methods for postmortem diagnosis.

IHC can be performed on cells from antemortem samples, including conjunctival scrapes, urine sediment, or buffy coat. These are not believed to be affected by recent vaccination so specificity is high, but due to variable shedding in these tissues, sensitivity is low and negative results do not rule out infection.

### Serologic tests

Serologic tests that measure IgM (early in infection) versus IgG (later in infection) have been used but are not reliable in a shelter where dogs are vaccinated at entry. Serologic tests are of greatest value in determining the immunologic status of dogs entering shelters or that are present at the time of a CDV outbreak. Those dogs that have antibody and are free of clinical signs are protected from infection and disease, whereas those dogs under 16 weeks of age that are most likely to have maternally derived antibodies (MDAs) are at risk of infection as the passive antibody decays. Acute and convalescent samples are of only limited value in a shelter situation because most dogs have been vaccinated at entry and more rapid tests are available for diagnosis (e.g. IHC, IFA, and PCR).

### Postmortem testing

Postmortem testing is the most reliable means to definitively diagnose distemper in an individual and a population because multiple tissue samples can be examined. Also, histologic changes and presence of viral inclusion bodies are diagnostic. (See Chapter 7 on necropsy.)

### Diagnostic strategy

Diagnosis of individual animals may be pursued in some animal welfare organizations. Recognizing disease and differentiating CDV infection from other potential pathogens may help management to design a treatment plan, identify concerns for rescue groups or adopters, and develop a response for handling other potentially exposed and susceptible dogs.

Diagnosing a group problem, such as a shelter with endemic levels of disease or an outbreak of CDV, should be a priority whenever suggestive signs are present within a population. Organizations that are having problems with canine respiratory disease complex should always be wary of the possibility that CDV may play a role. Some additional criteria for heightened suspicion that CDV is present in a shelter population include:

- shelter and community history of problems with CDV
- vaccination practices that do not ensure ALL dogs are vaccinated immediately on intake
- development of neurologic disease in any dogs either in the shelter or after release
- markedly increased frequency or severity of CRDC
- management practices that would favor transmission by allowing potentially infected dogs to remain in the general population or have contact with healthy susceptible animals

If these risk factors are present, necropsy testing of suspicious cases that die or are euthanized should be undertaken to permit definitive diagnosis. Alternately, if no necropsy specimens are available, samples should be obtained from multiple acutely affected dogs (ideally 10% to 30% of the population, a minimum of 5 to 10 dogs) and evaluated by PCR testing. Although vaccine-induced positives are possible, frequent positive results on PCR are cause for concern, and additional diagnostics, even in a recently vaccinated population, should be performed to confirm a CDV diagnosis.

## TREATMENT

Treatment recommendations for CDV focus largely on supportive care. Detailed information about the treatment of canine distemper can be found in other veterinary textbooks; only the basics will be covered in this chapter. As mentioned earlier, systemic disease may lead to severe dehydration and emaciation, respiratory disease may prog-

ress to pneumonia, and immunosuppression facilitates invasion by secondary pathogens. Supportive care primarily revolves around intensive nursing care, fluid replacement and systemic vascular support, nutrition, and treatment or prevention of secondary bacterial infection. This supportive care may reduce mortality as the viral infection runs its course. Dogs that have not developed neurologic disease have the best prognosis for recovery. Dogs that develop severe neurologic signs are unlikely to recover. Mild neurologic signs, such as myoclonus, may be more manageable, but neurologic disease is often progressive and irreversible. In every case where treatment is being considered, both risk of contagion to other animals, prognosis, and welfare of the individual animal should be considered carefully. Treatment of distemper in the shelter should only be undertaken if animals can be suitably isolated, housed in clean, warm rooms that are free of drafts, and provided with good nursing care.

Judicious use of broad-spectrum bactericidal antibiotics is recommended when treating respiratory disease associated with CDV. Viral pneumonia is often accompanied by secondary bacterial infections, or a primary bacterial pneumonia may be present due to CDV immunosupression. Bacteria associated with primary or secondary pneumonias include *Bordetella bronchiseptica, Streptococcus* species, *Pasteurella multocida, E. coli, Staphylococcus* species, and *Mycoplasma*. Secondary infections may be susceptible to different antibiotics than those most commonly used in shelters to treat suspected primary *Bordetella* infections; culture and sensitivity should be performed especially when treating groups of animals for pneumonia or in cases where dogs fail to respond to empirical therapy.

When gastrointestinal signs are present, broad-spectrum parenteral antibiotic therapy is essential. Fluid replacement therapy in the form of polyionic fluids such as Lactated Ringers solution corrects dehydration and helps prevent systemic collapse. B vitamins are also recommended. Antiemetics should be given when vomiting is present, and vomiting dogs should not be fed. For dogs that are unable or unwilling to eat, other forms of nutritional support should be considered since treatment may be prolonged, and wasting is common.

Treatment for neurologic disease is commonly less successful than supportive care for systemic signs. Administering anticonvulsants after the onset of systemic signs but prior to the development of seizure activity may prevent seizure circuits from becoming established. A single dose of dexamethasone given at an anti-CNS edema dose (2.2 mg/kg intravenously) has halted neurologic signs in some dogs. Subsequent treatment with tapering anti-inflammatory doses may be needed (Greene 2006). Use of corticosteroids is recommended even in the face of infectious disease because clinical signs may be related to the secondary inflammatory response.

## PREVENTION AND CONTROL IN THE SHELTER

### Vaccination

The single most important method to prevent CDV disease in shelters is to vaccinate all dogs and puppies at the time of intake (or before). The implementation of programs designed to increase vaccination rates for dogs in the community, especially those that may not receive regular veterinary care, would be quite helpful in increasing overall population immunity. Please refer to Chapter 5 on immunology and vaccinations for more information on this topic.

#### *Vaccine types*

There are two types of vaccines available: (1) modified live virus (MLV) CDV vaccine and (2) recombinant CDV (rCDV) vaccine. The CDV vaccine from Merial® has a canarypox vectored recombinant CDV component, whereas all the other products are conventional MLV vaccines. The two types perform similarly in adult dogs (over 16 weeks of age). The canarypox rCDV has the advantage of immunizing puppies that have MDAs at an earlier age than the MLV vaccines. (Please see section on juvenile animals.)

Measles virus (MV) CDV vaccine was previously manufactured but is now no longer available. MV vaccine was used primarily because puppies with MDAs could be immunized at an earlier age than CDV MLV vaccines were capable of immunizing, but it did not provide long-lasting immunity. The MV vaccination was given to puppies less than 12 weeks of age. Puppies were then revaccinated with an MLV vaccine later to provide long-lasting immunity. The practical use of the MV vaccine has been replaced by the rCDV vaccine.

#### *Vaccine efficacy and safety*

MLV vaccine CDV and rCDV vaccination provides significant protection even when dogs are challenged with exposure almost immediately following vaccination. One study (Schroeder, Bordt et al. 1967) showed significant benefit from MLV CDV vaccination of susceptible puppies compared to those that were unvaccinated even when puppies were placed immediately into a CDV-contaminated environment. More recently, a study by Larson and Schultz

(2006) showed similar onset of immunity with Recombitek™, the rCDV vaccine product by Merial.

It is important to recognize that the very early benefits from vaccination described in the studies above for both MLV and rCDV vaccines may not confer the same sterile immunity that can ultimately be expected from vaccination for CDV. Full immunity does develop quite quickly, but may not be reached for 3 to 5 days. Instead, the very early postvaccine immunity provides protection from the development of severe neurologic disease and death. Dogs challenged by exposure within 72 hours of vaccination may become infected, shed virus, and be a risk to other susceptible dogs in the population even though they do not develop fulminant disease.

Immune suppression following vaccination with an MLV combination product containing CDV, CPV-2, and CAV-2 [with or without canine parainfluenza (CPI)] occurs commonly in CDV–CAV–2 naïve animals, regardless of age. Immunosuppression can begin as early as 3 days after vaccination and can last as long as 12 to 15 days after vaccination. During this time, dogs can be at increased risk of developing more severe disease. Dogs with mild puppy pyoderma may develop severe pyoderma, localized demodex infections may become generalized, or dogs may develop CRDC. Suppression only occurs in dogs that are naïve to both CAV-2 and CDV, as it is only this combination of viruses within a vaccine that triggers this response. The authors have found that a combination vaccine containing recombinant CDV along with CAV-2, CPV-2, and CAV-2 (with or without CPI) does not induce immunosuppression (Phillips, Jensen et al. 1989).

The commercial CDV vaccines available from all the major manufacturers of vaccines (e.g., Fort Dodge Animal Health, Intervet, Merial, Pfizer Animal Health, and Schering Plough Animal Health) are excellent. These CDV vaccine products have been demonstrated to induce immunity that protects from infection and disease with at least 3 years' duration of immunity in greater than 99% of naïve animals who are vaccinated (Schultz 2006). Products not obtained from those companies should not be used, as their efficacy cannot be assured. While vaccines for CDV are among the most effective, rapidly acting vaccines available, if recently vaccinated animals are overwhelmed by exposure to high levels of pathogens, disease may occur.

When vaccinations are administered on intake; preventative management practices are put in place to minimize comingling, exposure, and stress; and sick animals are promptly isolated, the short lag between vaccination and onset of sterile immunity does not often lead to clinical problems. However, in environments where susceptible and potentially infectious dogs are housed or allowed to comingle together or share common space, disease may still occur in dogs that are vaccinated at intake and exposed shortly afterward.

### *Vaccine handling*

Because CDV is relatively labile, it is critical to reconstitute the vaccine shortly before use, taking care not to leave the vaccine at room temperature for more than 2 or 3 hours. If the room or ambient temperature is elevated, extra care should be taken so that vaccines are reconstituted just before administration. The vaccine can be administered subcutaneously or intramuscularly. If any portion of the vaccine fails to be administered subcutaneously (e.g., part of it is injected onto the skin or hair coat), a second full dose should be given immediately.

### *Vaccination protocols*

#### *Vaccine timing and revaccination*

Vaccination of all dogs entering a shelter should occur immediately at entry or prior to entry whenever possible. Vaccination on intake should be considered a minimum standard of care for animal welfare agencies.

Although it is commonly recommended to administer two doses of CDV vaccine in any dog over 16 weeks of age, one dose will provide immunity in a very high percentage of vaccinated dogs for up to a lifetime. Dogs that remain in the shelter for long periods of time need not be revaccinated more often than every 3 years as per the American Animal Hospital Association (AAHA) vaccination guidelines. Puppies must be revaccinated every 2 weeks until 16 weeks of age in an effort to effectively immunize while minimizing the window of susceptibility that results from waning maternal antibodies.

#### *Vaccination of juvenile animals*

As with other diseases, interference from MDAs can hinder effective immunization of puppies under 16 to 20 weeks of age, and it can never be certain which puppies will be effectively immunized. There may be variable efficacy of vaccines in overcoming MDAs even amongst the major vaccine manufacturers.

The canarypox vectored rCDV vaccine was licensed in 1997. Studies performed by the authors and others demonstrated that the rCDV vaccine is more effective than any of the MLV vaccines for vaccination of puppies less than 20 weeks of age that have MDAs. In any given puppy, it was found the rCDV can overcome maternal antibodies and immunize 2 to 4 weeks earlier than the MLV vaccine when MDAs are present. The canarypox vectored rCDV

vaccine not only has the advantage of providing early immunization, it is also very safe, especially when given as a monovalent vaccine, even to very young puppies (e.g. 2 weeks of age or older). The other components of the combination product may carry some risk when given before 4 to 6 weeks of age. The monovalent canarypox vectored rCDV vaccine is made for ferrets and is called PureVax Ferret CDV. Very young puppies at high risk of infection with CDV can be administered the monovalent product, rather than a combination product, starting as early as 2 to 3 weeks of age. Only 0.3–0.5 ml of the 1 ml PureVax Ferret CDV is required; thus each 1 ml vial can be used for up to three doses. This product should be given every 2 to 3 weeks until a combination rCDV product with CDV and CPV-2 plus other viruses (e.g., CAV-2 and CPI) can be started at 4 to 6 weeks of age.

Regular vaccination for puppies with combination vaccine products should begin at 4 to 6 weeks of age. It should be emphasized that vaccination alone will never be sufficient intervention when disease and exposure risk is high. Vaccination programs must work in concert with management plans that decrease infectious dose and risk of exposure, especially for puppies that may remain susceptible even after vaccination. The best management plan for susceptible juvenile animals is almost always housing outside the shelter, in an alternate, low-risk environment.

*Special considerations for dogs presenting to a shelter pregnant or ill*

Every animal over 4 to 5 weeks of age should be vaccinated prior to or upon arrival to a shelter, regardless of their health status at the time of arrival. Vaccines are unlikely to cause harm, whereas virulent virus is likely to be present. For animals that arrive ill, it is possible, though not likely, that the animal will be unable to mount an immunizing response. It is unlikely that the vaccine will adversely affect the animal, while there is a good chance much-needed protection will be provided.

If an animal arrives at a shelter pregnant, the risks and benefits of vaccination must be carefully weighed. Vaccine virus may present a risk, but in most cases the risk from virulent virus is greater as animals enter the shelter. While there may be a risk to the unborn puppies from vaccinating the dam if she has not been previously immunized, the risk to the dam entering a shelter environment unvaccinated and susceptible, followed by almost certain exposure, could be very high. In an effort to protect the fetuses from the possible adverse effects of vaccination, the mother and the puppies could all be lost to disease.

Titer checking pregnant animals on intake using a TiterChek™ kit is one way of evaluating risk prior to vaccination (see Chapter 5). The safest CDV vaccine to use in pregnant dogs is the canarypox rCDV vaccine, as the MLV vaccines in immunologically naïve (CDV antibody-negative) dogs have the potential and are likely to infect the fetuses, causing death and absorption or abortion. Pregnant dogs that have the antibody will not be infected with the vaccine virus; thus the embryos/fetuses will not be affected. However, the stress of vaccination, or one of the other vaccines in the case of a combination product (e.g., CAV-2), may infect the embryos/fetuses and cause absorption or abortion. The monovalent PureVax® Ferret rCDV product contains only the CDV component and so eliminates the risks from other vaccine virus components. Because canine parvovirus is likely also a risk, a monovalent product for CPV should also be strongly considered if the ferret rCDV product is used. When the monovalent PureVax® Ferret product is used, a dose of only 0.3–0.5 ml (one-third to one-half the regular dose of 1.0 ml) is required.

Whenever a combination product is used, both the benefit and the potential risk or adverse consequences of the other vaccines in the combination as well as the overall immediate risk from specific virulent virus in the shelter must always be considered. This is especially true during pregnancy.

*CDV vaccination of other species*

For species other than dogs (e.g., raccoons or ferrets), the PureVax® Ferret rCDV vaccine (1.0 ml dose) should be used rather than an MLV vaccine because of the adverse reactions the MLV vaccine may cause in these species. MLV CDV vaccines should only be used in the species for which they were licensed.

**Environmental control**

CDV is an RNA virus that is enveloped; thus the virus is rapidly inactivated outside the body by a variety of disinfectants. CDV is also rapidly destroyed by heat. At temperatures of 56 °C (130 °F), it has a half-life of 2–4 minutes; at 45 °C (113 °F), 10 minutes; at body temperature and room temperature, 37 °C (99 °F) and 21 °C (68 °F), respectively, about 1–3 hours; and 9–11 days at 4 °C (42 °F). Therefore, unlike canine parvovirus-2, which is very stable in the environment and resistant to many disinfectants and heat, CDV is very labile (unstable) and can be readily destroyed in the environment.

### *Isolation and separation*

As mentioned above when describing transmission, infected dogs, even those who are subclinically infected, serve as the primary reservoir for the virus. The virus is not hardy or long-lived outside the dog, but when infected dogs are intermixed with susceptible dogs, transmission is likely to occur. This makes isolation of all dogs with clinical signs of disease an essential component of distemper prevention and control. This is especially true for respiratory disease because of the strong potential for aerosol transmission and the frequent overlap of signs of canine respiratory disease complex and early or mild canine distemper. However, as a general practice, dogs with any clinical signs of potentially infectious disease (e.g., gastrointestinal, neurologic) should also be isolated from the general population.

Isolation ideally is achieved by use of a separated building or ward, including separate air flow. Staff must be trained in isolation procedures and either designated to work in that area only, or sequenced so that healthy animals are never handled or cared for after sick animals. Proper protective garments should be provided as well as separate equipment for use in the isolation area exclusively. In some cases, a separated ward is difficult to achieve. However, an isolation system where sick animals are promptly identified and removed, housed in a designated area separated by at least 25 feet from the susceptible population, and never cared for ahead of healthy animals is possible to implement for most organizations. This system is likely to have a dramatic effect on improving animal health. Housing and/or treating sick animals in the general population will ensure exposure of the entire population, and if CDV is present, it will lead to severe disease in at least some susceptible animals.

Isolating sick dogs removes the greatest source for exposure in the shelter. Subclinically affected dogs may still shed virus and go unrecognized as infectious. Still, the reduction in infectious dose in the environment that results from isolating the dogs that are most obviously a potential risk has a substantial effect on clinical disease reduction.

Separation of subpopulations of apparently healthy dogs and puppies works hand in hand with isolation to protect susceptible animals as they enter the shelter. In many cases, transmission can be interrupted by establishing defined housing areas and an order of care for specific susceptible groups. Special handling practices to reduce transmission can be targeted toward the most susceptible animals. In general, separation is most important for puppies because many are likely to remain susceptible even postvaccination. Healthy puppies should be housed in easily cleaned kennels separate from adult animals, with designated equipment for use exclusively in that area and handling by staff wearing clean, protective garments. Separation practices can also help protect incoming adult dogs during the first several days after admission when they have been vaccinated but have not had sufficient time to develop full immunity.

### *Planned comingling and all-in/all-out housing*

For shelters that must group-house recently admitted dogs, planned comingling of healthy dogs further reduces risk of transmission by defining cohorts or subgroups within the general population, thus reducing the number of animals to which each animal is exposed. To implement planned comingling, a system must be put in place defining which incoming healthy animals will be cohoused and interact with each other in play groups or other activities. The simplest method is to identify compatible dogs that are entering the shelter at similar times. Only those dogs who are part of the planned cohort would interact with each other.

All-in/all-out housing is an essential component of planned comingling. All-in/all-out housing dictates that when comingling is necessary, all dogs will be removed from the housing unit or housing area before new susceptible dogs are brought in. Ideally, animals are moved through the shelter in cohorts. New animals should not be added once the group has been established. When all-in/all-out practices are not used, it is possible that one subclinically infected animal could remain in an area long enough to expose another susceptible animal and so on, creating a cycle that allows persistence of the virus in the environment. All-in/all-out housing interrupts that cycle by creating small groups in which all dogs are less likely to have been infected. Each time one group leaves, the risk of exposure for the new group begins with just those dogs that have entered together, with no risk carried over from the previous group. All-in/all-out housing is an important component of halting a cycle of transmission.

## Outbreak management

Herd health management practices play an important role in the prevention of CDV transmission in the shelter setting. Common risk factors in shelters experiencing outbreaks or ongoing problems with CDV in their populations include: sporadic, late, or no vaccination on intake; crowding beyond capacity; kennels that are used inappropriately or in ways other than intended when designed; some-in/some-out housing; lack of separation between sick and healthy animals; poor or infrequent use of disease

detection methods; and lax response to respiratory disease that is believed to be "kennel cough." Receiving animals transferred from other shelters may also increase risk of CDV if the source shelters are in endemic communities or have any collection of these risk factors.

Once an outbreak occurs, it becomes even more essential that all dogs are vaccinated prior to or at entry. Response measures, beyond vaccination, must also be taken when disease has been identified in the general population.

If an outbreak of distemper does occur in a shelter, it is possible to control the outbreak, but strict measures must be put in place immediately. Total depopulation can be avoided by assigning risk categories to all dogs through a combination of careful observation of clinical signs and antibody testing. Outbreak response primarily consists of assigning risk categories, creating a sanitary environment for incoming dogs, and isolating or removing exposed potentially infectious animals. More information about general outbreak management can be found in Chapter 3.

***Risk assessment***

While assigning risk groups never gives an absolute guarantee of whether a particular animal will become infected or not, defining the level of risk for individual animals and subgroups can at least guide informed decisions. Risk assessment can be used to minimize the amount of euthanasia and other drastic or costly measures taken while still effectively controlling an outbreak. Establishing risk categories for exposed animals also limits the number of dogs subject to quarantine, isolation, or special rescue. Because some animals may have strong immunity to distemper demonstrable via serologic assessment, it may not be necessary to treat all who have been exposed as potentially infectious or "at risk."

Serologic risk evaluation is an especially valuable tool for CDV because the long incubation period, in many cases, makes quarantine of all exposed dogs difficult to impossible for many shelters to implement. Antibody testing correlates well with immunity for CDV, and both commercial and in-house tests (Synbiotics TiterCheck™) are available for this purpose. One caveat is that the long incubation period for CDV makes it somewhat more likely than for the parvoviruses that titers will rise faster than clinical signs in response to infection. This means low risk dogs (those with positive titers) for CDV are at slightly more risk for infection than when categorizing dogs as low risk for canine parvovirus by the same means. However, when using this system to manage several outbreaks, this theoretically increased risk has not caused a problem clinically. (See Chapter 5 on vaccination and immunology for detailed information on serologic testing and risk evaluation.)

When titer testing cannot be used to assign risk groups, most exposed dogs must be considered high risk. If complete vaccination records are available from veterinary records, dogs that had been vaccinated when older than 16 weeks and prior to admission should be considered low risk. Assertions by owners relinquishing dogs that their vaccinations are current are unacceptable.

*Quarantine requirements for high-risk/exposed dogs*

If high-risk dogs remain in the shelter, they must be well isolated from other dogs, especially those that have been recently admitted, recently vaccinated, and all puppies under 20 weeks of age. These dogs should be held for a quarantine period of at least 4 to 6 weeks to ensure that they are not incubating the disease. In many cases, this long holding time is impossible for the shelter; it also creates welfare concerns or runs the risk of actually contributing to more disease in the shelter due to crowding. Quarantine areas should have safety procedures equivalent to those described in the section on isolation and separation for isolation areas.

*Protection of incoming dogs during an outbreak*

When responding to an outbreak, all dogs, without exception, must be vaccinated prior to or within minutes of entry. All incoming dogs should be placed into clean, disinfected kennels. Housing for incoming dogs should be located at least 25 feet away from moderate-to-high risk dogs (based on titers, exposure history, or clinical signs) and from other dogs coming in with clinical signs of disease; ideally, this should be a separate building or at least a separate ward. If necessary, this can be a separate set of runs with clear visual barriers delineating at-risk versus clean areas. Separate staff and supplies should be used for new incoming dogs versus exposed/at-risk dogs. Dogs designated as low-risk based on titer testing can be housed with new incoming dogs if necessary based on space considerations. See Chapter 3 on outbreak control for more detailed recommendations.

*Summary of outbreak control*

Outbreaks within the shelter can be brought under control with careful attention to the measures described above. Clinical cases may continue to occur, but they should be limited to dogs infected prior to entering the shelter. If preventive management practices are put into place as part of the outbreak response, disease spread from these cases can be controlled and future outbreaks avoided.

## CONSIDERATIONS FOR ADOPTION

As noted earlier, recovered dogs may shed infectious virus for up to 16 weeks. Prolonged shedding is possible even in dogs that were subclinically affected, although the amount of virus shed is likely to be lower in dogs with no clinical signs. Adopters of recovered or exposed/at-risk dogs should be made aware that the dog may have been infected with CDV and be advised to keep the dog away from areas frequented by puppies, newly vaccinated animals, or other susceptible dogs (i.e., puppy classes, pet stores, boarding facilities, or doggy day care) for at least 16 weeks after recovery or exposure.

RT-PCR testing can help rule out continued shedding and may be more cost effective than holding dogs for prolonged periods after recovery. This method is unproven but may assist in risk assessment. Dogs that are negative on RT-PCR testing of oropharyngeal or nasal swabs at a reputable laboratory and completely free of clinical signs for at least 2 weeks probably pose a low risk to others, while dogs testing positive should remain isolated from susceptible groups.

## SUMMARY

Canine distemper remains an important disease, especially for animal shelters throughout the U.S. and world. Although effective control of CDV in well-cared-for pets has been achieved through vaccination, there has been a failure to control CDV in the poorly or uncared-for dogs that frequently enter shelters. Unlike the years prior to the 1980s, when there were many CDV unvaccinated dogs and thus viral prevalence was high enough to either naturally infect and immunize or to cause disease and death in the population as a whole, today, in most communities, there is little or no CDV to naturally infect and immunize dogs. Because of this, the canine population in the U.S. is dependent on vaccine-induced protection.

Canine distemper is a disease that is vaccine-preventable, and if effective vaccination programs are used in shelters, and, more importantly, if more dogs in the community were vaccinated just once after the age of 16 weeks, CDV could be eliminated as an important cause of disease. Revaccinating the same adult dog (over 16 weeks of age) multiple times provides no benefit for individual or herd/population immunity, but vaccinating all adult dogs (or as many as possible) at least one time after maternal antibodies have waned will make a significant difference in reducing or eliminating CDV for all dogs and all susceptible species.

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# 11
# Canine Influenza

*Cynda Crawford and Miranda Spindel*

## INTRODUCTION

A low level of infectious respiratory disease is common in any population of dogs housed in communal facilities. Most shelter managers are accustomed to managing "kennel cough" syndrome in a small percentage of dogs at any point in time. However, a large outbreak can have serious long-term implications for animal shelters and can ultimately impact an entire community. Canine influenza virus (CIV) is a recently discovered contagious virus that causes acute respiratory infection and must be considered in the diagnostic work-up along with other respiratory pathogens such as *Bordetella bronchiseptica*, canine distemper virus, and other causes of acute respiratory disease. Canine influenza is an important health issue for shelter veterinarians since this infection has had an impact on hundreds of dogs in multiple shelters across the United States. Increasingly, shelters are unable to break the infection cycle. In efforts to control infection, some shelters have elected to euthanize large numbers of infected dogs, and others have expended significant resources on therapy and management strategies. While there is no vaccine at this time to limit the spread of canine influenza, it may be possible to limit the consequences of widespread infection through rapid diagnosis and husbandry practices that may vary from those appropriate for management of other causes of infectious respiratory disease in shelter dogs.

The purpose of this chapter is to provide veterinarians with current information on diagnosis, therapy, and basic strategies for managing canine influenza in shelter environments.

## EPIDEMIOLOGY/DISEASE COURSE FOR CANINE INFLUENZA

### Etiologic agent

Influenza A viruses are negative-sense single-strand RNA viruses (family *Orthomyxoviridae)* that can cause acute respiratory disease in humans, horses, pigs, and domestic poultry (Webster, Bean et al. 1992). Influenza A viruses are subtyped based on the hemagglutinin (H) and neuraminidase (N) proteins on the virion surface (Webster, Bean et al. 1992). To date, 16 hemagglutinin and 9 neuraminidase subtypes have been identified, each of which is antigenically distinct (Webster, Bean et al. 1992). As examples, human seasonal influenza is caused by subtype H3N2 or H1N1 viruses, while equine influenza is caused by subtype H3N8 virus.

Canine influenza is a highly contagious respiratory infection of dogs caused by a novel influenza A subtype H3N8 virus. CIV was first isolated from the lungs of racing greyhounds that died from pneumonia during outbreaks of acute respiratory disease at tracks in Florida in March 2003 and January 2004 (Crawford, Dubovi et al. 2005). Subsequently, CIV has been associated with respiratory disease outbreaks involving thousands of racing greyhounds and non-greyhound dogs across the U.S. (Crawford, Dubovi et al. 2005; Crawford, Gibbs et al. 2006; Payungporn, Crawford et al. 2008; Yoon, Cooper et al. 2005).

Phylogenetic analyses of canine influenza viruses indicate that they are closely related to equine lineage H3N8 viruses isolated from horses in the U.S. since 2000

(Crawford, Dubovi et al. 2005; Payungporn, Crawford et al. 2008). The close genetic relationship suggests the interspecies transmission of influenza viruses from horses to dogs at some point in the recent past, followed by viral adaptation to the dog with efficient replication in the respiratory tract to cause clinical disease and sustained dog-to-dog transmission (Crawford, Dubovi et al. 2005; Payungporn, Crawford et al. 2008). Retrospective analysis of a respiratory disease outbreak in 2002 in foxhounds in the United Kingdom documented infection of the dogs with equine influenza H3N8 virus, but there is no evidence to date of ongoing influenza infections in dogs in the U.K. (Daly, Blunden et al. 2008).

**Susceptible species**

Because CIV is a novel pathogen, dogs of any breed, age, or vaccination status are susceptible to infection due to lack of preexisting immunity. Based on serological testing and virus cultures of cats housed in shelters during canine influenza outbreaks, there is no evidence at this time that cats are susceptible to infection with CIV (Crawford, unpublished data). Recent studies have shown that CIV still retains the ability to infect horses and replicate in the respiratory tract, but resultant clinical disease is very mild to inapparent (Long, Gibbs et al. 2007).

**Zoonotic potential**

Dogs are the only known susceptible species; there is no evidence at this time for canine-to-human transmission of CIV.

**Prevalence**

Since 2004, the University of Florida and Cornell University have conducted syndromic surveillance for CIV infection in non-greyhound dogs in the U.S. This surveillance is based on testing of serum, nasal/pharyngeal swabs, and respiratory tissue samples submitted by veterinarians from dogs with clinical signs of acute respiratory infection. Such surveillance is useful for defining risk groups for CIV and tracking virus activity, but does not represent true prevalence of the disease. At the time of this writing, syndromic surveillance has documented CIV infection in thousands of dogs in at least 28 states and the District of Columbia in the U.S. (Crawford, Gibbs et al. 2006). Shelter facilities are at high risk for CIV, and canine influenza has spread to multiple shelters in California, Colorado, Delaware, Florida, Kentucky, New York, Pennsylvania, Utah, and Wyoming. Canine influenza appears to be endemic in some regions of Colorado, Florida, Pennsylvania, New York, and Wyoming. Shelters in these regions report continual problems with canine influenza.

**Morbidity, mortality, and prognosis**

Like most influenza A viruses, canine influenza is a disease with high morbidity but low mortality. Nearly all exposed dogs become infected, and most have clinical disease while some have subclinical infection. Most dogs with clinical disease recover within 10 to 30 days. Based on data generated in Florida, the overall mortality rate is less than 8%, but with rapid diagnosis and appropriate therapy, mortality may be lower (Crawford, unpublished data).

**Modes of transmission**

Influenza viruses are rapidly transmitted between animals by a combination of aerosols, droplets, and direct contact with respiratory secretions or contaminated fomites (Tellier 2006). Coughing and sneezing generate substantial amounts of virus in droplets and aerosols, forming suspensions that remain airborne for prolonged periods and travel long distances before settling down on surfaces (Tellier 2006). As demonstrated for influenza in other species, aerosols are important contributors to the spread of CIV in shelters and may account for the explosive onset of disease in many dogs over a short period of time. Distances traveled by CIV-containing aerosols are unknown, but aerosol transmission of human influenza viruses has been documented at distances over 50 feet. Direct dog-to-dog transmission and fomite-associated transmission are two other important means of CIV transmission. Human handling of infected dogs followed by contact with other dogs without decontamination of hands and clothing has greatly contributed to spread of CIV in shelters. In several cases, shelter staff have transmitted infection to pet dogs at home via virus-contaminated clothing.

**Incubation period**

The incubation period is approximately 2 to 4 days from exposure to onset of clinical signs. This relatively short incubation period is typical for influenza in other species, and is shorter than for some other causes of acute respiratory diseases such as canine distemper virus and *Bordetella bronchiseptica*.

**Shedding period**

Studies in naturally and experimentally infected dogs have shown that CIV may be shed for up to 7 days in most dogs, and to 10 days in some dogs (Crawford et al. 2005; Rosas, Van de Walle et al. 2008). Peak viral shedding from the upper respiratory tract occurs 2 to 4 days postinfection;

since this overlaps with the incubation period, infected dogs may be most contagious prior to showing obvious clinical signs.

### Carrier state

Influenza A viruses do not establish persistent infections, and no carrier state has been described. Although some dogs have subclinical infection, there is no true carrier state. Once virus replication and shedding ceases, the dog is no longer contagious to other dogs.

### Clinical signs

Distinguishing canine influenza from other causes of acute respiratory disease can be very difficult. In a population of dogs with CIV, there may be a sudden increase in prevalence of acute respiratory disease, severity of illness, or a prolonged to complete lack of response to antibiotic therapy for *B. bronchiseptica*. When introduced into a naïve population, CIV typically causes an explosive onset and spread of "kennel cough" in most dogs in the shelter within a short period of time, usually less than 2 weeks. Once CIV has become established in a population, the classic rapid spread of disease is less apparent. Dogs of all ages are susceptible to infection with CIV and prior vaccination against canine distemper virus, adenovirus type 2, parainfluenza virus, and *Bordetella bronchiseptica* does not diminish introduction and spread of CIV within the shelter population.

Approximately 80% to 90% of infected dogs develop clinical disease. A small percentage (10% to 20%) of dogs are subclinically infected and appear healthy yet are shedding virus. Therefore, all exposed dogs in the facility should be considered an infectious risk, whether or not they are showing signs of respiratory infection. Coughing is the most predominant clinical sign and can persist for several weeks, even with antibiotic and antitussive therapy. Dogs may have mild anorexia, fever, and a purulent nasal discharge due to secondary bacterial infections. Approximately 1% to 20% of dogs may progress to more severe illness consisting of high fever, tachypnea, productive cough, pneumonia, and prolonged recovery. The fatality rate related to pneumonia is reported to be 5% to 8%, but with rapid diagnosis and appropriate therapy may be much lower. Peracute fatal hemorrhagic pneumonia has been reported only in the greyhound.

Canine influenza cannot be distinguished from respiratory disease caused by other infectious agents based on clinical signs alone. In addition, coinfections with other respiratory pathogens may occur, all producing the same clinical signs. Ultimately, diagnostic testing must be performed to differentiate the cause(s) of "kennel cough" outbreaks.

### Diagnosis

There are multiple laboratory methods available for detection of influenza infection, including virus isolation, virus antigen detection by immunoassays, virus nucleic acid detection by polymerase chain reaction (PCR), and serology for virus-specific antibody. Each method has strengths and weaknesses that are important for shelter practitioners to understand. The timing of sample collection relative to viral shedding relates directly to test performance. To institute optimal control measures, it may be necessary to combine several diagnostic approaches to identify the etiological agent accurately and rapidly.

#### *Swabs for immunoassays, PCR, and virus isolation*

During the first few days following infection, clinical signs are generally inapparent to mild, but viral shedding in nasal secretions is high. It is during acute influenza infection that achieving a diagnosis is often most critical for case management and outbreak control. Diagnostic methods aimed at detection of the virus (i.e., antigen detection methods, PCR-based assays, and virus isolation) are the preferred tests for early cases. Nasal and/or caudal pharyngeal swabs can be used for these tests. Swabs should be collected from exposed subclinical dogs or those with early clinical signs (1 to 3 days) to coincide with peak virus shedding. To maximize detection of CIV, swabs should be collected from multiple dogs in the population. If testing is being done through a commercial reference laboratory, it is recommended to contact the laboratory in advance for collection, handling and shipping preferences.

Patient-side immunoassay kits for human influenza A infection can be used for diagnosis of CIV. These kits detect the highly conserved nucleoprotein of influenza A viruses [see Web resources (b),(c)] but the sensitivity is unknown. Some shelters have these kits on site for in-house use. The tests do not require special equipment, are easily performed, and provide rapid results. Positive results are most likely correct, but negative results may be "falsely negative" due to critical timing of swab collection with peak virus shedding. Nasal and/or caudal pharyngeal swabs are also used for detection of CIV nucleic acid by PCR tests (Payungporn, Crawford et al. 2008; Spindel, Lunn et al. 2007). PCR testing is inexpensive and fast and is now offered by several reference [Web resources (a),(d)] and university [Web resources (e),(f)] diagnostic laboratories. The laboratories should be contacted in advance for collection, handling, and shipping preferences. PCR tests

are highly sensitive and specific and are more likely than virus antigen immunoassays to yield positive results when low amounts of virus are present. However, the assay's high sensitivity can produce false-positive results due to DNA contamination during sample collection as well as during sample processing in the laboratory. Shelter personnel should wear clean examination gloves for each dog and only touch the swab tip to the area sampled to avoid contamination by nucleic acid on hands and in the environment. False-negative results may occur due to inappropriate sample collection and handling or inappropriate timing of sample collection. Other diagnostic samples such as transtracheal washes, bronchoalveolar lavage fluid, and tissues can be submitted for CIV PCR.

Virus isolation from clinical samples is critical for epidemiological investigation and for future vaccine production, but it may have limited use for routine diagnostic purposes as it is a slow and specialized test. Laboratories that offer virus isolation [Web resources (a),(b),(e)] should be contacted in advance for collection, handling, and shipping preferences.

In general, the best results for virus isolation are often achieved by collecting nasal and/or pharyngeal swabs using polyester-tipped swabs. Cotton swabs should be avoided, as influenza viruses can adhere to the cotton fibers, thus decreasing the likelihood of virus isolation. The swabs should be placed in sterile dry tubes or tubes containing viral transport medium (depending on laboratory preference) and kept on ice packs for shipping to a laboratory. Depending on the amount of viable virus present in the sample and sample handling, virus isolation can take 3 to 5 days.

### *Serology*

Serology is the most reliable diagnostic test for confirmation of CIV infection and should be performed in conjunction with other tests to confirm canine influenza infection. CIV-specific antibodies can be detected in a hemagglutination inhibition assay as early as 7 days postinfection, but reliable detection occurs after 10 days of clinical signs (Anderson, Katz et al. 2006). Therefore, a negative antibody titer for serum samples collected before day 10 does not rule out infection. Because the presence of antibodies indicates exposure, but not necessarily active infection, comparing an acute titer and a convalescent titer (2 weeks apart) to confirm a fourfold rise in antibody titer (seroconversion) is necessary to prove recent active infection. Serum samples can be submitted to the NYS Animal Health Diagnostic Center [Web resource (a)], Colorado State University [Web resource (e)], or the University of Florida [Web resource (g)]. The relationship of timing of sample collection and performance of various diagnostic methods for CIV is shown by results from one Florida shelter in 2007 (see Table 11.1).

### *Ancillary diagnostic work-up*

Once a diagnosis of canine influenza is confirmed, further work-up may be very different in a single dog compared to a population of many dogs. Facilities with large numbers of symptomatic animals may not have the resources to perform a complete work-up on multiple dogs. Alternatively, veterinary decisions may be made that best utilize resources and allow for maximal numbers of dogs to be treated.

A complete blood cell count (CBC) with differential, serum biochemistry profile, urinalysis, and thoracic radiographs can yield important information. The CBC may be normal or show mild leukopenia suggestive of viral infection. If pneumonia is developing, leukocytosis consisting of neutrophilia with or without a left shift may be detected. Thoracic radiograph findings range from mild bronchointerstitial infiltrates to consolidation of all lung lobes.

CIV replicates in the epithelial layer lining the nasal passages, trachea, bronchi, and bronchioles, resulting in sloughing of the damaged epithelium and exposure of underlying tissues to potential bacterial infection. Bacterial cultures performed on nasal swabs from dogs with purulent nasal discharge and on transtracheal and endotracheal washes of dogs with pneumonia have revealed secondary infections with a variety of commensal gram positive and gram negative bacteria, including *Staphylococcus* spp., hemolytic and nonhemolytic *Streptococcus* spp., *Pasteurella multocida, Klebsiella pneumoniae, Escherichia coli,* and *Mycoplasma* spp.

The value of a necropsy should not be overlooked in the diagnostic work-up for respiratory infections, including canine influenza. If dogs are euthanized or die during respiratory disease outbreaks, a prompt necropsy with submission of tissues to diagnostic laboratories for histopathology, bacterial and viral cultures, and viral PCR can provide very valuable information. At a minimum, sections of trachea, lung, liver, spleen, kidney, and urinary bladder should be fixed in 10% buffered formalin for histopathology. For cultures and PCR, sections of fresh trachea and lung should be placed in a sterile container, refrigerated, and shipped to a diagnostic laboratory as soon as possible.

## Treatment

Not all dogs with canine influenza require therapeutic intervention. Therapy relies mainly on supportive care

**Table 11.1.** Diagnostic test results for a canine influenza outbreak in an animal shelter.*

| Dog ID | Clinical Signs | Duration | Influenza A Nucleoprotein | Influenza A Matrix Gene PCR | Virus Isolation | Acute Antibody Titer | Convalescent Antibody Titer |
|---|---|---|---|---|---|---|---|
| 1 | None – exposed | 1 day | negative | negative | not done | 4 | 64 |
| 2 | Sneeze/cough | 1 day | positive | positive | positive | 4 | 256 |
| 3 | Cough | 1 day | negative | negative | not done | 4 | 512 |
| 4 | None – exposed | 1 day | negative | positive | positive | 4 | 128 |
| 5 | None – exposed | 1 day | negative | negative | not done | 4 | 256 |
| 6 | None – exposed | 1 day | negative | negative | not done | 4 | 128 |
| 7 | Nasal discharge | 1 day | negative | negative | not done | 4 | 512 |
| 8 | Cough | 1 day | negative | negative | not done | 4 | 512 |
| 9 | Cough/nasal discharge | 1 day | positive | positive | positive | 4 | 1024 |
| 10 | Cough/nasal discharge | 1 day | negative | positive | positive | 4 | 512 |
| 11 | Cough/nasal discharge | 1 day | negative | positive | positive | 4 | 1024 |
| 12 | Cough/nasal discharge | 1 day | negative | negative | not done | 4 | 1024 |
| 13 | Cough/nasal discharge | 1 day | negative | negative | not done | 4 | 512 |
| 14 | Cough | 3 days | negative | positive | positive | 4 | 1024 |
| 15 | Cough | 3 days | positive | positive | positive | 4 | 1024 |
| 16 | Cough/nasal discharge | 3 days | positive | positive | positive | 4 | 1024 |
| 17 | Cough | 4 days | negative | positive | positive | 4 | 1024 |
| 18 | Cough | 4 days | negative | suspect | positive | 4 | 1024 |

* Nasal swabs were collected between days 1 to 4 of clinical signs for detection of influenza A nucleoprotein (Directigen Flu A®) and nucleic acid (matrix gene PCR). Virus isolation was performed on PCR-positive samples. Paired acute and convalescent serum samples were collected for CIV antibody titers using the hemagglutination inhibition test. Antibody titers <32 are negative.

while the viral infection runs its course. There is little evidence to support the use of antitussives for reducing frequency and duration of coughing. In addition, antitussives are contraindicated in dogs with productive cough. Antibiotics are indicated for dogs with secondary bacterial infections evidenced by fever, productive cough, purulent nasal discharge, or pneumonia. Ideally, a bacterial culture and antibiotic sensitivity should be performed on each dog to determine the most effective antibacterial therapeutic plan. Use of a reference for proper procedure and accurate interpretation of susceptibility results is recommended (CLSI 2008).

Bacterial cultures for each dog may not be practical or financially feasible in a population of many affected dogs, so many shelters opt for empirical treatment. Nasal discharge usually responds within days to empiric treatment with broad-spectrum bactericidal antibiotics. For pneumonia, empiric treatment with a combination of antibiotics that provide coverage against gram-positive, gram-negative, aerobic, and anaerobic bacteria has been effective in many cases; however, patterns of response may vary. Dogs with pneumonia usually require intravenous fluids in addition to antibiotics. Oxygen supplementation and nebulization with coupage have been very beneficial. Despite aggressive therapy, severe pneumonia may lead to death or become a criterion for euthanasia.

There is no specific antiviral treatment for canine influenza at this time. Although treatment with oseltamivir (Tamiflu®, Roche Pharmaceuticals) has been suggested, the doses, frequency of dosing, and efficacy and safety of this human drug have not been determined for use in dogs with canine influenza. For best effect in humans, the drug needs to be started within 48 hours of infection; canine influenza is rarely diagnosed this early. Most importantly, Tamiflu® represents a primary line of defense against human seasonal influenza and pandemic influenza, so veterinary use of this drug should be reserved for protection of human health.

### Postinfection immunity

CIV-specific antibodies have been shown to persist in naturally infected dogs for at least 5 to 6 years (Anderson, Grimes et al. 2007; Daly, Blunden et al. 2008). Theoretically, dogs that recover from infection should be immune to reinfection with the same viral strain. However, correlation of postinfection antibody titers with protection against reinfection and duration of protective immunity has not been established for natural infection with canine influenza. Furthermore, influenza viruses possess remarkable ability to mutate, so antibodies induced by infection with one strain may not be protective against infection by future strains that have mutated.

## PREVENTION AND CONTROL/RISK ASSESSMENT FOR CANINE INFLUENZA

### Risk assessment

As with any infectious disease outbreak, management of canine influenza requires breaking the cycle of transmission between exposed, infected, and naïve (new intake) dogs. The short incubation and virus-shedding periods make this a more manageable proposition with canine influenza compared with canine distemper and *Bordetella bronchiseptica*, which have prolonged incubation and shedding periods. Because of the high transmissibility of CIV, all dogs in the shelter at the time a case is suspected or diagnosed should be considered exposed/at risk.

### Quarantine/isolation

All exposed dogs pose an infectious risk for 7 to 10 days. Although it may be difficult to implement a quarantine in shelters, to be safe, they should be quarantined for a minimum of 14 days. Ensuring that fomite, aerosol, and direct contact transmission do not occur between the exposed population and unexposed dogs is crucial in breaking the transmission cycle. Exposure of just one naïve dog can defeat the quarantine.

For shelters that can discontinue intake and adoption of dogs for 2 to 3 weeks, the best plan is to quarantine the entire population while the infection runs its course. When discontinuation of intake is not an option, a clean area should be created for intake of unexposed dogs. Ideally, this should be a physically enclosed room with separate ventilation. When an isolation area like this is not available, exposed dogs can be consolidated into one ward located as far as possible from wards used for new intakes. When adequate physical separation of exposed from unexposed dogs is not possible on site, shelters can attempt to route new arrivals temporarily to other shelters. Alternatively, although a challenging task, the exposed population can be transferred to an off-site location. Foster care in a household with no other dogs is another option for holding exposed dogs for the quarantine period, especially adoptable dogs that have completed their stray holding period.

The quarantined population should be managed with strict biosecurity procedures to minimize CIV transmission, including the use of personal protective equipment (PPE) (gown or jumpsuit, gloves, booties) by staff. Ideally, personnel managing the quarantined population should not visit the area for unexposed dogs or common use areas. If this is not possible, then personnel should manage the unexposed population first, wear PPE for the exposed population, and wash hands thoroughly before entering common use areas. There should be no visitors to the quarantined area unless they are reclaiming their dogs. In this circumstance, if possible, the owner and dog should try to leave by an exit that does not risk contamination of the facility.

Shelters in communities where canine influenza is endemic may have continual reintroduction of CIV into their population. In this situation, quarantines, diversion of new admissions, and shutdown of adoptions may become impractical or financially unreasonable. Shelters may have no choice but to continue intake and release of dogs since canine influenza is a treatable disease with a good prognosis for recovery. However, this may contribute to spread of infection to other facilities or households and perpetuate the endemicity of the virus in the community. Clients should be educated about canine influenza, advised to quarantine dogs leaving the facility for 14 days, and informed about follow-up medical care. This information should be included in a written document. Shelters may also opt to release dogs only after their 14-day quarantine, thus ensuring that the shelter is not serving as a continual source of community infection. It must be acknowledged that many of these choices may be very difficult, if not impossible, for some shelters to implement.

### Environmental contamination and disinfection

Influenza A viruses do not persist in the environment for an extended period of time. These viruses can survive for 24 to 48 hours on nonporous surfaces (stainless steel, concrete, plastic), for 8 to 12 hours on porous surfaces (cloth, paper), and for minutes on hands (Bean, Moore et al. 1982). For canine influenza, routine cleaning and disinfecting are sufficient to inactivate infectious virus. Kennel surfaces should be cleaned first with a detergent to remove dirt and organic debris, followed by application of

virucidal disinfectants such as bleach (1:32 dilution), quaternary ammonium compounds, or potassium peroxymonosulfate (Trifectant®) with a contact time of at least 10 minutes. The kennel surface should be dried before returning the dog. All potential fomites (bowls, etc.) should also be cleaned and disinfected.

### Vaccination

Although several veterinary pharmaceutical companies are developing and testing vaccine candidates, there are no USDA-approved vaccines for canine influenza at this time. Current influenza vaccines licensed for use in horses appear to induce variable humoral immune responses to CIV (Crawford, Katz et al. 2006; Karaca, Dubovi et al. 2007), but their safety or efficacy for preventing canine influenza has not been demonstrated in the field. In a recent report, vaccination of dogs with an experimental equine herpesvirus vector containing equine H3 genes induced high levels of antibodies that provided partial protection against clinical disease and decreased virus shedding upon subsequent challenge with CIV (Rosas, Van de Walle et al. 2008). To minimize coinfections with other respiratory pathogens and the possibility of more severe disease, all dogs, regardless of age or health status, should be vaccinated before or at intake against canine distemper, adenovirus-2, parainfluenza virus, and *Bordetella bronchiseptica.*

### Euthanasia criteria

Canine influenza is a disease from which most dogs recover either on their own or with appropriate supportive treatment. However, several shelters have elected euthanasia of the entire or majority of the population in an effort to eliminate CIV from the facility. Many shelters have also euthanized individual dogs affected by CIV, particularly those with pneumonia. Treatment costs for large numbers of dogs, lack of space and staff to maintain quarantine, and lack of resources for isolation or intensive care of dogs with pneumonia have contributed to these decisions.

## CLIENT EDUCATION/IMPLICATION FOR ADOPTION

### Adoption

Following the minimum 14-day quarantine for canine influenza, it should be safe to adopt the dogs into private homes or transfer to rescue, foster care, adoption groups, and other sheltering facilities. Even though some dogs may still be coughing and recovering from pneumonia, virus shedding and infectivity to other dogs has ceased.

### Client education

Clients adopting, reclaiming, or rehoming dogs from affected shelters should be educated about canine influenza through verbal and written communication. This prevents common misconceptions such as persistent carrier states and confusion with parainfluenza virus and parainfluenza virus vaccination, and promotes better understanding of why canine influenza cannot be prevented by routine "kennel cough" vaccines. Ideally, a medical record should be provided for transfer to a veterinarian. This record should include clinical signs with dates of onset and resolution, diagnostic test results, and treatments administered.

### Community education

Shelters that experience outbreaks of canine influenza should consider open and rapid communication with other local sheltering facilities, veterinarians, adoption/rescue groups, boarding kennels, and the public to provide increased awareness of virus activity in the community. Proactive communication provides a beneficial "advisory" so that other potentially affected parties can step up surveillance and biosecurity measures, and enhances the shelter's reputation as a valuable and considerate member of the animal welfare community.

## WEB RESOURCES

(a) New York State Animal Health Diagnostic Center, Cornell University, http://diaglab.vet.cornell.edu/issues/civ.asp.
(b) Directigen Flu-A®, Becton-Dickinson, http://www.bd.com/ds/productCenter/256020.asp.
(c) QuickVue Influenza Test®, Quidel, http://www.quidel.com/products/product_detail.php?prod=56&group=1&cat=1.
(d) IDEXX Laboratories, Portland, ME, http://www.idexx.com/animalhealth/laboratory/realpcr/tests/641600.pdf.
(e) Colorado State University Veterinary Diagnostic Laboratory, http://www.dlab.colostate.edu.
(f) Lucy Whittier Molecular & Core Diagnostic Center, University California at Davis, http://www.vetmed.ucdavis.edu/vme/taqmanservice.
(g) P.C. Crawford, crawfordc@vetmed.ufl.edu.

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# Section 3
# Gastrointestinal Diseases

# 12
# Feline Panleukopenia

*Helen Tuzio*

## INTRODUCTION

Feline panleukopenia is a highly contagious, potentially fatal disease of cats. Although well controlled in pet cats thanks to widespread vaccination, an upsurge in this deadly disease has been reported in shelter cats in recent years (Lawson 2001). Fortunately, even in shelters, this disease can be largely prevented with careful vaccination, sanitation, and housing practices.

## EPIDEMIOLOGY/COURSE OF THE DISEASE

### Etiologic agent

Feline panleukopenia (FPV) is an extremely contagious viral disease that has been known by a variety of names, including feline distemper, pseudomembranous enteritis, laryngoenteritis, feline agranulocytosis, and show fever. Although the disease was recognized before 1900, it was not until 1928 that a viral agent was isolated, and the virus itself was not definitively identified until 1962.

The organism is a small, nonenveloped, single-stranded DNA parvovirus. It is extremely hardy and can remain infectious at room temperature for up to 1 year. It is resistant to many commonly used disinfectants (Gillespie and Scott 1973). It resists heating and is still fully infective after 13 months' storage at 4 °C to 25 °C (Pedersen 1988).

The virus is very virulent in susceptible animals and has an affinity for rapidly dividing cells, particularly those of the bone marrow, lymphoid tissue, intestinal epithelium, and of fetal and neonatal cerebellar tissue. Although FPV and canine parvovirus (CPV) are closely related (CPV may have emerged as a mutation of FPV), FPV has different biologic properties and has only one serotype (Sturgess 2003; Scott 1987). Recent evidence suggests that canine parvovirus type 2, although originally unable to infect cats, has spawned several variants (CPV-2a, CPV-2b, and CPV-2c) that have mostly replaced the original type 2. The variants not only can infect cats but can also cause clinical parvoviral disease in them (Ikeda, Nakamura et al. 2002; Nakamura, Ikeda et al. 2001; Chalmers, Truyen et al. 1999).

### Susceptibility

FPV affects cats of all ages. As with most parvoviruses, older cats often develop subclinical or mild infections (some outdoor cats may be naturally boosted by field exposure) while kittens are more severely affected. Therefore, it is most commonly associated with young (2 to 5 months old) unvaccinated kittens whose maternal antibodies have waned or who did not have adequate colostral transfer of antibodies. However, severe disease may develop in any susceptible animal regardless of age (Pollock and Postorino 1994).

The domestic cat is the primary host, but all members of the Felid family are susceptible. Procyonids such as raccoons are highly susceptible to feline parvovirus. Ferrets can be infected with the virus but develop only mild disease. Mink are highly susceptible to the mink strain but develop only subclinical disease to the feline strain (Scott 1987). In a shelter outbreak, these species should be considered at risk for infection and transmission regardless of clinical signs.

### Zoonotic implications

FPV does not infect people. However, when human bacterial diseases were first discovered, many people believed the disease in cats was related to human epidemics. It was thought to be similar or identical to typhoid, diphtheria, or cholera. Hence the origin of some of the disease's many other names such as cat plague, typhus, typhoid, and colibacillosis (Scott 1987).

### Prevalence

Feline parvovirus is widespread in nature, enzootic in all parts of the U.S., and reported from nearly all countries in the world. Although located essentially everywhere, the virus is much more concentrated in areas housing cat populations, such as barns and shelters. Over the past years, the overall prevalence has decreased due to widespread vaccination. However, the disease remains prevalent in shelters and rural environments where cats remain unvaccinated. It was once thought that the extreme prevalence of the virus in the environment would result in a high prevalence of antibodies in adult cats due to natural exposure (Lawson 2001). However, a survey of 61 feral cats in a Florida trap/neuter/release program found positive antibody titers in only 33% of the population (Fischer, Quest et al. 2007), while surveys of feral and shelter cats in Wisconsin found antibodies in only 53% and 48%, respectively (R Schultz, University of Wisconsin, personal communication, 2008).

Although panleukopenia occurs at any time of the year, the number of clinical cases depends on the percentage of immune cats in the population, as well as the virulence of both the particular strain of the virus and the intestinal bacteria in the infected cats. The result is a seasonal incidence with case numbers peaking in late summer and early fall when the maximum number of kittens is at the peak of susceptibility.

### Mode(s) of transmission

FPV can be transmitted by direct contact between infected and susceptible cats, by contact with the virus in the environment, or transplacentally. Prenatal infection usually occurs mid-gestation. The fetus is infected via the maternal circulation as the virus can pass the placental barrier in pregnant queens. The primary mode of transmission, however, is fecal–oral, either by direct contact or via fomites. Infected animals shed large amounts of virus in feces and urine, and susceptible animals ingest it.

Droplet transmission can also occur, particularly if concurrent infection with an upper respiratory virus produces sneezing (Scott 1987). The droplets containing the virus are expelled and travel through the air. They may be inhaled or ingested by neighboring individuals, or land on surfaces, thus contaminating the environment.

Environmental exposure is of special concern in shelters, boarding facilities, and catteries because fomites may remain infective for months or years. Barns inhabited by infected cats were found to still harbor the virus a full year after the cats were gone (Gillespie and Scott 1973).

Nearly anything can serve as an environmental reservoir for the disease. During the acute phase of the illness, the virus is shed in all body secretions and excretions, so food and water dishes, cages, bedding, litter boxes, toys and grooming supplies, rugs, and soil can become sources of infection. Even brief contact with a blanket used by an infected cat is sufficient to transmit the disease (Hindle and Findlay 1932). The hands, clothing, and shoes of handlers, or the bottom of a paw of an infected cat can transmit the virus to other fomites, thus widening the risk of exposure. Flies and fleas can serve as mechanical vectors, transmitting the disease from infected to susceptible cats (Torres 1947; Gillespie and Scott 1973; Scott 1987).

## PATHOGENESIS AND DISEASE COURSE

Following ingestion or intranasal inoculation, the virus replicates in the lymphoid tissue of the oropharynx and the gut. It then spreads into the bloodstream and causes an initial viremia by 18 hours postinfection. At this time, the virus is present in the thymus, heart, mesenteric lymph nodes, kidney, small intestine, and cerebellum. Within 48 hours, every tissue has significantly high levels of virus, which remain high as long as 7 days after inoculation. Gradually, circulating antibodies rise and virus titers begin to lessen. Serum antibodies usually appear 3 to 4 days after the onset of clinical signs and are followed 2 to 3 days later by a dramatic rebound in white blood cells. By 2 weeks postinfection, most tissues are free of virus, although small quantities may remain in some tissues such as the kidney. Although the virus can replicate in any cell, it prefers the intestinal epithelial cells of the crypts of Lieberkühn, lymphoid cells, bone marrow stem cells, and the cerebellum of fetal kittens. Because the virus most severely affects cells undergoing rapid mitosis, the rate of host cell proliferation directly affects the outcome of the disease.

Under normal circumstances, there is continuous turnover of intestinal epithelial cells. New cells form in the intestinal crypts and migrate up the villus to replace the older cells being shed into the intestinal lumen. Parvovirus infects the epithelium of the crypts, destroying any new cells. This leads to the blunting of the villus and eventually to the denuding of the lamina propria. This tissue destruction and inflammation, and the associated loss of epithelial surface area, greatly reduce the absorptive and digestive abilities of the small intestine and result in the severe enteric signs usually seen with this disease.

Viral infection of the lymph system destroys lymphocytes and causes depletion of lymphoid follicles of lymph nodes, spleen, thymus and gastrointestinal tract. Thymic atrophy can be seen in young affected cats.

The word "panleukopenia" is derived from the Greek words "pan" meaning "every," "leuk" meaning "white," and "penia" meaning "a reduction in the circulating blood." There is literally a reduction in the white blood cell count of affected animals. Viral invasion of the bone marrow produces lysis of both erythroid and myeloid cell lines, but the longer lifespan of circulating erythrocytes produces a more apparent leukopenia. This destruction, when combined with the increased demand, results in depletion of the bone marrow and frank panleukopenia. At the nadir, generally 4 to 6 days after initial infection, the count is so low that patients are very susceptible to secondary bacterial infections.

Nearly three-quarters of the small neurons of the feline cerebellum are formed after birth. In kittens infected in utero near birth, the virus destroys the cells programmed to become the granular layer of the cerebellum, thus preventing its normal development and resulting in permanent dysfunction.

**Incubation period**

The incubation period following natural exposure is 2 to 10 days following oral transmission, with the average incubation period being 5 to 7 days. However, the length of incubation will vary with the age of the animal, the dose of infection, and concurrent disease (Gillespie and Scott 1973; Csiza, Scott et al. 1971). Apparent incubation periods of up to 14 days have been reported in shelters (K Hurley personal communication, 2008).

**Carrier state**

Although a carrier state has not been proven, there is epidemiological evidence to suggest that one exists (Sturgess 2003). However, as noted below, the vast majority of cats appear to cease shedding within 6 weeks of recovery. Attempting to control infection by identifying carrier cats is impractical and generally unnecessary in the shelter environment. Outbreaks have been successfully controlled in shelters by focusing on clinically ill animals and cats that have been exposed to these animals. However, if an outbreak is not controlled by these measures, the possibility of carrier or subclinically affected cats must be considered.

**Shedding and recovery**

Large quantities of the virus have been found in the urine and feces for up to 6 weeks after clinical recovery, thus implying that animals may remain infectious even after resolution of clinical signs (Grace 2006; Sturgess 2003). Kittens infected mid-gestation (those with cerebellar hypoplasia) harbor and shed the virus for extended periods after birth (Pedersen 1988). However, the role of chronically infected cats in transmission of the disease is uncertain. Survivors generally have high antibody titers that neutralize the virus as it leaves the infected cells. As a result, most cats that have recovered do not remain viral shedders for more than 3 weeks. At minimum, cats should be held for this amount of time after recovery prior to adoption or introduction into vulnerable shelter populations. Enzyme-linked immunosorbent assay (ELISA) or polymerase chain reaction (PCR) testing can help verify whether shedding has ceased, although it should be noted that these tests are neither specifically designed nor validated for this purpose. Although a negative test result does not absolutely rule out intermittent shedding at clinically significant levels, it suggests it is less likely, and a positive result on either PCR or ELISA testing should be cause for continued careful isolation. The risk of releasing recovered cats must be balanced against the risks of prolonged postrecovery isolation, which may compromise shelter resources, socialization for kittens, and likelihood of adoption if kittens outgrow the most "adoptable" age.

**Immunity after recovery from natural infection**

Cats that survive clinical or subclinical panleukopenia infection develop a lifelong solid immunity to reinfection. Many kittens are passively immunized for the first few weeks to months of life by absorption of maternal antibodies. If these kittens are exposed to the virus, they may develop an inapparent infection that is no less immunizing than those that recover from full-blown illness.

**Morbidity and mortality**

Morbidity and case fatality rates vary greatly. In unvaccinated colonies, panleukopenia is arguably the most devastating disease of cats and may be the cause of great plagues that are believed to have almost wiped out the cat population in various areas of the world. In general, the incidence and severity of disease tends to be inversely proportional to age, probably due to the higher intestinal mucosa cell turnover rate and immature immune system of kittens. The many mild intestinal pathogens of kittens that further increase the cell turnover rate may predispose kittens to FPV as well (Pollock and Postorino 1994; Rohovsky and Griesemer 1967). However, even many adult cats will succumb to clinical illness unless protected by vaccination (Gillespie and Scott 1973).

If the population is susceptible, incidence of disease may be nearly 100%. Subclinical infection is possible, particularly in adult cats in otherwise good health (Pollock and Postorino 1994; Gillespie and Scott 1973). However, the combination of high exposure, environmental and

social stresses, as well as concurrent disease common in some shelter environments often results in severe illness amongst susceptible cats of any age.

The disease typically has an explosive short course and high case fatality rate. The mortality rate is nearly 100% in the peracute form due to its extremely rapid course. In the acute form, fatalities vary and generally approach 90% in untreated kittens less than 6 months old. With prompt intensive treatment and diligent nursing care, the high case fatality rate may be reduced by up to 50% even in severe cases. Recovery rates of >70% with treatment have been reported (Kirk 1971). If the cat survives 5 days of illness without developing secondary complications (bacterial infection, dehydration, etc.), there is a good chance of a rapid recovery. However, it may take several weeks for the cat to regain its former weight and condition. Even with treatment, the prognosis is less favorable for very young kittens (less than 8 weeks of age) than for older kittens (over 16 weeks of age) and adult cats; even in uncomplicated cases, death may occur in the first 5 days of illness (Kirk 1971; Sturgess 2003).

Neonatally infected kittens that survive the disease may be ataxic when they start walking, but will grow normally if they are coordinated enough to eat. Although cerebellar hypoplasia is nonprogressive, signs may be more apparent as the range of activities increases. The ataxia may be so severe as to make these cats unsuitable pets, or it can be extremely mild.

Animals that recover from full-blown panleukopenia frequently have diarrhea until the cells of the intestinal mucosa are replaced, which can take from weeks to months. However, they are generally eating and less depressed than prior to the crisis. It is important to note that the persistent diarrhea in these cats is due to extensive intestinal epithelial damage and fibrosis and not to persistent infection. Occasionally cats are left with chronic intestinal malabsorption–a result of fusing of villi and mucosal scarring.

## CLINICAL SIGNS

Feline panleukopenia virus can produce a wide range of signs depending on virulence of the infecting strain, resistance of the host, and type and severity of other viral and bacterial complications. Because the virus targets rapidly dividing cells, the age of the cat at the time of infection has great bearing on the clinical presentation. There are four recognized forms of clinical disease: peracute, acute, subacute, and in utero. As noted above, subclinical infection may also occur. Subacute infection may be seen in germ-free cats exposed to the virus. They develop leukopenia and fever and weight loss due to anorexia, but they do not develop signs of intestinal disease and they recover completely. This is due to a lower mitotic rate of crypt epithelial cells that leaves fewer cells for the virus to invade (Ott 1975; Rohovsky and Griesemer 1967).

### Peracute

Peracute is the most severe form; it is characterized by sudden death 4 to 9 days after exposure to the virus. Illness progresses extremely rapidly from severe depression to coma to death in just a few hours. Vomiting may occur, but death usually ensues before diarrhea or dehydration has a chance to develop. Peracute disease is usually seen in kittens under 6 months old, particularly in those that have been recently weaned, but it has also been recognized in adult shelter cats. Since a cat may be found extremely ill or dead after having been healthy and active 8 to 12 hours earlier, it is often presented to the veterinarian as a case of suspect poisoning. More recently, these fatalities have also been mistakenly attributed to virulent systemic feline calicivirus, particularly if the cat suffered a concurrent respiratory tract infection. In some cases, severe abdominal pain can be elicited on palpation early in the course of peracute disease. However, in most cases, shock is advanced and the body temperature is subnormal by the time clinical signs are evident. Death is usually within hours.

### Acute or typical

There is normally a sudden onset of clinical signs in the acute or typical form of the disease; a fever of 40 °C (104 °F) or higher that lasts for 24 hours is common. Occasionally, cats will die during this first febrile episode, usually due to dehydration, electrolyte imbalance, septicemia, endotoxemia, and/or disseminated intravascular coagulation (DIC). Afebrile cases also have been reported. This viremic phase is followed by a return to normal temperature for another 24 hours, and then another fever episode when the white blood cell (WBC) count drops. This crisis stage often determines the outcome and severity of disease; the more severe the leukopenia, the more severe the disease and the poorer the prognosis. WBC counts below 2 K/ul indicate a very guarded prognosis. In acute cases, illness seldom lasts more than 5 to 7 days. Eventually, the body temperature of the cat becomes subnormal, followed in a few hours by coma and death. Severe depression and complete anorexia take hold during the first fever and may become profound during the second.

Vomiting is the most common sign and initially consists of the last meal eaten but then changes to a white or yellow

(bile-tinged) frothy liquid. Severe fetid diarrhea – large amounts of liquid feces – usually develops in 24 to 48 hours. The stool is frequently hemorrhagic or dark with digested blood and often contains stringy casts of fibrin or shreds of intestinal mucosa that produce the typical necrotic "parvovirus smell." Diarrhea is not generally an early sign, so it often is not seen in quickly fatal cases. The profuse vomiting and persistent anorexia, particularly when combined with watery diarrhea, lead to severe dehydration and electrolyte imbalance. These cats may act as if they would like to drink but are reluctant to do so. This apparent desire for water lasts throughout the course of the disease.

On physical examination, the eyes are sunken and the third eyelids are generally raised. Often the eyes are caked with mucus even in the absence of concurrent respiratory disease. Mucous membranes often appear pale. The hair coat is rough, dry, dull and unkempt, and may be soiled with feces. The chin may be wet from vomiting or attempting to drink. There is a loss of skin elasticity due to dehydration. Abdominal palpation is painful; mesenteric nodes are usually enlarged and intestinal contents consist primarily of gas and liquid. These cats may meow plaintively, especially when handled, due to pain from intestinal inflammation. To help alleviate the pain and fever, they generally prefer to lie with their abdomen on a cool surface, or take a crouched position with their head between their paws or hanging over a water dish. FPV cats often will adopt this position just prior to death.

Due to the severely low WBC count and reduced resistance, cats may present with signs attributable to secondary infection as well. Panleukopenia is often reported either preceding or following upper respiratory infection in shelter cats. Other clinical signs of secondary infections may include purulent otitis, oral ulcers, mild jaundice, and iritis with aqueous flare. Areas of depigmentation have been reported to occur on the brown masks of Siamese cats. Rarely, there is necrosis of the ear tips – possibly due to fibrin thrombi.

### Subacute or mild form

Cats suffering from the subacute or mild form are mildly depressed and anorexic. Intestinal contents are mostly gas, but diarrhea is a common sign; body temperature may be slightly elevated. The illness lasts 1 to 3 days, followed by rapid and uncomplicated recovery.

### In utero/neonatal infections

As with any susceptible cat, unvaccinated queens may develop fulminant disease and die. However, queens that are partially protected by natural exposure or recent vaccination may show mild or no signs, but evidence of infection may be observed in the effects on the fetuses. Infection of the fetus generally results in abortion, stillbirth, early neonatal death, or cerebellar aplasia or hypoplasia depending on the age of the fetus at the time of infection. Infection early in gestation may cause fetal abortion or death with subsequent resorption, mummification, or stillbirth. Kittens infected in late gestation or during the first few days after birth may either die suddenly with no sign of disease, or develop ataxia at about 3 weeks of age.

Since the cerebellum continues to develop during the first 2 weeks after birth, cerebellar hypoplasia can develop in cats infected shortly after birth as well as in cats infected in utero. Ataxia associated with hypermetria, dysmetria, and incoordination becomes noticeable when the kittens start to walk. Affected kittens are symmetrically uncoordinated with exaggerated movements; they usually sway and may roll or tumble. They have a wide-base stance with tail held high and stiff for balance. Despite the ataxia, kittens are alert and strong, and mental ability is unaffected. The ataxia is nonprogressive, but may be more noticeable as kittens mature and their range of activity increases. Given time, most kittens learn to accommodate for the irregularity and become good pets. The degree of disability may vary greatly among members of the same litter. Some may be normal, as transplacental transmission may not occur in all the kittens of an infected queen.

## DIAGNOSIS

Clinical diagnosis of feline panleukopenia includes evaluation of the history, clinical signs, parvo ELISA SNAP test results and characteristic hemogram changes in a susceptible patient. Definitive diagnosis may be made postmortem via histopathology on tissue specimens. Panleukopenia should be suspected in any case of sudden death in a cat not known to be completely vaccinated.

### History

To determine disease susceptibility, the age and vaccination record should be readily available. A history of vaccination is not enough to rule out FPV, particularly in kittens under 16 to 20 weeks of age due to the possibility that maternal antibody interference may prevent effective immunization. Panleukopenia should also be suspected in cats vaccinated less than a week prior to exposure. Although rare cases of vaccine nonresponders or other issues with vaccination are possible, panleukopenia is extremely uncommon in fully vaccinated cats over 4 months of age.

**Fecal ELISA test**

The fecal enzyme-linked immunosorbent assay (ELISA) test developed to test for canine parvovirus is one of the most valuable means of diagnosing panleukopenia in the shelter setting, primarily because of its rapid-assay, point-of-care design. Other diagnostics, such as those listed below, may be more accurate but are less practical and cost effective. The fecal ELISA (a.k.a. canine parvovirus antigen fecal immunoassay) detects CPV-2 and is commercially available (Parvo SNAP Test®: IDEXX Labs, Westbrook, ME; AGEN CPV®: AGEN Biomedical Ltd., Brisbane, Queensland, Australia; WITNESS CPV®: Synbiotics Corp., San Diego, CA). Although not licensed for use in cats, these tests have been demonstrated to detect feline parvovirus in feces (Esfandiari and Klingeborn 2000; Neuerer, Horlacher et al. 2008; Patterson, Reese et al. 2007).

There are variations in sensitivity (ability to detect FPV antigens) and specificity (ability to avoid false positive results) among the tests. Of importance, sensitivity of canine parvoviral ELISA tests may be limited, meaning true positive samples (defined by viral isolation) may not always provide positive test results. In one small study, only 50% to 80% of 10 truly positive samples tested positive on various tests (Neuerer, Horlacher et al. 2008). Therefore, panleukopenia cannot be ruled out only on the basis of a negative ELISA test. The specificity of the test appears to be very good, ranging from 94% to 100% in one study, with both tests most commonly available in the United States (Idexx Snap® and Synbiotics Witness®) giving negative results in 100% of 190 negative samples.

The ability of modified live vaccination to cause positive ELISA test results is also a concern. In one study, the likelihood of this varied markedly between test brands: only 1/64 kittens tested weakly positive with the Idexx brand test within 14 days of vaccination, while 13/64 kittens tested positive on the Synbiotics brand test in the same time period, including one kitten that tested "strong positive" (Patterson, Reese et al. 2007). As with all tests, results should be interpreted in light of clinical signs, physical examination findings, and medical history; however, all kittens or cats testing positive should be treated as potentially infectious to others.

**Hematology**

A profound panleukopenia (500 WBC/ul or less) is the hallmark of the disease and is present in almost all infected cats even if they do not show clinical signs. An in-house blood smear can be readily performed to support questionable ELISA test results, and a full complete blood cell count (CBC) is a valuable confirmatory tool. There is a progressive decline in numbers of circulating WBCs that starts on the second or third day after infection (prior to the onset of clinical signs). The WBC count is usually 4–8 K/ul in subclinical cases and closer to 4 K/ul in clinical ones. By 4 to 6 days postinfection, there may be fewer than 200 WBC/ul of blood, sometimes making it impossible to do a differential count. This decrease in WBCs may be gradual or precipitous. Often, the decline is progressive with a precipitous drop at the time of crisis.

- Neutrophils in particular are affected. They may disappear as rapidly as up to 4000 cells/day.
- The lymphocytes also decrease, but not as rapidly, so an absolute lymphopenia with a relative lymphocytosis may be seen; the majority of circulating WBCs generally are lymphocytes.
- Monocytes also decrease slowly, resulting in a relative monocytosis, but their numbers are normally much lower than lymphocyte numbers.
- Eosinophil production is decreased, but due to their short life span (2–6 days), they may be absent or appear increased in number (Ott 1975; Sturgess 2003; Pederson 1988).
- Erythrocyte production is decreased as well, but their long life span (100–120 days) ensures that any anemia is mild. Anemia may develop if recovery is prolonged or if there is bleeding into the gastrointestinal tract (Scott 1987). In cases of severe dehydration, there may seem to be an increase in erythrocyte numbers (Ott 1975).

Following the crisis (approximately 5 days after the onset of clinical signs), the leukocytes rapidly return to circulation, usually at the rate of 4–6 K cells/day. The total count sometimes reaches 35,000 in 3 to 4 days, resulting in a neutrophilia with a left shift.

**Serology**

Because recent vaccination can cause an identical serological response to recent infection, the detection of virus antibody levels using hemagglutination inhibition has very limited diagnostic value in shelters where the majority of cats have been recently vaccinated. In addition, the need for convalescent samples makes this test useless for rapid diagnosis of current illness. Serology is therefore used mostly to measure response to vaccination and to perform risk analysis in the event of an outbreak (see the section on outbreak management).

### Postmortem examination

In-house postmortem examination can be a helpful adjunct to diagnose or confirm panleukopenia infection. With the exception of peracute cases, when changes may not be readily apparent, cats that succumb to FPV are gaunt with the sticky dry tissues and sunken, soft eyes that are typical of dehydration. Occasionally, the esophagus or mouth is eroded or ulcerated, and there may be sloughing of the palate or inflammation of the larynx.

Internally, mild to severe intestinal congestion with or without petechiation is common, particularly in the jejunum and ileum, and occasionally in the duodenum and colon. The intestines are thickened or inelastic. The serosal surface is roughened with a granular appearance that may be covered with fibrinous exudates. The mucosal surface is ragged with mucoid or membranous exudates. Intestinal contents may consist of fluid with mucosal debris and/or blood. Feces are scant, watery, and foul-smelling, often gray or yellow in color. Mesenteric lymph nodes are swollen and edematous, sometimes hyperemic or hemorrhagic. The stomach and esophagus are reddened and bile-stained. Bone marrow may be scarce, gelatinous or liquid, and yellow-white in color. See Chapter 7 on necropsy in this textbook for detailed information about performance of in-house necropsy and sampling for histopathology.

### Histopathology

Confirmatory diagnosis may be made via histopathology since parvovirus causes pathognomonic microscopic changes in the small bowel. Therefore, in any suspect case, samples (particularly of jejunum and ileum, bone marrow, and lymphoid tissue) should be submitted for histopathologic assessment.

### Other methods of diagnosis

Other less commonly used methods of diagnosis include viral detection and isolation. Virus can be detected via electronmicroscopy or via hemagglutination. Virus isolation via cell culture from feces is another method. The clinical laboratory should be contacted to determine adequate fecal sample preparation. Problems encountered with virus detection most commonly are false negatives that result from the rapid decline in virus particles in the feces that occurs once enteric infection is established, or reduction in the numbers of virus by dilution (diarrhea).

These methods are not commonly used because they are less accessible and/or practical; however, they may have application within research or in atypical cases.

### Diagnostic rule outs

Because panleukopenia is a deadly disease that can have a major impact on cats in shelters, it is important to rule out treatable diseases. Cats may be coinfected with more than one pathogen, so identification of one of the following pathogens does not rule out concurrent infection with panleukopenia. Most of these conditions are less likely in shelter cats, particularly as a cause of outbreaks or an acute cause of death. However, these should be strongly considered if well-vaccinated cats are affected and/or diagnostic test results are inconsistent with panleukopenia. Diagnostic rule outs include severe bacterial infections that result in a toxic leukopenia (particularly *Salmonella*, *C. perfringens*, and *Campylobacter*), and other major viral pathogens that can affect the intestinal tract, including feline calicivirus. Infectious causes less likely to be seen affecting multiple individuals include acute toxoplasmosis; feline leukemia virus, and to a lesser extent feline immunodeficiency virus; and any severe or prolonged diseases that will produce bone marrow suppression and leukopenia. Noninfectious causes include acute poisoning (which may affect individuals or groups), gastrointestinal foreign bodies, and intussusception (especially in kittens).

## TREATMENT

Treatment for panleukopenia is entirely symptomatic; therapy is designed to support the patient until the body's natural defenses can take over (usually in 5 to 7 days). The goals of treatment are to combat extreme dehydration by restoring and maintaining fluid balance, to minimize continuing losses by resting the gastrointestinal tract and providing nutrients and electrolytes, and to prevent secondary infections. All medications should be administered parenterally at least for the first few days since the intestinal lesions, as well as the vomiting and diarrhea, will decrease absorption.

Panleukopenia should only be treated in the shelter if strict isolation can be maintained and appropriate nursing care can be offered. Optimum treatment protocols are offered here, but many shelters will be unable to follow all of these recommendations and will have to make appropriate adjustments based on the cat's condition, response to therapy, and the shelter's resources.

### Fluid therapy

Fluids are the most important part of the treatment plan, and should be selected, administered, and monitored as for other conditions associated with vomiting, diarrhea, and dehydration. Acute dehydration and ongoing fluid and

electrolyte losses may need to be corrected. Neonates have significantly higher fluid requirements than adult cats (80–120 ml/kg/d), but need much slower dose rates (2–3 ml/hr) (Sturgess 2003). When a vein cannot be accessed, isotonic fluids may be administered by the intraosseous, intraperitoneal, or subcutaneous routes. When using subcutaneous administration, the fluids should be spread over the body surface to prevent delayed absorption or pooling of fluids in one area.

**Transfusions**

Blood transfusions should be given if the concentration of the patient's plasma protein is less than 4 g/dl or if the white blood cell count is less than 2 K cells/ul (Pedersen 1988). Administer fresh whole blood at 10 ml/lb body weight daily or on alternate days depending on the patient's response to treatment. Blood should be given slowly intravenously, or into the medullary cavity of a femur if a vein cannot be utilized. Blood should not be administered intraperitoneally (IP) to these patients (Ott 1975).

**Antimicrobial therapy**

Although antimicrobial therapy is not appropriate for routine treatment of acute nonspecific enteritis, it is indicated in these patients to prevent the secondary bacterial infection, sepsis, and bacterial overgrowth that are a result of the severe leukopenia and tissue destruction caused by FPV infection. Antimicrobials should be administered parenterally, particularly during the acute phase of the disease. *E. coli* is the most serious secondary invader, but other organisms may create complications; thus, an antibiotic with a broad spectrum of activity is warranted. A combination of an extended spectrum penicillin such as ampicillin 3 mg/lb, intramuscularly, every 8 hours given currently with gentamicin 2 mg/lb every 12 hours provides protection from gram-positive, gram-negative, aerobic, and anaerobic infections, but must be used with caution in dehydrated patients. The urine should be checked for granular casts that may be evidence of tubular nephrosis. Amoxicillin with clavulanic acid, cephalosporins, or potentiated sulphonamides may also be used. Antimicrobials should only be administered by mouth when the gastroenteritis has been controlled, and then only for 5 days (Scott 1987).

**Antiserum**

Antiserum is the only truly specific treatment for panleukopenia although there is no clear consensus on its benefit after clinical signs have appeared (Scott 1987). It may be helpful for colostrum-deprived littermates or nonimmune, exposed cases, but it must be given prior to clinical signs or in the early stage of illness to be of value. The minimum dose is 4 ml/lb daily (Sturgess 2003; Kirk 1971).

**Vitamin therapy**

Vitamin therapy is a useful component of the therapeutic regimen. B-complex is indicated and especially important when fluids are being administered; give parenterally until the patient is eating well. Vitamin A may assist healing and regeneration of severely damaged intestinal mucosa during the recovery period (Kirk 1971; Scott 1987; Sturgess 2003). The dose is 1.1–2.2 mg/kg orally every 24 hours (*North American Companion Animal Formulary* 2004).

**Food and water**

Initially, all food and water should be withheld for at least 24 hours, especially if there is severe colic, vomiting, and diarrhea (Pedersen 1988). After the first day, water in small amounts may be introduced, followed by a pureed bland diet once the gastroenteritis is controlled (approximately 48 hours after the crisis). If the bland diet is tolerated, the normal diet can be gradually introduced.

Use of an orogastric feeding tube may be beneficial for administration of oral medications as well as nutrients. Portions should be small initially and increased as the cat begins to tolerate the feedings. Portions of ½ oz/lb of bodyweight (BW) two or three times a day should be attempted for 2 to 3 days or until the cat eats its normal ration. The key is small quantities several times daily.

It is important to maintain adequate nutrition once the vomiting has subsided. This may require placement of an esophageal feeding tube. Appetite stimulants may be administered if necessary only after gastroenteric signs have dissipated.

**Antiemetics, motility modifiers, and gastrointestinal protectants**

The use of antiemetics for persistent nausea must be judicious and only administered early in the course of the disease. The effect of antiemetics is very limited in cats with panleukopenia. Metoclopramide or odansetron may be used in cases of uncontrolled vomiting, but their efficacy and/or use in cats is questionable. Phenothiazine derivatives such as chlorpromazine or prochlorpromazine cause hypotension and should not be used in dehydrated animals.

The use of gastrointestinal protectants is considered controversial. Some advocate the use of kaolin and pectin or astringents to control diarrhea once vomiting has sub-

sided. However, kaolin–pectin has not been effective in clinical trials (Pollock and Postorino 1994). The use of motility modifiers is also controversial. Anticholinergics and opiates reduce gastrointestinal motility, causing increased absorption of bacterial toxins and increased penetration of the bowel wall by bacteria and viruses. The watery intestinal contents, instead of being eliminated, become sequestered in the bowel lumen, causing distention and abdominal discomfort. However, when used with discretion, antiemetics and cholinergics may help prevent excess fluid loss (Scott 1987).

**Nursing care**

Although patients should be kept in isolation, young kittens require socialization and direct human contact for a healthy immune system and should be visited by designated staff members who understand the importance of adhering to strict sanitary and isolation procedures. All patients should be given compassionate care to stimulate their immune system and encourage their will to live. Closely monitored heating pads, frequent petting, hand feeding, as well as warm draft-free quarters and scrupulous sanitation are important treatment aids. Because of the real possibility of inadvertent fomite transmission from frequent handling of these animals and the fact that most shelters are not staffed to provide this level of nursing care, young animals that require this degree of care should be treated off site if possible.

**Euthanasia decisions**

The decision of whether to euthanize or treat must be based on patient and environmental factors. Patient comfort, chance of recovery and adoption, the risk of spreading the disease, and the financial cost of treatment must all be considered. There are many reasons why the decision may be made not to pursue treatment in the shelter: FPV is highly contagious, carries a guarded prognosis, can be expensive to treat, is resistant to disinfection and persists long term in the environment, requires an isolation area and trained staff to provide appropriate care, etc. The risk of spreading the disease to other occupants and the limited availability of funds are usually the deciding factors. As a result of all these factors, cats often are euthanized when there is a shelter outbreak to prevent both individual animal suffering and disease spread.

## PREVENTION AND CONTROL/RISK ASSESSMENT

The basis of control is centered on three fundamental principles: proper vaccination, close monitoring of the population with prompt isolation of affected animals, and careful cleaning and disinfection of all surfaces with which cats may have contact.

Each shelter should undergo a risk assessment to help identify and correct potential sources of outbreak. All aspects of the shelter situation must be taken into account when assessing risk, particularly the immune status of the population and the potential for environmental spread of the disease. Please see Chapter 3 on the management of outbreaks for additional information.

**Vaccination**

Vaccination is the cornerstone of prevention for feline panleukopenia. Since there is little viral antigenic variation, "vaccine-resistant strains" are highly unlikely. Current available research suggests vaccination against FPV induces cross-reactive antibodies that also protect against infection and illness from canine parvoviruses (Chalmers, Truyen et al. 1999; Nakamura, Ikeda et al. 2001; Ikeda, Nakamura et al. 2002). Modified live parenteral FPV vaccines are among the most rapidly protective vaccines available. In one study, a modified live virus (MLV) parenteral FPV vaccine conferred protection against clinical disease to specific-pathogen-free (SPF) kittens admitted to a contaminated environment immediately after vaccination, and provided protection against an intraperitoneal challenge just 72 hours after administration (Brun, Chappuis et al. 1979). FPV vaccines are inexpensive and confer long-term immunity. However, it is important to remember that no vaccine provides complete immunity in every vaccinated animal. Vaccination failure is most commonly due to maternal antibody interference and may also be caused by heavy challenge, mishandling of the vaccine, genetic factors, or severe concurrent illness.

***Vaccine types***

FPV vaccines may be inactivated (killed) or attenuated (modified live) and are usually delivered in combination products also containing the feline respiratory viruses [feline viral rhinotracheitis, calicivirus and panleukopenia (FVRCP)]. Both inactivated and modified live vaccines produce a long-standing immunity. Nevertheless, parenteral MLV vaccines should be the cornerstone of the shelter vaccination program. Parenteral MLV vaccines produce fast protection (usually 1 to 2 days), with full immunity by 5 to 7 days with one dose in animals over 4 months of age (Brun, Chappuis et al. 1979). Inactivated vaccines generally do not induce immunity until 1 to 2 weeks after a second administration of vaccine (usually 2 to 4 weeks after the first administration), and are more likely to be

blocked by low levels of maternal antibodies. This alone makes them inappropriate for routine use in a shelter setting.

Modified live vaccines for FPV are available for either parenteral or intranasal administration. Although vaccination by either route eventually confers immunity, parenteral vaccination may be superior for overcoming maternal antibodies and has been shown to provide very rapid protection, which has not been demonstrated for the intranasal vaccine. For this reason, the parenteral vaccine is recommended for all cats entering shelters or other environments where risk of exposure soon after vaccination is moderate to high (Richards et al. 2006).

Modified live vaccines do have the theoretical potential to attack the undeveloped nervous system and induce abortion and fetal malformation just as the field strain virus does. The frequency with which this occurs is unknown. A risk assessment should be performed to determine if the risk of FPV infection for queen and offspring outweighs the risk of adverse consequences from vaccination itself. The benefit of vaccination often outweighs the risk, particularly during an outbreak, in shelters where FPV risk is high, or if a spay or abortion is planned (Richards et al. 2006). Unvaccinated kittens and pregnant animals that are going to carry their fetuses to term should be removed from the shelter and placed in foster care to avoid the risk of infection.

### Vaccination guidelines

For initial vaccination of cats older than 16 weeks, a single dose of modified-live parenteral vaccine administered immediately upon intake should suffice, but a second dose 3 to 4 weeks after the first is recommended to increase the likelihood of immunization (Richards et al. 2006). A delay of vaccination of even a few hours may significantly compromise the efficacy of a vaccine program. Although concerns have been expressed about the shedding of vaccine virus among group-housed cats, this has never been documented to have clinical significance; group-housed kittens or cats should receive MLV parenteral vaccines as usual (Richards et al. 2006).

#### *Vaccination of kittens*

Maternally derived antibodies (MDAs) are the most common cause of vaccine failure and must be taken into consideration when establishing a vaccination protocol for kittens. If kittens received maternal antibodies (via nursing in the first 24 hours of life from a queen that was either vaccinated or naturally exposed), this may interfere with vaccination for the first 6 to 16 weeks of life. (See Chapter 5 on vaccinations and immunology for more detailed information about maternally derived antibodies.) Because many cats enter shelters with no evidence of prior exposure to FPV, shelter kittens may not have MDAs, and vaccination may be effective very early in life. As noted above, there is concern that modified live vaccines may have adverse effects on neurologic development when administered to neonatal kittens (less than approximately 4 weeks of age). To balance this risk best with the need for early protection, kittens should be vaccinated starting at 4 to 6 weeks of age in a shelter setting (4 weeks in a high-risk shelter or during an outbreak), and starting at 8 to 9 weeks of age in a very low-risk setting such as a pet home.

In order to minimize the window of susceptibility that occurs as MDAs wane, it is recommended that FPV vaccine be administered at 2-week intervals in high-risk environments (which includes many shelters), or at 3- to 4-week intervals in lower-risk environments such as clean foster homes. Revaccination should be continued until at least 16 to 20 weeks of age. Foster kittens should receive a vaccination at least 1 week prior to their return to a shelter or if they are attending an adoption event. It is important to recognize that complete vaccine protection cannot be assumed in kittens under approximately 16 weeks of age regardless of the number of vaccines received, so these kittens must also be protected by physical separation and protection from exposure.

#### *Vaccination of ill or injured cats*

Although vaccination during illness is generally not recommended for pet animals, due to the ubiquitous threat of panleukopenia in many shelters, the benefits of doing so far outweigh the risk (Richards et al. 2006). Cats with upper respiratory infection or other mild to moderate illness should be vaccinated as usual. An exception should be made for cats clinically ill with FIV or other immunosuppressive disease; these cats should receive a killed vaccine and be physically protected from exposure by careful isolation.

### Duration of immunity

Two recent studies indicate that cats with antibodies resulting from vaccination against FPV within the past 7 years had sufficient protection against the USDA challenge dose and strain of FPV (Lappin et al. 2002; Scott and Geissinger 1999). However, since titer studies for the upper respiratory viruses are not as reliable, it is recommended that a booster vaccination with MLV FVRCP be given 1 year following the last dose of the initial series and every 3 years thereafter (Richards et al. 2006).

**Vaccine safety**

Serious adverse events associated with FPV vaccines are rare. The possible effect of the modified live vaccine on fetal development and neonatal kittens has already been discussed. The most common events reported are local inflammation, swelling, or hair loss. Injection site sarcomas also have been reported [see American Association of Feline Practitioners (AAFP) guidelines at www.catvet.com for more detailed information]. Anaphylactic shock (type 1 hypersensitivity) is rare but possible. Fortunately, the more severe reactions are rarely seen and the benefits of vaccinating far outweigh the risks. However, all adverse reactions, even minor ones, should be noted on the animal's permanent record. Particularly in the shelter setting, it is important for adopters to be given this information.

***Protection of colostrum-deprived kittens or in the face of exposure***

Vaccination will not provide protection against panleukopenia if administered after exposure. Colostrum-deprived kittens and any susceptible cats or kittens that have been exposed to FPV may be passively immunized by the administration of commercial antiserum. A dose of 2 ml was effective when commercial antiserum from hyperimmune cats was used. Serum from healthy retrovirus-negative cats vaccinated at least 2 weeks previously may be used if specific antiserum or commercial feline serum is not available. If a noncommercial source is used, a generic dose for any serum is 2 ml/kg BW or 4 ml/lb daily (Scott 1987; Ott 1975). The efficacy of this is unknown. Vaccination of kittens given antiserum should be delayed for 2 to 4 weeks, and continued 2 to 4 weeks longer than usual. The routine use of antiserum in unexposed kittens is not recommended.

**Disease recognition and isolation**

It is not possible to eliminate the chance that FPV-infected cats will enter shelters from time to time. The goal in responding to a recognized case is to minimize suffering and loss. One of the most important aspects in controlling the disease, particularly in the shelter setting, is the rapid recognition of the signs of infection. This, of course, must be followed by immediate action to halt disease spread.

1. All staff should be trained to recognize the signs of panleukopenia.
2. All cats should be checked for signs of panleukopenia or other disease *prior to* cleaning the cage, socializing, or movement of the cat to another area of the shelter.
3. Sick cats should be isolated and tested as soon as disease is suspected to help prevent spread.
4. Written instructions should be provided to staff members that clearly outline the procedure to be followed if panleukopenia is suspected. These notes should include whom to contact, diagnostics to be performed, what to do with the suspect cat and exposed cats, and instructions for cleaning the cage and other areas that the cat may have contaminated.

*"When in doubt, take it out."* In other words, suspect animals should be removed. "Any case of fetid gastroenteritis should be considered as potentially contagious and isolated until proven otherwise," (Sturgess 2003). It is always better to err on the side of caution and isolate suspect cases. Waiting even several hours for confirmation of disease could prove disastrous in a shelter setting.

**Isolation guidelines**

Because panleukopenia is highly contagious and extremely durable in the environment, shelters must carefully assess whether adequate isolation capacity exists for housing of infected cats. Sick cats should be housed separately from exposed/at-risk cats (see the section on quarantine). Isolation must be in a separate room – ideally, in a separate building – that has no carpeting, furniture, wood, or grass, and that is thoroughly cleaned and disinfected on a daily basis. If foster families are used for sick or at-risk cases, they should be thoroughly counseled on the need and ways to prevent contamination of their home; they should also be counseled on the grave prognosis should the cats become ill. Whether in the isolation room or a foster setting, strict attention must be paid to hygiene.

Procedures should be completed within the isolation area whenever possible. Attendants should change gloves after handling each cat; neither hand washing nor hand sanitizers are sufficiently reliable against this extremely hardy virus. Everyone entering the isolation area should wear protective outer garments and shoe covers. All supplies used (scrub brushes, feeding carts, medical supplies, etc.), should be dedicated to the isolation area and not used elsewhere.

**Risk assessment**

If a single case is identified in a cat that is housed only with cats vaccinated on (or prior to) shelter entry with a MLV parenteral vaccine, if good husbandry is generally practiced at the shelter, and the area is carefully sanitized on a daily basis with a parvocidal disinfectant, quarantine

of all the ward inhabitants may not be necessary (UC Davis Koret Shelter Medicine Program, *Information Sheet: Feline Panleukopenia*). However, if only some of the recommended precautions are followed, the room and possibly the entire shelter may be at risk. (See Chapter 3 on outbreaks for more information about tools and limitations of risk assessment.)

It is possible to identify cats at low risk for developing panleukopenia by submitting serum samples to a validated laboratory for analysis. Those cats that are clinically healthy and have a protective IgG titer at the time of exposure can be considered immune and not in need of quarantine. Even in the absence of serology, risk can be assumed to be relatively low in cats over 4 to 5 months of age vaccinated at least a week prior to exposure. (See Chapter 5 on vaccination and immunology for more detailed information on use of serology for risk assessment.)

**Quarantine recommendations**

Cats determined to be at risk for development of panleukopenia as described above must be removed from the population to prevent further spread; if these cats are incubating illness, they may otherwise serve to perpetuate the infection. If resources exist to do so, these cats should be quarantined for a 14-day period from the date of exposure. Vaccination series and other prophylactic treatments should be continued as usual during this period, and cats should be carefully evaluated daily for development of clinical signs of FPV. Suspicious cases should be evaluated via ELISA testing and/or blood smears and CBC as described previously. The quarantine of kittens must be restarted with each newly recognized case in the quarantine group. Adult cats in quarantine may move into a lower-risk category if they have been vaccinated at least a week prior to a new exposure.

***Routine quarantine of new intakes***

Unless a known exposure history exists, the value of routine quarantines of newly admitted cats in shelters is questionable. In most cases, routine quarantine is impractical and may serve to increase length of stay, shelter crowding, and risk of infection. Routine quarantine of kittens, while meeting their developmental needs and preventing exposure to additional infections, is particularly problematic. However, when dealing with a high risk of panleukopenia in newly admitted animals (for instance when transferring kittens or unvaccinated cats from a shelter known to be high risk), an intake quarantine of 14 days is recommended.

**Protecting newly admitted animals during an outbreak**

Ideally, in the event of an outbreak, cat intake should be halted until the shelter can be thoroughly cleaned and disinfected and all exposed/at-risk cats are transferred to quarantine or otherwise removed. This is often not possible in shelters. At the very least, all incoming animals should be segregated from the already exposed and at-risk population. The numbers in each cage and in each room should be kept to a minimum to reduce risk. If possible, cats in foster care should be adopted directly from the foster residence and not be returned to the shelter. Any cats that must return to the shelter should be vaccinated at least 1 week prior to readmission. If cat intake must be continued during an outbreak, one clean area of the shelter should be designated for this purpose. (See Chapter 3 on outbreak management.)

**Disinfection and environmental control**

Feline parvovirus is one of the most stable viruses known. It resists time and many disinfectants. It can survive many years frozen or dried, and live for over a year in the environment on surfaces and objects such as food bowls, litter pans, cage doors, gloves, toys, and sponges, with no change in infectivity. It evades many common disinfectants including iodophors, quarternary ammonium compounds, alcohol, ether, chloroform, iodines, and phenols (Eleraky, Potgieter et al. 2002; Kennedy, Mellon et al. 1995; Scott 1980).

Sanitation is one of the keys to controlling panleukopenia; disinfection should be an ongoing process. (Please refer to Chapter 4 on sanitation.) The first step toward disinfection is the removal of dirt and debris (feces, kibble, litter, newspapers) that can serve as contaminants and inactivate disinfectants. This is followed by intense scrubbing of all contaminated surfaces and then a minimal 10-minute contact time with a disinfecting solution.

It is imperative that a disinfectant proven effective against FPV be used. Potassium peroxymonosulfate (marketed as Trifectant or Virkon-S and obtained from many animal supply outlets) will inactivate FPV (Eleraky, Potgieter et al. 2002). Sodium hypochlorite (5% household bleach solution at 32 parts water to 1 part bleach; or 4 ounces per gallon of water) has also been proven effective, is inexpensive and readily available, but must be used correctly on a precleaned surface (Scott 1980). Heavily contaminated areas should be cleaned, then disinfected and left to dry without rinsing. This process should be repeated before allowing access to incoming cats.

Alcohol hand sanitizers will not inactivate FPV reliably (Scott 1980). Staff should wear a new set of disposable gloves each time a suspect cat is handled and wash hands well with soap and water if an inadvertent exposure has occurred. As a general preventative practice, each cat should be assigned one cage for its entire stay. If a change is necessary, the cage should be thoroughly cleaned before introducing a new cat. Wood and plastics (litter boxes, carriers, etc.) should be eliminated or used only in areas housing well-vaccinated cats. All donated items (blankets, toys) should be laundered and bleached prior to use.

### Other recommendations

Documentation of panleukopenia cases and communication are important management tools. Other shelters, rescue groups, and local animal hospitals should be advised in the event of a serious outbreak. It is also important to recognize the emotional impact of the disease on employees, volunteers, and adopters, especially when apparently healthy kittens can suddenly die overnight and others must be euthanized. The disease can be truly heartbreaking.

## CLIENT EDUCATION/IMPLICATIONS FOR ADOPTION

Adopter education is a key factor in dealing with the disease. At the time of adoption, clients should be given their cat's complete medical history, including vaccinations, deworming, and treatment. In an outbreak, if there is a possibility that cats were adopted out before the first case of panleukopenia was identified, a phone call from shelter personnel after the adoption can ensure the kitten receives the necessary care. New owners should be educated about symptoms of the disease. If they observe any signs of illness, they should be advised to contact their veterinarian and the shelter immediately, and to isolate the kitten or cat to keep it from spreading the disease to other unvaccinated or at-risk animals that may be in the household. Clients should also be informed of the shelter's policy if the cat develops signs or becomes ill with panleukopenia (i.e., whom to call, who will pay, etc.).

Clients who adopt a cat that later becomes ill with panleukopenia should be provided with full written instructions on how to clean and disinfect their homes. Ideally, they should not bring a new unvaccinated cat into the home for at least a year since the virus can persist in sofas and carpets. A cat more than 4 to 5 months of age that has been fully vaccinated may be safely brought into the home.

## SUMMARY

Feline panleukopenia has long been a much-feared infection. The specter of a potential outbreak looms over even the best-run shelter. Fortunately, vaccination can provide excellent protection against this deadly illness. A solid vaccination program, coupled with good husbandry, effective sanitation and disinfection, physical separation of vulnerable kittens, and attentive monitoring of the population can greatly reduce this once-ubiquitous threat.

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# 13
# Canine Parvovirus and Coronavirus

*Leslie D. Appel and Stephen C. Barr*

## INTRODUCTION

Canine parvovirus (CPV) is one of the most significant infectious diseases in shelters mainly because of its highly contagious nature and the ability to survive long term in the environment. Although the prognosis for the individual patient is often good with adequate treatment, for most shelters, isolation and treatment is not an option due to lack of adequate isolation space and financial constraints. This chapter will review the epidemiology, course of the disease, treatment, prevention, control recommendations, client education, and implications of adopting dogs that have been exposed to, or recovered from, CPV. Special attention will be given to the control of CPV in shelter populations and its impact on an animal's adoptability.

## EPIDEMIOLOGY AND COURSE OF THE DISEASE

CPV was first diagnosed in the United States during a nationwide outbreak in the fall of 1978 (M Appel, personal communication). CPVs are small, nonenveloped, single-stranded DNA-containing viruses that require rapidly dividing cells for replication (Greene 2006). CPVs are extremely stable and resistant to adverse environmental influences, including most routine disinfectants, and can last for months to years in the environment. The virus that caused the first outbreak and clinical disease was CPV-2. Most, if not all, *Canidae* are susceptible to natural CPV-2 infections (Greene 2006). CPV and feline panleukopenia (FPLV) are closely related antigenically (Parrish 1999). CPV may have arisen as a mutation of FPLV (Truyen, Parrish et al. 1995), or from another wild carnivore parvovirus (Truyen 1999) such as mink enteritis virus (MEV) or raccoon parvovirus (RPV), or from artic fox parvovirus (Smith-Carr, Macintire et al. 1997; Truyen 1999). In 1980, CPV-2 evolved into type CPV-2a, and in 1984, CPV-2b appeared (Greene 2006). Today, CPV-2b is the most common isolate of parvovirus in the U.S. (Smith-Carr, Macintire et al. 1997), whereas in Europe the most common isolate is CPV-2a. CPV-2c has also been documented in many areas of the U.S. (Hong, Decaro et al. 2007). The clinical disease commonly referred to as CPV or "parvovirus" (hemorrhagic enteritis and leukopenia) is distinct and different from the disease caused by CPV-1, also called the minute virus of canines. The clinical signs and significance of CPV-1 will be reviewed later in this chapter.

Although the original CPV-2 isolate only produced systemic and intestinal disease in dogs, there are studies that demonstrate that CPV-2a, CPV-2b, and CPV-2c can infect, replicate in, and cause clinical disease in cats and wild felids (Nakamura, Ikeda et al. 2001; Truyen, Evermann et al. 1996). CPV-2a and CPV-2b can be transmitted from dogs to cats and were isolated from 10% to 20% of cats with natural parvovirus disease in Japan, Germany, and the U.S. (Parrish 1999; Mochizuki, horiuchi et al. 1996). This probably occurs for CPV-2c as well. CPV-2a and 2b show less virulence in cats than FPLV, but CPV-2c shows intermediate virulence in cats (Ikeda, Mochizuki et al. 2000). Because CPV can be transmitted from dogs to cats, for this and other reasons, it is highly recommended that cats be housed separately from dogs in the shelter. Although CPV only rarely causes clinical disease in cats, cats can act as reservoirs of the disease, be sources for contamination of the environment, and reinfect the shelter dog population.

### Transmission and risk factors

CPV is highly contagious; most infections occur as a result of the dog's contact with contaminated feces in the environment (Greene 2006). In the shelter, fomites also

play an important role in the transmission of the disease. Shelter staff and volunteers can all act as fomites, including their hands, shoes, clothes, as well as veterinary instruments, cleaning supplies, pens, or door handles. Rodents and insects can serve as vectors (Greene 2006), and shelter dogs (both exposed and infected) can carry the virus on their hair coats. Young puppies (6 weeks to 6 months of age) are more susceptible than adult dogs (Houston, Ribble, Head 1996); however, unvaccinated dogs of any age may be infected. Infection may be less severe in adult dogs, creating a risk that these cases may go undifferentiated from diarrhea due to other causes. Certain breeds such as Rottweilers, Doberman Pinschers, German Shepherds, American Staffordshire terriers (pit bulls), Alaskan sled dogs, and Labradors are at higher risk for CPV (Houston, Ribble, Head 1996; Greene 2006), while other breeds (toy poodles and cocker spaniels) seem to be at a decreased risk for the disease (Houston, Ribble, Head 1996). In addition, one study showed that in dogs older than 6 months of age, intact dogs, especially intact males, had a greater incidence of parvovirus than neutered dogs. This study also demonstrated that dogs were about 13 times more likely to be admitted to a veterinary clinic or shelter with CPV if they were not currently vaccinated, showing that lack of vaccination was a significant risk factor for contracting CPV. This study also showed a seasonal predilection for the disease, with dogs admitted to veterinary clinics or shelters in the summer months of July, August, and September being at increased risk (Houston, Ribble, Head 1996).

CPV is more common in shelter populations than in family pets, as most family pets have been vaccinated against CPV as compared with dogs in shelters. Predisposing factors for parvovirus infection that also help explain why CPV is more common in shelter dogs include lack of protective immunity (either from maternal antibody interference with vaccination or from an unvaccinated animal), internal parasites, overcrowding, and an unsanitary, stressful environment (Smith-Carr, Macintire, Swango 1997). Crowding and poor sanitation do not directly increase the severity of disease in individual animals, but increase the likelihood of exposure and infection (Barr and Bowman 2006). However, concurrent gastrointestinal disease or parasitic infestation resulting from exposure to such an environment can increase the severity of disease in an individual.

Although a human parvovirus exists, CPV cannot transmit from dogs to humans. In unvaccinated shelter and family dogs, CPV has a high morbidity rate. With optimal veterinary care, the mortality rate is relatively low, although this may not be an option in many shelters due to financial constraints or lack of isolation facilities.

**Pathogenesis**

CPV spreads rapidly from dog to dog via oronasal exposure to contaminated feces (Greene 2006). CPV proliferates in rapidly dividing cells. After exposure, replication of the virus starts in the lymphoid tissue of the oropharynx, including regional lymph nodes, pharynx, and tonsils. Replication then occurs in the thymus and mesenteric lymph nodes. Viremia occurs 1 to 5 days postinfection, after which the virus localizes primarily in the gastrointestinal epithelium lining the tongue, oral cavity, esophagus, and small intestine. CPV is disseminated to the intestinal crypts of the small intestines through viremia (Greene 2006), causing cell death and ultimately blunting of the intestinal villi. CPV also destroys mitotically active precursors of lymphoid cells and leukocytes. In addition to severe enteritis, CPV can also lead to secondary bacterial infections and septicemia as a result of the severe immunosuppression caused by depletion of white blood cells. After viremia occurs, CPV also localizes in the lymphoid tissue of the thymus, lymph nodes, and bone marrow. CPV has also been isolated from the lungs, liver, kidneys, and spleen, where it causes minimal pathology (Greene 2006).

**Incubation period and viral shedding**

The incubation period for CPV-2 was commonly 7 to 14 days (Greene 2006). The incubation period for currently circulating strains (CPV-2a and CPV-2b) is usually 4 to 6 days, although more prolonged incubation periods of up to 10 to 14 days have been reported in the field (K Hurley, personal communication). Active shedding of the virus into the feces usually occurs 3 to 4 days postexposure, soon after viremia but before overt clinical signs appear. CPV multiplies in the intestinal tract of infected dogs and a billion virus particles per teaspoon of feces can be shed during an infection (Legendre 2000). The virus may be shed in the feces for 7 to 12 days postexposure (Barr and Bowman 2006; Greene 2006). Thus, the authors recommend that shelters that wish to utilize a quarantine to rule out parvovirus use a period of 2 weeks that will encompass viral shedding.

There is no carrier state for canine parvovirus, and recovered dogs do not shed virus for more than 2 weeks postinfection. Although the virus can survive long term in the environment and on the hair coats of recovered and exposed dogs, once a dog recovers from parvovirus and is adequately bathed to mechanically remove any virus par-

ticles from the hair coat, the authors recommend that the dog can be safely adopted out of the shelter.

## CLINICAL SIGNS

Clinical signs of CPV are associated with two typical syndromes observed with CPV-infected dogs: acute myocarditis with high mortality in young puppies and hemorrhagic enteritis in older puppies (Ikeda, Mochizuki et al. 2002). CPV myocarditis can develop from infection in utero or in puppies younger than 6 to 8 weeks of age (Greene 2006). Cardiac myocytes can only support CPV growth within the first 2 weeks of the puppy's life, so the infection must occur in utero or within the first week of life (Barr and Bowman 2006). When CPV first appeared in the late 1970s, myocarditis was common, but it is rarely seen today because most neonates born to vaccinated or naturally exposed mothers are now protected by maternal antibodies (Smith-Carr, Macintire, Swango 1997). However, a high percentage of dogs entering shelters have negative titers to canine parvovirus; thus, this form of the disease may still be seen in shelter puppies (K Hurley, personal communication). Usually, all puppies in a litter develop myocarditis when CPV myocarditis develops and die after a short episode of crying, dyspnea, and retching, although the spectrum of myocardial disease varies within the individual (Greene 2006). Some puppies may show signs of diarrhea and death without cardiac signs, while others may show signs of diarrhea followed by apparent recovery only to be followed by death weeks or months later, when the puppy goes into congestive heart failure (Greene 2006). Apparently healthy puppies 6 weeks to 6 months of age may have acute onset of congestive heart failure. On necropsy, pale streaking of the myocardium is the lesion seen.

The most common clinical signs are related to parvoviral enteritis. These signs include vomiting and profuse diarrhea with or without blood (German 2005). Infected puppies are usually anorexic, dehydrated, and pyrexic (German 2005). Leukopenia is a characteristic finding, and in severe cases, the puppy can show signs of endotoxemia secondary to bacterial septicemia, shock, disseminated intravascular coagulation (DIC) and death (German 2005). Panhypoproteinemia (protein-losing enteropathy) can also occur in severe cases (Marks 2005). The clinical signs of CPV can be exacerbated by concurrent infections with intestinal parasites, coronavirus, canine distemper virus, salmonella, campylobacter, or *Giardia* (Marks 2005).

Clinical signs are usually worse in puppies 6 weeks to 6 months of age; older dogs may have subclinical infections (Houston, Ribble, Head 1996). As CPV grows in actively dividing cells, the incidence of CPV enteritis increases when puppies are weaned; at that age, the enterocytes of the intestinal crypts have a higher mitotic index because of the changes in bacterial flora and diet and are therefore more prone to damage from CPV (Houston, Ribble, Head 1996). The main factor that determines the severity of disease appears to be the rate of lymphoid and intestinal cell turnover; increased rates of turnover are directly correlated with virus replication and cell destruction, and concurrent parasitic disease or other viral infection also increase the pathogenicity of CPV (Smith-Carr, Macintire, Swango 1997). The individual's immune response also determines the severity of the disease: A rapid immune response may limit the magnitude and duration of viremia and therefore result in milder disease and a more rapid recovery (Smith-Carr, Macintire, Swango 1997).

Although kittens infected in utero with feline parvovirus, or panleukopenia, are at risk for developing cerebellar hypoplasia, this is an extremely rare event with CPV (Schatzberg, Haley et al. 2003).

Other uncommon clinical signs of CPV include thrombosis and bacteriuria, which mainly occur as a result of severe neutropenia. Dogs with CPV can have evidence of hypercoagulability, and these dogs may develop thrombosis or phlebitis (Greene 2006), especially at catheter sites. Asymptomatic urinary tract infection has also been seen in about 25% of puppies with CPV (Greene 2006). Fecal contamination of the external genitalia combined with the neutropenia caused by CPV can lead to urinary tract infections.

## DIAGNOSIS

The accurate diagnosis of CPV in the shelter is important and can be challenging. Although the sudden onset of bloody diarrhea and vomiting in a young puppy in the shelter is highly suggestive of CPV, it is important to remember that not all dogs with bloody diarrhea and vomiting have CPV. Other differential diagnoses include parasite infestation, infectious agents such as *Salmonella* or *Campylobacter*, dietary indiscretion, foreign body ingestion, inflammatory bowel disease (IBD), hemorrhagic enteritis (HE) toxins, as well as other systemic or metabolic disease (Barr and Bowman 2006). Parvovirus should be suspected especially if the patient is a puppy or an unvaccinated dog, or if the patient has been exposed to infected dogs (German 2005). The majority of parvo cases are severely panleukopenic (German 2005), and CPV may be distinguished from other causes of diarrhea by the presence of a severe neutropenia that is apparent on a stained

direct blood smear, even without cell counts (Barr and Bowman 2006). Therefore, the authors recommend the performance of a direct blood smear in conjunction with other diagnostic tests to make a definitive diagnosis of CPV.

The diagnostic test of choice in the shelter is the fecal enzyme-linked immunosorbent assay (ELISA) antigen test. This test is available for in-house testing and is relatively sensitive and specific for detecting CPV-2 infection (Greene 2006). In addition, fecal antigen test kits such as the SNAP Parvo Antigen Test (IDEXX) can detect both CPV viral antigen in canine feces and FPLV viral antigen in feline feces (Brower, Radi, Toohey-Kurth 2004). However, both false positive and false negative results can occur, and the test results should be interpreted in conjunction with history, clinical signs, and the direct blood smear. False negative test results can occur due to the relatively short time of viral shedding (Barr and Bowman 2006). The period of virus shedding in the feces is brief, and CPV is seldom detectable by 10 to 12 days after natural infection, which corresponds to 5 to 7 days of clinical illness (Greene 2006). In addition, systemic antibodies in the blood can pass from capillaries into the disrupted intestinal lumen and can terminate viral excretion into the feces, thereby causing a false negative in the face of acute infection (Smith-Carr, Macintire, Swango 1997). Finally, antibodies against parvovirus in blood in the fecal sample can bind to the virus, causing a false negative test result since these complexes are not detected by the parvo test. Some experts question whether a vaccine can cause a false positive test result, while others believe weak false positive test results can occur within 5 to 12 days of vaccination with a modified live virus (MLV) CPV vaccine (Greene 2006). In a study conducted in kittens, 1/64 kittens tested weakly positive on an Idexx brand parvo ELISA test within 2 weeks of receiving a modified live vaccination against feline panleukopenia. Other brands of tests had a greater number of positive results in recently vaccinated kittens. Although this documented that the modified live vaccination for feline panleukopenia may uncommonly cause weak false positives on the Idexx brand parvo test, it is unknown whether similar results would be obtained in puppies vaccinated against canine parvovirus (Patterson, Reese et al. 2007). Clearly, more research is required to elucidate this further.

Other diagnostic tests to confirm parvo virus infection include viral isolation using tissue cultures in the early course of the disease, electron microscopy scan of the feces, fecal polymerase chain reaction (PCR), fecal hemagglutination assay, and serum hemagglutination inhibition (Barr and Bowman 2006). Methods of diagnosis based on PCR have been shown to be more sensitive than by ELISA antigen test or by hemagglutination assays (Decaro, Elia et al. 2005). However, because fecal antigen tests are simple, reliable, and affordable and can be performed in house, the authors still recommend the ELISA antigen test, interpreted with the history, physical examination (PE), and white blood cell (WBC) smear in the shelter situation. The advantage of real-time PCR is that it is highly sensitive and reproducible, and it may allow for identification of dogs shedding CPV at low levels in their feces (Decaro, Elia et al. 2005). With other methods of diagnosis, dogs infected subclinically or recovering from CPV may not be identified, leading to environmental contamination and spread of CPV infection to other dogs (Decaro, Elia et al. 2005). However, the vast majority of shelters are able to diagnose and control parvovirus without resorting to PCR testing; it may be that dogs shedding at such a low level are not of great clinical importance in the face of reasonable cleaning, disinfecting and vaccination practices. In addition, real-time PCR may detect modified live vaccine virus shed in feces. Therefore, although real-time PCR is more sensitive, specific, and reproducible than fecal antigen ELISA tests, it is neither practical nor necessary for diagnosing most CPV outbreaks in shelters (Desario, Decaro et al. 2005).

A postmortem exam can also help confirm the diagnosis of CPV in the shelter. Early in the course of the disease, the lesions are most pronounced in the distal duodenum, while later the jejunum is more severely affected. The intestinal wall is thickened and segmentally discolored; there is denudation of the intestinal mucosa; and there can be a dark, sometimes bloody, watery material within the intestinal lumen. Histologic examination is usually definitive. Fluorescent antibody (FA) testing can be used to identify CPV antigen in a wide range of tissues including the tongue, pharynx, esophagus, planum nasale, small intestinal mucosa, bone marrow, spleen, thymus, mesenteric lymph nodes, palatine tonsils, and myocardium (Greene 2006).

## TREATMENT

### Treatment decisions

Once CPV has been diagnosed, the shelter staff must make the difficult decision about whether or not to treat the infected animals. Although the prognosis for recovery for individual CPV infected dogs is excellent with early diagnosis and appropriate treatment, widespread treatment in shelters is often cost-prohibitive. There is also some risk

involved in maintaining confirmed parvo cases within the shelter. Many shelters do not have adequate isolation facilities or sufficient staff to treat animals maintained in separate isolation areas. The shelter must not only decide whether to treat parvo cases but where to treat them as well. The authors recommend treating parvo cases at local veterinary hospitals or at isolation facilities separate from the shelter itself. Mild cases (puppies that are not vomiting and are not significantly dehydrated) can be treated on an outpatient basis in foster care homes, again provided suitable, readily disinfected "isolation facilities" exist in the home (Barr and Bowman 2006). Long-term contamination of a foster home may be an issue if puppies are treated in an area that is resistant to cleaning and disinfecting.

**Basic treatment guidelines and protocols**

Treatment of CPV is based upon principles of supportive care. Important principles include restoration of fluid loss associated with diarrhea and vomiting and prevention of secondary bacterial infections. The first step is to assess dehydration. Most puppies with CPV enteritis are 8% to 10% dehydrated, as indicated by sunken eyes, prolonged capillary refill time, skin tenting, dry mucus membranes, and signs of shock, including increased heart rates and weak pulses. A packed cell volume (PCV) and total plasma protein (TPP) can be useful to assess dehydration but can also be affected by blood loss in the diarrhea. A urinalysis usually shows markedly concentrated urine. The following formula can be used to estimate the fluid volume to be replaced during therapy:

$$\textit{Percentage dehydration} \times \textit{body weight in Kg} = \textit{liters of fluid to replace}$$

The estimated ongoing losses (vomiting and diarrhea) and insensible and sensible losses (about 15 ml/kg/day) should also be included in the replacement fluid calculation. A balanced fluid should be used, such as Lactated Ringers solution, Normosol, or 0.9% sodium chloride supplemented with dextrose and potassium. Potassium can be supplemented at 0.5 mEq/kg/hr (generally 20–30 mEq/L). Fluids containing dextrose are especially indicated in small puppies. The intravenous (IV) route of administration is recommended if a catheter can be properly maintained in the patient. Extreme care in catheter maintenance should be taken, as up to 22% of CPV patients develop bacterial colonization of IV catheters (Barr and Bowman 2006). The subcutaneous (SQ) route of administration should be used with caution, as the patient is usually leukopenic and SQ fluid in leukopenic patients can lead to infection. Often, due to lack of resources, the only choice is to use the SQ route of fluid administration. Care should be taken to insert the needle into a clean area of the skin, and dextrose should not be added to the fluid.

The use of broad-spectrum antibiotics is necessary in all CPV patients, as these animals are leukopenic and prone to sepsis. Enteric *Clostridium perfringens* frequently proliferate in dogs with CPV. Broad-spectrum antibiotics are recommended, such as cephalosporins, enrofloxicins, or combinations such as IV ampicillin and gentamicin. Dehydration should be corrected before using gentamicin.

A major component of supportive care of dogs with CPV includes control of emesis (Mantione and Otto 2005) because the profuse fluid losses from vomiting and diarrhea contribute to rapid dehydration. Vomiting can also put the patient at risk for aspiration pneumonia and gastric mucosal erosions. Because vomiting patients cannot be given oral medications, metoclopramide is the most effective antiemetic to use in the recovering dog. However, it must be used with caution because it stimulates GI motility (Mantione and Otto 2005), which predisposes puppies to ileus and intussusception. Other antiemetics include chlorpromazine and prochlorperazine. Serotonin receptor antagonists such as dolastron and ondansetron are also very effective. Gut motility modifiers (dephenoxylate or loperamide) are rarely indicated.

Careful abdominal palpation must be performed on animals with CPV to rule out secondary intussusception. Once vomiting has stopped, oral gastric protectants (carafate, famotidine, cimetidine, or ranitidine) can be used.

Treatment for *Giardia* and other parasites using a broad-spectrum anthelmintic should also be considered, as these infections can exacerbate the severity of the CPV infection. Fenbendazole is a good choice to consider once vomiting has ceased (Barr and Bowman 2006).

Whole blood or plasma transfusions may be indicated. Whole blood can help puppies that are severely anemic from GI blood loss from CPV enteritis as well as from concurrent parasitism; plasma transfusion can support puppies that become hypoproteinemic without anemia. A synthetic colloid such as hetastarch can also be used. Colloids should not be given until dehydration is corrected (Greene 2006).

**Other treatment modalities**

A relatively new treatment modality that has shown promise in the treatment of CPV infection is early enteral nutrition (EEN). Puppies provided with EEN administra-

tion showed earlier clinical improvement and significant weight gain. EEN also improved gut barrier function, which could limit bacterial or endotoxin translocation, therefore limiting bacteremia or endotoxemia (Mohr, Leisewitz et al. 2003). Furthermore, the most important stimulus for intestinal mucosal growth, repair, and integrity is the presence of nutrients within the gut lumen (Mohr, Leisewitz et al. 2003). EEN may help give shelters with limited financial resources the ability to treat parvo cases because a more rapid recovery time has the potential to decrease the length of the hospital stay and therefore decrease expenses (Mohr, Leisewitz et al. 2003). In one study, the enteral feeding tube was a nasoesophogeal tube, and although enteral tube feeding was not associated with severe complications, two dogs in this study developed moderate gastric tympany, so a nasogastric tube, where the gastric contents can be aspirated prior to feeding, may be preferable (Mohr, Leisewitz et al. 2003). EEN is better than starvation or total parenteral nutrition (TPN); the benefits of EEN include decreased intestinal mucosal permeability; increased weight and motility; decreased bacteremia, septicemia, and septic morbidity; attenuation of the acute phase response; decreased incidence of multiple organ failure; increased immunological status; decreased catabolism and preservation of a negative nitrogen balance; and a positive clinical outcome (Mohr, Leisewitz et al. 2003). Because of vomiting, the amount of enteral nutrition that successfully reaches the small intestines is not known, but at least 25% of total daily caloric requirements should be given enterally to prevent intestinal mucosal atrophy (Mohr, Leisewitz et al. 2003). This study showed that EEN can be done successfully in CPV enteritis patients, even with severe vomiting and diarrhea, and the significant weight gain indicated at least partially efficient nutrient digestion and absorption (Mohr, Leisewitz et al. 2003).

Other treatment options that have questionable efficacy and/or practicality for the shelter setting include antiendotoxin serum or hyperimmune plasma, granulocyte colony stimulating factor (G-CSF), recombinant feline interferon type omega, and Tamiflu. During the initial stage of CPV enteritis, adjunctive therapy with transfusion of specific hyperimmune plasma or antiendotoxin sera has been recommended (Greene 2006). These adjunct therapies reportedly decrease mortality and the length of hospitalization, but they are expensive (Greene 2006) and impractical for most shelter situations. Moreover, the use of hyperimmune plasma can be questioned because at the time of clinical signs, the levels of antibodies in CPV-infected patients are generally increased (Greene 2006). It is also difficult to separate the beneficial effects of protein as opposed to immunoglobin that binds virus or endotoxins.

G-CSF has been recommended for the treatment of the severe neutropenias that occur with CPV infection (Greene 2006). However, G-CSF has not been shown to change any aspect of the clinical outcome in CPV-infected puppies (Barr and Bowman 2006; Greene 2006).

Recombinant feline interferon type omega (antiviral therapy) has been shown to significantly improve the clinical signs of CPV and decrease mortality (Martin, Najbar et al. 2002; De Mari, Kaynard et al. 2003); this treatment modality is not available in the U.S. at the time of this writing.

The use of Tamiflu (oseltamivir phosphate) to treat CPV infection has been recently recommended but remains controversial, and the successes have been anecdotal. Tamiflu is an antiviral agent. The mechanism of action for this drug is inhibition of influenza viral neuraminidase (Roche Tamiflu drug insert). There is no proven efficacy of Tamiflu in any illness caused by agents other than influenza viruses types A and B (Roche Tamiflu handout). Currently, there is no evidence that Tamiflu improves the outcome of dogs with CPV.

In conclusion, there are several modalities for the successful treatment of CPV infection. When adequate treatment is possible, the prognosis for a full recovery is excellent. After successful treatment, the recovered dogs will most likely have immunity for life (M Appel, personal communication).

**Parvovirus and pediatric neutering**

The question has been asked if prepubertal gonadectomy predisposes puppies to CPV. In one study, parvoviral enteritis was the most commonly reported infectious disease, and CPV was reported exclusively in dogs that underwent prepubertal gonadectomy (Howe, Slater et al. 2001). However, the potential influence of anesthesia and surgery on the incidence of CPV infection could not be determined, as comparisons with puppies that did not undergo gonadectomy were not performed (Howe, Slater et al. 2001). It is important to remember that CPV is not uncommon in puppies from shelter environments, and in the authors' opinions, puppies became infected with CPV because they were exposed at a shelter when they were not protected either by maternal antibodies or by vaccination, not because they underwent prepubertal gonadectomy. In cases where neutering of a recovered parvo puppy is being considered, the authors recommend waiting until the puppy is completely recovered from CPV and the serum albumin and WBC count have returned to normal (usually

by 2 weeks or so after infection). Once fully recovered, the puppy can be safely spayed or neutered and will no longer be a source of contamination for the hospital or clinic, as viral shedding in the feces will have ceased. The puppy should also be carefully bathed after recovery and prior to surgery.

### Euthanasia decisions

Euthanasia decisions for puppies infected or exposed to CPV can be very difficult to make. The prognosis for patients with CPV is good with appropriate treatment. However, maintaining CPV-positive puppies in the shelter presents the risk of disease spread to the entire shelter dog population as previously discussed, and the prognosis for recovery without proper treatment is guarded to poor. Shelters should consider humane euthanasia for infected puppies if financial resources are limited and the shelter cannot provide adequate treatment. The authors do not recommend euthanasia of all exposed puppies or unvaccinated dogs in the shelter, but it should be considered for all puppies that test positive for CPV if treatment is not available. Furthermore, the authors do not recommend euthanizing the entire litter if only one puppy in the litter is confirmed with CPV. The other puppies may or may not become infected, and euthanizing the entire litter may be premature. Only puppies in the litter that test positive should be euthanized if treatment is not an option. Euthanasia of littermates may also be necessary if appropriate isolation with enrichment is not available.

## PREVENTION, CONTROL, AND RISK ASSESSMENT

The recommended quarantine period for the prevention of CPV is 14 days. This should be strictly adhered to in order to prevent CPV contamination of the shelter. A proposed idea is for shelters to test incoming dogs/puppies for CPV on intake in order to identify animals that may be shedding the virus before showing clinical signs. This may be useful in areas where parvovirus is very common; however, this will most likely be cost prohibitive for most shelters. A compromise approach is to train staff to be aware of factors that increase the suspicion of parvo infection. These may include susceptible breeds, puppies with an unthrifty appearance, those with evidence of diarrhea, and even dogs from a neighborhood known to be a common source of parvo. Some shelters keep a map on which they note the area in the community where cases have originated, such that extra care can be taken when receiving puppies from these locations.

If a shelter decides to set up an isolation area to treat CPV-infected dogs, strict isolation guidelines must be followed. It is best to use designated personnel to clean, feed, and medicate the animals in isolation only, rather than assigning them to work in other areas of the shelter. Isolation "gowns" or protective clothes, including shoe covers or dedicated boots, should be worn by staff attending to patients in isolation, and these should kept in the isolation area if the staff has to move on to other areas of the shelter. The use of footbaths is controversial; in one study, they were ineffective at reducing the bacterial count on barn floors even when correctly used (Stockton, Morley et al. 2006). Given the highly durable, contagious, and virulent nature of parvovirus, footbaths should not be relied upon for its containment. If the decision is made to use them, the best disinfectant to use is either bleach (diluted in a 1:32 ratio, or ½ cup per gallon of water) or Trifectant®. The disinfectant solution should be changed daily, or more often as fecal contamination occurs.

The same questions and precautions apply when housing exposed animals in quarantine; while perhaps not quite as great a risk to the rest of the population, infected dogs may shed for several days prior to development of clinical signs, so all dogs in quarantine following a possible exposure must be treated as if they are actively shedding infectious parvovirus.

Once puppies recover from CPV infection and it is safe to release them from isolation, it is best if they are adopted directly out of isolation or put into foster care until adoption rather than returning to the general shelter population. If these puppies must be returned to the general shelter population, it should be at least 14 days after the puppy was infected to ensure viral shedding has ceased. Each puppy should be properly bathed to mechanically remove CPV particles that may remain on the hair coat. If the hair coat is contaminated with CPV, the recovered puppy can act as a reservoir for CPV to contaminate the shelter even when the puppy is no longer shedding virus. Critics of in-shelter isolation areas are concerned because any dog or puppy with CPV infection can act as a reservoir for infection of other animals in the shelter, and it is difficult to properly staff isolation areas and ensure that all isolation protocols are strictly followed.

### Vaccination

Fortunately, safe and effective vaccines are available against CPV (Carmichael, Joubert, Pollock 1983). Modified live virus (MLV) vaccines should be used to prevent parvovirus infection in the shelter. MLV vaccines were shown to induce superior and longer-lasting immunity compared

with inactivated vaccines (Abdelmagid, Larson et al. 2004). They can also partially overcome interference with maternally derived antibodies. In addition, susceptible dogs are immunized by virus shed by vaccinates, a phenomenon that appears to occur with all attenuated strains studied (Pollack and Parrish 1985). CPV vaccines induce sterile immunity and immunity from MLV products (like natural infection) generally lasts for the life of the animal (Schultz 2006; M Appel, personal communication). All animals should be vaccinated at capture or on entry to the shelter. Where possible, animals should be vaccinated at least 1 week prior to shelter entry (e.g., puppies returning from foster care or owner-surrendered animals for whom appointments can be made).

***Vaccine schedule recommendations***

For puppies: vaccinate from ages 6 to 16 weeks on entry with MLV and then revaccinate every 2 weeks with MLV. It is important to recognize that repeated vaccinations are given because of the concern that maternal antibodies will interfere with vaccination. These are not booster vaccines. There is no benefit in holding puppies in a shelter for the sole purpose of administering multiple vaccines. In fact, this practice may simply serve to increase a puppy's risk of exposure.

There is a postulated risk of MLV vaccine-induced disease in puppies under 4 to 5 weeks of age. Killed vaccines can be used for puppies with unknown histories of nursing/maternal antibodies that are 3 weeks and older (M Appel, personal communication). However, killed vaccines will require a booster in 2 to 3 weeks to provide meaningful protection; therefore, extreme care must be taken to physically protect such puppies from exposure to disease.

For adult dogs: vaccinate once on intake (or at capture) with an MLV product (Schultz 2006). The American Animal Hospital Shelter Dog vaccine guidelines recommend revaccinating adult dogs once after 2 weeks or after adoption.

The commercially available vaccines for CPV are safe, and vaccine reactions are rare. Both Type II hypersensitivity and autoimmune hemolytic anemia (AIHA) have been suspected in rare cases after MLV vaccination in the dog (Greene 2006). Nonimmunologic reactions such as systemic fever and malaise lasting 1 to 2 days postvaccination can explain the transient depression and anorexia seen in some recently vaccinated animals (Greene 2006). Also, as previously mentioned, MLV CPV vaccines should not be given to puppies younger than 4 to 5 weeks of age because myocarditis and neonatal infection may develop (Greene 2006). Finally, a risk factor analysis should be performed before administering MLV CPV vaccines to pregnant dogs because, although fetal malformation, death, infertility, or abortion can occur (Greene 2006), the risk of contracting disease by failure to vaccinate or use of a killed product may be a greater concern in shelters.

There is a role for vaccination in the face of an outbreak, as immediate vaccination with MLV CPV after an animal has been exposed will reduce morbidity and mortality but will not prevent infection and disease. As previously mentioned, some authors believe (although it is controversial) that using modified live CPV vaccines can cause a weak false positive test result usually 5 to 6 days postvaccination (Smith-Carr, Macintire, Swango 1997). Individual patient test results should be interpreted in light of history, clinical signs, white blood cell count, and course of the disease.

Modified live CPV vaccines do cause shedding of the virus in the vaccinate's feces, but this is of no clinical significance. Although the amount of virus shed in the feces is much smaller than the amount of virus shed in the feces post natural CPV infection, it may cause seroconversion in naïve, in-contact animals (Greene 2006). However, fecal–oral spread or topical administration of modified live CPV does not provide suitable protection against CPV because it does not reach lymphoid tissue in sufficient concentration compared to parenteral administration (Greene 2006).

In summary, modified live CPV vaccines provide a high level of antibody and sterile immunity that prevent disease; they also prevent infection or shedding after challenge with virulent virus (Greene 2006). Therefore, dogs in shelters should be vaccinated with MLV vaccines immediately when they enter the shelter or even before if practicable (Greene 2006).

**Environmental control**

Environmental control of CPV in a shelter situation is challenging because the virus is stable and can persist for years in the environment. Disinfection should be accomplished with a product independently tested and proven effective against unenveloped viruses. Quaternary ammonium disinfectants have been repeatedly labeled as parvocidal by the Environmental Protection Agency (EPA) but have been shown to be incompletely effective by independent testing (Eleraky, Potgieter et al. 2002; Kennedy, Mellon et al. 1995). Sodium hypochlorite [household bleach (5% solution diluted at 1:32)] and potassium peroxymonosulfate (Trifectant) have been independently documented as effective against unenveloped

viruses. Other chlorine-based disinfectants may also be efficacious.

Disinfectants must be properly applied in order to be effective. Before application of disinfectant, the contaminated area must be thoroughly cleaned to remove dirt and organic material (such as feces), as organic material will compromise the efficacy of the disinfectant, especially bleach. After all organic material has been removed, freshly mixed disinfectant solution such as potassium peroxymonosulfate or bleach should then be applied in the appropriate dilution (1:32 for 5% household bleach), and left on the surface for a minimum of a 10-minute contact time prior to being rinsed off.

It is common to close off contaminated runs for up to 1 to 2 weeks. However, there is likely little or no benefit to this practice. If chemical disinfection and mechanical cleaning is inadequate, the virus can easily persist for months, so holding runs closed for a couple of weeks will not substantially reduce risk. However, it may be beneficial to complete several cleaning, disinfecting, and drying cycles prior to reuse of a contaminated area to ensure complete disinfection.

Outdoor areas can be especially difficult to disinfect adequately after contamination with CPV. If possible, cement and gravel runs should be disinfected with potassium peroxymonosulfate rather than bleach because of its superior activity in the presence of organic matter. Grass areas cannot be completely disinfected, and the focus for shelters should be on prevention of contamination of outdoor grassy areas. In addition, puppies should not be permitted to use outdoor grassy areas that may have been contaminated. Easily disinfected areas should be set aside for puppy socialization and exercise. All dogs allowed onto grassy areas should have been vaccinated on admission with a MLV CPV vaccine and dewormed. In high-risk shelters (where parvo is a frequent threat) or for dogs from high-risk groups (e.g., transfers from a shelter in which parvovirus is common), dogs should be quarantined for 14 days before exposure to grass play areas. Because the vaccine provides protection within 3 to 5 days, dogs unlikely to be incubating infection may be allowed in these areas sooner. If a grassy area is contaminated with CPV, it is impossible to say how long that area should be left unused. (M Appel, personal communication). Sunlight almost certainly will inactivate the virus, but there have been no studies to confirm how much time it will take (C Parrish, personal communication). While some experts recommend removal and replacement of the grass and soil, others think that this is a waste of time since future contamination will inevitably occur (C Parrish, personal communication). Repeated removal of grass and soil can be cost-prohibitive for many shelters as well. The best way to handle CPV contamination of outdoor grassy areas is through preventative measures, before contamination occurs.

Temperatures greater than 75°C will inactivate parvoviruses in normal media (C Parrish, personal communication), so hot steam cleaning can be an acceptable alternative to bleach or Trifectant for disinfection. Dishwashers that attain temperatures greater than 75°C can aid in the removal of CPV from food and water bowls and are less labor intensive for staff. The virus can probably be readily removed by washing, so dishwashers will reduce the virus titers, partly through the high temperature and partly just through the washing process (C Parrish, personal communication).

Other recommendations include being vigilant about vermin and pest control. Insects and rodents can serve as mechanical vectors (Greene 2006) of the disease. Overall, the shelter staff and volunteers who are involved in cleaning should be educated on proper disinfection procedures for CPV, and these disinfection procedures should be written down in a shelter operations manual and reviewed frequently.

## CLIENT EDUCATION AND IMPLICATIONS FOR ADOPTION

Animals that have recovered from CPV can be safely adopted out into the community. Client education is essential when adopting out puppies that either have been exposed to or are recovering from CPV. If a client adopts a puppy that subsequently becomes ill with parvovirus, that client is going to have a negative view of the shelter and will probably blame the shelter for adopting out sick animals. However, if each client is educated about CPV, including the risks of adopting any puppy from a shelter situation, that client is likely to be more understanding if the recently adopted puppy then becomes ill. Each new adopter should be counseled about CPV infection and assured that later complications are rare and immunity after recovery is usually life-long. The new adopter should also be counseled that CPV is unlikely to spread to other appropriately vaccinated pets already in the home.

If a new adopter wants to adopt or foster a puppy who has CPV or has been at high risk of exposure (e.g., a littermate of an affected puppy), special instructions should be given. The new adopter should be advised to have the puppy treated by his or her own veterinarian or be provided with other instructions regarding shelter policy. The new adopter should be advised to keep the puppy

confined to an easily disinfected area or kennel and to clean and disinfect where possible with dilute bleach or potassium peroxymonosulfate if available. After recovery, the puppy must be bathed to prevent continued contamination of the home environment. In addition, the adopter should be advised not to bring the puppy to public parks or other public areas for the first 2 weeks postinfection or following exposure to reduce the risk of spreading the disease to other animals. Puppies that have recovered from CPV can be safely adopted and have an excellent prognosis.

## CPV-1, THE MINUTE VIRUS OF CANINES

No chapter on canine parvovirus would be complete without the mention of CPV-1, also called the minute virus of canines (MVC). CPV-1 is distinctly differentiated from CPV-2; these are different viruses (Greene 2006).

The domestic dog is the only proven host for CPV-1, and serologic evidence suggests that CPV-1 has a widespread distribution in the dog population but usually only causes clinical disease (enteritis, pneumonitis, myocarditis and lymphadenitis) in puppies younger than 3 weeks of age. However, it has been observed infrequently in the feces of field dogs with mild diarrhea, as well as in the feces of clinically healthy dogs (Greene 2006). Many CPV-1-infected puppies die after vague symptoms, often being classified as having "fading puppy syndrome" (Greene 2006). The affected puppies usually present with diarrhea, vomiting, dyspnea, and constant crying; others present with respiratory signs with no enteric signs (Greene 2006). Sudden death can also occur in young puppies infected with CPV-1 (Greene 2006).

A diagnosis of CPV-1 should be considered in young puppies (less than 8 weeks old) that have mild diarrhea resembling CPV-2 clinically or histologically but that are serologically negative for CPV-2(Greene 2006). CPV-1 will not cross-react with any of the serologic or fecal detection methods for CPV-2, and electron microscopy can be used to confirm diagnosis (Greene 2006).

Once a puppy has been diagnosed, treatment of CPV-1 is usually unrewarding because of the rapid progression of the disease (Greene 2006). Mortality can be reduced by ensuring that newborn puppies are kept warm and have adequate nutrition and hydration (Greene 2006). There is no vaccine available for CPV-1 at this time, and there is no known public health risk (Greene 2006).

## CANINE CORONAVIRUS

Another enteric virus of concern in puppies is canine coronavirus (CCV). To date, several strains of CCV have been isolated from outbreaks of diarrhea in dogs (Greene 2006). CCV can remain infectious longer at frozen temperatures, but unlike CPV, CCV can be inactivated by most commercial detergents and disinfectants (Greene 2006). The true importance of CCV as an infectious disease of dogs is unknown, although coinfections with both CCV and CPV will increase morbidity for the puppy. The severity of clinical signs is more pronounced in dogs that had both CPV-2 and CCV infections, compared with dogs that have CPV-2 alone (Evermann, Abbott, Han 2005).

Although CCV has been generally regarded as a mild, usually sublethal, highly contagious disease of puppies less than 12 weeks of age, there are recent reports that CCV appears to be more virulent then previously recognized (Evermann, Abbott, Han 2005). A report of two case studies showed CCV-associated puppy mortality without evidence of concurrent CPV infection; these cases emphasize the importance of pursuing a diagnosis of CCV in young puppies when CPV-2 has been ruled out by diagnostic testing (Evermann, Abbott, Han 2005).

CCV has relevance for shelters, as it is highly contagious and spreads rapidly through groups of susceptible dogs, although the clinical significance in all but very young puppies may be minimal with most strains. In one study of shelter dogs, CCV was isolated from 59.3% of nondiarrheic dogs and 73.3% of diarrheic dogs, with no significant association with diarrhea (Sokolow, Rand et al. 2005). Neonatal puppies are more severely affected than weaning age and adult dogs (Greene 2006). Unlike CPV, CCV is shed in the feces of infected dogs for weeks to months after infection, and similar to CPV, fecal contamination of the environment is the primary source for infection (Greene 2006).

The incubation period for CCV is 1 to 3 days (Barr and Bowman 2006). CCV can generally be isolated from the feces of infected dogs between 3 and 14 days postinfection (Greene 2006). Differentiating CCV infection from other causes of canine enteritis can be difficult, but CCV infections are usually less severe than CPV infections (Greene 2006). In adult dogs, most infections are inapparent while puppies may develop severe, even fatal enteritis (Barr and Bowman 2006). Dogs often present with a sudden onset of vomit followed by diarrhea, which may be explosive, yellow-green or orange, loose or liquid, and typically malodorous (Barr and Bowman 2006). The diarrhea may persist for up to 3 weeks and even may recur later. Definitive diagnosis can be confirmed by electron microscopy of fresh feces (Barr and Bowman 2006). Most infected dogs recover without treatment, but hospitaliza-

tion for supportive fluid and electrolyte treatment is indicated in severe cases, especially if there is dehydration in young puppies (Barr and Bowman 2006).

Routine vaccination against CCV in shelters is not recommended because of the low cost:benefit ratio, although it is not contraindicated (Shultz 2006). Both inactivated and MLV CCV vaccines are available, but although these vaccines are relatively safe, they provide incomplete protection against the disease (Greene 2006). Benefit, if any, is more likely to be offered by a modified live vaccine than a killed vaccine due to the possibility of more rapid protection. CCV is not believed to infect people; however, because coronaviruses are not strictly host specific, the possibility of human infection cannot be completely ruled out (Greene 2006). Shelter workers should always practice safe handling and hand-washing techniques when working with sick puppies and handling fecal material from animals with diarrhea.

Overall, CCV is not a pathogen of great concern to shelters; the most significant aspect of CCV disease is when a puppy is concurrently infected with CPV.

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# 14
# Internal Parasites

*Dwight D. Bowman*

## INTRODUCTION

Many of the animals that enter shelters will either have received inadequate veterinary care or have been living on their own for months to years, and are therefore likely to be infected with internal parasites. Some common internal parasites cause significant clinical signs, are easily transmissible, and have public health significance. At the same time, many of the more unusual parasites are unlikely to be transmitted between animals in a shelter environment. Different types of shelters may have different goals and concerns with parasite treatment and prevention programs, and a tailored approach is often necessary. For example, the concerns are very different for shelters (sanctuaries) where animals are held long term and shelters where animals are not expected to become permanent residents. The goal may be to make the animal as parasite free as possible in the short holding time prior to adoption, or it may be to ensure that the animal has no parasites that could be detrimental to the health of the other animals already housed in the facility. It is very difficult to weigh all the different aspects of control and prevention and still provide an all-encompassing program.

There are three major concerns of shelters relative to parasites. The first concern is ensuring that untreated parasites in a dog or cat will not reduce the animal's chance of finding and keeping a new owner because of the unanticipated cost of treatment after adoption. The second concern is protecting the individual animal's health while preventing the introduction of pathogens that will adversely affect the overall health of the shelter population and environment. The third concern is protecting the shelter's staff, visitors, and adopters from potentially zoonotic agents carried by the animals. The goal of this chapter is to provide some guidance to help in alleviating these concerns.

## PARASITES THAT COMMONLY ENTER AND PERPETUATE IN SHELTERS

Internal parasites that can enter with a single animal and be efficiently transmitted between animals are of greatest concern in shelters. Because many parasitized animals show no outward clinical signs of disease, shelters must be diligent in creating protocols that aim to prevent internal parasites from perpetuating themselves in the population. For example, *Filaroides hirthi*, *Filaroides osleri*, and *Ollulanus tricuspis* are three nematodes that are infectious as soon as they leave the host. Other nematodes such as *Toxocara* spp., *Ancyclostoma* spp., *Strongyloides stercoralis*, and *Trichuris vulpis* are perhaps more commonly encountered in shelter animals but require time outside the host to become infectious. Although they are not directly infectious, they can still spread efficiently in several ways: they may have stages that are transmitted to puppies or kittens in utero or in milk or have resistant stages that persist in the environment. Some have stages that can repopulate the intestine and produce eggs detectable in a fecal examination weeks after a previous exam revealed no eggs of the same parasite. Most of these more common nematodes have a very difficult time completing their life cycles in a shelter environment unless there are outdoor areas (grass, soil, or dirt) that are difficult to sanitize. If dogs and cats have access to such outdoor areas, a perpetual cycle of infection may be created.

**Nematodes**

The nematodes that enter and easily perpetuate in shelters are of two types: common forms that are relatively easily transmitted in kennel-like arrangements, and unusual forms that are transmitted by direct (or almost direct) transmission and can flourish under close-quarter confinement. Examples of more unusual forms that can become problems in shelters or similar environs are *Ollulanus tricuspis*, which is transmitted in feline vomitus; *Filaroides hirthi* and *Filaroides osleri*, which are transmitted in saliva or fresh feces; and in dogs, *Strongyloides stercoralis*, which have larvae that develop fairly well to the infective stage under shelter conditions. The common forms that do well in kennel environments are roundworms, hookworms, and whipworms.

***Ollulanus tricuspis***

*Ollulanus tricuspis* is a parasite of the stomach of cats; it is also found in the stomach of other carnivores and the pig. The females are 1 mm long, and males are even smaller (Blanchard, Hargis, Prieur 1985). The worm is difficult to detect, but it has been reported in cats in Europe, the Americas, Egypt, and Australia (Hargis, Prieur et al. 1981; Hasslinger 1984; Hasslinger, Omar, Selim 1988; Kennedy, Kralka, Schoonderwoerd 1984; Pomroy 1999; Tiberio, Greiner, Humphrey et al. 1983).

This worm seems to be more common in catteries than in the general cat population (Bell 1984; Caldwell 1984). One German study of 155 stray cats reported a prevalence of 12% (Schuster, Kaufmann, Hering 1997). It does not infect people; thus there are no implications for adoptions or special instructions for adopters.

*Ollulanus tricuspis* appears to be transmitted directly through consumption of cat vomitus, which is where the infective larvae are found. It is ovoviviparous, and the female gives birth to infective third-stage larvae. The larvae mature within the lumen and superficially within the mucosa of the stomach; the adults live in the stomach lumen. Indirect transmission among singly housed cats via fomites is unlikely, but worms have been shown to survive in vomitus for up to 12 days (Wittmann 1982). The prepatent period is not known.

Most infected cats do not have clinical signs. Because infections with *O. tricuspis* are usually inapparent, they are usually recognized only at necropsy (Dennis et al. 2006; Hargis, Prieur et al. 1982; Reindel, Trapp et al. 1987; Wilson and Presnel 1990). The worms cause inflammation along with increased mucus secretion, hemorrhagic gastritis, and hyperplasia of the stomach epithelium. When clinical signs are present, infected cats may present with a history of chronic vomiting that may or may not be associated with wasting, anorexia, and dehydration (Greve 1981).

Antemortem diagnosis requires the careful examination of vomitus and stomach irrigation fluids. Recently, the diagnosis has been made by gastric biopsy (Cecchi, Wills et al. 2006). Diagnosis at postmortem is much easier and is made by the examination of washings and scrapings of the stomach wall (Hargis, Blanchard, Prieur 1983; Hargis, Haupt, Blanchard 1983). Some cats can have as many as several thousand worms present in their stomachs. Most outbreaks occur in large catteries where animals are housed in groups.

Treatment with tetramisole (a mixture of stereoisomers of which levamisole is the active component) has been efficacious and without side effects. It is unknown whether cats develop any immunity to the infection. If cats are treated, they usually respond very well to therapy. Isolation of known infected animals is recommended to prevent transmission between animals; however, this is unlikely to be practical in most shelter situations, given the difficulty in establishing an antemortem diagnosis. Quarantine of incoming animals to observe for signs of this parasite is also unlikely to be a successful control strategy. There is no vaccine available.

The worms in the vomitus are probably very easy to kill with most routine disinfections or hot soapy water. Free larvae on hard surfaces would not survive for more than a few hours and will die rapidly if dehydrated. As noted above, they can, however, survive in vomitus for several days as long as it does not dry out.

***Filaroides hirthi***

*Filaroides hirthi* is a parasite of the lung parenchyma of dogs and other canids (Georgi and Anderson 1975) that shows up periodically in research animal facilities (Bahnemann and Bauer 1994; Crippa 1995; Vajner, Vortel, Brejcha et al. 2000; Waner, Pirak, Nyska et al. 1991); thus, there is every reason to believe that this pathogen should be of concern in a shelter facility.

This worm is difficult to diagnose because the diagnostic stage is the larva that is found in saliva and feces. Thus, cases occur sporadically without any realistic estimate as to what the actual prevalence is in the canine population. This worm does not infect people and there are no implications for adoptions or special instructions for adopters.

*Filaroides hirthi* is transmitted by the ingestion of larvae found in saliva or in fresh feces (Georgi 1976; Georgi, Fahnestock et al. 1979; Georgi, Georgi et al. 1979). The larvae migrate to the lungs within 6 hours via the hepatic

portal circulation or mesenteric lymphatics. The prepatent period is 5 weeks (Georgi, Georgi et al. 1977).

Most dogs probably do not show clinical signs of the infection; however, infections can cause dyspnea, nonproductive coughing, exercise intolerance, and other signs of respiratory distress (Caro-Vadillo, Martinez et al. 2005; Pinckney, Studer, Genta 1988; Rubash 1986; Spencer, Rushton, Munro 1985; Torgerson, McCarthy, Donnelly et al. 1997), and may lead to radiographic changes (Rendano, Georgi et al. 1979). There have been fatal cases described in severely stressed and immunodeficient animals (August, Powers et al. 1980; Carrasco, Hervas et al. 1997; Genta and Schad 1984; Valentine and Georgi 1988).

Diagnosis is best accomplished by finding the larvae in the feces using a zinc sulfate centrifugation method flotation or by examination of tracheal wash material. (The reader is referred to Chapter 15 for a description of the zinc sulfate centrifugation method.) The larvae can be differentiated morphologically from those of *Filaroides osleri* by the morphology of the tip of the tail.

Ivermectin and albendazole are two drugs that are routinely used to treat infections (Bauer and Bahnemann 1996; Erb and Georgi 1982). Treatment of dogs with albendazole (25 mg/kg/day for 5 days, repeated in 4 weeks) reduced the prevalence of infection in two kennels from 65% to 0.2% and 100% to 24%, respectively. It is not known if dogs develop any immunity to infection. Treated dogs seem to recover very well once the worms are cleared.

Because the diagnosis is so difficult to make, quarantine is unlikely to be a workable means to keep the organism from entering a shelter. If an infection is diagnosed, the affected dog should be isolated and all exposed dogs should be treated with ivermectin.

When the worms are found in the saliva and feces, they are probably very easy to kill with most routine disinfections or hot soapy water. If the worms are found on a clean surface, they will probably only survive a very few hours or until dry; even in moist soil, they will probably survive only hours to days.

### *Filaroides osleri*

*Filaroides osleri* is found in dogs and other canids throughout the world (Barr, Lavelle et al. 1986; Kotani, Horie et al. 1995; Randolph and Rendano 1984). Infections with this worm appear sporadically. It is likely that infection is often subclinical and thus underdiagnosed. It does not infect people. There are no implications for adoptions or special instructions for adopters.

Transmission is by the ingestion of larvae in saliva or feces (Lappin and Prestwood 1988). This infection is probably not readily transmitted by fomites, but it could be a possibility if the conditions were appropriate (e.g., large amounts of saliva, high humidity, short span between hosts, etc.). The prepatent period is 6 to 7 months.

Most dogs probably do not show clinical signs of the infection. When seen, disease is represented by a spasmodic dry cough brought on by exercise. Young dogs tend to be more severely affected and can develop respiratory distress, anorexia, and become emaciated.

Lung nodules that can be observed by bronchoscope are pathognomonic for infection by this worm. It is also possible to find the larvae in fecal flotations using zinc sulfate centrifugation.

Anthelmintics used to treat *Filaroides osleri* infections include doramectin, ivermectin, albendazole, thiabendazole, and others (Levitan, Matz et al. 1996; Outerbridge and Taylor 1998). Some recommend endoscope-guided debridement of the lesions to the extent possible to improve the success of treatment. It is not known if dogs develop any immunity to infection. Treated dogs seem to recover very well once the worms are cleared.

Because the diagnosis is so difficult to make, quarantine is unlikely to be a workable means to keep the organism from entering a shelter. In the case where an infection is diagnosed, isolation of the infected dog during treatment would be advisable. There is no vaccine available.

When the worms are found in the saliva and feces, they are probably very easy to kill with most routine disinfectants or hot soapy water. If the worms are found on a clean surface, they will probably only survive a very few hours or until dry; in soil, they would probably survive only hours to days if kept moist.

### *Strongyloides stercoralis*

*Strongyloides stercoralis* is a parasite of people, dogs, and probably other canids (Koutz and Groves 1953). The very tiny threadlike parasitic forms of this genus of worms live entwined within the mucosa of the small intestine. Cats are host to two species of *Strongyloides*: *Strongyloides tumefaciens* and *Strongyloides felis*. *Strongyloides tumefaciens* lives in the mucosa of the large intestine and is probably a wildlife species that infects cats of the southeastern United States (Malone, Butterfield et al. 1977). Cats in Asia and Australia can become infected with *Strongyloides felis*, which is very similar to *Strongyloides stercoralis*, but it does not seem to infect dogs (Speare and Tinsley 1986).

*Strongyloides stercoralis* develops equally well in both dogs and people. A caretaker in an animal facility acquired the infection from dogs under his care (Georgi and Sprinkle

1974). Dogs that are known to be infected should not be allowed to enter new homes until they are treated and examined on several occasions a couple of weeks after treatment to make certain they are no longer shedding larvae; thus there are no special instructions for adopters other than routine follow-up surveillance for parasites.

The infection is difficult to diagnose because the stage in the feces is a larva (Ferreira, Goncalves Pires et al. 2006; Jaskoski 1971). For this reason, individual cases are identified sporadically and unexpectedly. Prior to the use of ivermectin, these worms commonly became prevalent throughout breeding kennels. Now, outbreaks may occasionally appear in a breeding kennel, but ivermectin will quickly clear the infection from the affected dogs.

Transmission to animals and humans occurs by penetration of the skin by infective larvae; these larvae develop in dirt and debris around pens to the infective stage from the first-stage larvae passed in the feces of an infected dog (Schad, Aikens, Smith et al. 1989). After skin penetration, the larvae then migrate to the lungs, are coughed up, swallowed, and reside in the small intestine. The eggs produced by the parthenogenetic female that lives embedded in the intestinal mucosa hatch within the mucosa, so first-stage larvae are found in the feces. It is possible for infections to become chronic and persistent without causing severe disease (Mansfield, Niamatali et al. 1996). Skin-penetrating larvae will be passed to puppies when they are nursing if the mother acquires an acute infection during lactation (Mansfield and Schad 1995; Shoop, Michael et al. 2002). The prepatent period is about 2 weeks.

Many dogs are likely to be infected and act as carriers without showing clinical signs. Based on World War II veteran soldiers, both American and Japanese, it appears that humans can remain infected for 40 or more years after they have acquired their infections, so it is likely that dogs can remain infected for life without treatment. Although most infections occur without clinical signs, in heavy infections there will be diarrhea associated with mucosal damage and damage to the lungs and other tissues by migrating larvae (Grove, Heenan, Northern 1983; Grove, Warton et al. 1987; Schad, Hellman, Muncey 1984). Puppies with heavy infections can have mucoid diarrhea.

The first-stage larvae can be found in feces of infected animals using the Baermann funnel technique (preferred) or zinc sulfate flotation.

Ivermectin (200 µg/kg repeated in 1 week) can be used to treat dogs (Aikens and Schad 1990; Mansfield and Schad 1992). In a shelter situation, all dogs sharing the same areas should be treated at the same time. Dogs probably do not become immune to reinfection, and they are unlikely to clear an infection spontaneously. Dogs do respond very well to therapy.

Quarantine is unlikely to be an effective means of preventing the infection because it is so difficult to diagnose. If animals are infected, they should be isolated during treatment and for 1 or 2 weeks thereafter. There is no vaccine available.

When worms are found in the saliva and feces, they are probably very easy to kill with most routine disinfectants or hot soapy water. These worms thrive in swampy conditions, so areas of damp soil or damp, heavily soiled cage areas are highly conducive to harboring larvae.

### *Roundworms: Toxascaris leonina, Toxocara canis, Toxocara cati, and Baylisascaris procyonis*

The adults of *Toxascaris leonina* are found in the intestines of dogs, cats, and various other canids and felids. *Toxocara canis* adults are found in the intestines of dogs and other canids. *Toxocara cati* adults are found in the small intestines of cats and other felids. *Baylisascaris procyonis* is a parasite that is found as an adult in the small intestines of raccoons but can on occasion be found in the small intestines of dogs (Kazacos 2006).

All these roundworms can cause zoonotic disease. The most serious is *Baylisascaris procyonis*. The larvae of this parasite cause severe disease associated with visceral larva migrans and have killed more than 120 different species of host, including humans (Gavin, Kazacos, Shulman 2005). *Toxocara canis* is considered one of the most common infections of people around the world and is the cause of most cases of visceral and ocular larva migrans. *Toxocara cati* is known to be capable of causing visceral larva migrans, but until recently it was not considered as important as *Toxocara canis*. *Toxascaris leonina* is capable of causing infections in primates, but no cases of visceral larva migrans in humans have been described as attributable to this parasite.

The prevalence of *Toxocara canis* in shelter dogs was reported on a national level to be 14.5%, and the prevalence of *Toxascaris leonina* was reported to be 0.7% (Blagburn, Lindsay et al. 1996). When the data were examined by age, *Toxocara canis* was found in 30% of the samples from dogs less than 6 months of age, and *Toxascaris leonina* was found in 0.5% of the dogs sampled from this age group. A survey of 450 cats in Connecticut revealed an overall prevalence of *Toxocara cati* of 39.8%, with 67.5% of shelter cats and 30.4% of client-owned cats being infected (Rembiesa and Richardson 2003). A survey of cats less than 1 year of age in central New York State revealed that 33% were infected with *Toxocara cati*, as

were 27% of owned cats, and 37% of sheltered cats (Spain, Scarlett et al. 2001). A number of dogs have been found infected with *Baylisascaris procyonis* and shedding the eggs in their feces. (Kazacos in 2001 reported on 28 such dogs.) This is of considerable concern because of the indiscriminate defecation habits of dogs compared to raccoons, and the fact that some skill is required to distinguish the eggs of this parasite from those of *Toxocara canis* in dog feces.

In most cases, dogs and cats become infected in the shelter environment through the ingestion of eggs containing infective larvae. All these ascarids can use paratenic hosts (rodents, birds, etc.), but this mode of transmission would be unlikely in most shelters. Puppies can be infected in utero with *Toxocara canis*. Kittens can be infected with *Toxocara cati* larvae via nursing from an infected queen (Coati, Schnieder, Epe 2004). The secret to the successful transmission of these parasites in shelters is the hardiness of the eggs. In addition, *Toxascaris leonina* does well in zoos and cool climates because the eggs embryonate very rapidly compared to those of *Toxocara canis* and *Toxocara cati* (Okoshi and Usui 1968).

The prepatent period of *Toxascaris leonina* is about 10 weeks. The prepatent period of *Toxocara canis* following egg ingestion is about 5 weeks, but puppies infected in utero can shed eggs within about 3 weeks after birth. The prepatent period of *Toxocara cati* is 6 to 8 weeks following the ingestion of eggs, and from about 6 weeks following lactogenic transmission (Coati, Schnieder, Epe 2004). The prepatent period of *Baylisascaris procyonis* in dogs is approximately 8 weeks (Bowman, Ulrich et al. 2005).

Most dogs have no clinical signs of their roundworm infections. Thus the majority of infected dogs will be asymptomatic carriers. In addition, some dogs will harbor worms that remain as larvae for extended periods; some of these worms will, at some undefined interval (months to years) and for unknown reasons, develop to the adult stage. Thus, untreated dogs that have had negative fecal examinations for extended periods can develop patent infections even though they have been removed from a source of incoming infective eggs or larvae.

*Toxascaris leonina* and *Baylisascaris procyonis* infected dogs typically have no clinical signs. In the case of *Toxocara canis*, puppies infected prenatally can have clinical signs that include coughing and nasal discharge. Heavy infections in puppies can cause vomiting, anorexia, abdominal distension, mucoid diarrhea, debilitation, reduced growth rate, allergic pruritus, a characteristic foul oral odor, and possibly epileptiform seizures and death due to bile duct blockage or intestinal perforation. Cats and kittens infected with *Toxocara cati* typically have no clinical signs, although kittens can sometimes develop thickened bowel walls.

Diagnosis can best be made by finding the characteristic eggs in a zinc sulfate centrifugation fecal examination. However, negative fecal flotation results do not rule out infection.

Many products can be used to treat ascarid infections in dogs and cats, including pyrantel pamoate, fenbendazole, and milbemycin oxime. Intrauterine infection of puppies with *Toxocara canis* can be minimized by administering ivermectin (1 mg/kg) or doramectin (1 mg/kg) to the pregnant bitch 40 to 50 days after conception (Epe, Pankow et al. 1995). However, neither treatment prevented all puppies from developing patent infections in either group although there was a very marked decrease in environmental contamination. The Centers for Disease Control and Prevention (CDC) suggests that puppies be dewormed with a product that covers hookworms and roundworms every other week from week 2 of life, and kittens beginning at 3 weeks of life until they are 12 weeks old. Pregnant and nursing animals should also be treated (http://www.cdc.gov/ncidod/dpd/parasites/ascaris/prevention.htm.). The Companion Animal Parasite Council also has guidelines regarding parasite control that can be found at www.capcvet.org. Dogs and cats seem to become refractory to infection with adult worms as they become older. However, it is still possible for adult dogs and cats to be infected with these worms; in shelter dogs, 6% of dogs over 7 years of age were infected with *Toxocara canis*, and 0.5% of these dogs had *Toxascaris leonina* (Blagburn, Lindsay et al. 1996).

There is no need to quarantine or isolate infected animals. There is no vaccine available. While the eggs are difficult to kill, they can be killed with heat and disinfectants such as ammonia or chlorine bleach when located on hard surfaces. Aqueous iodine also works well to kill the eggs. Once eggs enter the soil, it becomes very difficult to impossible to inactivate fully and kill them.

It should be expected that most of the dogs and cats that enter a shelter have the larvae of ascarids in their tissues. There is insufficient data about the migration of these larvae back to the intestine to make any firm claims that they do or do not spontaneously begin shedding eggs again; however, this author has observed small developing forms and large adults in dogs that were held for months in raised pens. These worms may be stunted in their development, but the author believes it is much more likely that worms periodically migrate back to the lumen and begin development. Thus, a dog that has tested negative could

spontaneously become positive without ever ingesting another ascarid egg.

These are some of the most common parasites of people in the world. New owners should be reminded that regular veterinary visits and good parasite surveillance and control are very important parts of responsible animal ownership for maintaining both human and animal health.

### *Hookworms: Ancyclostoma caninum, Ancyclostoma braziliense, Ancyclostoma tubaeforme, and Uncinaria stenocephala*

The adults of *Ancyclostoma caninum* are found in the intestines of dogs and various other canids. *Ancyclostoma tubaeforme* adults are found in the intestines of cats and other felids. The adults of *Ancyclostoma braziliense* are found in the intestines of dogs, other canids, cats, and other felids in the coastal areas of the southeastern U.S. and along the Caribbean. The adults of *Uncinaria stenocephala* are found in the small intestines of dogs, foxes, other canids, and occasionally cats; in Europe, *Uncinaria stenocephala* appears to be more common in cats than in the U.S., where feline infections are rare.

The species within the genus of *Ancyclostoma* most typically associated with zoonotic disease is *Ancyclostoma braziliense*, the worm that causes the majority of cutaneous larva migrans in the U.S. The larvae of the other species are capable of causing cutaneous larva migrans, but typically these worms do not cause the same type of serpiginous tracks on the skin that are found in the other species. This is because they apparently spend considerably less time in the dermis before seeking deeper muscle tissues in which they will ultimately persist as larvae. Therefore, although cases of cutaneous larva migrans can be caused by other hookworm species, they are typically not seen commonly outside of the range of *Ancyclostoma braziliense* (Diba, Whitty, Green 2004).

The prevalence of *Ancyclostoma caninum* in shelter dogs was reported on a national level to be 19.2%; the prevalence of *Uncinaria stenocephala* was reported to be 1% (Blagburn, Lindsay et al. 1996). When the data were examined by age, *Ancyclostoma caninum* was found in 15% to 20% of dogs from all age groups from less than 6 months to more than 7 years of age. For cats, a survey of 450 cats in Connecticut revealed an overall prevalence of hookworm eggs in the feces of 0.4%; the authors cite previous surveys with ranges varying from 0.9% to 84.6% (Rembiesa and Richardson 2003). The differentiation of *Ancyclostoma braziliense* infections from the other *Ancyclostoma* species found in dogs and cats typically requires the identification of worms at necropsy. In a survey in Rio de Janeiro, Brazil, it was found that of the 135 cats over 1 year of age that were examined, 66% were infected with *Ancyclostoma braziliense*, and 9% were infected with *Ancyclostoma tubaeforme* (Labarthe, Serrão et al. 2004).

Infections of dogs and cats with hookworms most likely occur through either skin penetration by infective-stage larvae or by the ingestion of the larvae that developed in the soil. These larvae are also capable of persisting in the tissues of various paratenic hosts where they can survive for extended periods; thus, the ingestion of rodents or other infected animals is another source of infection. Finally, dogs are capable of becoming infected by the larvae of *Ancyclostoma caninum* found in the milk of the bitch; this does not appear to occur with the other species that are found in the dog, nor with the species that occur in cats.

The prepatent period for hookworms is basically 2 weeks; puppies acquiring infections via their mother's milk can begin to shed eggs within 2 weeks of delivery.

Most dogs and cats show no clinical signs from their hookworm infections; therefore, the majority of infected animals should be considered carriers. It is well known that dogs will become recurrent hookworm egg shedders with the constant migration of larvae from either the intestinal wall or deeper tissues; these larvae develop into adult worms within 2 weeks after their arrival in the intestinal lumen. This phenomenon of "larval leak" of hookworms back to the intestine has not been as carefully examined in the cat as it has been in the dog.

Anemia is the major clinical sign associated with a hookworm infection. In puppies with *Ancyclostoma caninum* infections, including the very young animals infected by transmammary transmission, signs may include mucosal pallor, diarrhea, weakness, progressive emaciation, cardiac failure, and death. Mature, well-nourished animals often have no signs of infection other than mild hypochromic anemia. Less frequent signs include dermatitis and pruritus due to larval skin penetration in older, sensitized dogs, and coughing and dyspnea due to larval migration in younger dogs. In the case of cats with *Ancyclostoma tubaeforme*, infections lead to weight loss and regenerative anemia, while heavy infections may cause death. Infections with *Ancyclostoma braziliense* cause less relative blood loss than the other two *Ancyclostoma* species of the dog and cat found in the U.S. *Uncinaria stenocephala* infections are unlikely to cause clinical disease.

The diagnosis is best made by finding the characteristic eggs in a zinc sulfate centrifugation fecal examination. As

with roundworms and many other internal parasites, a negative exam does not rule out infection.

Many products can be used to treat hookworm infections in dogs and cats, including pyrantel pamoate, fenbendazole, moxidectin, and milbemycin oxime. The CDC suggests that all puppies be dewormed with a product that covers hookworms and roundworms, every other week from week 2 of life and kittens beginning at 3 weeks of life until they are 12 weeks old and then monthly until 6 months of age. Pregnant and nursing animals should also be treated (http://www.cdc.gov/ncidod/dpd/parasites/ascaris/prevention.htm). There does not appear to be a great deal of immunity to infection, and dogs and cats are almost as likely to be infected when they are older as when they are immature (Blagburn, Lindsay et al. 1996). There is no need to quarantine or isolate infected animals. There is no vaccine available.

The eggs are not as hardy as ascarids and are probably destroyed fairly rapidly with dehydration if located on dry surfaces. The eggs start to develop rapidly after deposition onto the ground, and larvae can hatch 1 to 2 days after deposition. The worms then molt and grow in the soil and infective-stage larvae can become common a week later. Some people like to treat soil with varying concentrations of chlorine bleach, which might have some effect on the ensheathed larvae. Since infections are easier to control by not allowing them to become established, prophylactic treatment of all animals on intake and repeat treatment of puppies is advised.

It should be expected that many of the dogs and cats that enter a shelter harbor the larvae of hookworms in their tissues. With hookworms, it is suspected that dogs that are negative at the time of adoption may begin to shed eggs again later. Thus, it is important that clients be made aware that their new pets should visit a veterinarian promptly after adoption, be placed on a monthly broad-spectrum heartworm preventative with efficacy against hookworms and have their feces disposed of properly in garbage that will be landfilled or incinerated to protect the environment. Clients also need to be reminded that regular veterinary visits and good parasite surveillance and control are very important parts of responsible animal ownership for maintaining both human and animal health.

### *Whipworms: Trichuris vulpis*

The adults of *Trichuris vulpis* are found in the cecum and colon of dogs and other canids. When animals have only a few whipworms, they are isolated within the cecum; when animals have heavier infections with larger numbers of whipworms, the worms are also found threaded through the colonic mucosa.

The zoonotic potential for canine whipworms is low. Human whipworm infections are not uncommon, but the human whipworm is a separate species from the canine whipworm. There have been very rare reports of finding *Trichuris vulpis* eggs in the stools of humans (Dunn et al. 2002), but it is thought that eggs of the human whipworm *Trichuris trichiura* can appear similar to those of the canine whipworm and thus confuse the diagnosis (Yoshikawa, Yamada et al. 1989).

The prevalence of *Trichuris vulpis* in shelter dogs in the U.S. was reported in 1996 as 14.3% (Blagburn, Lindsay et al. 1996). When the data were evaluated for age, *Trichuris vulpis* was more common in dogs over 6 months of age and was found in anywhere from 10% to more than 15% of the animals.

The life cycle of the whipworm is direct. Dogs are infected by ingesting the egg(s), often found in contaminated soil. The eggs can take days to months to reach the infective stage, and they are hardy and resistant to many environmental extremes.

The prepatent period for whipworms is approximately 3 months. Most dogs have no clinical signs associated with a whipworm infection unless they have very large numbers of worms. Due to the low number of worms, the lack of clinical signs, and the long prepatent period, dogs often serve as carriers of the infection and contaminate the surrounding environment.

When clinical signs are observed in heavily infected dogs, they include weight loss, abdominal pain, and mild to severe diarrhea that sometimes contains blood. The worms live with their anterior ends threaded through the intestinal mucosa, so there must be some lesions associated with the worms living in the intestinal tissue. The diagnosis is best made by finding the characteristic barrel-shaped egg in a fecal centrifugation sample.

Many products can be used to treat whipworm infections, including fenbendazole and milbemycin oxime. There does not appear to be a great deal of immunity to infection, and dogs are as likely to be infected when they are older as when they are puppies (Blagburn, Lindsay et al. 1996).

There is no need either to quarantine animals or to isolate infected ones. There is no vaccine available. The eggs are probably hardier than ascarid eggs. Although no studies have been performed on the topic, the polar plugs may make these eggs somewhat more susceptible to chlorine bleach than ascarid eggs. The problem is that once these eggs

contaminate the soil of runs or outdoor kennels, they are almost impossible to eliminate.

It should be expected that many dogs entering shelters will have whipworm infections, and the infections may not be patent at the time of arrival due to the 3-month-long prepatent period. Thus, new owners should plan to visit a veterinarian who will perform a fecal examination on the new pet so any treatments administered at the shelter can be followed up before the dog contaminates its new environment. Furthermore, new owners should be advised to seek regular veterinary care that will include fecal examinations and the possible use of monthly heartworm products that also routinely treat any existing whipworm infections.

### Tapeworms: cestodes

Three tapeworms with life cycles that could allow their perpetuation in shelters under certain circumstances are *Dipylidium caninum*, *Taenia taeniaeformis*, and *Echinococcus multilocularis*. These are the parasites that utilize fleas or rodents as their only intermediate hosts. Thus, *Dipylidium caninum*, which has fleas as the intermediate host, could be perpetuated in a shelter if there are fleas developing from eggs through to the adult stage on the premises (fleas become infected by larvae in carpet, floors, or soil). *Taenia taeniaeformis*, which has a rodent intermediate host, could be perpetuated through a cat–rodent–cat cycle if there was a sufficient rodent population in a shelter where cats were housed for extended periods. *Echinococcus multilocularis* could also be perpetuated in a dog/cat–rodent–dog/cat cycle in shelters if there was a significant rodent problem.

*Dipylidium caninum* is found wherever dogs or cats and fleas coexist. *Taenia taeniaeformis* exists wherever cats and rodents share the same space. *Echinococcus multilocularis* is typically a parasite of foxes and rodents; however, the parasite can make its way into domestic situations through the infection of dogs or cats that enter the fox/rodent ecosystem. *Echinococcus granulosus* (with its canid–ruminant–canid cycle) does not develop well in cats, but *Echinococcus multilocularis* can develop to some extent in cats. Both species of tapeworms flourish in the domestic dog and other canids. It is believed that the cat is only of minimal importance as a host of *Echinococcus multilocularis* in domestic (dog–rodent) cycles (Thompson, Kapel et al. 2006). Adult *Echinococcus* tapeworms are exceedingly small, so eggs will appear in the feces, but segments will not be grossly observed. In foxes, *Echinococcus multilocularis* has been found in the continental U.S. and has a distribution that extends down from Canada with a southernmost front along the southern border of Wyoming, eastward through central Nebraska and central Illinois into Indiana and Ohio. Thus, in these parts of the U.S. it is possible that dogs, especially stray dogs or retired sled dogs, could be infected with this parasite.

The most reliable drug for treatment of tapeworms is praziquantel. If this is cost-prohibitive, the other choice is fenbendazole, but this will not treat *Dipylidium caninum*. Flea control should also be undertaken.

Zoonotic disease is possible from two of these tapeworms: *Dipylidium caninum* and *Echinococcus multilocularis*. *Dipylidium caninum* has upon occasion developed to the adult stage in children who have ingested a flea, and the effects of an infection are the same in people as they are in dogs and cats, i.e., minimal or no clinical signs. This is of marginal concern to shelters. Zoonotic hydatid disease due to the larvae of *Echinococcus multilocularis* (the alveolar hydatid) is of significant concern. The larva of this parasite grows typically in the hepatic tissue of the human host much like a cancer and the infection is 100% fatal without treatment (Wilson, Rausch, Wilson 1995). The ingestion of one egg can be lethal. The parasite grows slowly and insidiously, so there may be a lag time of months to years from the time of infection until the development of first signs. Thus it is important to make staff in endemic areas aware of the potential risk of exposure to eggs in canine feces. Staff at shelters in Alaska and Canada need to be especially wary.

## PARASITES THAT MAY ENTER SHELTERS BUT ARE UNLIKELY TO BE PERPETUATED

Animals may bring many other parasites into shelters that are less likely to be perpetuated within the shelter environment. Many of these parasites can be easily eradicated by treatment after the animals are appropriately diagnosed.

### Nematodes

There are a number of nematode parasites that will enter shelters with dogs but will have no chance of being perpetuated. These parasites include those that require intermediate hosts as part of their life cycles. The nematodes that will not be transmitted except under the rarest of circumstances within shelters include the metastrongyloid lungworms (*Crenosoma vulpis* and *Angiostrongylus vasorum* of the dog, and *Aelurostrongylus abstrusus* of the cat), the spirurid nematodes (*Dracunculus insignis*, *Gnathostoma spinigerum*, *Physaloptera* spp., and *Spirocerca lupi*), and the capillarid nematodes that go through intermediate hosts (*Aonchotheca putorii*, *Eucoleus aeroph-*

*ilus*, *Eucoleus boehmi*, and *Pearsonema plica*). The lungworms require snails as an intermediate host; *Dracunculus* and *Gnathostoma* species require water with copepods as a first host and then a second host; *Physaloptera* spp. and *Spirocerca lupi* require insect intermediate hosts (beetles, cockroaches, crickets, etc.); and most of the capillarids require earthworms as intermediate hosts. If a shelter has outdoor runs that are not screened to keep out insects, and if snails or earthworms are present, these parasites would be potentially transmissible within the facility. The zoonotic risk to any shelter staff is minimal even if the animals arrive infected because all these nematodes require intermediate hosts, and the staff would only become infected by eating these hosts.

**Trematodes**

Trematodes are acquired by animals either through the ingestion of an intermediate host or through skin penetration by cercariae (a special case of the *Schistosomatidae*, e.g., *Heterobilharzia americana* in the southeastern U.S.). There is a chance that free-roaming animals will have acquired the infection by eating a fish, amphibian, lizard, or crayfish. However, within the shelter, there will be neither the proper snail first intermediate host nor the invertebrate or vertebrate second intermediate host to perpetuate the cycle. Thus, for the parasite, these are dead ends in every single scenario. Trematodes do not do well outside of the wild. These parasites pose no threat to shelter staff as zoonotic agents.

**Cestodes**

Cestodes of dogs and cats, like trematodes, will develop into adult tapeworms in dogs and cats only if there is the ingestion of an intermediate host. Some cestodes, because their life cycles require wildlife intermediate hosts, are very unlikely to be perpetuated in shelter situations. These tapeworms include *Diphyllobothrium latum*, *Spirometra mansonoides*, *Mesocestoides lineatus*, *Taenia pisiformis*, *Taenia serialis*, and *Echinococcus granulosus*. Of those unlikely to be in shelters, the intermediate hosts (with the associated tapeworm in parentheses) that would be ingested by dogs or cats to initiate an infection are fish (*Diphyllobothrium latum*), vertebrates (*Spirometra mansonoides* and *Mesocestoides lineatus*), rabbits (*Taenia pisiformis* and *Taenia serialis*), and ruminants (*Echinococcus granulosus*). *Diphyllobothrium* and *Spirometra* have to go through copepods to infect the host that is then ingested by the dog or cat, and *Mesocestoides* spp. go through some unknown host before they make their way into the host that can infect the dog or cat via ingestion. It is highly unlikely that dogs in shelters would have access to eating rabbits or ruminants to an extent that would allow the cycle to be perpetuated within a shelter environment.

Of these tapeworms, there are only two that could pose a threat of zoonotic disease to shelter staff when dogs first enter the shelter; they are *Taenia serialis* and *Echinococcus granulosus.* People have become infected with the larval stage (the coenurus) of *Taenia serialis* on very rare occasions (there have been only six cases reported in North America). The eggs are infectious when passed in the feces of dogs and might infect people if they are ingested. The larval cysticercus of the other taeniid tapeworm of dogs in North America, *Taenia pisiformis*, has not been reported as a larval stage in people (Ing, Schantz, Turner 1998).

Zoonotic hydatid disease due to the larvae of *E. granulosus* (the unilocular hydatid) is of much greater concern. Adults of this tapeworm are tiny and live in the intestinal tract of dogs; the eggs are passed in the feces, and they are infectious at the time of defecation. This is a case where geographic distribution is important in determining risk. This parasite exists in a few small foci in the mountains of the western U.S., in coyotes in the central valley of California, in dogs (with associated hydatidosis in people) in central Utah, and on Native American land in Arizona and New Mexico (Anderson 1997). *Echinococcus granulosus* also occurs commonly in wolves and their cervid prey in the circumpolar tundra and taiga in the Arctic and sub-Arctic (Rausch 2003). Dogs can replace wolves in the cycle, and thus, when dogs scavenge or are fed offal in these areas, they can become infected with these parasites. Therefore, dogs from these areas of the world should be considered by shelter staff as potentially infected with this tapeworm, and if infections have ever been diagnosed in an area, it would be prudent to treat all dogs prophylactically when they enter the facility. Care must be taken to dispose of all the feces from possibly infected dogs with the utmost caution, as the eggs are infectious when passed. Individuals would become infected through the accidental ingestion of the eggs passed in canine feces. Potential sources of infection would include ingestion of contaminated food or sprays contaminated with fecal matter while washing cages, fomites, etc.

**Acanthocephala**

All acanthocephala require an arthropod intermediate host for transmission to occur. To date, there have been no reports of acanthocephalan infections in cats in the U.S. There is only one acanthocephalan that occurs with any regularity in dogs in the U.S., *Macracanthorhynchus ingens*. This is a parasite of raccoons that requires the

ingestion of a millipede intermediate host and that sometimes appears in dogs with unusual gustatory habits. As with some of the nematodes, this parasite could perhaps be transmitted between dogs in outdoor pens if millipedes are capable of surviving in the same space. The risk of zoonotic infection of shelter staff is minimal to nil, and would require the ingestion of the millipede host.

## TREATMENT OF THE ANIMAL AT THE TIME OF ARRIVAL IN THE SHELTER

There are three concurrent goals related to the initial diagnosis and treatment of internal parasitic infections and infestations of shelter animals when they arrive at a facility: preparing the individual animals for adoption, limiting zoonoses, and protecting the other animals within the facility from incoming infections, which includes preventing environmental contamination. The problem is that there is no single inexpensive means of easily managing the large and diverse group of parasites potentially coming into a facility. Thus, shelters are left with the conundrums of how much of a diagnostic work-up is sufficient, how much treatment can be afforded, and how much treatment is necessary. There are, unfortunately, no simple or straightforward answers to these questions. One has to develop a general scheme of operation with a goal of optimizing prevention and conserving resources for diagnosis and treatment.

If eliminating parasites were the only goal of a shelter and expense was no object, every animal entering the facility would be held in quarantine, treated with products that would remove all ectoparasites, screened for all internal parasites of importance, and treated as necessary. Then the animal could be considered temporarily parasite free and ready for adoption. The trouble is that this expensive and time-consuming approach is impractical and likely even to be detrimental (due to the prolonged holding time and cost entailed) in most, if not all, shelter situations. So, what is to be done?

There are several prophylactic therapies that shelters can consider. By far the most common recommendation and practice for control of internal parasites in shelter animals is the treatment of all incoming animals with pyrantel pamoate, as roundworms and hookworms are nearly ubiquitous and zoonotic, and roundworm eggs are extremely difficult to remove from the environment. This is a cost-effective approach even for very high-volume shelters. Additional treatments for whipworms, tapeworms, etc., can be reserved for adoptable animals and those for whom diagnostics have been performed. Treatment for 3 days with fenbendazole is another option, although it may be prohibitive in large shelters or those where animals are routinely group housed. In these shelters, the time of intake may be the only opportunity to provide treatment to an individual animal, and provision of the second and third days of treatment would be unlikely.

In shelters with additional resources that desire broader spectrum coverage, treatment with Drontal® Plus (pyrantel, febantel, and praziquantel) will provide the broadest coverage against internal parasites. This product will treat and remove most intestinal nematodes, tapeworms, and also the unusual intestinal trematode. A product with an almost equivalent spectrum of activity is Panacur® (fenbendazole), which will provide treatment for everything except for *Dipylidium* and *Echinococcus*; it also will remove a few of the more unusual worms from dogs. For cats, Drontal® is an effective, all-purpose anthelmintic. Although not approved for cats, fenbendazole at the same dose used for dogs is also excellent for general purpose use. It should be noted that Drontal® Plus adds very substantially to the cost of prophylactic treatment, to the point that its cost becomes prohibitive for many shelters.

The presence of tapeworm segments in an animal's stool can be disconcerting to owners, so some shelters elect to treat animals if they are being placed for adoption regardless of confirmation of infection. These parasites are often difficult to diagnose because the segments are only shed by the dogs and cats sporadically. Treatment with the cestocidal dose of praziquantel also removes most intestinal dwelling trematodes from dogs and cats.

For dogs that are known to be heartworm-negative, there are many monthly heartworm preventative products that will treat internal parasites as well as provide protection against heartworms. The author of this chapter is of a very firm conviction that it is inappropriate to use these products in heartworm-positive animals except under extreme conditions (as in the immediate placement of the dogs displaced by the Katrina hurricane into foster homes around the country) for reasons explained in depth elsewhere (Bowman, Torre et al. 2007). These all vary slightly as to their ability to control internal parasites, both in spectra of activity and in ability to kill developing forms of the parasites. Some provide protection against ectoparasites while also providing treatment of intestinal infections. A great deal of the choice of product will be based on availability, price, and the spectrum of activity required as determined by the attending veterinarian in the shelter.

Use of these broader-spectrum approaches may be beyond the means of some shelters or may require an

investment that would detract from the ability to provide other needed services and care. The focus of shelter treatment must remain on the parasites that cause disease in the animal, contaminate the shelter's environment, pose significant risk of zoonosis, or readily spread between animals.

Thus, when designing the ideal shelter parasite control protocol in order to prepare an animal for adoption, the plan should include (1) treatment for external parasites (covered elsewhere in this text), (2) determination of heartworm status, and (3) administration of pyrantel pamoate to treat the majority of common internal parasites. Praziquantel could be included if it was felt that treatment of tapeworm infection warranted its use and cost. For broad-spectrum deworming, the pyrantel and praziquantel combination could be replaced with the liquid large-animal formulation of fenbendazole for 3 days, with the understanding that *Dipylidium caninum* would not be treated. With any of these approaches, adopters can then be informed that the animal has received appropriate initial treatment for common internal parasites. Owners should be advised that the animal may still harbor parasites that need professional diagnostics or additional treatment. They should be encouraged to set up an appointment as soon as possible with a veterinarian to perform a physical examination of the animal and an extensive fecal examination, and to start a preventive medicine program.

## CONCLUSION

In summary, it is probably wisest not to expend a large proportion of the establishment's funds to treat all animals for all possible parasites at the time of animals' admission to the shelter. Animals entering a shelter should receive treatment for the most common internal and external parasites found in that area. Much of what additional therapy long-term shelter residents will receive is going to depend on the ability of the shelter to critically assess the need for diagnostics, treatment, and disease prevention. It should not be expected that shelters can be entirely parasite free, but policies should be implemented to regularly examine animals to make certain that the parasites that may have slipped into a shelter have not been allowed to multiply to such an extent that they pose a serious threat to animal or human health.

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# 15
# Bacterial and Protozoal Gastrointestinal Disease

*Michael R. Lappin and Miranda Spindel*

## INTRODUCTION

One of the greatest challenges for small animal shelter veterinarians is the management of gastrointestinal disease. Determining the cause of vomiting or diarrhea is often complicated, particularly in the shelter environment where stress, dietary change, and immunodeficiency are inherent and may play significant roles. There are a multitude of infectious agents that can be associated with vomiting and diarrhea. Some animals that harbor infectious agents can have severe clinical signs while others show none, yet they can be shedding potentially pathogenic organisms into the shelter environment. The gastrointestinal diseases of highest infectious concern with the poorest prognosis, such as panleukopenia and parvovirus, are frequently the first to be ruled out by shelter veterinarians. Bacterial and protozoal causes of gastrointestinal disease may be overlooked entirely or the diagnostic workup for these agents delayed (see Tables 15.1 and 15.2). However, in the animal shelter environment, these organisms are commonly associated with clinical disease, can be transmitted within the shelter, and, for some agents, have zoonotic potential (Table 15.1). Thus, there are situations where bacterial and protozoal causes of gastrointestinal disease should be considered early in the diagnostic workup.

Prevalence rates for the protozoal and bacterial agents associated with gastrointestinal signs of disease vary amongst regions of the country (Hill, Cheney et al. 2000; Spain, Scarlett et al. 2001; Hackett and Lappin 2003; Nutter, Dubey et al. 2004, Carlin, Bowman et al. 2006). For the most part, prevalence work has been performed with client-owned animals, not shelter animals. Thus, the relative risk for the individual agents is usually unknown in individual shelters, and shelter veterinarians must perform risk assessments based on extrapolated information. While these agents are easy to detect with a variety of tests, each can also be detected in healthy and ill animals, and so positive test results do not always correlate with the presence of illness. In addition, it is simply not realistic to test for every organism in every clinically ill shelter animal because of financial limitations. Out of necessity, shelter veterinarians must often treat animals' gastrointestinal signs with empirical therapies (Table 15.3). While many of the bacterial and protozoal causes of gastrointestinal disease are zoonotic, healthy animals without parasites are not considered to be significant health risks (Brown, Elston et al. 2003; www.cdc.gov) (see Table 15.1). In addition, animals with protozoal or bacterial infections with normal stools are unlikely to be shedding large numbers of organisms, and the fecal matter is easier to control than that from animals with diarrhea, facts that also potentially lessen zoonotic risk. Thus, shelters should strategically deworm and strive to adopt out animals without gastrointestinal signs of disease.

The purpose of this chapter is to provide an overview of some of the common small animal bacterial and protozoal gastrointestinal pathogens and to provide current information concerning diagnostic procedures, primary therapies, zoonotic risks, and means of prevention.

## BACTERIAL AGENTS

There are many bacterial agents in the gastrointestinal tract that have the potential to induce gastrointestinal disease. *Campylobacter* spp., *Clostridium* spp., *Escherichia*

**Table 15.1.** Characteristics of common feline and canine bacterial and protozoal gastrointestinal pathogens.

| Agents | Species Affected[a] | Herd Risk | Zoonotic | Modes of Transmission |
|---|---|---|---|---|
| **Bacterial** | | | | |
| *Brachyspira* spp. | D, C, O | Unknown | Unproven | Fecal–oral, fresh feces |
| *Campylobacter* spp. | D, C, O | Yes | Yes | Fecal–oral |
| *Clostridium* spp. | D, C, O | Yes | Unlikely | Fecal–oral |
| *E. coli* | D, C, O | Yes | Yes | Fecal–oral |
| *Helicobacter* spp. | D, C, O | Unknown | Unlikely | Fecal–oral suspected |
| *Salmonella* spp. | D, C, O | Yes | Yes | Fecal–oral suspected |
| *Yersinia* spp. | D, C, O | Unknown | Yes | Fecal–oral |
| **Protozoal** | | | | |
| **Flagellates** | | | | |
| *Giardia* spp. | D, C, O | Yes | Some species | Fecal–oral |
| *Tritrichomonas foetus* | C, D (rarely) | Yes | No | Fecal–oral |
| **Coccidians** | | | | |
| *Cryptosporidium* spp. | D, C, O | Yes | Some species | Fecal–oral |
| *Cystoisospora* spp.[b] | D, C | Yes | No | Fecal–oral, transport hosts |
| *Toxoplasma gondii*[b] | C, D | No | Yes | Fecal–oral, transport hosts, transplacental, lactational (cats). |

[a] D = dog; C = cat; O = other species.

[b] Requires a sporulation period to be infectious.

**Table 15.2.** Diagnostic assays commonly used to confirm infection by common bacterial and protozoal agents associated with gastrointestinal disease.

| | Assay[a] | | | | | |
|---|---|---|---|---|---|---|
| Agents | Flotation | Wet Mount | Cytology[a] | Culture | Immunologic | PCR assay |
| **Bacterial** | | | | | | |
| *Brachyspira* spp. | NA | NA | Spirochete[b] | Yes | NA | Yes |
| *Campylobacter* spp. | NA | NA | Spirochete[b] | Yes | NA | Yes |
| *Clostridium* spp. | NA | NA | Spores[a] | Yes | ELISA | NA |
| *E. coli* | NA | NA | NA | Yes | NA | Yes |
| *Helicobacter* spp. | NA | NA | Spirochete[b] | NA | NA | Yes |
| *Salmonella* spp. | NA | NA | NA | Yes | NA | Yes |
| *Yersinia* spp. | NA | NA | NA | yes | NA | NA |
| **Protozoal** | | | | | | |
| **Flagellates** | | | | | | |
| *Giardia* spp. | Cyst | Trophozoite[b] | NA | Yes | AG or IFA | Yes |
| *Tritrichomonas foetus* | NA | Trophozoite[b] | NA | Yes | NA | Yes |
| **Coccidians** | | | | | | |
| *Cryptosporidium* spp. | Oocyst | NA | Oocyst | NA | IFA | Yes |
| *Cystoisospora* spp. | Oocyst | NA | NA | NA | NA | NA |
| *Toxoplasma gondii* | Oocyst | NA | NA | NA | NA | Yes |

[a] None of the test results described have 100% positive predictive value because the agents can also be detected in healthy animals. NA = Not applicable for this agent; AG = Antigen test; IFA = Immunofluorescent antibody assay.

[b] Presumptive diagnosis.

**Table 15.3.** Drugs commonly used in the management of bacterial and protozoal agents associated with gastrointestinal disease in dogs and cats.

| Drug Name[a] | Commonly Used Protocols | Primary Disease/Organisms |
|---|---|---|
| Amoxicillin | 22 mg/kg, daily, for 5 days, PO | *Clostridium* spp., bacterial overgrowth |
| Ampicillin | 22 mg/kg, q8 hr, for 3–7 days, IV | *Salmonella* spp., anaerobic sepsis |
| Azithromycin | 10 mg/kg, q24 hr, for 10 days minimum, PO | *Cryptospordium* spp., *T. gondii* |
| Cefoxitin | 22 mg/kg, q8 hr, for 3–7 days, IV | Gram positive, gram negative, and anaerobic sepsis |
| Clindamycin | 12.5 mg/kg, q12 hr, for 28 days PO | *T. gondii* |
| Erythromycin | 15–25 mg/kg, q12 hr, for 7–10 days, PO | *Campylobacter* spp. |
| Febantel/pyrantel praziquantel | Dog – Label dose for 3–5 days, PO | *Giardia* spp. |
| | Cat – Approximately 50 mg/kg based on febantel, for 5 days, PO | *Giardia* spp. |
| Fenbendazole | 50 mg/kg, q24 hr, for 3–5 days, PO | *Giardia* spp. |
| Furazolidone | 4 mg/kg, q12 hr, for 7 days, PO | *Giardia* |
| | 8–20 mg/kg, q24 hr, for 7 days, PO | *Cystoisospora* spp. |
| Metronidazole | 10–25 mg/kg, q12 hr, for 7 days, PO | *Giardia*, bacterial overgrowth |
| Nitazoxanide | 25 mg/kg, q12 hr, for 7 days, PO | *Cryptosporidium* spp., *Giardia* spp. |
| Paromomycin | 150 mg/kg, q12–24 hr, for 5 days, PO | *Cryptosporidium* spp., *Giardia* spp. |
| Ponazuril | 5–20 mg/kg PO once and repeat in 7 days | *Cystoisospora* spp. |
| Ronidazole | 30 mg/kg, q12 hr, for 14 days, PO | *T. foetus*, *Giardia* spp. |
| Sulfadimethoxine | 50–60 mg/kg, daily, for 5–20 days, PO | *Cystoisospora* spp. |
| Trimethoprim-sulfa | 15 mg/kg, q12hr, for 5 days, PO | *Cystoisospora* spp., *T. gondii* |
| Tylosin | 10–15 mg/kg, q12hr, for 7–21 days, PO | *Clostridium* spp., bacterial overgrowth, *Cryptosporidium* spp., *Campylobacter* spp. |

[a] Clinicians are advised to verify drug information before administration.

spp., and *Salmonella* spp. are all commonly associated with gastrointestinal disease. *Brachyspira* spp., *Helicobacter* spp., and *Yersinia* spp. are also potential pathogens that may be associated with disease in some animals. *Campylobacter* spp., *Escherichia* spp., and *Salmonella* spp. may also be of public health concern. The following is a brief description of each organism.

### *Brachyspira* species

#### *Agent and host range*

Previously known as *Serpulina* spp., *Brachyspira* spp. are spirochetes found in the intestinal tract of dogs, pigs, rodents, birds, and primates (Hampson and La 2006). *Brachyspira* spp. have multiple species including *B. aalborgi*, *B. innocens*, and *B. pilosicoli* (Hampson and La 2006). *Brachyspira pilosicoli* has been found in many species. The clinical importance of this organism group is not known, and so prevalence has yet to be established.

#### Transmission

There is very little known about the transmission and pathogenesis of disease associated with this organism group. It is unclear whether a relationship exists between the presence of organisms and disease, as the bacteria has been isolated in similar numbers from both healthy animals and those with diarrhea (Oxberry and Hampson 2003). If transmission occurs between animals, it is thought to be by the fecal–oral route, making fomite transmission likely (Smith 2005). Densely housed, stressed, and immunocompromised animals seem to be at higher risk for shedding large numbers of *Brachyspira* spp. in diarrheic samples.

#### Clinical signs

*Brachspira* spp. are thought to be associated with gastrointestinal disease in dogs as well as in other species such as humans, birds, and pigs (Oxberry and Hampson 2003). The presence of the organisms in stools has usually been associated with clinical signs of large bowel diarrhea, including tenesmus, mucus, hematochezia, and increased frequency. Pathogenesis of disease from *Brachyspira* spp. may relate to the spirochetes attaching to the intestinal epithelium, causing inflammation.

#### Diagnosis

Presumptive diagnosis of *Brachyspira* spp. infection has been made by noting multiple spirochetes (see Figure 15.1) on fecal or rectal cytology of animals with diarrhea

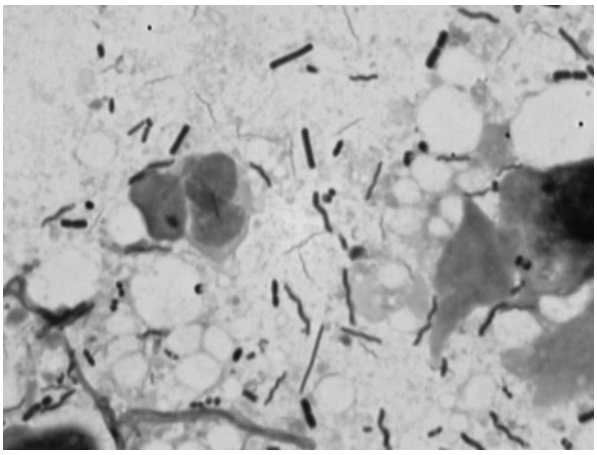

**Figure 15.1.** Rectal cytology stained with Dif Quick stain showing multiple different spirochetes (1,000X).

(see the diagnostic protocols section). Definitive diagnosis is made by bacterial culture, polymerase chain reaction (PCR) assay, or by histopathologic examination of intestinal biopsies.

### Treatment

Optimal treatment protocols have not been established; however, animals with suspected *Brachyspira* spp. infections have had clinical signs of disease resolve after administration of amoxicillin or tylosin (see Table 15.3).

### Prevention

Preventative measures to reduce fecal contamination in the shelter environment include prompt removal and disposal of feces, disinfection with most common disinfectants, stress reduction, and prevention of overcrowding in facilities.

### Zoonotic considerations

Whether *Brachyspira* spp. infections are shared between small animals and people has not been established. The zoonotic potential of this organism probably exists under proper circumstances (Hampson, Oxberry, La 2006).

## *Campylobacter* species

### *Agent and host range*

*Campylobacter* spp. are curved, gram-negative flagellated rods that infect multiple species including dogs, cats, and humans (Hald and Madsen 1997). There are many *Campylobacter* species, with *C. jejuni* reported as the agent responsible for over 2 million cases of human bacterial intestinal illness annually (www.cdc.gov/ncidod/diseases/index.htm). However, *C. coli*, *C. helveticus*, and *C. upsalensis* have also been associated with diseases in both small animals and people (Brown, Elston et al. 2003).

Prevalence studies vary between dogs and cats, source of the animals, and diarrheic and nondiarrheic animals. In two studies of shelter source cats in north central Colorado (Hill, Cheney et al. 2000) and central New York State (Spain, Scarlett et al. 2001), *Campylobacter* spp. were cultured from the stool of 1.8% and 0.0% of the cats, respectively. In a recent study in California, *Campylobacter* spp. were cultured from the feces of 10.5% to 18.7% of the dogs with diarrhea and from 0% to 11.1% of the dogs with normal stools (Marks 2003). In a similar study in cats, *Campylobacter* spp. were cultured from the feces of 11.1% of cats with diarrhea and 19.6% of cats with normal stools (Marks 2003). The rate of shedding and disease association may be greater in individuals stressed by other disease states and animals less than 6 months of age. While colonization is common, since both healthy and diseased animals are culture or PCR assay positive, the prevalence of disease is unknown.

### *Transmission*

Transmission is fecal–oral, generally through contact with animal feces, contaminated food, water, or via fomites that have become contaminated in the environment.

### *Clinical signs*

Most dogs and cats that are culture positive for *Campylobacter* spp. appear clinically normal. When animals are clinically ill, symptoms generally include anorexia, vomiting, and mild to severe large bowel diarrhea.

### *Diagnosis*

Presumptive diagnosis can be made by detecting the characteristic "seagull" bacterial shape motility on a saline mount under phase contrast microscopy or via fecal cytology (see diagnostic protocols section). Definitive diagnosis is made by culture of the organism. Because cytological findings cannot be used to definitively distinguish between *Campylobacter* spp. and nonpathogenic spirochetes, if a definitive diagnosis is needed because of zoonotic considerations, or because large numbers of characteristic organisms are seen on a slide in an animal with diarrhea, culture is indicated. However, the organism

can be fragile and difficult to grow, requiring specialized transport media and culture techniques (see Appendix 15.1). PCR assays can also be used but do not provide antimicrobial susceptibility. Because the organisms are commonly detected in healthy animals and culture- or PCR-assay-positive results do not prove a disease association, some shelter veterinarians may reasonably choose to empirically treat animals when they lack the resources to perform cultures.

#### *Treatment*

Clinical signs of disease associated with *Campylobacter* spp. infections are generally self-limited. However, some animals that exhibit signs of systemic illness, particularly young animals and those with parasites or other underlying disease, generally require supportive therapy and antibiotics to control the clinical signs. Treatment is usually empirical; tylosin or erythromycin is commonly administered for 5 to 7 days (Table 15.3). These protocols may also decrease the shedding of the organism in feces and thus the potential zoonotic risk.

#### *Prevention*

*Campylobacter* spp. are susceptible to heat, dryness, and most routine disinfectants, and survive no longer than a week in the environment. Thus, cleanliness and general biosecurity measures, including proper sanitation and disinfection, isolation of sick animals, posting of cage signs indicating the condition and precautions to be taken regarding animal handling, frequent hand washing, etc., can help reduce spread of the organism within shelters.

#### *Zoonotic considerations*

Humans are usually infected with *Campylobacter* spp. by ingestion of contaminated water or food, but fecal matter is directly infectious when organisms are present. Dogs and cats have been associated with *Campylobacter* spp. infections in people (Holt 1981). Thus, strict personal hygiene should be practiced with all dogs and cats known or suspected to have been infected. Sequential cultures can be used to attempt to establish success of therapy, but animals with normal stools are unlikely to be a human health risk (Brown, Elston et al. 2003). When an animal with a previously proven *Campylobacter* infection is to be adopted, potential risks should be discussed with prospective owners so that a risk/benefit decision can be made by the adopter. Some shelters may choose not to adopt out animals with previously documented infection, especially to families with young children, elderly, or immunocompromised people; however, if the animal has normal stools and is otherwise healthy, the risk of disease transmission is small.

### *Clostridium* species

#### *Agent and host range*

*Clostridium* spp. are commensal, gram-positive, spore-forming obligate anaerobes. *Clostridium perfringens* and *Clostridium difficile* are the two species most commonly associated with gastrointestinal disease in dogs and cats (Lefebvre, Arroyo, Weese 2006; Marks 2003). *Clostridium* spp. colonize many animals (Marks, Kather et al. 2002). However, since both healthy and diseased animals are culture or enterotoxin positive, the prevalence of disease in shelter animals is unknown.

#### *Transmission*

*Clostridium* spp. can exist in normal dogs and cats. Gastrointestinal disease may result from overgrowth of the organisms resulting in production of enterotoxins. The production of enterotoxin is coregulated with production of large numbers of environmentally resistant spores which may be transmitted amongst animals by fecal–oral ingestion.

#### *Clinical signs*

Vomiting, large bowel diarrhea, flatulence, and abdominal pain are possible clinical sequelae associated with *Clostridium* spp. infection. Clinical disease can be recurrent in some animals. Stress and dietary change may play a role in whether individual animals develop clinical disease.

#### *Diagnosis*

Presumptive diagnosis is often made by correlating classical clinical signs, history, and demonstration of the characteristic “safety pin” type spores on fecal or rectal cytology (see Figure 15.2). However, spores can be detected in both healthy and diseased animals (Hackett and Lappin 2003). Similarly, detection of the organisms by culture or detection of specific enterotoxins fails to correlate to the presence of disease (Hackett and Lappin 2003; Marks and Kather 2002). Thus, clinical response to treatment is used as an indirect means of confirming a diagnostic suspicion.

#### *Treatment*

Diarrhea suspected to be associated with acute *Clostridium* spp. infection seems highly responsive to antibiotic therapy. Classical antibiotic choices include amoxicillin, metronidazole, and tylosin (Table 15.3).

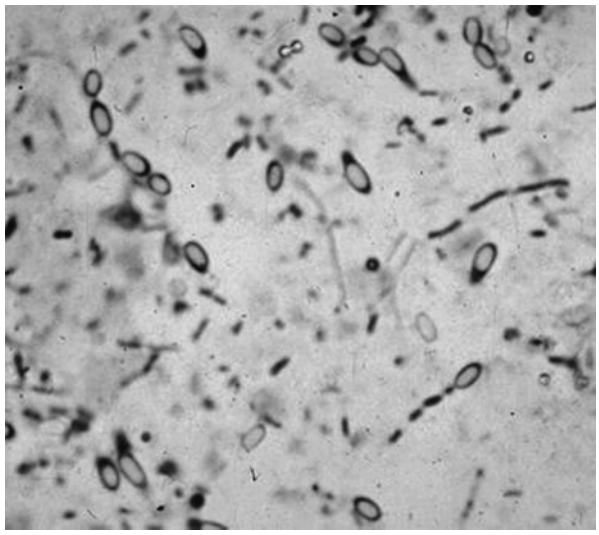

**Figure 15.2.** Rectal cytology stained with Dif Quick stain showing multiple spore-forming rods that are morphologically consistent with *Clostridium* spp. (1,000X).

***Prevention***

*Clostridium* spp. spores are environmentally resistant and it is imperative to maintain environmental cleanliness in order to avoid nosocomial transmission. Increased fiber in the diet and reduction of stress may lessen the occurrence of diarrhea in *Clostridium* spp. carriers housed in crowded animal environments like shelters.

***Zoonotic considerations***

Human strains of *Clostridium* spp. have been identified in dogs, suggesting the possibility of interspecies transmission exists (Lefebvre, Arroyo, Weese 2006). However, direct transmission between animals and man has not been documented. Hand washing, proper disposal of feces, and other biosecurity and hygiene principles are advised to limit possible zoonotic transmission.

### *Escherichia coli* species

***Agent and host range***

In general, *E. coli* are normal enteric bacteria. However, there are particular strains that are pathogenic in many species, including dogs, cattle, pigs, and humans (Beutin 1999). Some studies have produced equivalent percentages of pathogenic and nonpathogenic strains in normal animals versus those with diarrhea (Marks 2003). The prevalence of pathogenic *E. coli* in shelters around the United States is unknown.

***Transmission***

Fecal-oral and fomite transmission are both possible with pathogenic strains of *E. coli*.

***Clinical signs***

Dogs or cats infected by enteropathogenic (EPEC) *E. coli* spp. may develop intestinal cell damage and malabsorption resulting in small bowel diarrhea. There are also enterocytotoxic (ETEC) strains that can cause severe bloody diarrhea, sepsis, and even death.

***Diagnosis***

Presumptive diagnosis of pathogenic *E. coli* can be made through combining clinical signs, signalment, and bacterial culture. However, for most infections, disease is self-limited and so a culture is generally not performed. If *E. coli* infection is documented and more information is needed because of zoonotic considerations, isolates can be assessed for specific toxin genes and/or characterized by molecular typing. Toxin analysis in addition to molecular typing can be helpful because all genes identified may not be functionally expressed (Kruth 2006).

***Treatment***

Therapy should be tailored to the severity of disease. When septicemia is suspected, parenteral antibiotics and fluid therapy are indicated. Antibiotics based on culture and sensitivity are recommended as *E. coli* tend to develop resistance patterns. If empirical choices need to be made, suggested first choices are amoxicillin-clavulanate or cephalosporins (Table 15.3).

***Prevention***

Routine hygiene and biosecurity should limit the spread of pathogenic *E. coli* in the shelter environment.

***Zoonotic considerations***

The possibility of zoonotic transmission exists, but cleanliness and routine personal hygiene should lessen potential for spread between species (Rodrigues, Thomazini et al. 2004). In addition, if stools are normal, the potential for transmission is small; these animals can be adopted.

### *Helicobacter* species

***Agent and host range***

*Helicobacter* spp. are spiral organisms found in the stomach and intestinal tracts of dogs, cats, humans, and

other species (Simpson, Neiger et al. 2000). Many *Helicobacter* spp. have been isolated from dogs, cats, or humans, including *H. pylori*, *H. felis*, *H. pametensis*, and *H. bizzozeronii*. These bacteria have been isolated from the gastrointestinal tracts of both healthy and ill dogs and cats (Eaton, Dewhirst et al. 1996 1996). While prevalence rates in shelter animals are largely unknown, it is likely that many dogs and cats in shelters carry *Helicobacter* spp. Prevalence has been found to be higher in animals sampled from high-density situations. *Helicobacter*-like organisms were observed in gastric biopsies of 82% of pet dogs and 76% of pet cats as opposed to nearly 100% of laboratory and shelter cats and dogs (Fox 2006).

#### *Transmission*

Transmission between species may occur, but most disease spread appears to be limited within species. Fecal–oral transmission is suspected but not proven. Oral–oral transmission is also suspected, and licking may be a mode of transmission.

#### *Clinical signs*

The actual relationship of naturally occurring *Helicobacter* spp. infections to gastrointestinal disease in dogs or cats is still unclear, although experimentally induced infections cause illness. Vomiting without diarrhea is thought to be a common manifestation.

#### *Diagnosis*

Serological test results have not been predictive of illness in dogs and cats because of the large number of subclinical carriers (Fox 2006). Presumptive diagnosis is made in dogs and cats by combining the identification of spiral organisms in gastric and other tissues by histopathological examination and exclusion of other causes of vomiting. Gastric mucosal biopsies can also be placed on a urea slant; *Helicobacter* spp. are urease positive. *Helicobacter* spp. DNA can be amplified from tissues or feces as a diagnostic procedure. However, these diagnostic tests are not commonly utilized by shelter veterinarians. In shelter situations, empirical therapeutic trials are usually utilized if these bacteria are suspected. Diagnosis in humans can be performed through a fecal PCR, but in animals, diagnosis is still generally made via biopsy, which is unlikely to be performed in the majority of shelter settings.

#### *Treatment*

Antibiotic therapy is not well defined as a treatment for *Helicobacter* spp., but empirical therapy with amoxicillin, metronidazole, and an antacid may be prudent as a trial treatment if the animal is clinically ill (Table 15.3). Alternately, a macrolide such as azithromycin can be used.

#### *Prevention*

Since the organisms may be transmitted directly between animals and by the fecal–oral route, limiting contact between vomiting animals and others housed in the shelters seems prudent. The organisms are not environmentally resistant and so routine cleaning and disinfection combined with biosecurity procedures should lessen spread within a shelter.

#### *Zoonotic considerations*

Multiple studies have examined the risk of animal contact and the development of helicobacteriosis in people (Brown, Elston et al. 2003); the majority suggest that there appears to be minimal risk for zoonotic transmission from animals to man. While many dogs and cats harbor *Helicobacter* spp., studies have found species other than *H. pylori*, the most important human pathogen (El Zaatari, Woo et al. 1997). Good hygiene is recommended when handling known infected animals. The AAFP Zoonoses Guidelines states that people should avoid being licked on the face and should not share food utensils with cats (Brown, Elston et al. 2003).

### *Salmonella* species

#### *Agent and host range*

*Salmonella* species are nonspore forming, gram-negative bacterium in the family *Enterobacteriaceae*. *Salmonella* have a broad host range and can affect dogs, cats, and humans among other species. There are over 2,000 known serovars, identified based on flagellar and somatic antigen characteristics. *Salmonella enterica typhimurium*, *S. enterica enteritidis*, and *S. enterica arizonae* are three serovars that commonly cause illness in domestic animals. S*almonella typhimurium* is the organism most frequently isolated from dogs and cats and is seen periodically in migratory songbird populations, thus affecting outdoor hunting cats. Multiple antibiotic resistant strains have also been detected in some cats (Wall, Davis et al. 1995).

The true prevalence of *Salmonella* in a population varies depending on factors such as population density, sanitation, and age of animals. It has been reported that the prevalence of *Salmonella* in cats varies between 1% and 18% and dogs 1% and 36% (Greene 2006a). Based on fecal culture results, prevalence rates were 0.8% and 0.9% in client-owned cats from Colorado (Hill, Cheney et al.

2000) and New York (Spain, Scarlett et al. 2001), respectively, and 1.3% and 0.7% in shelter cats from the same regions.

#### *Transmission*

*Salmonella* species are transmitted by fecal–oral contact via contaminated food, water, or fomite transmission. In utero transmission is also possible, and abortions, stillbirths, and neonatal illness can occur. The organism is relatively hardy, and environmental contamination can be a problem. Many factors can contribute to spread of illness, including dense population, unsanitary conditions, coprophagia, stress, immunocompromise, and disruption of gastrointestinal flora through antimicrobial therapy.

#### *Clinical signs*

Clinical disease associated with salmonellosis can vary from subclinical carrier status to mild, moderate, and severe life-threatening disease. It is estimated that approximately 50% of culture-positive animals are subclinical carriers. When clinical signs are present, vomiting; small, large, or mixed bowel diarrhea; and fever are typical. Disease can be self-limiting, responsive to routine treatments, or result in septicemia and death in young or stressed animals.

#### *Diagnosis*

*Salmonella* spp. can be detected in feces or blood (septic animals) via a fecal culture or PCR assay (see Appendix 15.1). A culture has the advantage of having antimicrobial sensitivity testing performed concurrently, which may help guide the treatment plan. Culturing for *Salmonella* spp. should be considered in animals with clinical signs, especially in outdoor cats, animals that have received prior antimicrobial therapy, and if a definitive diagnosis is needed because of zoonotic considerations. Testing should also be utilized when an environment is known to have been contaminated.

#### *Treatment*

Treatment for *Salmonella* is generally recommended only for bacteremia, and parenteral antibiotics should be used. For most animals with *Salmonella* bacteremia without sepsis, ampicillin administered intravenously is usually sufficient (Table 15.3). For animals with clinical signs of sepsis, a combination of ampicillin with a fluoroquinolone is often prescribed. Use of oral antibiotic therapy is controversial as administration of oral drugs is commonly associated with development of resistant strains.

#### *Prevention*

Preventative measures in a shelter environment should include routine hygiene and biosecurity measures, periodic environmental culture, removal of potential rodent and insect species vectors, and the avoidance of raw meats or unprocessed diet sources. Judicious use of antibiotics is an important consideration in preventing the development of drug resistant *Salmonella* strains.

#### *Zoonotic considerations*

*Salmonella* spp. are directly infectious to humans. Most outbreaks appear to be caused by indirect contact with a contaminated environment. Individual shelters will need to assess their resources and the potential risks when considering therapy for animals diagnosed with salmonellosis. Strict hygiene when handling infected animals and the environment is recommended. Removal of carrier animals from an environment may be warranted to avoid large-scale contamination. As discussed in the section on campylobacteriosis, when an animal with previously proven salmonellosis is to be adopted, potential risks should be discussed with prospective owners so that a risk/benefit decision can be made (Brown, Elston et al. 2003). Some shelters may choose not to adopt animals with previously documented infections. It is beyond the scope of this text to discuss salmonellosis in humans but serious, life-threatening disease does occur and can be spread from clinically normal animals.

### *Yersinia* species

#### *Agent and host range*

Yersiniosis is a clinical syndrome caused by the bacteria *Yersinia enterocolitica* and *Yersinia pseudotuberculosis* (Greene 2006b). *Yersinia* spp. are nonmotile, gram-negative coccobacilli that belong to the family *Enterobacteriaceae*. *Yersinia pseudotuberculosis* is widespread in animals, and *Yersinia enterocolitica* is restricted more to dogs, cats, and humans, and appears to be responsible for the majority of human cases of yersiniosis. Both *Y. enterocolitica* and *Y. pseudotuberculosis* species can be isolated from normal dogs and cats as well as from animals with diarrhea; it remains unclear how often this bacterium is truly a primary cause of disease in animals. *Yersinia* spp. are cultured most often from animals under 6 months of age. The prevalence of the agents in shelter animals is unknown.

#### *Transmission*

The bacteria can be transmitted via fecal contamination and fomites in the environment.

### *Clinical signs*

Clinically affected animals develop a mesenteric lymphadenitis, which can cause variable clinical signs. Some animals remain asymptomatic, while others experience mild to severe diarrhea of several weeks' duration.

### *Diagnosis*

There is no diagnostic test available to make a presumptive diagnosis. Both organisms can be cultured from stool and can be identified in tissues by histopathology (see the diagnostic protocols section).

### *Treatment*

*Yersinia* spp. infections generally respond to empirical therapy with routine doses of cephalosporins, trimethoprim sulfa, or chloramphenicol. Antibiotic therapy based on susceptibility testing is recommended when possible.

### *Prevention*

Hygiene and separation of animals by life stages within a shelter may help to prevent the spread of disease. It is theorized that this disease may also be prevented by eliminating diets of raw meat or unprocessed dairy products that may harbor the bacteria. Good sanitation within a building will eliminate fecal exposure.

### *Zoonotic considerations*

Infected animals can shed this organism for several months in their stool following clinical recovery. Zoonotic outbreaks of gastroenteritis following exposure to infected dogs and cats have been reported (Greene 2006b). As discussed for campylobacteriosis and salmonellosis, potential risks should be discussed with prospective adopters of animals with previously documented infections.

## PROTOZOAL PATHOGENS

There are many pathogenic protozoans that might be encountered in small animals housed in shelters. The most common flagellates are *Giardia* spp. and *Tritrichomonas foetus*. The most common coccidians are *Cryptosporidium* spp., *Cystoisospora* spp., and *Toxoplasma gondii*. The pathogenic potential of these agents varies. *Giardia* spp., *Cryptosporidium* spp., *and T. gondii* have public health considerations. The ciliate *Balantidium coli* and the amoeba *Entamoeba histolytica* are extremely rare in small animals of the U.S. and will not be covered in this chapter. There are other coccidians of dogs or cats, including *Besnoitia darlingi*, *Hammondia hammondi*, *Neospora caninum*, and *Sarcocystis* spp. However, these agents are not usually associated with gastrointestinal disease.

### *Giardia* species

#### *Agent and host range*

These binucleate, flagellated protozoal organisms infect dogs, cats, and humans, among other animals. The organism has two forms: a motile trophozoite and an environmentally resistant cyst. After infection, the prepatent period varies from 5 to 16 days. There are six recognized species of *Giardia* (Thompson, Hopkins, Homan 2000). The most commonly recognized in dogs, cats, and humans is *Giardia lamblia* (also known as *duodenalis*, *intestinalis*). *Giardia lamblia* is further differentiated into six genotypes or assemblages via molecular methods. These assemblages are typically restricted to the species the organism affects, although microscopically the organisms are indistinguishable.

While the reported prevalence rates of *Giardia* spp. in animals vary by the region and assay, the organism is thought to be one of the most common parasites of animals in the U.S. (Carlin, Bowman et al. 2006). For example, in one study of shelter kittens in New York State, fecal antigen was identified in feces of 8.1% (Spain, Scarlett et al. 2001). In another study of shelter animals with diarrhea in Colorado, 0% of cats were positive and 68.4% of dogs were positive for fecal antigen (Spindel, Riggenach, Lappin 2006).

#### *Transmission*

Infection with *Giardia* spp. occurs after ingestion of the resistant cyst stage of the organism, which can be on the fur of infected animals or in a contaminated environment. Young or otherwise immunocompromised animals seem more susceptible to development of diarrhea.

#### *Clinical signs*

Most animals that harbor *Giardia* spp. are clinically normal. However, some small bowel diarrhea, with or without mucous, occurs in some animals. Coinfections with other potential pathogens such as *Clostridium* spp. or *Cryptosporidium* spp. are common and may influence whether clinical illness occurs.

#### *Diagnosis*

*Giardia* spp. trophozoites are detected by wet mount examination or cytology; cysts are detected by fecal flotation (Appendix 15.1 details the zinc sulfate centrifugation method) or IFA (see Figure 15.3); the antigen is detected by immunoassay; DNA is amplified by PCR assay and can

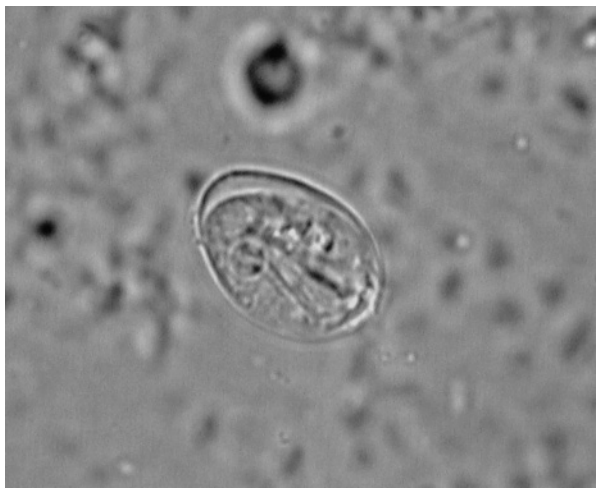

**Figure 15.3.** An 8 µm × 10 µm *Giardia* spp. cyst showing characteristic internal detail (1,000X).

be used to genotype the organism; and rarely the dog and cat strains can be grown in culture (Table 15.2 and Appendix 15.1). Each of the tests has a different sensitivity and specificity; none are 100% reliable (Appendix 15.1). Moreover, none of these tests may prove the diarrhea is from *Giardia* spp. because subclinical infection is common. *Giardia* is fairly often missed as a cause of diarrhea outbreaks in shelters because of intermittent shedding/poor sensitivity of techniques commonly used in shelters.

***Treatment***

If *Giardia* spp. is detected in the feces and there is no other explanation for the diarrhea, treatment is indicated (Table 15.3). Metronidazole, fenbendazole, or febantel are used most frequently in dogs or cats (Barr, Bowman et al. 1998; Payne et al. 2002; Scorza and Lappin 2004; Scorza, Radecki, Lappin 2006; Zajac et al. 1998). There are probably differences in antimicrobial susceptibility between *Giardia* isolates, and so it is impossible to determine the optimal anti-*Giardia* drug. In a recent study of canine field cases, there was no difference in efficacies between three different drugs (Miro, Mateo et al. 2007).

Administration of *Giardia* vaccine as immunotherapy has had variable results (Olson, Ceri, Morch 2000; Stein et al. 2003). Most dogs or cats with diarrhea due to giardiasis rapidly respond to therapy. However, recurrence of clinical signs can occur; it is unknown how many of these apparent recurrences are from incomplete clearance or reinfection from a contaminated environment. In these animals, use of an alternate anti-*Giardia* drug may be effective. Concurrent administration of metronidazole with fenbendazole is advocated by some clinicians. Addition of fiber to the diet and treating again with an anti-*Giardia* drug is effective in some cases. If an animal with *Giardia* infection and diarrhea is still clinically ill after two drug protocols, a search for concurrent abnormalities or infections (like *T. foetus* or *Cryptosporidium* spp.) should be made.

***Prevention***

Cleanliness, lessening of stress, isolation of clinically ill animals, and reduction of moisture/standing water may help lessen spread of disease within a population. *Giardia* is readily killed in the environment with quaternary ammonium disinfectants, so proper biosecurity protocols should prevent outbreaks from occurring. Thorough drying of the environment on a routine basis is also important. In the shelter environment with a *Giardia* outbreak, thorough cleansing of the animal's coat and the environment may help reduce the chances of fecal–oral recontamination (Payne et al. 2002). Use of the canine vaccine has not lessened prevalence of *Giardia* infection in crowded environments (Anderson et al. 2004). This may relate to the *Giardia* spp. used in vaccine production. To date, data concerning efficacy of the feline product using field cases have not been reported. Some shelters that have frequent *Giardia* problems treat all incoming animals with a course of fenbendazole, especially if they also have endemic whipworms, but there is no evidence that pretreatment is effective.

***Zoonotic considerations***

Most dogs and cats with *Giardia* are carrying host-adapted strains and so risk of zoonotic transmission is likely to be low. The infective species of *Giardia* can be determined by PCR assay. If *Giardia* spp. are detected in a healthy animal, most clinicians recommend a course of therapy with a recheck fecal flotation approximately 9 days after treatment (Brown, Elston et al. 2003). Because infection may not be eliminated by treatment, reinfection can occur within days, and healthy animals are not considered human health risks (Brown, Elston et al. 2003), there is usually no benefit of repeated testing after 9 days of treatment. As discussed previously with campylobacteriosis and salmonellosis, when an animal with previously proven giardiasis is to be adopted, potential risks should be discussed with prospective owners so that a risk benefit decision can be made by the owner (Brown, Elston et al. 2003). The AAFP recommends rechecking one fecal float after successful

treatment of client-owned animals (Brown, Elston et al. 2003).

### *Tritrichomonas foetus*

#### *Agent and host range*

*Tritrichomonas foetus* is a flagellate associated with diarrhea in some cats (Gookin, Breitschwerdt et al. 1999). While the agent also can infect dogs, the importance is unknown at this time. The organism does not produce a cyst. Feline *T. foetus* isolates are genetically similar to that isolated from cattle but it is unknown if *T. foetus* is shared between species. *Pentatrichomonas hominus* is another flagellate that also can be isolated from dogs and cats but the significance of this organism is unknown.

While the prevalence of *T. foetus* was 31% among international purebred cats attending a show (Gookin, Copple et al. 2006), it is unknown how often the agent is associated with diarrhea. The prevalence in shelter animals is unknown at this time.

#### *Transmission*

Close and direct vertical contact transmission between cats is assumed, as the organism is frequently demonstrated in densely housed populations of animals and does not produce an environmentally resistant cyst. Fecal–oral transmission is also possible.

#### *Clinical signs*

Most cats with diarrhea thought to be from *T. foetus* are under 1 to 2 years of age and found in crowded or stressful facilities. Shelters and catteries seem to be at particular risk. Clinical signs of infection can include diarrhea with blood, mucus, tenesmus, and even rectal prolapse.

#### *Diagnosis*

Diagnosis of *T. foetus* can be made using a fresh fecal sample saline wet mount, fecal culture, or PCR assay (Table 15.2; Appendix 15.1). The trophozoite of *T. foetus* has an undulating membrane that surrounds the entire organism, and the organism moves in a relatively straight line motion when seen on examination of a fecal wet mount. It is important to distinguish *Giardia* spp., which have a characteristic "fallen leaf" motility. *T. foetus* should be a differential diagnosis in situations where *Giardia* is suspect but animals are not responding to appropriate therapy.

#### *Treatment*

Some cats with *T. foetus* infection have coinfections that respond to administration of specific drug therapy. Other cats will initially improve and then worsen again post-therapy. With time, clinical signs of disease resolve, but this may take months (Foster, Gookin et al. 2004). Recently, administration of ronidazole (Table 15.3) has led to parasitological cure and resolution of clinical disease in some experimentally and naturally infected cats (Gookin et al. 2006). This drug can induce central nervous system toxicity and so should be used cautiously.

#### *Prevention*

In the shelter setting, *T. foetus* has a poor prognosis for eradication with short-term therapy. The housing of affected kittens with normal kittens should be avoided. Reduction of overcrowding may be the most important preventive measure.

#### *Zoonotic considerations*

There has been only a single reported case of human *T. foetus* infection, in a severely immunocompromised individual (Okamoto, Wakui et al. 1998).

### *Cryptosporidium* spp.

#### *Agent and host range*

*Cryptosporidium* spp. are coccidian parasites found in the gastrointestinal tract of dogs, cats, humans, and other animals (Morgan, Monis et al. 1999; Xiao, Fayer et al. 2004). *Cryptosporidium parvum*, found most frequently in cattle and humans, has the greatest zoonotic potential. *Cryptosporidium hominis* is native to humans and unlikely to infect dogs and cats (Morgan-Ryan, Fall et al. 2002). Dogs are most commonly infected with *C. canis*, and cats are most commonly infected with *C. felis*; neither species is common in immunocompetent people.

Dogs and cats are commonly exposed to *Cryptosporidium* spp., but the incidence of diarrhea induced by the organisms is unknown. The seroprevalence of *Cryptosporidium* spp. antibodies detected using an IgG ELISA test was measured at 15.3% and 8.3%, respectively, in cats in Colorado (Lappin 1997) and the U.S. (McReynolds, Lappin et al. 1998). Oocysts or antigens were detected in the feces of 5.4% of cats in Colorado (Hill 2000), 3.8% of kittens in New York State (Spain, Scarlett et al. 2001), and 3.8% of dogs in Colorado (Hackett and Lappin 2003).

#### *Transmission*

Infection following direct fecal–oral or water contamination is most common. There is a 3- to 5-day prepatent period.

### *Clinical signs*

Infection is often subclinical, but small bowel diarrhea can occur, especially in young, immunosuppressed animals.

### *Diagnosis*

*Cryptosporidium* spp. oocysts are small in diameter (4–6 μm), and dogs, cats, and people shed small numbers of oocysts per gram of feces. Thus, fecal flotation is generally falsely negative (Table 15.2, Appendix 15.1). Use of a modified acid fast stain on a thin rectal or fecal smear has greater sensitivity than fecal flotation alone and can be done as a point of care test (Marks, Hanson, Melli 2004). The only immunological assay (Appendix 15.1) that reliably detects *C. felis* or *C. canis* is a fluorescent-antibody-based assay that is offered by most commercial veterinary laboratories (Marks, Hanson, Melli 2004; Scorza, Brewer, Lappin 2003). Assays for *C. parvum* antigen in human feces are inadequate for use with dog and cat feces. PCR assays are the most sensitive testing methods available and the products can be sequenced to determine the infective species (Scorza, Brewer, Lappin 2003). However, since many animals are healthy carriers of *Cryptosporidium* spp., PCR assays should only be used with clinically ill animals.

### *Treatment*

No drug has proven effective in eliminating this organism from the gastrointestinal tract. However, infections can be self-limiting, and administration of several different drugs has proven effective in the control of clinical signs in some infected dogs and cats. The authors have used tylosin, azithromycin, paramomycin, or nitazoxanide most frequently (Table 15.3). Some animals have required administration of antimicrobial agents for weeks to achieve maximal response.

### *Prevention*

The oocysts are immediately infectious when passed in the feces, and so routine cleanliness and biosecurity measures should be maintained. As most disinfectants require extremely long contact times to be effective, the only practical way to inactivate the oocysts on surfaces is with steam cleaning.

### *Zoonotic considerations*

Humans are usually infected with *C. parvum* or *C. hominus*, but *C. felis* and *C. canis* have been detected in people with Acquired Immune Deficiency Syndrome (AIDS) (Morgan, Weber et al. 2000). In one study, there was no statistical link between pet ownership and cryptosporidiosis in people with AIDS (Glaser, Safrin 1998). If *Cryptosporidium* spp. are detected in feces, genotyping is available but is generally not performed because healthy animals are unlikely to be the source for human infections. As discussed previously for campylobacteriosis, salmonellosis, and giardiasis, when an animal with proven cryptosporidiosis is to be adopted, potential risks should be discussed with prospective owners so that a risk/benefit decision can be made by the owner (Brown, Elston et al. 2003).

## *Isospora* species

### *Agent and host range*

The principal *Isospora* spp. in dogs are *Isospora canis* and *Isospora ohioensis*. In cats, *Isospora felis* and *Isospora rivolta* are most common. *Isospora* spp. have a worldwide distribution, and tend to be very host specific.

Clinical disease is most common in young, debilitated, and immunocompromised animals. One study showed 5% of shelter dogs to be passing oocysts in their feces (Blagburn 2003).

### *Transmission*

*Isospora* spp. have a complicated life cycle. Infection can occur following ingestion of sporulated oocysts or through indirect transmission via ingestion of an infected intermediate host, such as a rodent. Insects like flies or cockroaches can act as important vectors in the transmission cycle. Unsporulated oocysts (noninfectious) are shed in the stool 5 to 9 days after initial infection. Sporulation can occur in as little as 12 hours in an environment with proper conditions.

### *Clinical signs*

*Isospora* spp. are generally only associated with disease in young animals; however, oocysts are often isolated from fecal samples taken from clinically normal animals. Clinically ill animals demonstrate mild to severe large bowel diarrhea, abdominal pain, vomiting, and illness. Disease can lead to dehydration and death in young animals.

### *Diagnosis*

Diagnosis is made by identifying the characteristic oocysts after fecal flotation (see Figure 15.4). Because oocysts can be present in normal animals, it is important to rule out other causes of gastrointestinal disease. Most puppies and kittens with clinical signs of disease are shedding large numbers of oocysts, so false negative results are uncommon. However, because signs can precede the presence of

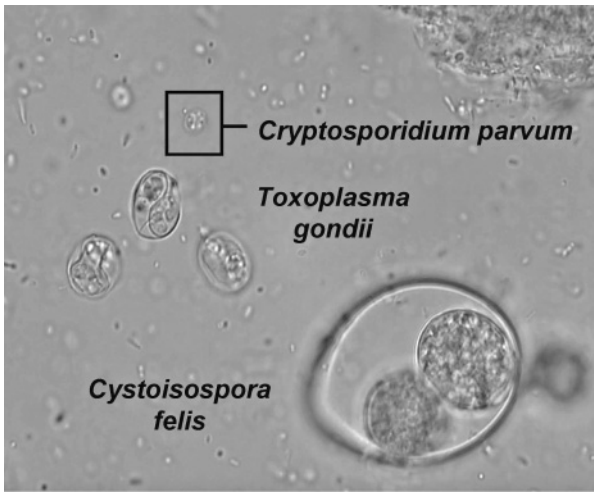


**Figure 15.4.** *Isospora felis., Toxoplasma gondii,* and *Cryptosporidium felis* oocysts (1,000X).

oocysts in acute disease, false negatives do occur. In some cases, a repeat fecal examination might be required to prove infection.

***Treatment***

The disease is generally thought to be self-limiting, and spontaneous cure in relatively healthy animals occurs without therapy. However, the majority of shelter animals with diarrhea and *Isospora* infections are likely to benefit from treatment, which may also lessen shedding of oocysts into the environment. The most commonly prescribed drug is sulfadimethoxine; trimethoprim sulfa or clindamycin can also be used (Table 15.3). Ponazuril (Table 15.3) has shown good success in shelter animals (Lloyd 2001). This drug has the advantage of requiring only one to two doses and is one of the few coccidiocidal (versus static) medications available. Toltrazuril/diclazuril have also been used in countries where these are the more readily available choice.

***Prevention***

Because of the prepatent period and time to sporulation, facilities that practice good isolation and hygiene are less likely to develop nosocomially transmitted *Isospora* infections. Oocysts can be very difficult to eradicate in the environment. Routine disinfectants do not kill *Isospora* spp. Steam cleaning, best accomplished with commercial machines, may help in environments that are contaminated. Animals at high risk for infection should therefore be housed in environments amenable to such cleaning—this means no carpeted items, upholstered furniture, and the like in puppy and kitten housing. Isolation of animals known to be shedding oocysts is highly recommended, along with segregating animals by age groupings. Frequent stool removal (every 12 hours minimum) will minimize environmental contamination. Forethought should be given to the housing of young animals (i.e., foster animals) in environments that are amenable to cleaning.

***Zoonotic considerations***

The *Isospora* spp. of dogs and cats are not known to have zoonotic implications.

***Toxoplasma gondii***

***Agent and host range***

*Toxoplasma gondii* is an obligate intracellular coccidian that is found in a variety of species, including dogs, cats, birds, and humans (Dubey and Lappin 2006). It is estimated that 30% to 40% of cats and humans and 20% of dogs in the U.S. are seropositive and thus presumed to be infected with this organism (Dubey and Lappin 2006, Vollaire, Radecki, Lappin 2005). However, the clinical disease is thought to be uncommon.

***Transmission***

The sexual phase of the life cycle of *T. gondii* can be completed only in the intestinal tract of cats, resulting in the passage of resistant, unsporulated noninfectious oocysts. Once passed into the environment, the oocysts sporulate in 1 to 5 days, and then are infectious by the fecal–oral route. Infected intermediate hosts develop tachyzoites and bradyzoites in tissues that are also infectious when ingested. There are several less apparent modes of transmission, including transplacental, lactational, and, rarely, via blood transfusion.

***Clinical signs***

*Toxoplasma gondii* is generally not associated with vomiting or diarrhea in dogs or cats. Most cats experimentally infected with *T. gondii* maintain normal stools even when shedding millions of oocysts. Thus, the main importance of *T. gondii* infection of the gastrointestinal tract relates to potential zoonotic risk. However, the organism is associated with a number of polysystemic syndromes in shelter animals. Illness is most frequently noted during the intracellular replication of tachyzoites, with neonates showing the most severe signs. Clinically, these kittens or puppies may be stillborn or never thrive, or may have variable

signs of multiple organ disease. The liver, pulmonary parenchyma, pancreatic tissue, and central nervous system are most frequently affected. Chronic clinical syndromes also occur; fever with or without ocular, respiratory, gastrointestinal, and neurological disease manifestations are common (Dubey and Lappin 2006).

### *Diagnosis*

During the enteroepithelial stage of infection in cats, the $10\,\mu m \times 12\,\mu m$ oocysts are easy to identify after fecal flotation (Figure 15.4). However, this stage lasts less than 21 days and usually only occurs once, so detection of *T. gondii* oocysts in fecal surveys is uncommon (Hill, Cheney et al. 2000; Spain, Scarlett et al. 2001; Nutter, Dubey et al. 2004). When systemic toxoplasmosis is considered likely, serum antibody testing to detect elevated IgM titers or rising IgG titers are used most frequently to support the diagnosis. Because antibody titers can be detected in both ill and healthy animals, serology only documents prior exposure to *T. gondii*. Diagnosis is usually made on the basis of several criteria such as the demonstration of antibodies documenting exposure, clinical signs compatible with current disease, exclusion of other disease, and a positive response to appropriate therapy (Lappin 1996).

### *Treatment*

Oocyst shedding is usually completed in less than 21 days. If oocysts of the appropriate size are noted on fecal flotation, administration of clindamycin can shorten the oocysts shedding period (Table 15.3). If systemic toxoplasmosis is suspected, administration of clindamycin, trimethoprim sulfa, or azithromycin is often effective in alleviating clinical signs but does not eliminate the organism from tissues (Table 15.3).

### *Prevention*

*Toxoplasma gondii* oocysts are environmentally resistant. Like *Isospora* spp. and *Cryptosporidium* spp., cleaning with scalding water and steam cleaning (best with a commercial machine) are the only practical ways to attempt to destroy the organism in a contaminated environment. Cats should be fed processed foods, not raw food diets, and not be allowed to hunt to lessen likelihood of exposure to *Toxoplasma gondii*, and, thus, oocyst shedding. Because cats housed in shelters have often been hunters, removing feces from the litter boxes daily, before oocysts can sporulate, will lessen the risk of naïve cats or intermediate hosts (including humans) coming in contact with the organism. Disposable litter pans can aid in this process. When disposables are not in use, pans should be thoroughly washed to remove organic matter and disinfected. A daily cycle is advised and, minimally, when soiled.

### *Zoonotic considerations*

Toxoplasmosis can be a significant zoonotic risk, particularly to the unborn human fetus and immunosuppressed individual. However, in most studies, there is no difference in prevalence rates between cat owners and people who do not own cats (Wallace, Rossetti, Olson 1993). To avoid *T. gondii* infection, people should avoid exposure to old cat feces in the environment and should not ingest undercooked meat. Cats that are thought to have clinical toxoplasmosis are unlikely to be shedding *T. gondii* oocysts, as the enteroepithelial cycle is generally complete by the time clinical disease is noted. Previously infected cats almost never repeat cyst shedding; thus, a cat that is seropositive for *T. gondii* is unlikely to shed oocysts in the future (Brown, Elston et al. 2003).

## DIAGNOSTIC PROTOCOLS

There are many laboratory procedures utilized in the diagnosis of bacterial and protozoal gastrointestinal diseases (Table 15.3); descriptions of the most commonly used tests are listed in Appendix 15.1 and are discussed with the appropriate individual organisms. While many of the bacterial and protozoal organisms encountered in shelters have the potential for zoonotic transfer to people, healthy pets are generally not considered human health risks, and with the exception of fecal flotation, the tests discussed herein are generally not needed for animals with normal stools (Brown, Elston et al. 2003).

Because of the large number of infectious agents associated with diarrhea, the American Association of Feline Practitioners Zoonoses Guidelines Committee recommended the following workup for cats with diarrhea: (1) fecal flotation, preferably zinc sulfate; (2) fecal wet mount examination; (3) rectal cytology; and (4) acid-fast stain for *Cryptosporidium* spp. (Brown, Elston et al. 2003). Most veterinarians at Colorado State University follow these guidelines for both dogs and cats (MR Lappin, unpublished observation, 2006). Each of these tests can be performed with simple equipment and stains and should be considered at shelters with a laboratory facility and staff members capable of performing the assays. This is of particular importance for animals that join the homes of immunodeficient people.

Because of budgetary constraints or lack of equipment, shelter veterinarians may not be able to perform a complete work-up on each individual animal with diarrhea but

may need to resort to a combination of dietary modification, limited work-up, and therapeutic trial to establish a diagnosis or management plan. In some cases, prior to a therapeutic trial, a bland diet (high fiber, highly digestible protein, hypoallergenic, or other diets) or withholding food for a day may be helpful to establish the cause of the problem. The drugs most likely to be effective for control of diarrhea from bacterial or protozoal agents are metronidazole (*Giardia* spp., bacterial overgrowth), tylosin (*Campylobacter* spp., *Cryptosporidium* spp., *Clostridium* spp., and bacterial overgrowth), and fenbendazole (*Giardia* spp., helminths). However, if an infectious or zoonotic diarrhea outbreak is suspected (i.e., unusual numbers of ill animals, illness not responding to typical therapies, or symptomatic humans noted in proximity to sick animals), performance of a complete diagnostic work-up on at least some of the affected animals to identify the causal agent is highly recommended to identify and plan a course of action to stop the spread of the disease. In these situations, use of an outside laboratory for further testing such as culture and sensitivity, immunologic techniques, PCR assays, or full necropsy may be of great benefit. Lastly, routine screening of a portion of a large population (e.g., 10 random samples/100 animals/month) would be ideal to provide an indication of infectious agent prevalence within a given population.

## MANAGEMENT IN THE SHELTER ENVIRONMENT

It is impossible to prevent protozoal and bacterial gastrointestinal disease entirely in any large, fluctuating population of animals, particularly since each of the agents can be carried by healthy animals. Instead, veterinarians should set the primary goals of limiting disease and preventing nosocomial infections. Proper attention to all aspects of husbandry within the shelter will significantly reduce disease incidence. Cleanliness, reduction of stress, isolation of clinically ill animals, and limiting animal density are some of the best strategies for avoiding clinical disease outbreaks from gastrointestinal infectious agents. The reality of diarrhea in animal facilities is that not every animal with gastrointestinal disease can be fully worked up or strictly isolated. The goal of environmental management should be to limit transmission and rapidly identify serious infections.

Most protozoal and bacterial agents are readily killed by routine disinfection, with the exception of the coccidians, *Cystoisospora* spp., *T. gondii*, and *Cryptosporidium* spp., which are resistant to most disinfectants with limited contact time. It must always be remembered that a single animal with gastrointestinal disease could jeopardize an entire animal and human population if the proper procedures are not in place. Implementing standard written policies for general biosecurity and for the management of specific infectious agents when diagnosed in single animals or multiple animals is advised. The reader is referred to other chapters in this textbook, as well as *Shelter Medicine for Veterinarians and Staff* (Miller 2004) for more detailed discussion of overall disease management in an animal shelter.

## IMPLICATIONS FOR ADOPTERS

It is of utmost importance that shelter veterinarians understand zoonotic diseases. While many of the bacterial and protozoal agents discussed herein have zoonotic potential (Table 15.1), healthy animals without parasites are generally not considered to be human health risks (Brown, Elston et al. 2003; www.cdc.gov/hiv/pubs/brochure/oi_pets.htm; www.cdc.gov/ncidod/diseases/index.htm). Thus, the shelter staff should always strive to adopt out clinically normal, healthy animals. However, because of variable incubation or prepatent periods, normal animals will occasionally be adopted, only to break with vomiting or diarrhea within several days. Thus, shelters should provide information on how to minimize nosocomial and zoonotic spread of infectious agents within the home after adoption. When animals develop vomiting or diarrhea after adoption, shelter veterinarians then must be skilled at handling public health issues and public relations, not just with adopters but with the local veterinary community.

## CONCLUSION

Management of bacterial and protozoal gastrointestinal disease in animal shelters will never be simple. There will always be complicated diagnostic and treatment decisions based on individual situations. Diagnostic rule-outs for gastrointestinal disease in shelter animals must include stress, change in diet, toxicosis, GI parasites, foreign body ingestion, neoplastic, metabolic, and immunodeficiency disease, etc. Fortunately, the field of shelter medicine has advanced rapidly over the past decade, and many shelter animals are being treated more extensively than ever before. Veterinarians must continue to elevate both the preventative and therapeutic standards of care offered to shelter animals by increasing awareness, management, and study of bacterial and protozoal causes of diarrhea in shelter animals. Ideally, the long-term result of properly

managing any infectious disease in a shelter is placement of more animals into lifelong homes.

## APPENDIX 15.1. DIAGNOSTIC TECHNIQUES FREQUENTLY USED IN THE DIAGNOSIS OF BACTERIAL AND PROTOZOAL GASTROINTESTINAL DISEASES

**Fecal flotation techniques.** Most parasite eggs, oocysts, and cysts can be easily identified during microscopic examination of feces after flotation. Fecal samples should be fresh for accurate results. If samples are more than 2 hours old, refrigeration is recommended until examination is completed. This should limit overgrowth of yeast, which may confuse the diagnosis of giardiasis. All samples should be labeled clearly with an indelible marker in a spill-proof container. There are multiple fecal flotation procedures that can be used in shelters. Centrifugation techniques have the best sensitivity and specificity and should be used if possible.

The following is a description of the zinc sulfate centrifugal flotation procedure:

Place 1 g fecal material (at least the size of a large pea) in a 15-ml conical centrifuge tube. Add 8 drops of Lugol iodine and mix well. Add 7 to 8 ml of $ZnSO_4$ (1.18 specific gravity; approximately 330 g $ZnSO_4$ mixed into 670 ml of distilled water) and mix well. Add $ZnSO_4$ until there is a slight positive meniscus. Cover the top of the tube with a coverslip. Centrifuge at 1,500–2,000 rpm for 5 minutes. Remove the coverslip and place on a clean microscope slide for microscopic examination. Examine the entire area under the coverslip for the presence of eggs, cysts, and oocysts at 100X while changing the plane of the microscope stage. Increase magnification to 400X or 1,000X to evaluate for appropriate internal detail if suspected parasites are identified.

**Fecal wet mount.** This technique is most valuable for detection of the motile trophozoites of *Giardia* spp. and *T. foetus* and for recognition of motile spirochetes like *Brachyspira* spp. in fresh feces. *Giardia* spp. and *T. foetus* are commonly detected in the mucus on the surface of feces. Mix a 2 mm × 2 mm × 2 mm amount of fresh feces or mucous sample with a drop of 0.9% NaCl on a microscope slide. Mix in a circular motion until the specimen is 1 cm × 1 cm. Add a coverslip and immediately examine for motile organisms at 100X.

**Rectal or fecal cytology**. A cotton swab moistened with 0.9% NaCl should be used to collect rectal material for cytological examination if tolerated by the animal. The swab should be gently passed into the rectum, rolled several times against the rectal wall, and then removed. The swab should be rolled on a slide in several lines of varied thickness; at least two slides should be made. If rectal passage is not tolerated, gently roll the swab on the surface of the feces and roll on a microscope slide. The slides should be allowed to air dry and then one slide can be stained with a rapid stain like Diff-Quick. (Diff Quick; Baxter Diagnostics, Inc., Deerfield, IL) After staining, the slide should be scanned at 100X to evaluate for the presence of white blood cells. When appropriate areas are identified, increase magnification to 400X or 1,000X to evaluate for organisms with characteristic morphologic forms like *Clostridium* spp., *Campylobacter* spp., or *Brachyspira* spp. (Figures 15.1 and 15.2). White blood cells may indicate inflammation induced by *Salmonella* spp. or *Campylobacter* spp. and may be an indication to follow through with a fecal culture. The second slide can be stained with modified acid-fast stain (Modified acid fast, Becton Dickinson, Franklin Lakes, NJ) to aid in the detection of *Cryptosporidium* spp. oocysts, which stain pink.

**Culture.** Culture of feces for *Salmonella* spp. or *Campylobacter* spp. is occasionally indicated. Approximately 2–3 grams of fresh feces should be submitted to the laboratory immediately for optimal results; however, some *Salmonella* spp. and *Campylobacter* spp. will remain viable in refrigerated fecal specimens for 3–7 days. Use of an appropriate transport media (Cary-Blair media; Bectin-Dickinson Microbiology Systems, Sparkes, MD) may increase sensitivity. The laboratory should be notified of the suspected pathogen so appropriate culture media can be used. More than one culture may be needed to prove infection. *Tritrichomonas foetus* can be cultured from the feces of dogs or cats using a commercially available kit (Inpouch™, Biomed Diagnostics, White City, OR). Some *Giardia* species isolated from dogs or cats will grow on culture media, but this technique is not frequently performed.

**Immunologic techniques.** *Cryptosporidium parvum* and *Giardia* spp. antigen detection procedures are available for use with feces. The SNAP® *Giardia* antigen assay (IDEXX Laboratories, Portland, ME) has been shown to detect antigens of *Giardia* isolates from dogs and cats and can be used as an adjunct test to fecal flotation and fecal wet mount, or to confirm questionable results in other tests. Currently available *C. parvum* antigen assays utilize monoclonal or polyclonal antibodies against *C. parvum* and do not consistently detect *C. felis* or *C. canis*. An indirect fluorescent antibody assay (Merifluor Crypto/Giardia kit, Meridian Diagnostic Corp., Cincinnati, OH) for the concurrent detection of *Giardia* spp. and *C. parvum* in human feces has been assessed with samples from dogs and cats. This assay can be used to detect *C. felis* and *C. canis* but requires a fluorescence microscope and so is usually performed at diagnostic laboratories.

**Polymerase chain reaction.** Polymerase chain reaction (PCR) assays are currently available to detect DNA of *Giardia* spp., *Cryptosporidium* spp., *T. foetus*, and several bacterial agents in feces. Most laboratories request that fresh feces should be kept cold and submitted within 24 hours to the

laboratory for PCR analysis. For *Giardia* spp. and *Cryptosporidum* spp., genotyping of PCR-positive samples can also be performed to determine the infective species in an attempt to assess zoonotic risk.

**Necropsy.** A thorough necropsy can often lead to determination of a definitive diagnosis and should be considered during any gastrointestinal disease outbreak, especially if affected animals are dying or being euthanized. Samples for histopathology, culture, and the techniques discussed previously can be collected.

Note: Each of the above tests has a different sensitivity and specificity, none of which are 100%.

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# Section 4
# Dermatological Disease

# 16
# Dermatophytosis

*Karen A. Moriello and Sandra Newbury*

## INTRODUCTION

Dermatophytosis, commonly referred to as ringworm, is one of the more complex infectious disease problems facing shelters. If given enough time, and assuming the cat is healthy and in a stress-free environment, this disease will resolve in most pet cats. However, because the disease is highly contagious to cats and other animals and is a known zoonosis, it can be "life threatening" in shelters. Outbreaks have resulted in serious problems for shelters, especially when people contract the disease from animals adopted from the shelter. It has long been believed that the disease is too difficult for shelters to diagnose and treat and that successful environmental decontamination of the long-lived, resistant spores is virtually impossible to achieve. Based on the experiences of the authors with the establishment of a successful screening and treatment program at a large Midwestern shelter and consulting work done with other shelters and facilities that house multiple animals, it is the authors' conclusion that dermatophytosis can be managed successfully in many shelters without resorting to widespread depopulation (Newbury, Verbrugge et al. 2005a; Newbury, Verbrugge et al. 2005b; Newbury, Moriello et al. 2007). Because outbreaks of dermatophytosis in shelter cats have been so much more frequently reported as a problem severe enough to debilitate an entire organization, the emphasis of this chapter will be on management of feline dermatophytosis in a shelter setting; information on the treatment of dogs and other animals in shelters is also included.

## ETIOLOGY

### Agent description

The dermatophytes consist of a group of fungi of the genera *Microsporum*, *Trichophyton*, and *Epidermophyton*. These organisms have adapted to digest keratinous debris. Pathogens in these genera infect the stratum corneum, hair shafts, and claw. Species may be divided into three classes: anthropophilic, zoophilic, and geophilic. The anthropophilic species have evolved on humans and rarely affect animals. The species that are adapted to animal hosts are termed "zoophilic" but these may spread to in-contact humans. The soil-adapted "geophilic" dermatophytes are less often a cause of human disease, but sometimes affect animals.

Although there are more than 30 species of dermatophytes that affect dogs, cats, and birds, the most commonly isolated pathogens from cats and dogs are *Microsporum canis*, *M. gypseum*, and *Trichophyton* spp. *M. canis* is the most important pathogen of cats, and *M. gyspeum* is isolated more frequently from dogs. *Trichophyton* infections are more common in dogs than in cats, although the latter may also be affected. *Trichophyton* spp. infections are also more common in rodents and hedgehogs.

Approximately 90% of feline dermatophytosis is caused by *Microsporum canis*; dogs may be infected with *M. canis*, *M. gypseum*, or *Trichophyton mentagrophytes*. Infection and clinical signs are significantly more common in cats than in dogs. In regions with colder winters, infection in dogs is uncommon. Cats can also be infected with alternate species such as *M. persicolor* or *Trichophyton* spp. *M. canis*, which may be readily transmitted between humans, cats, and dogs, is the pathogen of greatest significance in shelters.

### Key factors affecting susceptibility to infections

In many regions, there is a strong seasonality associated with dermatophyte infection. Infections in animals tend to be more common in warm, humid geographic regions of the world. In more temperate climates, infections may be

more common in warm months than in winter. Increased incidence of infection in shelters may also coincide with breeding season, i.e., "kitten season." For example, in the United States, the authors have found that in the northern Midwest, October and May tend to have the largest influx of infected cats and kittens (Newbury, Verbrugge et al. 2005a; Verbrugge, Moriello, Newbury 2006). Kittens are more susceptible to infection and often present to shelters in poor body condition, stressed, and infested with external parasites. Animal welfare organizations in the warm, humid southern regions of the U.S. and northern shelters that receive transports from those more southern regions report problems with dermatophytosis in dogs more frequently than northern shelters that do not receive transports from southern shelters. Infections are rarely reported as problematic in shelter dogs originating from the Northeast and northern Midwest.

There are many factors that influence infection, but in general, age is the most important factor. Juvenile animals (cats and dogs) are most commonly affected by this disease. Young animals are also relatively likely to suffer from severe, generalized infections (e.g., lesions covering much of the body), while infections in adult animals are more commonly limited or focal infections/lesions. Infection tends to be most common in cats that have been living in close proximity to other cats and outgoing, friendly cats, probably because of the increased chance for exposure through contact. Overcrowding of cats in shelters, whether singly housed, free roaming, or group housed, should be considered a major risk factor. Animals from environments where many animals are present, such as barns or hoarding situations, are also at higher risk of infection. The authors have not found any correlation with intake status, such as stray or owner-surrendered (Verbrugge, Moriello, Newbury 2006).

Dermatophytosis more commonly affects cats than dogs. Dogs that run free or are housed outside in dirt runs, hunting dogs, and dogs housed in overcrowded environments are at increased risk of infection (Cafarchia, Romito et al. 2004). Yorkshire terriers are one well-known dog breed that is predisposed to infection; the reason is unknown and may be related to the hair length or that dogs that require frequent grooming are at higher risk for contagious skin diseases (Cafarchia, Romito et al. 2004; Cerundolo 2004).

Dermatophytosis may also be encountered in other species sometimes housed in shelters, including rabbits, ferrets, mice, rats, guinea pigs, and hedgehogs. Clinical signs will be similar, as the pathogenesis of the disease is the same. Treatment protocols acceptable for kittens are generally safe; however, the reader is cautioned to always check for species susceptibility and potential toxicity to systemic antifungals prior to using them in species other than cats and dogs.

## PATHOGENESIS

Exposure occurs from contact with another infected animal, a fomite, or a contaminated environment. Simply being exposed to spores does not necessarily result in an infection. For an infection to become established, spores must reach the skin surface and defeat host-protective mechanisms. Natural skin flora, sebum, grooming, and the skin's immune system are the first lines of defense.

Dermatophyte spores require some type of microtrauma or trauma to gain access to the skin and cause an infection. An often-overlooked source of "microtrauma" is maceration of the skin due to high humidity. External parasitism is another common source of microtrauma to the skin that can predispose animals to infection. Infection is usually the result of exposure to infected spores coupled with one or more predisposing factors, including but not limited to youth or old age, debilitating disease, compromised immunologic status, poor body condition, matted hair coat, and/or predisposing environmental factors associated with poor husbandry. These factors are often found in combination. In settings where animals are not stressed, ill, or in poor body condition, an infective spore that reaches the hair coat may merely fall off, be groomed off, or simply be mechanically carried and never trigger an infection. In shelter animals, where stress, parasitism, and concurrent illness may be impediments to normal grooming behavior and have a negative impact on the immune system, exposure will more readily lead to infection.

## DISEASE COURSE

### Incubation

In general, the incubation period from exposure until development of clinically obvious lesions is approximately 2 to 4 weeks. In experimentally induced infections, infected hairs have been noted in less than a week (DeBoer and Moriello 1994). Lesions may be detected soonest by a highly trained observer. Development of clinical lesions is preceded by infection of the hair follicle. The relatively long incubation period compared to other infectious diseases must be considered when attempting to map an outbreak or determine potential origin of infections (in-shelter spread versus community source). Owing to the long incubation period and variable clinical signs, simply quarantining potentially exposed animals to watch for development

of dermatophytosis is not recommended. (Please see sections on risk assessment and treatment below.)

### Immunity after recovery

Studies on the immune response of cats have shown that cats develop both a humoral and cell-mediated immune response to infection, but recovery is associated with the strong cell-mediated response, not the humoral response, in contrast to immunity to many other infections (Sparkes, Gruffydd-Jones, Stokes 1996; DeBoer and Moriello 1993). Lack of a cell-mediated response is associated with prolonged infection. Immunity is also relative. Most recovered infected animals are immune from infection but when challenged with large numbers of spores, infection is possible. Recovered animals should be protected from exposure in order to prevent reinfection. The duration of immunity is unknown.

### Carrier state

The authors have not seen any cases in a shelter setting of unaffected "carrier state" animals nor animals with persistent infections in the face of appropriate treatment. Studies on the fungal flora of cats have shown that *Microsporum canis* is NOT part of the normal fungal flora of cats (Moriello and DeBoer 1991a, 1991b). A positive fungal culture from a cat indicates one of three situations: a cat with obvious clinical lesions, a cat with subtle lesions, or a cat that is mechanically carrying spores on its hair coat. All three situations require some type of action, as these spores can be transmitted to other animals and humans. The concept of "asymptomatic carriers" with respect to dermatophyte infections is unlike that of other diseases encountered in shelters where "latent" infections can be activated. The authors strongly discourage the use of the terms "carrier" or "asymptomatic carrier."

Dermatophytosis is a treatable and curable disease. When animals have long-standing or unresolving infections, treatment choices and medications, as well as environmental contamination should be evaluated. In many cases, the animal continues to culture positive because there are spores remaining in the housing environment. The authors have not encountered any cases in a shelter setting where cats with long-standing or "incurable" infections could not be cured once appropriate treatment was instituted, underlying diseases concurrently treated and resolved, and appropriate environmental decontamination instituted. (Please also see the section on treatment.)

Animals can culture positive for dermatophytes if they are truly infected or if they simply have spores resting like dust on their hair coat. These two situations present very different challenges and risks, so differentiation is essential. Cats that mechanically carry spores on their hair coat ("dust mop" cats) may become infected if the spores are not removed, but in many cases, cats will remove those spores themselves by grooming.

It is unclear what risk these "dust mop" cats pose to other animals or to the shelter environment. Although the hair coat of animals often carry spores representative of those found in their environment, dermatophytes are not considered normal flora of dogs or cats. When large quantities of spores are being carried on the hair coat, at least some risk does exist that infection will develop or spores will be shed into the environment. When the numbers of spores carried is low, the risk diminishes. Quantitative fungal culture can help distinguish between these two scenarios; please see the section on risk assessment.

## TRANSMISSION

Naturally infective hairs and spores are easily shed into the environment from infected animals. Infective spores are small, approximately the size of dust, and can easily collect or be transferred to the hair coats of other animals that are either housed in or passing through a contaminated area. Infective spores can be transmitted to a susceptible host by direct contact, via contaminated fomites (such as environmental surfaces, bedding, blankets, toys, brushes, lab coats, or human hands), or even by external parasites.

In some cases, such as when medicating cats, it is possible for staff to transmit dermatophytosis mechanically when moving sequentially from one cat to the next giving pills, feeding, or providing other nursing care. These activities can also cause microtrauma to the skin, increasing the likelihood that infection will become established.

Airborne transmission is commonly reported as a concern by shelters and other facilities that house multiple animals. Many questions have arisen about the likelihood of environmental contamination resulting from the travel of spores through heating and cooling ducts. Although airborne transmission of dermatophyte spores is possible via infective spores floating across distances, in most cases, when husbandry and disinfection practices are adequate, airborne transmission is of minimal significance. In the authors' work in a facility at a shelter with a heating and cooling unit similar to that of a home, airborne transmission of spores did not occur. In this facility, infected cats were confined to cages, and caretakers swept floors daily and used detergent to mop floors once or twice weekly. On multiple occasions when the facility was completely filled with infected cats, fungal culture plates

were left open and exposed to the air throughout the facility. In addition, fungal culture plates were placed directly (culture-medium side down) over heating vents to see if spores were being spread through forced air heating vents. All plates were consistently negative even when infective spores could be isolated from areas where contamination was expected (e.g., cages of actively infected cats). However, fungal cultures of the furnace filter were always positive. These results indicate that infected hairs and spores were drawn into the air vents and trapped in the furnace filter, not being blown throughout the facility. This example also suggests that in most shelter situations, dermatophyte transmission can be effectively controlled without providing separate air circulation, provided that adequate treatment is concurrently administered to minimize infectious dose and environmental contamination. However, airborne transmission has been noted by author Moriello in a cattery where the owner used fans to cool cats and circulate air in the isolation room. The potential for airborne transmission should be minimized whenever possible, but large investments of resources for separate air circulation or duct cleaning are probably not warranted unless a particular problem has been demonstrated.

In the authors' experience, transmission in shelters can be reduced by paying rigorous attention to fomite and environmental control. Mechanical cleaning and disinfection at regular intervals substantially lowers the likelihood of environmental contamination. Environmental contamination is greatest in foster homes and shelters, in areas where hair has been allowed to accumulate, or in homes where there are large numbers of infected kittens (Mancianti, Nardoni et al. 2003).

Spores will persist in the environment and remain potentially infectious for weeks to months unless the area is thoroughly cleaned and disinfected, including specific steps to mechanically remove infective material. (See the section on decontamination.)

Increased infectious dose and frequency of exposure increase the likelihood of transmission. Transmission of dermatophytosis is particularly problematic in situations such as shelters and rescue homes when animals are housed together, either in cages or in cage-free environments. Higher turnover shelters, with a constant influx of new, potentially infectious cats, may present a higher risk of introduction and/or greater exposure to a critical mass of infective material, but any time an infectious animal is admitted to a group setting, especially when infection goes unrecognized, infection may be transmitted to others in the population.

## CLINICAL PRESENTATION

Classic lesions of dermatophytosis are usually described as circular areas of alopecia with inflammation and scaling. Those "classic" round hairless lesions gave rise to the initial theory that a worm running in a ring within the skin was causing the lesions, hence the name "ringworm." Many cases of dermatophytosis will present with those classic clinical signs. Many others will not. In addition to the classic presentation, dermatophytosis has a wide variety of presentations.

Dermatophytosis is one of the most pleomorphic skin diseases encountered in veterinary dermatology. Clinical signs in dogs and cats include, but are not limited to, any combination of the following: hair loss, erythema, easily broken hairs, excessive shedding, minimal to marked pruritus, follicular plugging, hyperpigmentation of the skin, hair loss that varies from focal to generalized in severity, otitis externa, ear margin inflammation, pododermatitis, papules and pustules, "feline symmetrical alopecia," mild to severe scaling and crusting, and presentations severe enough to mimic immune mediated skin diseases (see Figures 16.1 to 16.6).

Lesions can be any shape or size, and the degree of inflammation, crusting, and hair loss varies widely. Lesions most often involve some degree of inflammation with or without hair loss. Skin lesions may mimic or be hidden by many other noncontagious, noninfectious skin diseases.

In many cases, subtle lesions may be missed without a careful, complete examination. In other cases, lesions that have the classic appearance may not be due to dermatophytosis at all. While cats with a classic presentation of dermatophytosis are often actually infected with dermatophytes, skin lesions in adult dogs that look like classic ringworm lesions are much more likely to be caused by a bacterial pyoderma or demodicosis rather than dermatophytosis. Skin lesions in puppies are more likely to be a result of dermatophytosis than in adult dogs, but may also be caused by bacterial pyoderma or demodex. Because dermatophytosis can present in so many forms, diagnosis cannot be based solely on the presence of "characteristic" skin lesions, although examination of lesions is an integral part of identification, diagnosis and outbreak response. (Please see the section on diagnosis.)

## DIAGNOSIS

Diagnosis of dermatophytosis in animals within shelters and other animal welfare organizations can be challenging. Decisions about which animals will be able to go to foster care or be made available for adoption are often affected. Because of the infectious potential for humans and animals,

**Figure 16.1.** Puppy with area of hair loss caudal to the ear. This was caused by *M. gypseum* but other differential diagnoses included demodicosis and bacterial infection.

**Figure 16.2.** Hair loss in the preauricular area of a cat. It was initially assumed to be "normal" until the cat was examined with a Wood's lamp, and glowing hairs were found.

**Figure 16.3.** Ear margin crusting due to dermatophytosis. This was caused by a *Trichophyton* spp. infection. Ear margin infections are common presentations of *Trichophyton* spp. infections in the authors' experience.

**Figure 16.4.** Multifocal areas of hair loss on the trunk of a dog caused by a dermatophyte infection. Note that the lesions extend to the head. The most common cause of circular areas of hair loss in an adult dog is bacterial pyoderma; however, it is rare for bacterial pyoderma to involve the face. (Courtesy of Dr. Gail Kunkle.)

early identification and prompt response are essential. A detailed description of the recommended systematic screening process, including specifics of how each diagnostic tool can be effectively used in animal welfare organizations, is provided below.

### Basic diagnostic tools

A meticulous and thorough dermatologic examination is the foundation for appropriate use of all other diagnostics. The diagnostic tools described below must be used as part of an overall screening process that includes a careful, thorough physical examination of the skin and hair coat by a trained observer. Every reasonable effort should be made to obtain a history of the source of the animal, previous housing situation, and prior health problems. Information about the potential for exposure can be very

**Figure 16.5.** Kitten with "common classical" lesions of dermatophytosis in the periocular and muzzle region. The site of this infection is difficult to treat because it is close to the eyes.

**Figure 16.6.** *Microsporum canis* infection on the ear of kitten. The initial clinical signs were ear pruritus. Not only did the ear pinna glow but also the hairs inside the bell of the ear. It is important in these cases to be sure to treat the inside of the ear. Also, note that suspect cats should be handled with gloves.

helpful to identify higher risk animals. After the history and physical examination, the most common and practical diagnostic tools include use of a Wood's lamp, direct microscopic examination of suspect hairs, and fungal culture. Skin biopsy is rarely used, but a biopsy of unusual skin lesions may surprisingly reveal dermatophytosis as the cause, especially when dermatophytosis has not been previously ruled out. Information regarding the use of these tools has been incorporated in the systematic screening process steps described below.

**Diagnostic protocols for preventive management and control: systematic screening process**

The recommended systematic screening process described here consists of coordinated and consistent use of the five basic diagnostic tools: history, visual examination, Wood's lamp examination, direct examination of fluorescing hairs, and fungal culture. A thorough understanding of all five aspects of this screening process is required in order to develop a working protocol for screening, prevention, and treatment in a shelter setting. In some cases, specific staff may be trained to focus on particular steps (e.g., reading fungal culture plates). Use of these five basic diagnostic tools simplifies early recognition and helps guide housing and treatment decisions. This systematic screening process can be used at admission, any important control point, or when responding to an outbreak. (The use of diagnostic tools to monitor treatment is discussed in the section on treatment.)

Screening is crucial at the time of admission to prevent disease transmission. Admission screening provides an opportunity to identify infected, potentially contagious animals, take preventive action, and start treatment promptly when resources allow. Screening for dermatophytosis using this step-by-step process, in the author's experience, adds only a few minutes to admission procedures if the designated area is properly equipped for the screening examination and intake staff have been properly trained. At a minimum, the examination steps of the screening process should be repeated at critical infectious disease control points (such as when moving animals into public areas, group housing, or foster or adoptive homes) in order to identify any lesions or infections that may have been missed or developed since intake. This systematic screening process is also essential as part of an outbreak response plan. Other diagnostics work best in conjunction with information gathered during the screening process to help guide treatment and management decisions.

***Step one: history***

All relevant historical information for each individual animal and group of animals examined should be reviewed. Animals from the same household as infected animals should be treated as highly suspect. Littermates or cage mates of confirmed infected animals should be treated

as infected because of the close exposure and direct contact even if not all members of a litter show clinical signs.

***Step two: visual examination***

Animals should be examined for skin lesions under bright light. A strong, directed examination light greatly helps identify subtle lesions. If this is not available, a strong-beamed flashlight should be available. Sometimes more lesions are found using only the light from a flashlight rather than with overhead lights because the beam is concentrated on one area. Particular attention to the following areas is needed, as these are common sites where lesions are overlooked: muzzle, lips, periocular area, ear margins, skin inside the cone of the ear, digits and nail bed area, abdomen, medial aspects of limbs, and the tail. Staff must be trained to differentiate scars or other quiet, noninflammatory skin lesions from possible dermatophyte lesions. All inflammatory lesions should be noted, even if another obvious cause is identified. As an example, ear mites may cause inflammation in the ear canal and inner pinnae of cats. The infestation or the associated self-trauma may seem like an obvious cause of inflammation or hair loss in and around the ears. However, the ear mite infestation does not rule out concurrent dermatophytosis. In the authors' experience, an ear mite infestation can actually increase the likelihood of dermatophytosis because the associated microtrauma would facilitate development of infection. Fleas have been found to be culture positive and may be one way spores can spread in a shelter. Also, even if there is an obvious cause of an animal's pruritus (e.g., louse infestation), it is important to remember that cats, especially kittens, may have more than one disease present. In addition, this careful visual examination of animals is a valuable way to identify other medical problems.

***Step three: Wood's lamp examination***

The next step is to examine animals with a Wood's lamp for fluorescing hairs. A Wood's lamp is an ultraviolet light with a wavelength of 365 nm. The only veterinary pathogen of importance that can produce fluorescence is *M. canis*. A positive examination allows one to select hairs for microscopic examination. A negative examination does not rule out dermatophytosis.

A plug-in Wood's lamp should be used; in the authors' experience, battery-powered UV lamps rarely give sufficient illumination of appropriate wavelength. Smaller handheld models make examination easier than bulky wands or lamps with built in magnification. If additional magnification is needed, a handheld magnifying glass works nicely.

The lamp needs to warm up for 5 minutes to obtain a stable wavelength. In addition, it takes several minutes for the examiner's eyes to adapt to the light; otherwise, glowing hairs can be missed. The room should be darkened and the lamp held close to the hair coat and skin; the entire body should be examined slowly and carefully to avoid missing any affected areas. When using the Wood's lamp, attention should be focused on the examination of common sites of infection and the frequently overlooked lesion sites.

Fluorescence associated with dermatophytosis is seen at the base of the hairs, near the hair follicle, and not just on the tips of the hairs. Infected hairs fluoresce because the fungus in the hair follicle deposits a metabolite on the hair shaft as it grows. In many cases, it will look as though the whole hair shaft is glowing. The metabolite coating the hair does not make the hairs stick together. In some cases, infected hairs will be broken and only the stubble will glow at the base, very close to the skin.

Fluorescence from infected hairs will most commonly have a bright apple green appearance (see Figure 16.7). During a study conducted by the authors in which cats were examined daily, author Newbury noted that very early fluorescence was blue-white eventually turning apple-green. Other colors are most often artifact. Sebum on the skin, which may or may not be associated with inflammation, will glow a fainter, dull yellow color that is

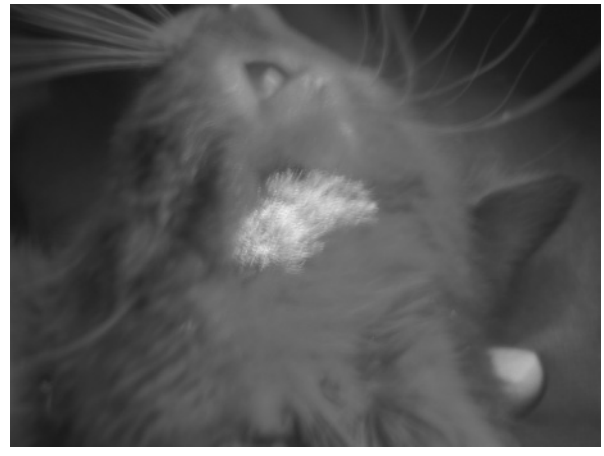


**Figure 16.7.** "Classic" fluorescence of hairs with a Wood's lamp.

not indicative of dermatophyte infection. Doxycycline or terramycin gives a yellow glow when smeared or crusted on the fur and should not be confused with infection. It is not possible to brush off the fluorescing substance if it is caused by dermatophyte infection. If there is any uncertainty, gently pluck hairs and examine the roots for fluorescence.

If thick crusting is present, it is important to gently remove the crusts and look for infected hairs because crusting may obscure them. In many cases, broken hairs underlying the crusts will be Wood's positive while the crusting is not.

It is commonly cited that approximately 50% of cases of dermatophytosis caused by *M. canis* will fluoresce with a Wood's lamp. Only *M. canis* produces the metabolite that creates the fluorescent glow, and not every strain of *M. canis* will produce the metabolite. However, in the authors' experience of examining hundreds of infected cats presenting to animal shelters, careful examination reveals glowing hairs on the vast majority of infected, lesional cats. In many cases, cats that appear to be nonlesional on visual examination will have fluorescing hairs that suggest preclinical infection or help to identify subtle lesions that were missed on initial examination.

***Step four: direct examination of fluorescing hairs***

Direct microscopic examination of fluorescing hairs is a quick and simple method of obtaining an immediate diagnosis of *M. canis* dermatophytosis when a Wood's lamp examination is positive. Interpretation of the microscopic examination takes some training and practice but is not difficult to master. When staff are initially training to evaluate direct examinations, each direct exam procedure should be confirmed by a fungal culture until an acceptable accuracy rate has been achieved. When performed properly, Wood's lamp and direct examinations of hairs are very cost effective and may save the cost and time of performing a fungal culture. There is one area of caution: If any legal circumstances surround the case, a fungal culture should always be performed even if the Wood's lamp and direct examination of hairs confirms the diagnosis. Fungal cultures are considered the "gold standard." In addition, if legal issues are present, it is prudent to take both gross photographs of the animal and photographs of any microscopic examinations. This is easily performed using a digital camera through the microscope lens.

A Wood's lamp, microscope, and a curved tip hemostat are the only required equipment. Supplies needed are glass microscope slides, microscope coverslips, and mineral oil as a suspension solution. Clearing agents such as potassium hydroxide (KOH) can be used instead of mineral oil. Clearing agents cause the background material to swell, rendering hairs and spores more refractile. Caution should be used with KOH solution because KOH can be caustic to the animals' skin and microscope lenses. In the authors' experience, mineral oil is a good, readily available, benign alternative for use in shelter settings.

Procedure:

1. Place a drop of mineral oil on a microscope slide, which should be set aside where it will not be easily knocked to the floor but still close to the examination area.
2. Pluck a few glowing hairs, following the direction of growth to ensure the hair root is retrieved for examination. This process requires at least one assistant to hold the animal and the Wood's lamp while the other person identifies and carefully plucks the glowing hairs. The Wood's lamp can be used to carefully examine the hairs in the hemostat before they are placed in the suspension solution on the slide.
3. Place the hairs on the drop of mineral oil or KOH on the microscope slide and place the coverslip on the slide. Again, the Wood's lamp can be used to confirm that glowing hairs are present on the slide (see Figure 16.8).
4. Place the slide on the microscope stage and examine the slide on 4X magnification with the microscope light off and the room lights dim. Hold the Wood's lamp next to the microscope stage, directed toward the slide. This process highlights glowing hairs so they can be placed within view through the eyepiece and lens (see

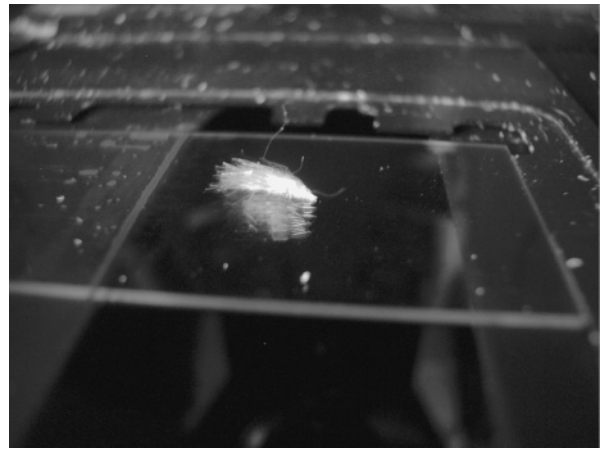


**Figure 16.8.** Glowing hairs on a glass slide.

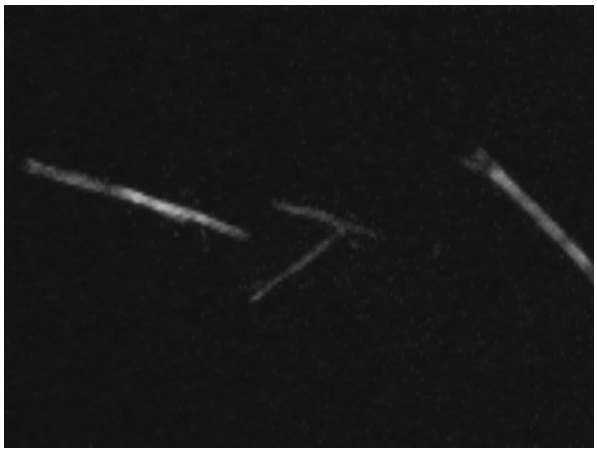


**Figure 16.9.** The Wood's lamp can be used to locate hairs on glass microscope slide to facilitate examination.

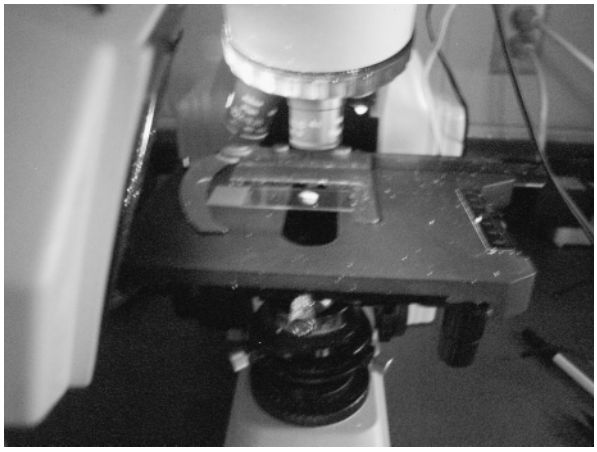


**Figure 16.10.** Note the glowing hairs on the glass slide on the microscope stage. This allows the specimen to be positioned beneath the lens.

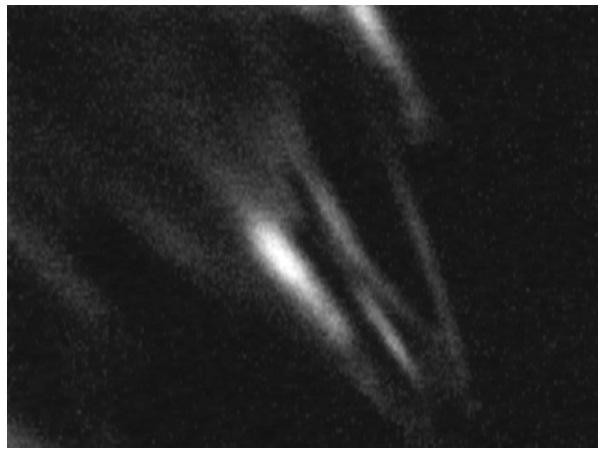


**Figure 16.11.** Glowing hairs seen through the microscope lens. In this situation the Wood's lamp is being held to the side of the stage. Once the hairs are located, the Wood's lamp is not needed and the slide can be examined normally.

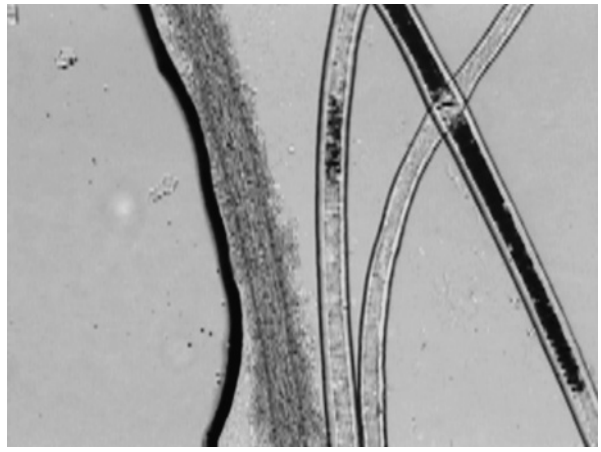


**Figure 16.12.** Normal and affected hairs are present. Note that the infected hairs are lighter in color, wider, and more filamentous in appearance (10X).

Figures 16.9 and 16.10). Once the fluorescing hair can be seen through the eyepiece, the Wood's lamp is no longer needed, and both the microscope and room lights can be turned on (see Figure 16.11).

5. Infected hairs are wider, irregular, and appear more filamentous than normal hairs at low power (see Figure 16.12). At higher magnification, cuffs of refractile spores and hyphae can be seen. A 10X lens is usually sufficient to confirm infected hairs, but a 40X magnification lens may be needed to confirm the presence of ectothrix spores. Oil immersion is not needed. Again, the examiner is looking for stacks or rows of small beads on either side of the hair shaft and/or hair shafts that appear swollen, broken, filled in, or frayed in appearance compared to normal hair shaft structure (see Figure 16.13).

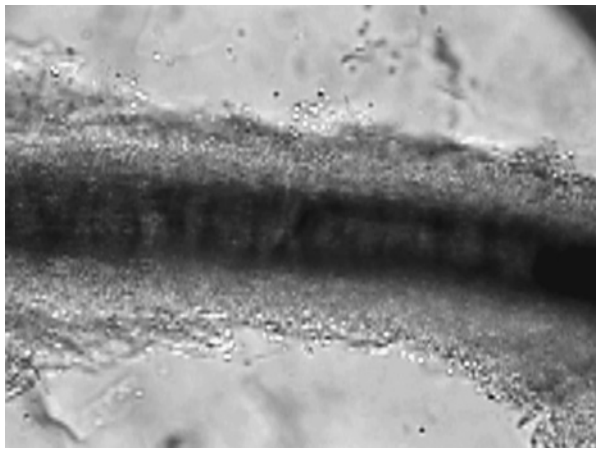


**Figure 16.13.** Cuffs of ectothrix spores seen around an infected hair (40X).

*Please note: After completion of the first four diagnostic steps described above (history, visual exam, Wood's lamp, and direct exam), an initial risk assessment and response should be made. Please see below for risk evaluation and response information.*

***Step five: fungal cultures***

*Prioritized or comprehensive fungal culture screening*

Fungal culture of individual animals is the best method for diagnosis of dermatophytosis. In shelter settings, fungal cultures may be used to screen all animals at intake in a comprehensive fashion regardless of whether lesions are detected, or prioritized fungal cultures may be performed only on animals identified as suspect via the first four steps of the systematic evaluation described above.

Comprehensive fungal culture screening is the most cautious approach and offers a safety net to identify any infectious animals that may be missed at intake. Fungal cultures are essential for diagnosing or ruling out dermatophytosis in animals with lesions that do not fluoresce. Screening all cats by culture also ensures that fomite carriers or "dust mop" cats are identified. Sample collection must be done in conjunction with effective intake screening, as described in steps 1–4 above, to identify suspect cats. Even if all cats are going to be cultured, screening at the time of admission is crucial to identify suspect animals and allow preventative planning while awaiting results. In an ongoing clinical project, comprehensive fungal culture screening of all cats at intake has effectively controlled dermatophytosis in a shelter (Newbury, Verbrugge et al. 2005a). For this project, a team of volunteers was trained to read fungal culture plates. This screening added an additional cost of approximately $2 per cat. Fungal culture plates were purchased in bulk through a medical laboratory supply company. In a previous study, fungal culture plates were prepared by volunteers in a research laboratory for a cost of approximately $0.75 each.

Resource investment and waiting time for fungal culture growth and identification, in addition to other factors, may make comprehensive fungal culture screening a difficult or impractical tool in many high turnover animal welfare organizations. Animals may instead be prioritized for cultures based on potential risk. Even if comprehensive fungal culture screening is not possible, careful intake evaluation using the diagnostic tools described above will identify the vast majority of suspect and infectious cats at the point of entry, and greatly reduce infectious risk from dermatophytosis. Prioritized fungal culture screening supports this process by confirming or ruling out infections in positive or suspect animals and is required to diagnose infection for animals with lesions that do not fluoresce. Cautious, prioritized use of fungal cultures to confirm or rule out infections in animals identified as suspect through the first four steps of the systematic process will not identify every infected cat with subtle lesions, or "dust mop" cats, but will contribute to risk reduction.

Fungal culture screening for all animals is probably most important for shelters or organizations that commonly house animals in group or community settings, house animals in rooms that are difficult to disinfect, send animals to private temporary homes for foster care, or have intake staff that cannot reliably screen for lesions. If screening prior to entry is required for admittance to certain rooms or foster homes, advance planning and culture setup help reduce animal waiting time while cultures grow. Animals should be sampled and cultures inoculated as soon as possible so that the waiting time to review the results is minimized. For animal welfare organizations that plan to screen only some animals by fungal culture, similar priority should be given to animals that are likely to be made available for adoption, housed in group settings, or housed in foster homes or other public places (e.g., satellite adoption centers). The highest priority for fungal culture should be given to cats that have some type of inflammatory skin condition or hair coat abnormality.

*Sample collection and preparation technique*

A new toothbrush must be used for each animal. New toothbrushes in their original packaging are mycologically

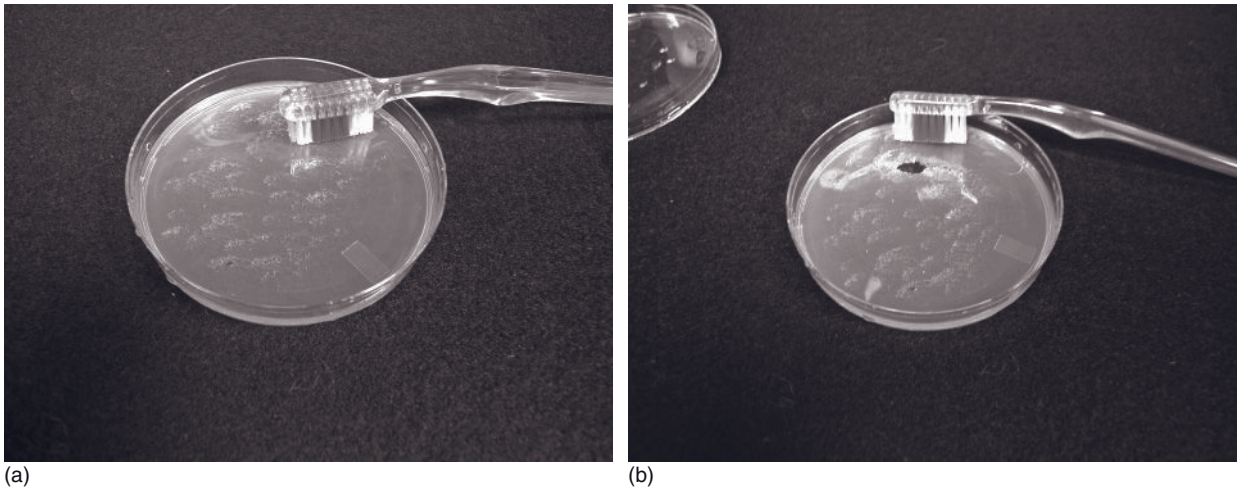
sterile. Individually wrapped toothbrushes can be purchased in bulk for as little as $0.05 to $0.10 from hotel supply companies. For cats, vigorously brush the toothbrush over the cat's entire body until hairs are visible in the bristles of the brush. If lesions were identified, the area with the lesions should be brushed last in order to avoid spreading spores throughout the hair coat. For dogs, sample lesional areas only unless there are no lesions and the dog is only being sampled because there has been known or suspect exposure. Fungal cultures from a dog's entire hair coat are commonly overgrown rapidly by contaminant organisms; watch these cultures carefully and be prepared to reculture dogs if needed.

Next, inoculate the fungal culture plate. Gently stab the toothbrush bristles onto the surface of a fungal culture plate. Cover the entire plate and use a consistent system each time to help support the pathogen scoring system described below. Start in the center of the plate, working outward, and cover the entire surface of the plate. It is important to embed the bristles in the plate so that the spores are transferred, but not so hard as to lift off the medium [see Figure 16.14(a) and (b)].

If inoculation just after collection is not possible or practical, toothbrushes may be placed into plastic sandwich type bags and then double bagged into a sealable Ziplock™ type bag. If cultures are inoculated at a later time, this must be done in a clean area that is easily disinfected. Careful identification of toothbrush samples cannot be emphasized enough; preprinted labels with blank spaces for ID numbers and dates can be printed. If a sample is highly suspect, this should also be noted on the bag. When inoculating many samples, inoculate high-risk samples last to prevent cross-contamination. Always wear gloves when handling samples and discard used toothbrushes into trash that is sealed.

Culture plates can be difficult to mark. Plates are often wet if they have been refrigerated; wipe the plates dry prior to writing on the plate. If using petri dishes, mark identification and dates on the bottom of the plate and not the cover to ensure that there are no mix-ups in the laboratory. Culture plates should always be marked with the animal's identification information (name or booking number), the date sampled, and the date inoculated.

Author Moriello completed a series of laboratory tests to determine if one type of fungal culture plate was superior to another with respect to time to sporulation. Dermatophyte test medium (DTM) from six commercial companies was tested, including flat trays, jars, and "micromedium plates" (In-Tray) (see Figure 16.15). Some of the medium advertised "rapid sporulation." Multiple replicates of each DTM brand were tested on several strains of *M. canis*, *M. gypseum*,and *Trichophyton* spp. In addition, the effects of light exposure and temperature on time to growth were tested (Verbrugge, Kesting, Moriello 2007). Based on these studies, the author reported the following observations: With the exception of one fungal culture medium that did not perform as well as the others, there was no advantage of one brand over another with respect to time to growth. The smaller the surface area, the more difficult it was to identify growth and pathogens;



(a) (b)

**Figure 16.14.** (a) Toothbrush cultures being inoculated on a plate. (b) Toothbrush culture pressed too hard into the medium pulling the medium away from the plate.

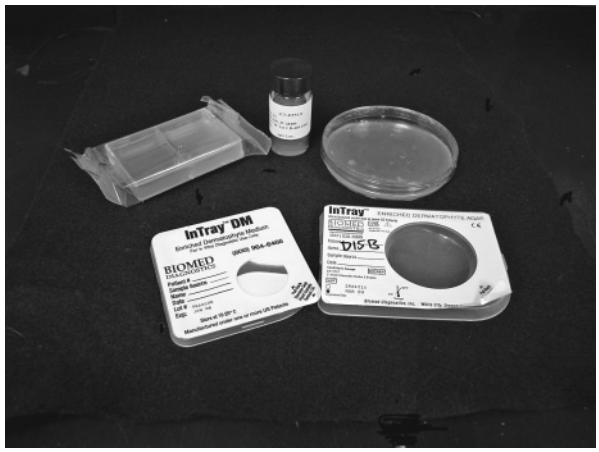



**Figure 16.15.** Various commercial fungal culture mediums. Small-volume and small-size plates are not recommended.

once the surface turned red the usefulness of the color indicator was lost. In addition, the smaller-surface-area culture plates often dried up before the pathogen grew. Light had no effect on time to growth. The most important factor affecting growth was temperature. Cultures sporulated best when grown between 27 °C and 30 °C. The authors recommend the purchase of DTM plates that have a large flat surface area that is easily inoculated. Jars should be avoided because it is difficult to inoculate the surface and sample colonies. Furthermore, bacteria and yeast often swarm over the surface.

*Animal holding time for culture results*

Fungal cultures take time to incubate and grow before pathogens can be identified or the fungal culture can be deemed negative. When legal or required holding periods are similar to the time needed for culture incubation and identification, or when animals are generally expected to stay for long periods of time, waiting for fungal cultures has little impact on length of stay or level of crowding. However, if holding all cultured cats leads to increased holding time, this could have negative consequences for individual and population health. Balance must be found between the risks of exposure to other illness, stress, and the contribution to shelter crowding caused by holding animals for extended periods of time as compared to the risk of potentially moving an infectious animal through the system. There is no feeling of success in ruling out dermatophytosis in an animal that has developed clinical signs of respiratory disease while waiting for culture results. In many cases, if adequate examination screening is provided as described above, the risks from holding animals while waiting for culture results are greater than the risk of missing a dermatophyte infection, unless there is a reason for increased suspicion. Even when using a comprehensive screening protocol, only truly suspect cats need be held in isolation while awaiting culture results. Animals without suspect lesions may be moved forward to adoption even before results are available. If animals are identified as culture positive after leaving the shelter, the new owners or foster parents can be promptly notified.

Performing fungal cultures in-house or in a lab that will give regular progress reports on cultures (online) instead of just reporting results once cultures are finalized will shorten the waiting time dramatically. The authors are strong advocates of performing fungal cultures in-house as this is a skill that is not difficult to learn. In-house management of fungal cultures also significantly reduces costs associated with a screening program and permits daily monitoring of cultures. Additionally, community practitioners may want to consider developing in-house culture systems as a service to clients, including shelters and rescue groups. When data were retrospectively examined, over 95% of positive fungal cultures were identified between days 10 and 14 postinoculation. Suspect growth was almost always noted in these cultures by day 7 postinoculation. In animals with severe infections, cultures were often finalized within 7 days. Cultures that are not suspect by day 7 or positive by day 10 are unlikely to be *M. canis*. Although not foolproof, in most cases, when cultures are kept warm and evaluated in house, decisions can be made by day 10 of fungal culture growth. Some of the *Trichophyton* species grow more slowly; however, these are of lesser clinical significance in shelters.

*Fungal culture processing, pathogen identification, and reporting culture results*

Typically, cultures are reported as "culture positive" with a pathogen being identified or "culture negative." In the authors' experience, this is an inadequate amount of information for designing and implementing an effective management program that minimizes infectious risk while maximizing life-saving opportunities for infected or suspect cats. The number of colony-forming units on the plate is very important to decision making when interpreting culture results, just as it is when interpreting results from bacterial cultures. The authors use a semiquantitative system of reporting fungal culture results that was developed in the laboratory of author Moriello for treatment

studies on cats with dermatophytosis (Deboer and Moriello 1995; Moriello and Deboer 1995; Deboer, Moriello et al. 2003; Moriello, DeBoer et al. 2004b).

The following is a summary of how the authors' colony-forming unit (CFU) scoring system is used to report fungal culture results, interpret the results in light of physical findings (lesions or not), and make treatment decisions. In order to make the language of CFU more "user friendly" for staff, the authors' refer to this as a Pathogen score or P-score. In order to use this system, DTM culture petri dish plates or similar large flat-bottom plates need to be used. The following steps describe an in-house system for inoculating, incubating, and reading fungal culture plates. Tables 16.1 to 16.5 summarize "practice tips" from the authors on setting up an in house system and reading cultures.

1. Plates must be adequately identified in a systematic manner. Plates should have the animal's ID/name, date of culture (DC) and date of inoculation (DI). Other information such as age, sex, hair length, and source can be entered on the ID label and entered into a spreadsheet for identification of trends for infection in a particular organization or community.
2. Recording both the DC and the DI is important when plates are not immediately inoculated at the time of sampling. If the time between the DC and DI is long and the culture is positive in a cat that was not suspect, it may explain an unexpected outbreak in a previously unaffected facility.
3. Samples are inoculated onto DTM. Petri-dish-style plates are ideal because of ease for evaluating cultures, inoculation, and sampling. Purchased DTM plates work nicely.
4. The key to early and fast identification of pathogens is a daily examination of fungal culture plates. Daily checks of culture plates allow for early identification of suspects as well as prompt diagnosis. Contrary to popular belief, this is NOT a time-consuming activity. One hundred or more plates can be quickly scanned in less than 7 to 10 minutes. Any small white colonies with a red ring of color change around them as they are growing should be considered suspect. Often the colonies will be too young for definitive identification, but once a plate is identified as "suspect," it can be observed more closely. A system of communication to quickly report positives to the shelter is essential. Positives found on daily review of cultures should be reported immediately to allow for rapid intervention.
5. Plates are held for 21 days and "officially" read out on day 7, day 10, day 14, and day 21. Day 10 is an especially useful time point since most positive cultures show suspect growth by this date.
6. Identification of suspect colonies is not difficult. When using DTM plates, the colonies to look for on daily checks are white or buff colored with a red ring around them as they are growing. *The red color change is not diagnostic for a dermatophyte*, but it "flags" colonies that need to be microscopically identified and are suspect. Pigmented colonies are not pathogens and can be ignored. Pale or white colonies with no red ring of color can be ignored.
7. If a suspect colony is identified and it is too small or too soon to sample, it can be circled with a marker so it can be observed.
8. If plates become rapidly overgrown, they are useless for screening and the animal should be recultured. Plates that are rapidly overgrown with contaminants in the first 7 to 10 days are of concern because rapid overgrowth of the plate may result in a false negative or uninterpretable fungal culture. This is seen most commonly in kittens and stray cats. These cats should be recultured as soon as overgrowth is noted, especially if a suspect lesion was noted. In addition, once the entire surface of the plate turns red, the usefulness of the red color change is lost.
9. A shorthand system for recording culture results was developed by the authors to allow data to be easily entered into a spreadsheet. In addition, this short hand system is easy for lay staff to understand.
   - "NG": no growth; it is not uncommon for cats to have no growth on their fungal culture plate due to their fastidious grooming skills.
   - "C": contaminant growth.
   - "HC": heavy growth of contaminants; it signals the staff to reculture the cat. This may not be cost effective in every shelter, but minimally cats with skin lesions or kittens with HC should be recultured.
   - "S": suspect growth; many culture positive plates will have S growth in the first week. Identified pathogens are listed by name. If a pathogen (e.g., *M. canis*) is found, the number of CFUs is counted and recorded. The significance of the latter will be discussed in detail below.
10. Plates should be held for 21 days unless a pathogen is identified sooner, the plate turns completely red, or the plate is overgrown. In the authors' experience, when cultures are held in a warm room or incubator

(approximately 80 °F to 86 °F or 27 °C to 30 °C), most *M. canis* positive cats have been identified within 7 to 14 days of culture. Plates are held for 21 days because *Trichophyton* spp. dermatophytes take longer to grow. From a practical perspective, if cats are culture negative for *M. canis* after 10 to 14 days, they can be considered "culture negative" at the time of admission. Holding cultures, not animals, for the full 21 days is still recommended since that is considered a standard culture incubation time by reference laboratories; individuals infected by less common and less contagious species may still benefit from identification and treatment.

*The pathogen scoring system: using colony-forming units to aid in management and treatment decisions*

The determination of the number of CFUs is an important aid to guide treatment. Simple reporting of a fungal culture as positive or negative may not be very helpful as a component of a management plan because no distinction can be made between fomite carriers or "dust mop" cats and truly infected cats. Incorporating the number of CFUs found on the plate via a Pathogen score ("P-score") helps further guide diagnosis and treatment decisions.

If a culture has been properly obtained and inoculated, the number of CFUs per plate generally corresponds to the severity of infection for cultured animals or degree of contamination when evaluating cultures of the environment. The system is very simple: P-1 score = 1–4 CFU/plate, P-2 score = 5–9 CFU/plate, and P-3 score = 10 or more CFU/plate [see Figures 16.16(a), (b), and (c)]. Shelter staff can readily learn the significance of a P-1, P-2, or P-3 cat even if they are not involved or trained in the laboratory aspect of fungal cultures. This information, along with the presence or absence of lesions at the time of culture, can help speed identification of culture-positive cats and differentiate fomite carriers from those who are truly infected. When the laboratory alerts the shelter that a positive animal has been identified, the P-score would ideally be included. The animal should be immediately reexamined for lesions. Most commercial laboratories do not currently report CFUs or P-scores and only report one finalized result after 3 weeks, making in-house culture evaluation even more important for shelters.

P-1 cats: These cats fall into two categories. The first are cats that are fomite carriers. These cats are lesion free and Wood's lamp negative when carefully reexamined. In the authors' clinical studies, on reculture 1 to 2 weeks following an initial screening culture, all nonlesional P-1 and P-2 cats were negative without any intervening treatment. These cats probably groomed the spores from their coats. It is also possible that the initial sampling process

**Table 16.1.** Practice tips for collecting samples and data.

- Package culture material into "culture kits" that have a toothbrush inside a plastic bag with a preprinted label attached.
- Use preprinted labels that contain all of the information the organization wants documented for the culture. Commercial sheets of labels are sold that contain instructions on how to format the page. Below is a sample label used by the authors. Note that it asks for three key pieces of information: Wood's lamp status, presence or absence of lesions, and whether or not lesions are suspected of being caused by dermatophytosis.

ID #_____ Date: _____
Sex: M F N Hairlength: S M L
Age: Kitten Juvenile (6–12 months) Adult
Wood's Positive? Y N Any Lesions? Y N
Do you suspect lesions from ringworm? Y N

- Set up an Excel sheet for recording data and making treatment plans as detailed in Tables 16.2 and 16.3. This allows for sorting of data to look for trends. An Excel spreadsheet allows for rapid searching of culture results from a particular animal via booking number. Macros can be made that make it easy for lay staff to enter data in a consistent manner. For example, a macro can be set up to change the status of a culture from "pending" to final once a pathogen has been identified or a week 3 culture has been entered. It can also be set up to report culture results as negative when the final outcome is no growth or contaminant growth.

**Table 16.2.** Sample Excel Sheet for Recording Data.

| Cat ID | Results | FINAL | DC | DI | Lesions | Wk 1 | Wk 2 | Day 10 | Wk 3 | P-score | Age | Sex | Hair | Source | Other comments |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|

Cat ID: Identification number or name.
Results: List as "Negative" if the final culture results are no growth or contaminants. List the pathogen if "Positive."
FINAL: This indicates whether or not the culture is finalized. Cultures are held for 21 days but can be finalized sooner if a pathogen is isolated or if the plate is overgrown.
DC: Date cultured.
DI: Date inoculated.
Lesions: List as Y or N. These are the data reported by the intake staff.
Wk 1, Wk 2, Day 10, Wk 3: Cultures are examined daily for evidence of growth, but it is only practical to "officially" read cultures once a week. However, if a daily scan of the plates reveals a suspect colony that should be examined sooner it is obviously appropriate to read out the culture on that day. Day 10 is a very useful data point as explained in the text.
P-Score: This is P-1 (1–4 CFU/plate), P-2 (5–9 CFU/plate), and P-3 (>10 CFU/plate). This semiquantitative reporting system coupled with the pathogen identification is very useful in decision making.

NG: no growth
C: Contaminant
HC: Heavy overgrowth of contaminants
S: Suspect

**Table 16.3.** Sample of an "ACTION PLAN" for culture-positive animals.

Develop an ACTION PLAN sheet for dealing with positive culture results. Below is an example of one used by the authors. This action plan lists the cats' ID numbers, location, pathogen, P-score, who will examine the animal, and the clinical findings plus a decision as to whether or not to move the cat to the treatment annex or treat as a "dip and go." These Action Plan sheets can be kept in an Excel file as record of the "response" for each animal.

| 7/1/05 Shelter Name | | | Culture Results | | | Action Plan for Evaluating NEW POSITIVES | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| New Positives | | | | | | | | | | |
| Cat ID # | Name | Loc | Organism | P-Score | Examiner | Exam? (Y/N) | Wood's (Y/N) | Lesions? (Y/N) | To Annex? (Y/N) | Needs in-house Cult Dip/Go |
| | | | | | | | | | | |
| | | | | | | | | | | |
| | | | | | | | | | | |
| | | | | | | | | | | |
| | | | | | | | | | | |

**Table 16.4.** Organizing large numbers of culture plates.

Use plastic containers to store fungal culture plates (Figure T1).
Use one container per week for Week 1, Week 2, and Week 3 plates. As plates are read each week they are moved from one container to the next.
Each fungal culture plate should be placed in a plastic sandwich bag. This will minimize the chance of cross-contamination and minimize problems with media mites. An inexpensive digital fish tank thermometer can be used in the area where the cultures are kept to monitor temperature (Figure T2).
Media mites should be suspected if the media rapidly turns red and "tracks" are seen on the plate. If this happens, this is a "laboratory emergency." The entire laboratory area should be thoroughly cleaned and the area sprayed with a pyrethrin flea spray immediately. Media mites are a common environmental mite found associated with foodstuffs (Figure T3).
An inexpensive incubator can be made by using a small thermal cooler and inserting a fish tank heater into the drain hole. The "correct" temperature can be monitored with the thermometer.

Key Points for Identification of Pathogens:
- Cytological identification is mandatory to identify a pathogen.
- Pathogens are never heavily pigmented either gross or microscopically.
- Pathogens are ALWAYS pale, and a red color change in the medium occurs as they are growing if cultured on DTM.

For help with microscopic identification see www.doctorfungus.org or *Applied Cytology: Microscopic Examination of Fungal Cultures* at www.clinicansbrief.com, April 2008.


**Figure T1.** Box for cultures.

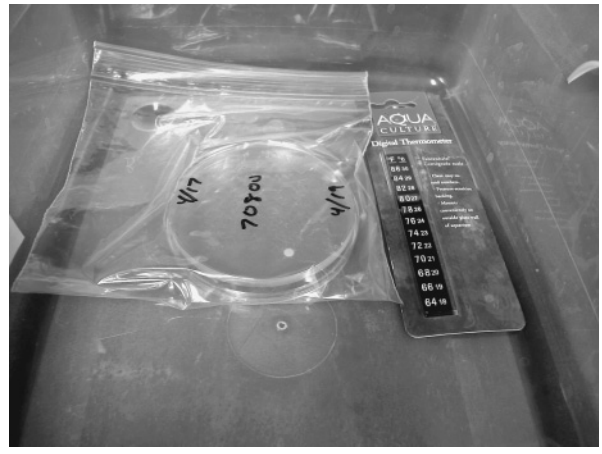



**Figure T2.** Culture in bag with thermometer.

**Figure T3.** Plate showing media mite growth.

**Table 16.5.** Quick guide to reading fungal culture plates.

**Equipment:** Clear or frosted acetate tape, new methylene blue stain or lactophenol cotton blue stain, glass microscope slides, microscope coverslips, forceps, clear nail polish

**Making Slide Mounts:**

- The most common stain used is lactophenol cotton blue stain because it kills the organism; however, new methylene blue stain works equally well but it does not kill the spores.
- Put a drop of stain on a glass microscope slide.
- It is easiest to work with clear acetate tape, but frosted tape can be used too.
  - Using clear tape, touch the target colony and then place it STICKY SIDE DOWN directly over the drop of stain on the glass slide.
  - With frosted tape, touch the target colony and then place the tape STICKY SIDE UP over the drop of stain on the glass side.
  - Place a second drop of stain over the sample, then cover with a coverslip.
  - Wipe off any excess stain the seeps through the edges of the "sandwich mount."
  - Wipe off any stain that touches the microscope lens IMMEDIATELY or it will damage the lens.
- If necessary, the sides of the slide can be sealed with clear nail polish, making a permanent mount.

**Rapid Culture Plate Sorting Method (Figure T4):**

- LOOK FOR THE RED AND WHITE!
  - Possible pathogens will be pale with a red color change developing in them as they grow [Figure 16.16(a) and 16.16(b)].
  - Circle these for sampling.
- IGNORE THE FOLLOWING (Figure T5)
  - Grossly pigmented colonies regardless of whether or not a red color change in the medium occurs.
  - Pale colonies WITHOUT a red color change in the medium as they grow.
- SPECIAL THINGS TO NOTE
  - Toothbrush samples from cats with severe infections can sometimes grow very rapidly and the entire plate will rapidly turn red. The colonies all look the same [Figure 16.16(c)].
  - Yeast or bacterial contamination will turn the plate red very quickly.
- GROSSLY OVERGROWN PLATES
  - Once the entire surface of the plate turns red, the usefulness of the color indicator is gone and all suspect colonies need to be examined. *Microsporum canis* colony (arrow). Glistening colonies are yeast or bacteria (Figure T6).
  - Once the plate is overgrown it is often difficult or impossible to find a pathogen. Reculture the animal.


**Figure T4.** This photograph shows a large number of cultures prior to being sorted for reading. Using the Quick Sort tips in Table 16.4, these plates were examined and sorted, data were recorded, and target colonies were examined in less than 1 hour.

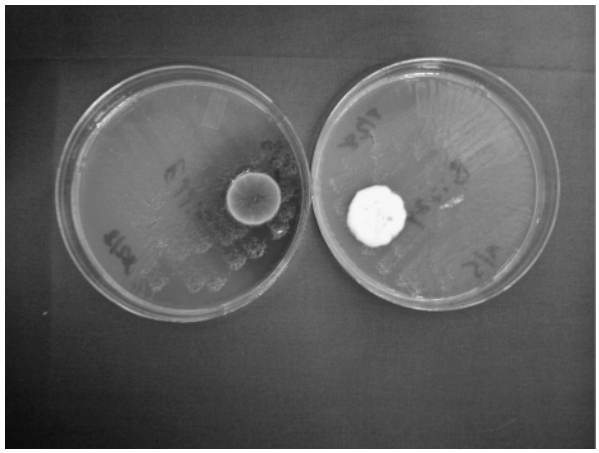


**Figure T5.** This picture demonstrates how useful the "look for the red and white" is in sorting plates. One plate shows a red color change around the darkly pigmented colony. This is not a pathogen regardless of the "red color change" because the colony is grossly pigmented. The other plate shows a white colony. This is not a suspect pathogen because it does not have a red color change in the surrounding medium.

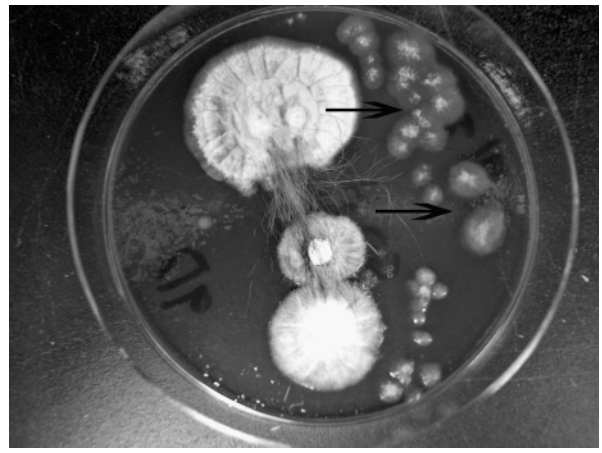


**Figure T6.** This picture shows a fungal culture plate where the entire surface is red. Close inspection of the picture shows four different grossly appearing pale colonies. Only the small white colonies (arrow) are pathogens, but all four colonies need microscopic examination to determine this.

**Microscopic Examination of Slides:**

- Scan slide at 4X and 10X to find areas where there are both hyphae and spores.
- Ignore microscopic colonies that are pigmented (Figure T7). Pathogens are hyaline (pale) and have septate hyphae.
- *Microsporum* genus is "boat shaped."
- *Microsporum gypseum* rapidly produces large number of macroconidia compared to *M. canis* (Figure T8). These are thin walled and the edges are smooth.
  - *Microsporum canis* colonies are tapered at the ends. Close examination reveals the surface is rough, and there is a "knob" at one end [(Figures T9(a) and (b)].
  - Odd variations of the shape of *M. canis* can be seen, especially in cultures from shelter animals (Figure T10).
  - Young *M. canis* cultures can show few macrocondia or odd features. One macrocondia has the typical shape with thick walls but no subdivisions. The other shows a developing macrocondia "fingerlike" projection (Figure T11).
- *Trichophyton* spp.
  - These colonies are often slow to grow.
  - Microscopically there are large numbers of round microconidia and rare macroconidia.
  - Large numbers of microconidia, rare large marcoconidia and spiral hyphae are the key characteristics (Figure T12).

For more help on microscopic identification of fungal cultures, see www.doctorfungus.com

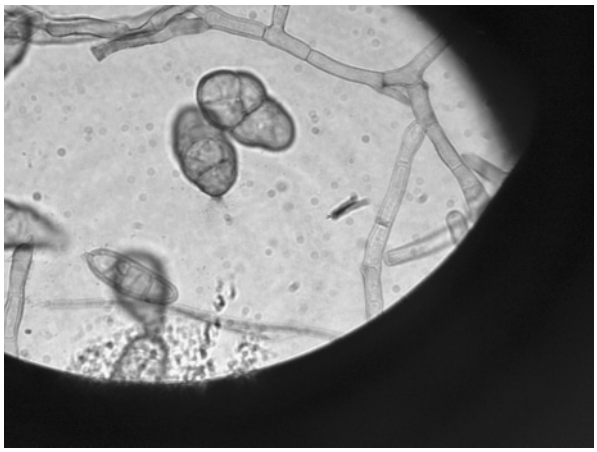


**Figure T7.** Microscopic examination of suspect colony. Note the dark pigmentation of the spores; this is a contaminant and not a pathogen (100X).

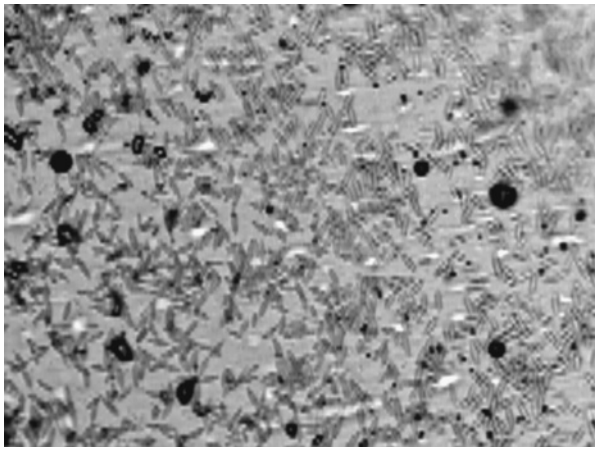
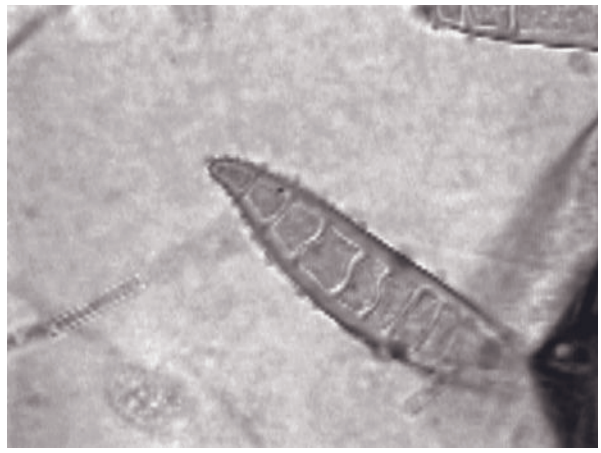


**Figure T8.** Microscopic view of tape preparation of *M. gypseum*. Note the large numbers of macroconidia.



(a)

(b)

**Figure T9 (a), (b).** Microscopic examination of macroconidia of *M. canis*. Note the thick walls, rough surface, and "knob" at the end. The number of subdivisions is less reliable.

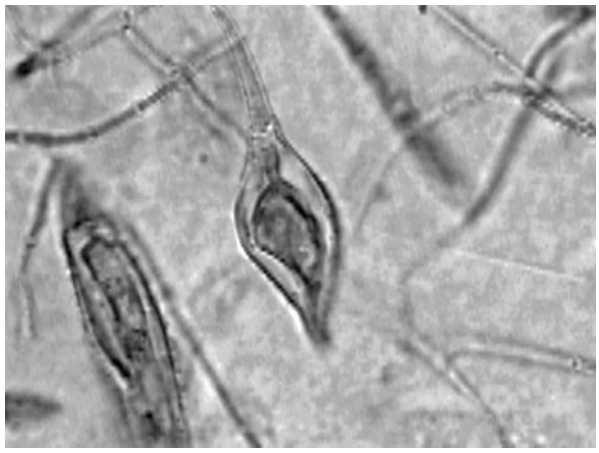


**Figure T10.** *M. canis distorum*. Note the distorted form of *M. canis*. This strain is isolated more commonly from shelter cats than from pet cats in author Moriello's experience.

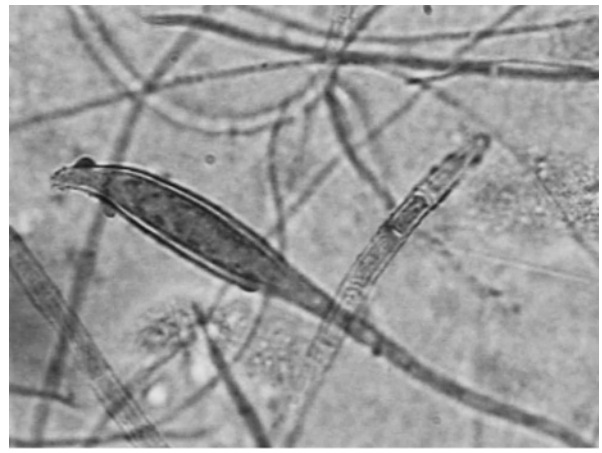


**Figure T11.** Microscopic view of a young culture of *M. canis* showing common features of developing macroconidia. The first is the development of a boat-shaped spore with thick walls and no subdivisions. The second is the development of thick figure like projections that will eventually develop into mature macroconidia.

**Figure T12.** Microscopic view of a *Trichophyton* spp. Note the large numbers of macroconidia and spiral hyphae.

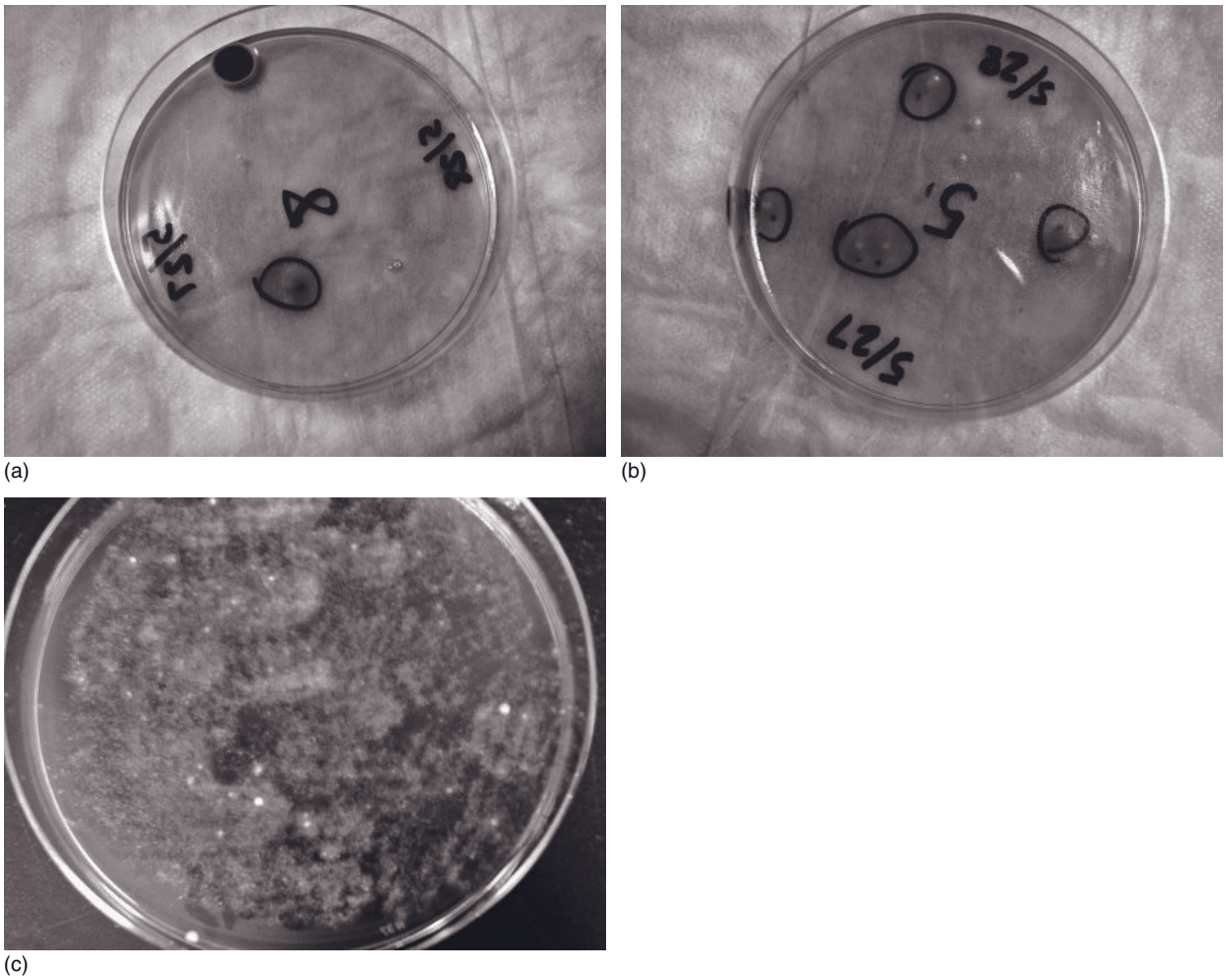


**Figure 16.16.** (a)–(c) This series of pictures is representative of a P-1, P-2, and P-3 fungal culture scored plate. Note that many of the colonies are circled. These colonies were identified as "suspect" colonies during daily examinations; circled colonies alert staff to pay special attention the colonies.

of brushing vigorously with a toothbrush may have removed the majority of the spores. These cats are recultured as a safeguard and treated with one topical application of lime sulfur. These animals are referred to as "dip and go" cats.

The second group of P-1 cats are those that were incubating infections at the time of admission. Lesions in these cats may have been very subtle and overlooked at admission. At the time of reexamination, lesions can still be very subtle. Closely inspect the face, hairs in the bell of the ear, ear margin, chin, lips, and the ear canal. Wood's lamp examinations may or may not be positive depending upon the strain of *M. canis*; *Trichophyton* infections do not fluoresce. Animals whose lesions are identified after reexamination because of positive culture results should be treated as truly infected.

P-2 cats: These cats most commonly fall into the "infected group" but may be fomite carriers. The major difference with these cats is that if lesions are found they tend to be more noticeable, and often shelter staff report these lesions almost simultaneously with the reporting of the fungal culture. When reexamining a cat with a "positive P-2" culture, the index of suspicion for a missed lesion should be higher than for a P-1. As with P-1 cats, those

cats that are lesion free on a very careful second examination may be dipped once in lime sulfur and placed for adoption as usual, while those with lesions must be treated as truly infected.

P-3 cats: These cats should be immediately removed from the general population regardless of whether or not lesions are identified. In general, when thorough intake examinations have been performed, these cats have already been identified as suspect. Lesions are often found in difficult-to-find locations on reexamination of P-3 cats that were initially reported as nonlesional. P-3 cats are considered a risk to others and should not be housed in the general population. A small number of cats with P-3 cultures have been "dust mop" cats. These cats usually had a history of coming from a contaminated environment and often did not groom well or had a thick or long coat. When treatment data were examined, these cats generally were found to be become culture negative very rapidly, often after the first week of treatment.

The P-scoring system is also very useful when monitoring treatment. Animals under treatment should be cultured once weekly with P-scores reported. As animals cure, the P-score becomes lower. (Please also see section on treatment.)

The P-score system and CFU counts are also helpful when reporting the results of environmental cultures. Environmental cultures help to identify contaminated areas so that cleaning may be targeted and focused. Reporting a site as culture positive, with some indication of the level of contamination, is very helpful to staff charged with the task of cleaning and disinfecting the site. The P-score system has resulted in acceptance and improved compliance by shelter staff and volunteers. (Please also see section on disinfection.)

## INITIAL RISK EVALUATION AND RESPONSE

As part of a systematic screening process, an initial risk evaluation and response must be made for animals as they are examined and screened. Information to consider for this initial response is collected during the first four steps of the screening process described previously. The initial response should be made at intake, or after an initial evaluation if screening is happening at a time other than intake (e.g., during an outbreak). The initial response plan should be developed *prior to incubation or confirmation of fungal culture results*. Positive, suspect, and high-risk animals should be clearly identified to staff, volunteers, and the public.

A prompt, definitive response should be planned for animals with a positive diagnosis. When a thorough systematic examination has been performed, only those animals with suspect inflammatory lesions need be considered suspect while awaiting further results. An initial response plan for suspect animals or high-risk animals should include, at the very least, separation or isolation from the general population as described below. Isolation is ideal but where it is not possible, adequate separation practices must be put in place pending a definitive diagnosis. (Please see section on isolation and separation for more detailed information.) Suspect animals must be clearly identified as a zoonotic health risk for staff, volunteers, and the public. If suspicion is high and treatment would be initiated if a positive result were confirmed, starting treatment while awaiting results may help to shorten the length of stay while also reducing the risks of transmission.

### Isolation and separation

Positive, suspect, and high-risk animals should be isolated from the general population as soon as possible. Ideally, isolation includes a physically separated housing ward, including cleaning and care staff designated to work in that area only, and separate equipment. Newer facilities with designated isolation areas may be designed with separate air circulation. This can be extremely costly and the investment may not be warranted for dermatophytosis when resources are limited. In older facilities, separate air circulation may simply not be possible. Instead, strict adherence to minimizing fomite transmission and environmental contamination is likely to bring a higher reward. (Please see section on transmission.) Because of the potential for zoonosis, animal attendants assigned to work in isolation areas should be required to wear protective clothing including gowns, gloves, shoe covers, and caps. All materials located in the isolation ward should be dedicated to that ward and cannot be moved to other areas for use. In shelters where separate staffing for an isolation area can be a problem, staff who work in multiple areas should work in isolation wards only after working in other areas. They must always completely change all garments before moving to other areas. Staff who work in isolation areas should *not* subsequently work with high-risk animals, especially juveniles. All shelter staff should change clothes before going home at the end of the day. The risk of carrying infected spores home is minimal if staff members adhere to these guidelines. Environmental cultures of homes of shelter staff were all negative in one study conducted by the authors.

Within the isolation area, "clean" and "dirty" areas should be defined. These need not be physically separate rooms or wards, but clear visual and practical separation

**Figure 16.17.** In this facility, red tape is used on the floor to designate a "dirty" area.

**Figure 16.18.** To control environmental contamination, a conscious effort has been made in this facility to minimize clutter and keep food, bedding, and other materials in closed containers.

should be maintained (e.g., by colored tape or painted lines). Areas in the immediate vicinity of the housing units should be defined as "dirty" (see Figure 16.17). In-contact bedding, litter, and food should be bagged within the "dirty" area in an effort to control environmental contamination with spores. Infected animals should remain within the "dirty" area.

Protective garments worn within the dirty area should remain in that area except when bagged and removed to go directly for laundering. A clean area should be designated to provide a safe area for supply storage, food preparation, or other activities (see Figure 16.18). When creating an isolation area for treatment of cats with dermatophytosis, a separate contained section within the isolation area for cats with both dermatophytosis and upper respiratory infections may be beneficial.

When immediate physical isolation is not possible, temporary separation of suspect or positive animals in a defined section may be sufficient to help control the spread of disease and avoid depopulation. For temporary separation to be effective, it must be clearly indicated that there is a possibility that the animals housed within may be infectious to humans and to other animals; specific precautionary care procedures must be in place, and staff must be carefully trained and comply well with control procedures. A "dirty" zone should be defined surrounding these housing units (see Figure 16.17). Housing suspect or high-risk animals near to or intermingled with uninfected animals or in areas where uninfected animals are commonly housed risks exposing the group as a whole, as well as in-contact humans. It may also contaminate the environment with infective spores that are difficult to eliminate. Treating suspect animals with topical lime sulfur reduces the infectious risk by reducing the number of spores being shed into the environment. It should be emphasized that fungal culture-positive animals should be housed in this area only temporarily while awaiting a definitive plan. Suspect animals should be held in this type of separation area only long enough to confirm results of diagnostic testing. In general, incomplete physical separation for the duration of treatment should not be considered a sufficient precaution against disease transmission. Isolation is strongly recommended. (Please see the sections on treatment and housing below.)

## TREATMENT

Treatment studies performed by the authors have used the following protocol: itraconazole orally, given once daily for 21 days in combination with twice-weekly topical lime sulfur treatments. This protocol is recommended for treatment of dermatophytosis in shelter cats and dogs. After completion of the itraconazole, topical treatment should be continued until the animal has reached a mycological cure. (See the section on verification of cure.)

### Topical treatment

Miconazole, enilconazole, and lime sulfur are consistently identified as the most effective antifungal agents against *M. canis* when tested in vitro (Moriello and Verbrugge

2007; Moriello DeBoer et al. 2004b). Enilconazole is an effective topical treatment, but it is not available in the U.S. and is labeled for use in dogs and horses only. Miconazole alone or in combination with chlorhexidine has been shown to be equally as sporocidal when compared to lime sulfur in vitro (Moriello and Verbrugge 2007). In vivo, however, although it did help to hasten a cure, it was not as effective as lime sulfur (Newbury and Moriello, unpublished results). Several other topical products that have been used to treat dermatophytosis include povodine iodine, Captan, chlorhexidine shampoos, and sodium hypochlorite (bleach) (Deboer and Moriello 1995; Moriello, DeBoer et al. 2004b; White–Weithers and Medleau 1995). These products are ineffective or otherwise problematic and should not be used.

Lime sulfur is an effective topical treatment (both in vivo and in vitro) both to eliminate infection and to reduce shedding of spores that lead to environmental contamination (Newbury, Moriello et al. 2007; Moriello and Verbrugge 2007; Moriello, DeBoer et al. 2004b). Diluted and applied properly, lime sulfur has been consistently shown to be inexpensive, available, safe and effective; in the authors' opinion, it is the best choice to use as a topical component of a shelter treatment protocol.

Commercial lime sulfur products have been found to be equivalent to one another in efficacy, including commercial products with masking agents for the odor. Although lime sulfur tends to be malodorous and may stain certain fabrics, the odor disappears fairly quickly and should not be considered a deterrent to its use. Because animal welfare organizations should prioritize treatments that minimize animal care days and the potential for contagion or environmental contamination, the application of topical lime sulfur any time an animal welfare organization is going to treat animals for dermatophytosis is strongly recommended by the authors.

### *Application of lime sulfur dip*

Lime sulfur should be used at a dilution of 8 ounces to a gallon of warm water (the higher dilution of the two given most commonly on the commercially available products). When mixing the product, it is important to put 8 ounces of the concentrated lime sulfur in the mixing container FIRST and then add the warm water. Although the term "dip" is commonly used, it is not necessary to immerse the animal in the solution. Instead, the solution should be applied topically to the animal's coat. A simple, inexpensive and portable "dip" sink can be made using a laundry sink that is set up to drain into a bucket (see Figure 16.19).

Do not pre-wet the cat. The properly diluted lime sulfur solution is easily applied with a gallon or half-gallon garden rose sprayer (see Figure 16.20). The nozzle of the sprayer should be held very close to the cat's skin so the spray flows over it like a gentle shower. Often, the solution will bead up and initially roll off the hair coat. The solution

**Figure 16.19.** This is a portable treatment station. It comprises a plastic utility sink with a bucket beneath to collect dip. This station is portable, allowing cats to be treated in areas with improved ventilation so that the odor of lime sulfur in a facility is minimized. No plumbing is required.


**Figure 16.20.** Portable rose garden sprayer used to apply topical treatment solutions.

**Figure 16.21.** Application of lime sulfur to a cat using a garden sprayer. Note that the nozzle is held very close to the cat's skin, in effect "showering" the cat rather than spraying.

should coat the entire hair, reaching the base of the hairs. The cat must be soaked to the skin in order for the treatment to be effective. Cloths should be used to gently sponge the dip around the face and inside the ears, on the nose, etc. These areas are most important as the lesions found there tend to be the most difficult to resolve. Surprisingly, cats tolerate this application method much better than being soaked in towels or drenched with watering cans (see Figure 16.21). It is also a very cost-effective method of application. Fractious cats can be sprayed through a wire carrier. An attempt should still be made to keep the spray close to the cat's skin because cats seem most tolerant of the treatment when the nozzle is close enough so the liquid does not spray out at them or make a hissing noise. Do not rinse off the solution. Both rinsing and pre-wetting will cause dilution and could lead to less efficacious treatment.

Lime sulfur is safe to apply topically, even for very young kittens and nursing queens. The authors have treated kittens as young as 4 weeks of age; hypothermia is a concern in young kittens. When lactating queens are treated, teats should be wiped clean of the solution after dipping. Animals must be kept warm while they are wet. This is especially true of kittens and puppies or other animals that may have some difficulty with thermoregulation. Adverse effects are uncommon. During the authors' experience treating hundreds of cats, they have not found it to be necessary to put E-collars on the cats after treatment. The only time oral ulcers were seen in cats treated with lime sulfur was when cats had concurrent severe upper respiratory disease. The nature of the oral ulcers was consistent for a cat with upper respiratory infection, not an irritant reaction to the lime sulfur dip.

#### *Clipping the hair coat prior to topical treatment*

Clipping the hair prior to topical treatment has often been recommended. The authors have not found that clipping is necessary for short- or medium-haired cats. However, for a long-haired cat with a high pathogen score or a cat that appears unkempt, matted, unwilling, or unable to groom, the cat's entire body should be clipped with a #7 or #10 blade (not a surgical blade). Clipping can also be helpful for cats whose coats get clumpy or matted from the dipping process. Caution is advised: hair must be contained in order to avoid environmental contamination that is likely to result from clipping. The environment must be carefully and thoroughly cleaned and disinfected after clipping an infected cat.

Clipping should be done in a designated and controlled area that will not be used to house other animals, using clippers dedicated only to that purpose. Be sure to alternate between two clippers or take breaks and allow the clippers to cool to avoid causing thermal injuries; deep thermal burns can result from overheated clippers. In some cases, these burns may not become apparent until several days after clipping when an escar begins to form.

### Systemic treatment

Dermatophytosis is an intrafollicular disease. Systemic treatment is responsible for shortening the course of infection by reaching the fungus within the follicles. Itraconazole is the drug recommended for systemic treatment of dermatophytosis in shelter cats. In this chapter, all treatment information is based on the combination protocol using itraconazole for systemic treatment and lime sulfur topically. As part of the recommended combination topical and systemic treatment protocol, itraconazole is given orally, once daily at 5–10 mg/kg for 21 days.

Although many drugs and alternate schedules for systemic treatment are available, they are not recommended as the treatment of first choice in a shelter environment. In some cases, this is due to potential problems associated with alternate drugs. In other cases, the drug has been shown to be safe and effective, but the treatment regimen

has not been documented to cure cats reliably after two negative fungal cultures, as itraconazole has when used in the manner described above.

### *Itraconazole*

Itraconazole is currently the most commonly used drug for the treatment of dermatophytosis in both dogs and cats. Itraconazole, a triazole antifungal that accumulates and persists in hair and epidermis, can be used to treat dermatophytosis in a daily or pulse-therapy protocol, or a short-term treatment protocol when coupled with effective topical therapy.

In practice, the most common pulse therapy protocol is a week-on/week-off protocol (5–10 mg/kg) until cured; this is how the drug is licensed for use in Europe. Pulse therapy may require a 14-day daily dose-loading period to achieve appropriate therapeutic levels prior to initiating pulse therapy. Pulse therapy is not ideal for animals that are ill or have limited body fat because the drug is stored in body fat. For stressed, thin, or debilitated animals, 21 to 28 days of daily therapy coupled with topical therapy is recommended.

Itraconazole is available in 100-mg capsules that can be divided into smaller doses manually and repackaged in empty gelatin capsules or mixed with a small amount of food; alternatively, one can use the oral solution. Toxicity problems are rare, but occasionally animals may be inappetant. If this is persistent, the drug should be stopped, and liver enzymes should be checked.

As a note of caution, the authors are aware that some owners have obtained bulk itraconazole powder inexpensively in foreign countries; anecdotally, this treatment often fails. There have also been many separate reports of shelters using compounded itraconazole having problems with unexpectedly long times to cure that resolve when a change is made to the brand name product. Itraconazole requires careful formulation in appropriate vehicles in order to ensure its absorption, and use of any material other than the "official" approved products is not recommended, as it may result in treatment failure.

### *Fluconazole or terbinafine*

Fluconazole has received some recent attention as an alternative to itraconazole. Fluconazole has not been used as extensively as itraconazole and there is limited information about it in shelter cats. Author Moriello treated two groups of cats with fluconazole, one group at 5 mg/kg and another at 10 mg/kg. Cats treated at 10 mg/kg cured faster than those given the lower dose. If used, 10 mg/kg orally once daily is recommended until studies determine that lower doses can be used effectively. This drug is available as a generic.

Oral terbinafine (Lamisil®, Novartis) is another treatment option. The drug is very expensive and, in a shelter situation, currently appears to offer no advantages over itraconazole. Cats with *M. canis* infections documented to be resistant to azole drugs (rare!) can sometimes be treated successfully with terbinafine. Various doses have been used (10–40 mg/kg, once daily, orally, but cats treated at the higher end of the dosage range cure significantly faster). It is recommended that liver enzymes be monitored; this drug may elevate alanine aminotransferase (ALT) in cats, although no clinical toxicity is necessarily seen. Recently the drug has been shown to have residual activity in the skin similar to that of itraconazole and may be useful for pulse therapy (Foust, Marsella et al. 2007).

### *Griseofulvin*

Griseofulvin is not recommended for use in shelter cats because it has a narrow margin of safety and may require a longer time to cure dermatophytosis. In one study, griseofulvin therapy alone required a mean of 70 days of treatment to cure experimentally infected cats, compared to 56 days of treatment with itraconazole (Moriello and Deboer 1995). It is highly teratogenic and must not be used in pregnant animals. It can cause bone marrow suppression in cats; this side effect is severe, unpredictable, and not dependent upon the dose, breed, or length of therapy. To use it safely, white blood cell counts are recommended pretherapy and biweekly thereafter; this makes the drug cost-ineffective. Cats should be tested for feline leukemia virus (FeLV) and feline immunodeficiency virus (FIV) infection before use because there may be an association between infection and these adverse reactions. Although the authors do not recommend griseofulvin use in cats, it may be less expensive per dose than itraconazole when treating large dogs. Over the full course of treatment, though, considering all costs and times to cure, itraconazole may still be the more cost-effective treatment. The dose is dependent upon the formulation (microsize versus ultramicrosize). Absorption is enhanced with a fatty meal. Vomiting, diarrhea, and inappetence are common adverse effects. This drug is increasingly difficult to obtain.

### *Ketoconazole*

The true clinical efficacy of ketoconazole in dermatophytosis is unknown; there are limited anecdotal reports on its efficacy. Some strains of *M. canis* are resistant to ketoconazole. The drug is not well tolerated and has a narrow therapeutic margin in cats and so is not recommended for

use in this species. The use of ketoconazole as a systemic antifungal is best reserved for infections in dogs, particularly *Trichophyton*. Ketoconazole has become inexpensive over the past few years, but other than this, it has no advantage over other drugs in routine cases of dermatophytosis.

### *Lufenuron*

A published case caused speculation that lufenuron (Program®, Novartis) may be beneficial in treatment of feline or canine dermatophytosis (Ben-Ziony and Arzi 2000). Although there have been anecdotal reports of "cures" with lufenuron treatment, controlled studies have consistently shown that lufenuron is ineffective as both a treatment and preventive drug (Deboer, Moriello et al. 2003; Moriello, DeBoer et al. 2004a). Controlled studies using feline experimental infection models and natural exposure models consistently found that lufenuron did not prevent initial establishment of dermatophytosis in cats, did not result in faster cure once the infections were established, and was not synergistic with terbinafine. Lufenuron is NOT recommended for the treatment of dermatophytosis.

## Verification of cure

Successful treatment of dermatophytosis must be verified through repeated fungal cultures. Resolution of some of the clinical signs, including reduction of scaling, erythema, and pruritus, etc., may be seen within 2 weeks of treatment, with hair growth in clipped cats starting shortly thereafter. When effective and recommended treatment protocols are used, mycologic cure may actually precede hair regrowth. However, when times to cure are longer or lesions are mild, cats may appear clinically cured before mycologic cure has been achieved; if released into the general population or adopted out prematurely, these cats may continue to spread infection. This is particularly likely if an ineffective treatment is used. Mycologic cure has been defined most frequently by three consecutive negative cultures at weekly intervals; cultures should be held for 21 days. Treatment monitoring should start after 1 week of treatment. In a shelter treatment trial performed by the authors, it was found that, using the recommended combination treatment protocol, no cats became positive again after two consecutive negative weekly fungal cultures (Newbury, Moriello et al. 2007). Cats were held in the treatment facility and received continued topical treatment until the fungal cultures were finalized. Using two negative cultures rather than three to define mycologic cure shortened waiting time for release to adoption with no negative consequences; however, this has only been demonstrated to be reliable when using the combined lime sulfur and systemic itraconazole treatment described above. Using any other treatment still requires three negative cultures to be reasonably certain of cure.

As treatment progresses, P-score values are expected to drop rapidly. Fluorescence of hairs on Wood's examination becomes more and more faint. In fact, monitoring animals under treatment with a Wood's examination can be an effective means of verifying that topical treatment is being correctly applied. Most commonly, in the authors' experience, topical solution is not applied carefully enough to the face, probably because of caution around the eyes and nose for the animal's sake, thereby leaving brightly fluorescing, minimally treated hairs in these areas that contribute to prolonged times to cure. Showing these hairs to treatment staff who were applying topical treatment resulted in more attention being paid to these areas, which dramatically changed the amount of fluorescence seen on reexamination.

In the treatment trial discussed above, the mean number of days of treatment required for cure was $18.4 \pm 9.5$ Standard Error of Mean (SEM) (range 10–49 days). Cats with more severe infections required longer therapy. These time-to-cure data do not include an additional 21 days required to finalize the fungal cultures in order to demonstrate cure. In general, an average treatment and housing time of at least 1 month should be estimated when considering an animal for treatment. The time it takes to cure and release an animal back into the population for adoption may be an especially important consideration for kittens. In some cases, kittens that undergo treatment may be young adults by the time mycologic cure has been finalized. Culturing animals weekly during treatment helps reduce total treatment time by limiting the time when a cat has actually reached mycologic cure but no culture has been taken.

## Treatment housing

Infected or suspect animals should not be permitted to roam freely throughout any part of the facility. Animals should be treated for dermatophytosis in an isolation area, as described above, in small family groups, bonded pairs, or housed individually. Housing animals individually or separating into small groups of two or three kittens helps to prevent cross-infection and potential cross-contamination with spores that could confound the fungal culture process, and allows better monitoring of general health and behavior. Animals should be released for adoption only when all cohoused animals have reached mycologic cure, so housing fewer animals per housing unit may also

prevent delays in release. Since animals are likely to be housed and treated for at least 1 month without opportunity to roam freely, housing size and quality should be adequate for an extended stay. Enrichment should be provided, including toys and regular positive interactions with humans. Staff or volunteers must be trained to follow isolation protocols for enrichment as well as treatment. Bedding may be used for animals under treatment but should be changed daily, identified as contaminated, and kept contained when transported dirty to the laundry area. In the treatment trial referenced above, all cats had bedding in their cages. Bedding was removed and washed each day in the shelter's standard washing machine and heated dryer. Although separate laundry facilities were not used, bedding was washed and dried separately from all other shelter laundry.

***Environmental decontamination: cleaning, disinfection, and preventive planning***

Environments can become contaminated with naturally infective hairs and spores. Studies have shown that the most cost effective and consistently effective disinfectants are sodium hypochlorite and enilconazole (Clinafarm™) at dilutions of 1:10 and 1:100, respectively. Clinafarm™ is available as a spray or a fogger and is most commonly used in poultry farms; it is usually found in agriculture supply stores. A commonly used disinfectant labeled for use against ringworm—potassium peroxymonosulphate (Trifectant™)—and the quaternary ammonium products are ineffective, as is chlorhexidine (Moriello, DeBoer et al. 2004b). Heat (50 °C) will inactivate *Trichophyton* spores better than repeat chilling and freezing. The same is most likely true for *M. canis* as author Moriello left toothbrush cultures from severely infected cats in a car on a sunny day only to find that all cultures were negative. Numerous studies have looked at the effect of UV light on various aspects of the growth of dermatophytes; however, data from these studies cannot be translated to practical application because the studies used the mycelial (culture plate) state and not naturally infective material.

The key to minimizing contamination and effectively decontaminating the environment is a combination of daily mechanical removal of infective material thorough sweeping or "Swiffering" of the floor and mechanical scrubbing with a detergent (see Figure 16.22). Disinfection of the environment should be performed ONLY after a thorough cleaning; its purpose is to kill any remaining spores that were not mechanically removed. Although use of bleach is recommended for disinfection, mechanical removal is the cornerstone of environmental cleanup. Even


**Figure 16.22.** The use of commercial Swiffer™ cloths is an excellent way to mechanically remove spores from surfaces. These cloths readily collect spores, dirt, and dust. The only negative is that they are expensive to use. Shelters can consider requesting donations of this product on their "wish list."

though bleach has been shown to inactivate spores in vitro, achieving equivalent or sufficient contact for an appropriate duration of time is difficult or impossible on many surfaces. Spores may linger in cracks and crevices. In the authors' experience, enthusiastically cleaning an area three times in a row, followed each time by disinfection with bleach, often results in negative environmental cultures as long as there are no items in the room that could not be effectively cleaned.

In general, it is very difficult to effectively decontaminate areas that contain soft, carpeted or upholstered furniture, and other unwashable items. Lime sulfur solution has been used in combination with direct sunlight to disinfect cat trees from community rooms (cat trees were placed outside because light filtered through windows will not be effective). Cat trees were cultured until two negative cultures were obtained. Steam cleaning and vacuuming may be helpful in those cases, but difficult items should be carefully evaluated for contamination after cleaning since they may remain a source of exposure for humans and animals. Discarding these contaminated items is often safer and more cost effective.

Environmental cultures of rooms and furniture are an extremely helpful tool to target cleaning efforts and verify successful decontamination. Environmental cultures can be particularly helpful to verify that difficult-to-clean areas such as group rooms or foster homes have been suffi-


**Figure 16.23.** "Swiffer™ kit" for environmental sampling.

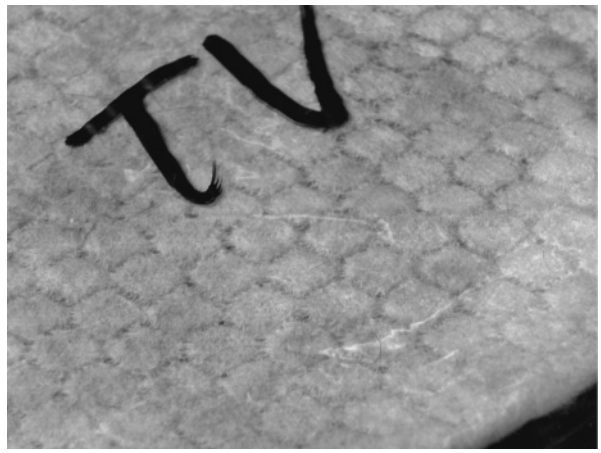


**Figure 16.24.** Swiffer™ should be wiped over the target area until visibly soiled. The soiled side is then pressed onto the surface of a fungal culture plate to inoculate the sample.

ciently decontaminated and are safe enough to admit new animals. They may also be helpful prior to investing in expensive procedures such as cleaning of ductwork; cultures may reveal that such procedures are unnecessary. Cultures can be obtained by using clean Swiffers™ to sample the environment, identify contamination, and verify decontamination (Heinrich, Newbury et al. 2005). A sheet of Swiffer™ is cut into four sections in a clean area and placed in a resealable plastic bag (see Figure 16.23).

Several locations from each potentially contaminated area or room should be sampled, pains being taken to include locations frequented by infected animals or where hair or dust is likely to accumulate. Swiffer™ samples should be wiped over an area until visibly soiled (see Figure 16.24). Items that may be particularly difficult to disinfect should also be sampled. Swiffer™ sections can then be used to inoculate fungal culture media by pressing them firmly onto the fungal culture plate. Fabric-covered furniture is often easier to culture using a toothbrush. The P-score system described previously can be used to evaluate relative levels of contamination in each area.

Preventive room design should include plastic or vinyl furniture that can be easily washed or hosed down if needed, combined with soft, removable, washable bedding, and disposable items such as cardboard or a simple log to be used as a scratching post. Walls, floors, cages, and kennels should be smooth, in good repair and easily sanitized. Cracked walls and baseboards create many opportunities for spores to collect and evade efforts at disinfection. Preventive management should include performing physical examinations, Wood's lamp and/or direct examination screening, and/or fungal cultures prior to admitting animals to difficult-to-clean areas such as community rooms or foster homes; regular monitoring of animals housed in those areas for possible late development of lesions; and regular, thorough cleaning and removal of hair from the environment. Because stress and lack of normal grooming are important risk factors for dermatophyte infection, low-stress housing that facilitates normal behavioral expression is also helpful. There are no controlled studies on whether or not exposure to the outside is beneficial or not, but it is commonly observed in bovine practice that calves with dermatophytosis allowed to go outside in the sunshine recover faster than calves housed indoors. Management and housing issues and their impact on treatment of dermatophtysois is an area of shelter medicine in need of further investigation. (See Chapter 2 on wellness.)

## OUTBREAK MANAGEMENT AND RESPONSE

Successful management of dermatophytosis must be a continual preventive process, using the systematic screening procedures and environmental prevention practices described in this chapter. When outbreaks do occur, the same systematic screening process guides diagnosis, separation, and treatment decisions as well as environmental clean-up.

The first step is often answering the question, "Is this an outbreak?" It is difficult to define what number of cases or which particular situations may constitute an outbreak. Anytime in-shelter transmission is occurring, some type of intervention and organized response is necessary to assess the number of animals affected and disrupt further spread. Outbreaks are far more common in shelter cats than shelter dogs, but they can affect either or both species as well as in-contact humans.

A step-by-step process is recommended using the basic tools described previously for screening. When an outbreak is suspected, all potentially exposed animals should be screened and cultured. Every effort must be made to allocate appropriate resources to accomplish this. Evaluating or responding to an outbreak or potential outbreak without comprehensive screening of all at-risk animals will make resolution unlikely and may result in unnecessary treatment or removal from the population. In some cases, inadequate training or insufficient diagnostics may lead to unnecessary euthanasia. Outbreak response is time consuming, emotionally draining, and costly for any organization. Attempting to respond without using all the tools available will virtually ensure the need for another response in a short period.

It is equally important to recognize that outbreak responses must be followed by diligent prevention practices. Otherwise, the cycle may begin again almost immediately after the previous outbreak is resolved when another unrecognized yet infected animal enters the facility.

When responding to an outbreak or suspected outbreak of dermatophytosis:

1. Clearly identify all known cases and remove, isolate, or separate infected animals from the general population.
2. Assess potential for exposure for each animal or group of animals by mapping the location and movement of known cases in and out of each shelter area as well as the movement and routines of staff and volunteers. In some cases, exposure may have been confined to a particular area or ward. In many cases, when the number of known cases is relatively high, all cats in the shelter must be considered potentially exposed.
3. Systematically screen all at-risk animals as described previously in this chapter using the five basic diagnostic steps.
4. Discontinue the movement of exposed animals while awaiting culture results.
5. Plan an initial response for each animal based on results of the first four steps of the systematic screening process.
6. Establish a "clean break" between unexposed animals who are just entering the shelter and those who may have been exposed. Create separate housing areas for the exposed and unexposed groups. If possible, have separate staff care for each area and do not handle animals in the "clean" area after handling animals in the exposed group. At a minimum, ensure separate protective garments, gloves, and equipment are available when handling exposed and unexposed cats.
7. Perform environmental clean-up as described previously.
8. Assess culture results as they become available, using culture results to guide treatment and other animal movement decisions as described previously.

## CONSIDERATIONS FOR ADOPTION

Dermatophytosis is a zoonotic disease. (See Chapter 23 on zoonosis). Not everyone who is exposed to the disease will become infected and develop clinical lesions. Although it is most likely to affect the immune-compromised, elderly, infants, and very young children, disease can occur in immune-competent adults as well. Animals infected with dermatophytes should not be adopted out until they have been treated and a mycological cure has been verified as described above. High-risk, exposed, or in-contact animals, or animals with any type of suspicious skin lesions should never be adopted to members of the at-risk categories identified above. On the other hand, animals who have been treated and achieved a confirmed mycologic cure pose no greater risk to adopters than any other shelter animal. In fact, since they have been so thoroughly monitored, the risk they pose to adopters is likely to be even lower.

## SUMMARY

Unlike many infectious diseases encountered in a shelter setting, dermatophytosis is a treatable, curable disease that has no associated long-term sequelae. In fact, left untreated, many cases will eventually clear up on their own in healthy, stress-free cats. Yet, because of the potential for contagion and zoonosis, infection may be life threatening for the individual shelter animal carrying the infection as well as damaging to the entire organization. The preventive management practices described in this chapter have demonstrated that it is possible to effectively control dermatophytosis in a shelter setting. While treatment of infec-

tion may not be a viable option for every animal welfare organization, planning and training make it possible to avoid situations that put large numbers of animals, shelter workers, and the public at risk.

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# 17
# Ectoparasites

*Karen A. Moriello, Sandra Newbury, and Alison Diesel*

## INTRODUCTION

Cutaneous ectoparasites cause common and contagious diseases in shelter animals. It is important to always consider parasites when evaluating animals with skin disease. This chapter is divided into three sections.

The first section contains a discussion of "point of care" diagnostic tests for parasites.

The second contains a "most important facts" discussion of parasites that cause significant problems in shelters. Parasites selected for discussion include those that are commonly encountered or highly contagious, have the highest potential to affect the health of shelter animals, and/or can transmit diseases to other animals or people (zoonosis). A brief discussion of nonparasitic insect-associated conditions often encountered in individual animals that necessitate immediate treatment or recognition (e.g., bites of venomous insects, mosquito bite hypersensitivity, etc.) is included. The reader is referred to parasitology or dermatology textbooks for detailed descriptions of parasitic diseases of small animals (Scott, Miller, Griffin 2001). Table 17.1 contains a list of common ectoparasites of shelter animals.

The third section focuses on protocols for the treatment or control of parasites in a shelter situation. The purpose of this section is to present treatment options or suggestions that have been successful in shelter situations. Finally, it cannot be stressed enough that no parasiticidal agent is 100% effective. Many animals, even those surrendered from homes, will present with existing infestations. It is time and cost effective to treat all animals for parasites as part of the intake process to reduce the risk of spread throughout the shelter. Safe combination therapies are recommended to minimize relapses, subclinical infestations, etc. It is strongly recommended that ectoparasite treatment protocols be circulated to local veterinarians in the shelter's area or upon request. This will allow optimum follow-up treatment of adopted pets. Appendix 17.1 contains a list of ectoparasiticides.

## PROCEDURES FOR PERFORMING COMMON DIAGNOSTIC TESTS FOR ECTOPARASITES

The following is a brief summary of proper technique and/or usefulness of point of care diagnostic tests for ectoparasites that could be performed in a shelter. Detailed procedures are provided in Tables 17.2, 17.3, and 17.4 for performing key diagnostic tests. Not described are skin biopsy techniques, skin cytology, and allergy testing as they are less likely to be commonly performed in a shelter- or population-based practice. Excellent descriptions of these procedures can be found in many dermatology textbooks and the recommended resources (Jackson 2001).

### Visual examination with or without magnification

Good lighting is extremely important when examining the skin of animals. A simple strong-beam flashlight will often suffice. Visual examination can reveal the presence of fleas, stick-tight fleas, ticks, lice, breathing pores of *Cuterebra*, *Otodectes* mites (usually requires magnification), and myiasis.

### Flea combing and visual inspection of debris

A fine-tooth plastic or metal comb can be used to find fleas, flea excreta, ticks, lice, louse egg sacs or *Cheyletiella* mites attached to hairs, *Cheyletiella* mites, and fur mites. Examination of this material is enhanced with magnification. Flea excreta can often be found with this technique and can be discriminated from other debris by wetting the brown-black debris with water. Flea excreta is "C" shaped and composed of digested blood. It dissolves when wet, leaving a red-brown color. Flea combs are more successful

**Table 17.1.** Commonly encountered ectoparasites in shelter animals.

| Parasite | Common Name/Condition | Species Affected | Zoonotic Potential | Major Clinical Sign | Distribution |
|---|---|---|---|---|---|
| *Ancylostoma, Uncinaria* | Hookworm dermatitis | Dogs | Yes | Pruritus | Paws, ventrum, can be generalized |
| *Pelodera strongyloides* | Pelodera dermatitis, "rhabditic dermatitis" | Dogs | Rare | Erythema, papules, hair loss | Predominantly distributed to areas in contact with ground |
| *Otobius megnini* | Spinous ear tick, soft ticks | Warm-blooded animals | Yes | Irritation, blood loss | Primary ears |
| *Rhipicephalus Dermacentor* | Hard ticks | Warm-blooded animals | Yes. Many species transit blood-borne parasites or other infectious diseases | Irritation, blood loss | Any body part |
| *Dermanyssus gallinae* | Poultry mite | Primarily wild and caged birds, but also dogs and cats | Yes | Pruritus | Intense pruritus on back and extremities in birds, variable in dogs |
| *Lynxacarus radovsky* | Cat fur mite | Cat | Not reported | Pruritus | Generalized |
| *Otodectes cynotis* | Ear mite | Cat and dog | Rare, but possible | Obvious pruritic otitis externa, hypersensitivity reaction | Ears and whole body in severe cases |
| *Cheyletiella* | "Walking dandruff mite" | Cats, dogs, rabbits, other small mammals | Yes | None to severe scaling with variable pruritus | Primarily dorsal distribution |
| *Demodex canis* | Demodectic mange, follicular mange, red mange | Dogs | No | Highly variable, commonly causes hair loss, pruritus, scaling, deep pyoderma | Focal to generalized in distribution |

| | | | | | |
|---|---|---|---|---|---|
| *Demodex cati* | Feline demodicosis | Cats | No | Highly variable | Focal or generalized |
| *Demodex gatoi* | Feline demodicosis contagious mite | Cat | No | Most commonly moderate to intense pruritus, evidence of contagion | Usually generalized lesions, pattern of contagion often present |
| *Sarcoptes scabiei var canis* | Scabies | Dogs | Yes | Intense pruritus | Ventral distribution, ears and elbows, will rapidly become generalized, highly contagious |
| *Notoedres cati* | "Feline scabies" | Cats, dogs, rabbits | Yes | Intense pruritus and scaling | Often starts on head, highly contagious |
| *Trichodectes canis Linognathus setosus Felicola subrostratus* | Lice | Lice are species specific | No | Pruritus, inflammation, sucking lice can cause anemia | Generalized |
| *Ctenocephalides* spp. *Echidnophaga* spp. | Fleas, stick-tight fleas | Warm-blooded animals | Yes | Pruritus, inflammation, anemia | Highly variable |
| Flies | Fly bite/strike dermatitis | Warm-blooded animals | N/A | Pruritus, hemorrhagic crusts | Ears, face |
| Myiasis | Maggots | Warm-blooded animals | N/A | Secondary invaders to open wounds | Any open wound is susceptible |
| Cuterebra | | Dogs, cats, rabbits | N/A | Cutaneous nodule, breathing pore commonly seen | Any skin location possible, dorsal back and face common |

in finding fur mites (e.g., *Cheyletiella* or *Lynxacarus*) than skin scrapings or Scotch tape preparations. Flea combs can transmit parasites and other infectious agents and should be cleaned after use with soap and water and allowed to soak in dilute bleach (1 : 100) for 10 minutes. More concentrated dilutions of bleach (i.e., 1 : 10 is required to kill ringworm spores) can be used but require extra care, because they can damage plastic and metal flea combs and countertops, and can cause an irritant reaction in people and animals. Some examiners prefer to spray the comb just prior to combing the hair coat. Alcohol-based flea sprays labeled as "quick knock down" work well with flea combs; cutaneous parasites are killed or temporarily "knocked down" pending examination. Material from the comb should be examined immediately. If flea comb material cannot be examined immediately, it is best stored in a plastic self-sealing bag labeled with the animal's identification number and other pertinent information. A positive test or visual identification is diagnostic, but a negative test does not rule out parasitic infestations (see Table 17.2).

**Acetate tape preparations**

Acetate tape or "Scotch tape preparation" has long been recommended as a diagnostic test for ectoparasites. In practice, its use is limited to the capture of macroscopic parasites. This technique requires the use of clear acetate tape. If the parasite cannot be immediately identified, the tape can be adhered to a glass microscope slide sticky side down until it can be examined later. This technique is often recommended when trying to find *Cheyletiella* mites. In author Moriello's experience, this technique is less successful than flea combing. Proper use of this technique to find mites on the surface of the skin requires clipping of the hair coat with scissors and firmly pressing the tape to the skin to collect debris and scale. If this technique is used, a minimum of five samples should be obtained. A positive test is diagnostic but a negative test does not rule out mite infestation (see Table 17.3).

**Skin scrapings**

Skin scrapings can be used to aid in the diagnosis of infestations of fur mites, *Cheyletiella*, *Notoedres*, and *Sarcoptes*, as well as canine and feline demodicosis. Skin scraping can also identify *Pelodera infestations* (free-living nematodes acquired from contact with soiled organic bedding such as straw or hay). A positive test is diagnostic, but a negative test does not rule out the above parasites, with one exception. A properly performed deep skin scraping from a suspect lesional area on a dog can rule out the presence or absence of canine demodicosis.

Given the risk of injury to humans or animals, as well as the increasing recognition of bloodborne infectious diseases of animals and the need to prevent human blood exposure, skin scrapings should NOT be performed using scalpel blades. There is too great a risk of injury to the animal (i.e., unintentional laceration) and too great a risk that staff may be cut, injuring themselves or exposing others to human bloodborne pathogens. Furthermore, inadequate sterilization of blades between patients poses a risk of transmission of bloodborne animal pathogens. Finally, it is cost-prohibitive to use new scalpel blades on

**Table 17.2.** Procedure for performing flea combing.

- Flea combing is a core diagnostic test. It is indicated in any pruritic or scaling skin disease.
- The fine-tooth combs can be used to find fleas, flea excreta, ticks, lice, and *Cheyletiella* spp and fur mites.
- The hair coat is combed using a fine metal- or plastic-tooth comb. The material can be examined with a hand held magnifying lens or under a microscope.
- Soil particles can be confused with flea excreta and water can be used to differentiate these two; the flea excreta dissolves leaving a reddish brown smear.
- Shampoo residue may mimic excessive scaling. It appears as a fine powdery debris on the distal tips of the hairs.

**Table 17.3.** Procedure for performing an acetate tape preparation.

- Acetate tape preparations are indicated to find or capture fleas and/or flea excreta, ticks, and scales associated with *Cheyletiella* mites.
- *Cheyletiella* spp. mites are more reliably found on skin scrapings or flea combings; the usefulness of this technique is greatly overemphasized.
- The sticky side of a clear piece of acetate tape is pressed against the object of interest and then placed on a glass microscope slide over a drop of mineral oil. Another drop of mineral oil is placed on top of the tape and then a coverslip is added. This enhances visualization of mites. The slide is examined under increasing magnification.
- Common artifacts include crinkling of the tape, using frosted tape, clothing treads, pigmented fungal spores, and plant matter.

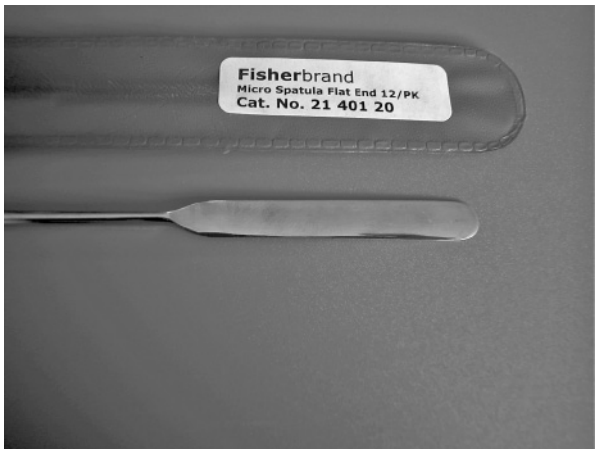


**Figure 17.1.** Skin scraping spatula.

each animal. The authors recommend the use of skin scraping spatulas (see Figure 17.1). These can be purchased from a variety of sources including chemical supply houses; skin scraping spatulas are chemical weighing spatulas and are inexpensive and easily cleaned and disinfected after use (see Table 17.4).

**Hair trichograms**

A "hair trichogram" is a microscopic examination of a hair shaft. It is most commonly used on glowing hairs when dermatophytosis is suspected. (Please see Chapter 16 on dermatophytosis.) This same technique can be very useful for finding canine and feline *Demodex* mites, for identifying the egg cases of *Cheyletiella* mites on hair shafts, and for confirming the presence of louse eggs (nits) on hair shafts. Hair trichograms are recommended in place of skin scrapings when target skin lesions are near the eyes or areas that cannot be easily sampled.

When canine or feline demodicosis is suspected, hairs are gently plucked or pulled in the direction of growth via gentle traction. It is important to obtain the hair bulb or root. The hairs are carefully placed in a drop of mineral oil on a glass microscope slide. A glass coverslip is highly recommended as this puts the entire slide into one plane and makes examination of the hairs easier. Examination for *Demodex* mites should concentrate on the hair bulb and the proximal third of the hair. Mites can be seen at 10X magnification, but usually 40X magnification is needed for confirmation. Egg sacs of *Cheyletiella* spp. or lice can be found anywhere on the hair shaft. If the parasite cannot be identified, the edges of the slide can be sealed with clear nail polish and examined later.

**Table 17.4.** Procedure for performing a skin scraping.

- This is a core diagnostic test and is used primarily to look for mites. At some point, all animals with skin disease should have a superficial and deep skin scraping performed.
- Superficial skin scrapings collect material from the skin surface and stratum corneum. Deep skin scrapings collect material from the intrafollicular and superficial dermal areas. They are called deep because when properly done, the technique causes capillary bleeding.
- Skin scraping is the test of choice for *Demodex* spp. mites. It can also be used to find *Sarcoptes* spp., *Cheyletiella* spp., and *Notoedres* spp.
- Several drops of mineral oil are applied to the skin. A skin-scraping spatula is held perpendicular to the skin and the area firmly scraped. Deep skin scrapings are performed as described above; the only difference is that the area is firmly squeezed between the fingers prior to scraping and gently scraped until there is capillary bleeding.
- The mineral oil and skin debris mixture is collected on the edge of the scraping instrument and transferred to a glass microscope slide and coverslipped. Sometimes it is necessary to add a drop of mineral oil on the microscope slide.
- The specimen is examined under low power with maximum contrast (move the condenser down). Mites are colorless translucent objects; movement is often the first clue that a mite is present.
- The following are artifacts: red-brown globules (blood cells), brown-black granules (melanin granules), colored threads, broken hair shafts, plant pollen, or mold spores (usually darkly pigmented). *Microsporum canis* macroconidia are never seen on skin scrapings.

**Ear swab cytology**

Ear swab cytology involves the collection of debris from the ear canal of an animal, rolling the debris in a drop of mineral oil on a glass microscope slide, and examining it for parasites. The most common use of this test is for identification of *Otodectes* mites. However, canine and feline *Demodex* mites can be found using this tool as well.

### Fecal flotation

Fecal flotation examinations are rarely considered as a diagnostic test for ectoparasites, but they can yield valuable information. Feces being prepared for a fecal flotation may reveal tapeworm segments, indicating the animal has fleas; excessive hair may be found, raising the suspicion that pruritus is present; or actual parasites may be found on fecal flotation, including fleas, *Cheyletiella* mites, canine or feline *Demodex* mites, and *Sarcoptes* or *Notoedres* mites. The finding of hookworm eggs on a fecal examination may explain pedal pruritus in dogs.

### Response to treatment trials

In many cases, bathing prior to surrender, intermittent or incorrect use of parasiticidal agents, improper diagnostic technique, or poor sensitivity of a test may make it impossible to definitively diagnose a parasitic infestation in an animal. In these situations, response to treatment trials may be the only way to confirm infestation. When time and personnel resources are limited, response to treatment trials may be the best approach to diagnosis and treatment for some conditions.

**Table 17.5.** Common parasitic causes of pruritus by body region.

| | |
|---|---|
| Pruritic ears | *Otodectes cyanotis, Demodex,* ticks, *Notoedres* |
| Pruritic pinnae/ear margins | *Otodectes, Sarcoptes, Notoedres*, fly bites |
| Pruritic head (cat) | *Notoedres*, *Otodectes*, feline *Demodex*, fleas |
| Pruritic head (dog) | *Otodectes*, *Demodex,* fly bites |
| Dorsal pruritus | Lice, *Cheyletiella*, fleas, *Demodex* |
| Ventral pruritus | *Sarcoptes, Pelodera*, hookworm dermatitis |
| Hind end | Fleas |
| Feet | *Pelodera*, hookworm dermatitis, *Demodex,* |
| Whole body | Fleas, ticks, insect bite hypersensitivity, lice, canine *Demodex*, feline *Demodex* |
| "Mad itchy cats" | Fleas, *Demodex, Cheyletiella* |

## ECTOPARASITES OF IMPORTANCE IN SHELTERS

The presence of a parasitic disease in a shelter animal or population may be readily apparent and diagnosis may not be the challenge (e.g., fleas jumping off the animal). It is, however, more common for animals to present with patterns of disease, making knowledge of typical parasite infestation patterns extremely useful.

Most parasitic infestations are irritating to animals and cause some degree of pruritus. Pruritus leads to hair loss, inflammation, and secondary infections of the skin with bacteria and yeast. The location and pattern of lesions, in combination with any available history, help guide diagnostics, treatment, and other interventions (see Table 17.5).

### Hookworm dermatitis

#### *Disease presentation*

Hookworm dermatitis is caused by the aberrant migration of the larvae of *Ancyclostoma* and *Uncinaria* into the skin of animals and people. In people, the disease is called "creeping eruption" and is intensely pruritic. People and animals contract the parasite by contact with larvae on the grass and in the soil of contaminated runs and other areas during the spring and summer months. The disease is most common in animals kenneled in runs or on grass where there is heavy fecal contamination and poor sanitation. The initial lesions are small papular eruptions, especially on the ventrum. The feet are particularly affected, but any area in contact with the ground is at risk. Intense pedal pruritus is the most common clinical sign; the larvae tend to invade the skin at the junction of the pad and haired skin. The diagnosis is made based upon clinical signs, positive fecal examination, and history of poor housing and sanitation. Hookworm dermatitis has a seasonal presentation in climates with distinct seasons. It can present year round in warm and semitropical areas.

#### *Treatment, control, and/or prevention*

Control of hookworm infestation involves cleaning of the environment, improved sanitation (particularly daily removal of feces), and routine anthelmintic treatment of the animals. Treatment when the animal is admitted to the shelter helps prevent environmental contamination. Human exposure in the shelter is easily prevented by mandating the wearing of closed toe shoes and socks.

### Pelodera strongyloides

#### *Disease presentation*

This disease is caused by percutaneous infestation by these nonparasitic nematodes. It most commonly affects dogs exposed to damp, decaying bedding such as straw marsh

hay, rice hulls, and dirt. Clinical signs tend to be located on areas of the body in contact with the bedding. Pruritus is common and infestation causes diffuse erythema and self-trauma. Diagnosis is easily made based upon a history of poor sanitation, clinical signs, and skin scrapings. Unlike hookworm dermatitis, this free-living nematode is large and easily found on skin scrapings or even in the associated bedding.

***Treatment, control, and/or prevention***

*Pelodera* dermatitis is controlled by removing and destroying the contaminated bedding. Complete removal of bedding and cleaning of dog crates and cages is mandatory. Gross cleaning with a detergent and thorough rinsing followed by the application of an insecticide suitable for environmental control of fleas is recommended. The affected dogs should be bathed in an antibacterial shampoo (e.g., benzoyl peroxide, chlorhexidine) and treated with systemic antibiotics. Treatments effective against scabies mites will also kill the nematode. These include ivermectin, amitraz dips, and lime sulfur. Amitraz dips pose a risk to the person performing the application, so they should be used carefully in a shelter setting and should be avoided if large numbers of animals require treatment. Amitraz is a monoamine oxidase inhibitor (MAOI); it can interfere with insulin secretion, and thus contact with the solution should be avoided in people with diabetes mellitus and people taking MAOIs. Pregnant women should not come in contact with the solution. The efficacy of spot-on flea control products is unknown and not recommended to target *Pelodera strongyloides*. Topical spray steroid treatment may be beneficial and help to make animals more comfortable until clinical signs resolve.

***Other comments and/or client education***

*Pelodera* dermatitis is an individual animal disease, and if encountered in a population, will be related to housing, as this is a disease of filth and neglect. Straw and other similar materials may be very cost-effective bedding in shelters, provided the material is kept dry and replaced daily.

**Ticks**

***Disease presentation***

Ticks are blood-sucking parasites. Most are not host specific and will feed on a wide range of warm blooded species. In general, ticks feed for 3 to 5 days before disengaging from the host. They are divided into two general groupings: soft ticks or Argasid ticks, and hard ticks or Ixodid ticks. The most commonly encountered soft tick is *Otobius megnini*. It is found in the southern and western United States. It most commonly affects dogs and cats and has a predilection for invading the ear canal.

Affected animals present with acute otitis externa, pain, severe head shaking, and (rarely) convulsions. There are anecdotal reports of hundreds of ticks packing the ear canal of animals. Affected animals suffer from blood loss and complications associated with otitis. Diagnosis is made by finding ticks during physical examination. Treatment involves mechanical removal of the ticks. Severely infected animals may require whole body treatment with parasiticidal dips to facilitate removal.

*Rhipicephalus* and *Dermacentor* are the two most common hard ticks that infest dogs, cats, and other small mammals. *Ixodes scapularis* (deer tick) is also problematic as it transmits Lyme disease. Tick infestations are highly variable and presentation can range from no clinical signs to severe pruritus. Other complications are tick bite reactions, which present as small nodules at the site of prior attachment.

Tick bite paralysis can occur in both dogs and cats as an ascending flaccid paralysis resulting from a toxin; it is most commonly associated with *D. variabilis*. Tick bite paralysis results from the feeding of a female tick and release of a salivary neurotoxin that interferes with acetylcholine release at the neuromuscular junction. Signs occur 5 to 9 days after tick attachment. Anecdotally, a single tick has been implicated in causing clinical signs, so it is important to remove all ticks. Blood loss (anemia) and secondary inflammation are the most common complications.

***Treatment, control, and/or prevention***

Treatment of hard ticks involves mechanical removal of the ticks. Heavy infestations in dogs can be treated with whole body treatment with fipronil or permethrins. Spot-on therapies are more appropriate for prevention or treatment of limited infestations; whole body or heavy infestations are best treated with whole body dips or sprays. Permethrins are toxic to cats; fipronil is recommended as the treatment of choice, although ivermectin has been anecdotally reported to be successful.

Ticks are best controlled at the point of entry into a shelter using a product labeled for the control of ticks. Of major concern in shelters is the infestation of the premises with ticks; *R. sanguineus* will infest buildings and can be difficult to eradicate. Professional extermination is often needed.

***Other comments and/or staff and adopter education***

It is important to educate shelter staff on the safe removal of ticks from animals. If staff report tick bites that are

extremely painful or if target lesions ("bull's eye") develop at the site of tick bite, advise immediate medical attention. Ticks should not be handled with bare hands; remove ticks with forceps, gently pulling in the direction of hair growth and making certain to remove the entire tick.

Ticks can transmit a number of systemic infectious agents including Rocky Mountain spotted fever, *Babesia*, canine ehrlichiosis, granulocytic ehrlichiosis, Lyme disease, and canine hepatozoonosis. (More information on vector-borne disease can be found in Chapter 21.)

Adopters and rescue groups need to be made aware if a pet has had a tick infestation. Tick bite reactions may occur weeks or months postattachment and the sudden development of a "lump" is worrisome to all clients. In addition, ticks carry bloodborne diseases; known tick exposure may expedite diagnosis of an illness.

**Figure 17.2.** Cheyletiella mite egg.

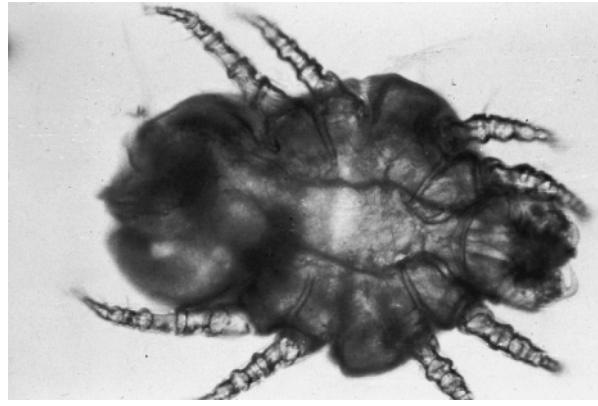

**Figure 17.3.** Cheyletiella mite.

### Fur mites

#### *Disease presentation*

The most common fur mites of dogs and cats include *Dermanyssus gallinae*, *Lynxacarus radovsky*, chiggers (*Eutrombicula, Walchia americana*), and *Cheyletiella* spp.

*Dermanyssus gallinae* or the poultry mite is most common in wild birds and pet birds. Pet birds can be affected if they are in contact with wild birds. Contact does not need to be direct; mites can be mechanically transmitted to pet birds via contact with contaminated material or close exposure to nests. Dogs and cats are only rarely affected. Clinical signs in dogs and cats vary from none to pruritic papular eruptions; contact with poultry is an important part of the history.

*Lynxacarus radovsky* infestations have been reported in Hawaii, Texas, and Florida. Clinical signs varied from mild to severe pruritus and papular eruption. Mite infestations were generalized.

Chiggers are an underdiagnosed cause of pruritus in dogs and cats. Chiggers can be found in living or decaying organic material, and it is the larvae that are parasitic and feed on animals. Bites can occur anywhere but tend to be localized to areas in contact with grass or soil. Typically, chigger infestations cause a severe papular eruption. One common clue to diagnosis is the concurrent affliction of people. Chiggers are seasonal and outbreaks tend to occur in late summer and fall. *Walchia americana* is a species of chigger found in small rodents in the southeastern and eastern U.S. and can affect cats. Affected cats have pruritic lesions on the ventrum and on their feet.

*Cheyletiella* (Figures 17.2 and 17.3) are the most well known of the fur mites and most commonly affect cats, dogs, rabbits, and other small mammals. These mites are highly contagious and are of zoonotic importance. Mites do not reproduce on people but do cause a pruritic, papular eruption. There are several different species, but all are generally similar in appearance. Infested animals can be asymptomatic carriers, sometimes identified only after transmitting symptomatic infections in other people or animals.

Clinical signs are predominantly found on the dorsal surface but can be generalized, and consist of excessive scaling and pruritus that varies from mild to severe. The pruritus is less severe than that seen with scabies. *Cheyletiella* mites live superficially on the skin and lay eggs on the hair coat. The major differential diagnoses include lice, fleas, flea allergy dermatitis, other fur mites, and secondary bacterial infections of the skin.

Definitive diagnosis of fur mite infestation is made by finding mites on skin scrapings, Scotch tape preparations, hair trichograms, flea combings, and/or fecal examinations. Definitive diagnosis can be difficult because the pathology of some of these infestations can involve a hypersensitivity reaction, and the mites are susceptible to many commonly used flea control products, thereby making the numbers low. It is common to make a presumptive diagnosis of fur mite infestation and treat animals based upon suspicion of infestation.

***Treatment, prevention, and control***

Treatment protocols for fur mites are outlined later in this chapter. It is important to note that while these infestations are not life-threatening and will most commonly resolve with treatment, they may be highly contagious. Ideally, animals should be housed separately from other susceptible animals. "Isolation" protocols used for fleas are adequate. If isolation and/or treatment is not possible within the facility, animals should be removed as soon as possible.

It is not possible to prevent the introduction of *Cheyletiella* or *Lynxaracus* into a facility, and either can live for short periods of time off the host. But routine cleaning of a facility and protocols acceptable for the control of fleas and ticks should be adequate for environmental control of these mites. Treatment of all fur-bearing animals at admission with a flea control product labeled as safe for use in the species is the best control protocol.

***Other comments and/or staff and adopter education***

Many of the common products used to successfully eradicate fur mite infestations require more than one application. Adopters of animals suspected or known to have fur mite infestations should not necessarily be discouraged from adopting these animals. However, adopter education is crucial, and if other animals are in the home, the potential adopter should consult with a veterinarian first about required precautions. All animals in the home should be treated with flea control prior to the arrival of the new pet, and owners should report any increase in pruritus and/or scaling to their veterinarian. It is important to emphasize that these diseases will commonly resolve with treatment. Adoption counseling should stress the importance of follow-up treatment by a primary care veterinarian.

**Ear mites**

***Disease presentation***

Ear mite infestations with *Otodectes cyanotis* (see Figure 17.4) are most commonly encountered in dogs, cats, and ferrets. Rabbits are infested with *Psoroptes cuniculi*. Ear mites can live on or in the ears and on the hair coat. Eggs are cemented to host skin substrate most commonly on the ear margins. Mites feed on the epithelium of the ear. The irritation caused by the mites is responsible for some of the classic signs of the disease.

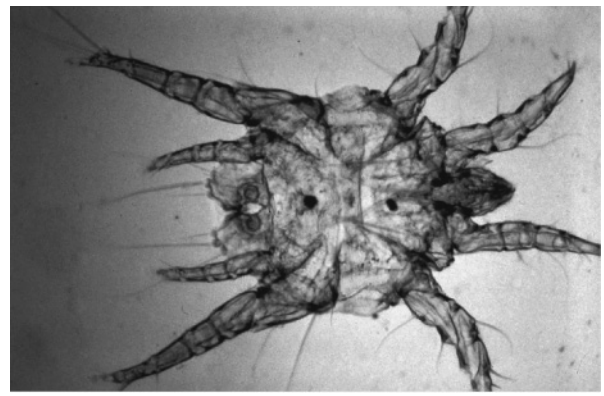

**Figure 17.4.** *Otodectes cyanotis.*

Dogs with ear mite infestations tend to have pruritic ears with minimal discharge compared to cats. Clinical lesions in cats can vary from none (asymptomatic carriers) to ear canals massively impacted with concretions of cerumen, blood, and mite debris. Kittens are recognized as a high-risk group, but any animal can be affected, so adult animals should be examined with the same care. The typical clinical sign is a coffee-ground discharge and pruritus. Hypersensitivity reactions in cats can develop secondary to mite infestations. Pruritus will be severe, yet mites are often not found in these cases. Untreated or inappropriately treated ear mite infestations can lead to secondary infections, purulent otitis externa/media, and aural hematomas (especially in cats), and may be involved in the development of chronic otitis media in adult cats. Severe ear mite infestations can occur over the entire body, leading to a pruritic, papular skin disease that can mimic many other parasitic and nonparasitic diseases. Ear mite infestations in rabbits are characterized by thick adherent crusts on the inner pinnae; the ears are pruritic.

Diagnosis of ear mite infestation can be made by finding the mites by direct examination with an otoscope or, more commonly, by finding mites on mineral oil ear swab cytology. One mite or egg is diagnostic for an infestation. Positive pinnal-pedal reflexes are common in cats with gross or subclinical infestations; when the ear is manipulated or swabbed the cat scratches with the ipsilateral hindlimb. Mites can often be found on skin scrapings of

the ear margins in animals that are suspect, but mites cannot be found on ear swab cytology.

***Treatment, prevention, and control***

Ear mites are highly contagious and all animals that have been in contact with them should be treated. It is not unreasonable to treat all animals at admission for possible ear mite infestations with the intent of controlling or minimizing outbreaks in a facility. Treatment must consist of eradicating the infestation, treating for secondary infections, and managing the associated pain and discomfort. The reader is referred to the section on treatment protocols for details of treatment for individual animals.

***Other comments and/or staff and adopter information***

Ear mites are highly contagious and material removed from ears of affected animals should be disposed of carefully and immediately. Mites can be mechanically transferred from one animal to another by fomites. Effective eradication of ear mites in an individual animal optimally requires treatment for at least 4 weeks. Products labeled as effective for the treatment of ear mites require repeat applications. Adopters should be instructed to continue treatment even if the ears appear normal at the time of adoption, either with medications prescribed by the shelter veterinarian or through their primary care veterinarian.

**Canine demodicosis**

***Disease presentation***

Canine demodicosis is caused by a proliferation of *Demodex canis* (Figure 17.5), a mite normally found in the skin of dogs. The mite lives in the hair follicle and clinical signs are related to its proliferation in the hair follicle.

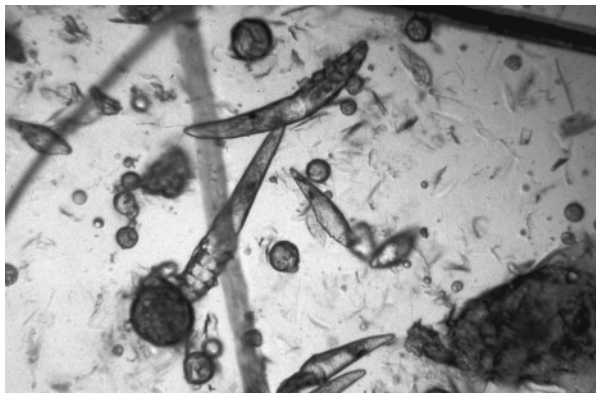

**Figure 17.5.** Canine *Demodex* mite.

Classic clinical signs include, but are not limited to, any combination of hair loss, follicular plugging, erythema, deep pyoderma, and pruritus. Chronic cases can present with marked hyperpigmentation, scaling, lichenification, draining tracts, and pododermatitis. Lymphadenopathy and systemic signs of illness (fever, depression, anorexia) can occur. Severely affected animals can be septic.

There are three classic presentations. The first is localized demodicosis, in which there are one to five focal areas of hair loss that are positive on skin scraping. This is most common in young dogs. The second is generalized demodicosis. These animals have severe, dramatic skin disease, often with deep pyoderma and signs of systemic illness. This can occur in both young and adult dogs. The last presentation is adult-onset demodicosis, the development of demodicosis (focal or generalized) in an adult dog secondary to an underlying medical disease.

In a shelter situation, any skin lesion in a dog of any age should be considered suspect for demodicosis. Diagnosis is made by deep skin scraping and/or hair trichograms. A positive skin scraping in any dog is considered diagnostic for demodicosis. Stress is a major precipitating factor for the development of this disease, and minimizing stressors is part of the treatment protocol.

***Treatment, prevention, and control***

Dogs with localized demodicosis have the best chance of cure in a shelter situation. If stressors can be minimized, that chance improves. In a pet situation, 9 of 10 localized cases will self-cure, and no treatment is needed. In a shelter situation, treatment is recommended because stress is a major trigger for the development of generalized demodicosis. Euthanasia of dogs with generalized demodicosis is not unreasonable owing to the prolonged treatment required and guarded prognosis for cure. These dogs require intense treatment including daily bathing if deep pyoderma is present, a minimum of 4 weeks of antimicrobial therapy, and long-term treatment coupled with regular skin scrapings to determine if they have or can be cured. Author Moriello advises private pet owners to be prepared to treat dogs with generalized demodicosis for at least 16 weeks, if not longer. Demodicosis is treated with weekly amitraz whole body dips, daily ivermectin 0.4–0.6 mg/kg or milbemycin 0.5–2 mg/kg daily. Ivermectin can be given orally at the recommended dose. Oral administration is preferred because ivermectin given by injection causes pain and irritation at the injection site. Concurrent treatment with antimicrobial therapy is often needed. The reader is referred to the section on treatment protocols for details of treatment for individual animals.

***Other comments and/or staff and adopter information***

Demodicosis in dogs is not considered a contagious disease. There is a well-recognized, heritable predisposition for dogs to develop this disease, and affected animals should not be bred. Clients who adopt animals with demodicosis or a history of demodicosis should understand that relapses are common and that cure occurs in less than 50% of dogs with generalized demodicosis.

**Feline demodicosis**

***Disease presentation***

Feline demodicosis is increasingly recognized as a cause of skin disease and pruritus in cats. The disease is caused by *Demodex cati*, a long slender mite, or *Demodex gatoi*, a short rounded mite (Figures 17.6 and 17.7). There appears to be a third species of feline *Demodex* mite, but this is currently a subject of much debate.

Skin disease may be limited to the ears, causing pruritic otitis. Localized or generalized skin lesions may also be seen. As with dermatophytosis, the clinical presentation is highly variable. Localized lesions are usually characterized by patchy hair loss, scaling, and erythema, and are most commonly found around the eyes, or on the head or neck. Generalized lesions may or may not be pruritic. Erythema, scales, crusts, easily epilated hairs, symmetrical alopecia, or just intense pruritus mimicking feline "hyperesthesia-like" quivering may be all that is found.

In the authors' experience, *Demodex cati* is most commonly found in cats with pruritic ears or in cats with skin lesions and concurrent disease such as diabetes mellitus, feline hyperadrenocorticism, feline immunodeficiency virus (FIV), feline leukemia virus (FeLV), toxoplasmosis, systemic lupus or other immune mediated diseases, and neoplasia. *D. cati* is not considered to be a contagious mite; however, the authors have received reports from shelters where *D. cati* appeared to follow a pattern of contagion.

*Demodex gatoi* is increasingly recognized as a pruritic skin disease of cats with clinical evidence of contagion that has been noted in animal shelters. Diagnosis is made by demonstration of the mite on skin scrapings, fecal flotation, ear swab cytology, or hair trichogram. *Demodex gatoi* can be especially difficult to find. The mite lives in the superficial layers of the stratum corneum and routine grooming of cats often removes the mite.

***Treatment, prevention, and control***

*Demodex cati* often resolves without treatment if the underlying disease can be identified or managed. It has been successfully treated with lime sulfur rinses administered every 4 to 7 days for 4 to 8 weeks. Lime sulfur treatment can be paired with daily oral ivermectin. Ivermectin treatment alone is not recommended, and if lime sulfur is not an option, topical spray fipronil weekly is a viable option. No controlled studies have been done to compare the efficacy of fipronil to ivermectin or lime sulfur, but anecdotally it seems equally effective. If fipronil is used and the response to treatment is less than satisfactory, treatment can be changed to ivermectin or lime sulfur. *Demodex gatoi* responds to treatment with lime

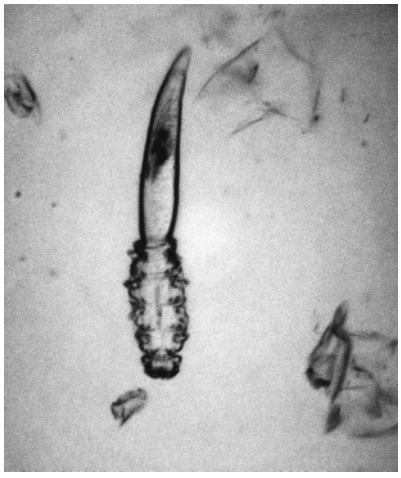

**Figure 17.6.** *Demodex cati* mite.

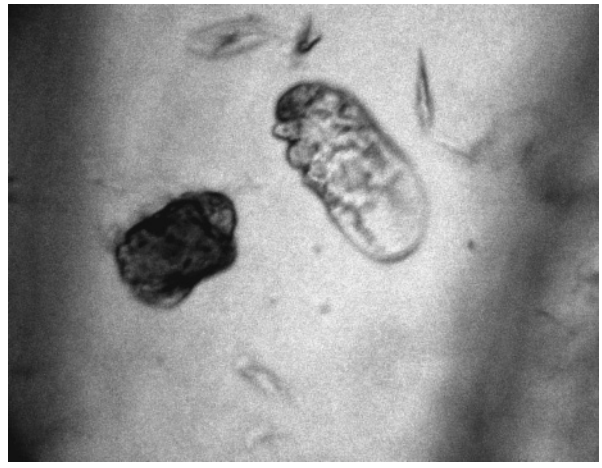

**Figure 17.7.** *Demodex gatoi* mite.

sulfur topical rinses administered every 4 to 7 days for 4 to 8 weeks. In the authors' experience, these cats often present with acute marked pruritus that rapidly responds to treatment. It is impossible to prevent the introduction of either mite into a facility. Cats with suspect or known *D. gatoi* must be isolated during treatment. All in-contact cats should be treated.

***Other comments and/or staff and adopter information***

When possible, cats with *D. cati* should be evaluated for systemic illness. If such cats are made available for adoption, potential adopters should be warned that they may have an undiagnosed systemic illness. It is possible that stress may be a precipitating cause.

Potential adopters of cats with a history of or suspicion of *D. gatoi* should be warned that this mite can be highly contagious. Animal welfare organizations should carefully evaluate risk prior to making cats available for adoption; however, this mite infestation is curable, and this point should be taken into consideration when making decisions about adoptability of a cat.

**Sarcoptic mange (scabies)**

***Disease presentation***

Sarcoptic mange (scabies) in dogs is caused by an infestation with *Sarcoptes scabiei var canis* (Figures 17.8 and 17.9). This mite lives and burrows in the epidermis, and infestations start in the thinly haired areas of the body; the mite has a ventral distribution. As the disease progresses, crusting develops on the elbows, ear margins, and periocular area. In severe infestations, clinical signs become generalized. Mite infestations cause intense pruritus, and infested dogs will often continue to scratch and self-mutilate even during the most stressful of experiences. This mite is contracted via contact with other infected animals, fomites, or contaminated environments. Mites can live for short periods of time off the host in the environment. The mite can be found on skin scrapings in cases with heavy infestations, but more often than not, the mite is not found. A low mite burden can cause intense pruritus, as hypersensitivity is part of the pathogenesis. Another reason mites are hard to find is that the mites live very superficially and are easily dislodged when the animal scratches. This is why areas of excessive self-trauma are rarely skin-scraping positive. The most common method of diagnosis is response to therapy. This mite is highly contagious, and if there is any suspicion of the disease, suspect dogs should be treated.

***Treatment, prevention, and control***

There is no way to prevent completely the introduction of this mite into a facility. If a suspect animal enters, that dog should be isolated and treated immediately along with any other animals that have been in direct contact. This mite is highly contagious, and the use of topical lime sulfur is strongly recommended to minimize spread of the contagion. The dog can be isolated to a run. Ideally, the location of the run should be out of the main traffic flow of animal movement, and adjacent runs should be vacant. If the latter is not possible, animals in the adjacent runs should be prophylactically treated for scabies to prevent them from contracting the mites. Mites can live off the host for a period of time with females being hardier than males. Routine use of premise sprays for fleas and ticks are effective at killing mites in the environment. Treatment options for scabies are listed later in this chapter. Exposed bedding

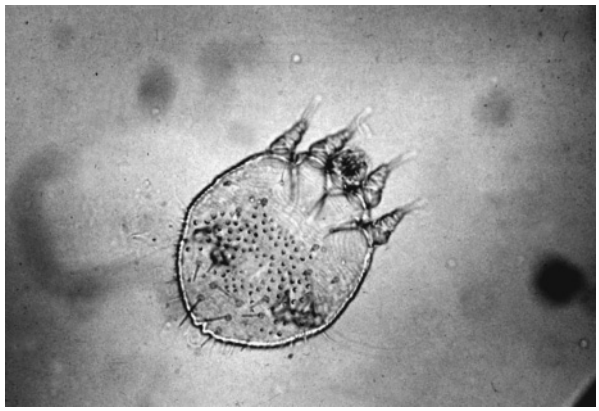

**Figure 17.8.** Canine scabies adult mite.

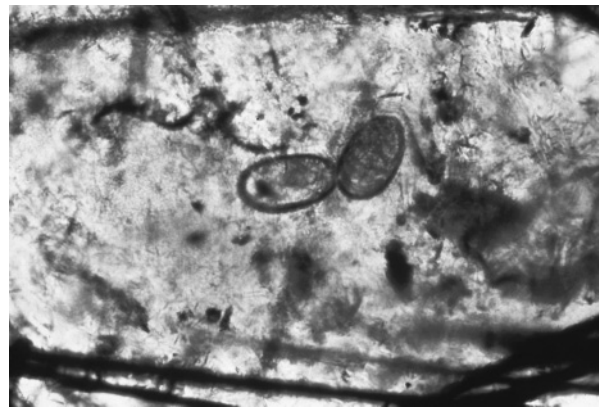

**Figure 17.9.** Canine scabies mite egg.

should be disposed of and collars washed. The prognosis for cure is usually good.

***Other comments and/or staff and adopter information***

This mite is highly contagious and causes lesions in people that present as an intensely pruritic, papular eruption on areas in contact with dogs. Experimentally, mites have been found to transiently infest people and lay eggs, but infestations in healthy people usually resolve rapidly. (However, people with skin lesions are advised to seek medical care from their physicians.) In the U.S., this mite rarely infects cats, but infestations of *Sarcoptes* mites in cats in Europe have been reported.

**Notoedres**

***Disease presentation***

*Notoedres cati*, also known as "feline scabies" is an intensely pruritic skin disease of cats. It is rare, being found most commonly in catteries and multiple cat households. Affected cats present with intensely pruritic crusting and scaling on their face, ears, head, neck, feet, and perineum. As the infestation progresses, the skin becomes lichenified, hyperpigmented, alopecic, and excoriated. It is diagnosed via skin scraping and the mite is very similar in appearance to scabies mites. However, unlike canine scabies and *D. gatoi*, these mites are easily found.

***Treatment, prevention, and control***

*Notoedres cati* is highly contagious and will infest dogs, rabbits, and people. Affected cats benefit from gentle bathing to remove crusts and scales. Treatment options are found later in the chapter.

**Fleas**

***Disease presentation***

Fleas are the most common ectoparasites encountered in a shelter (Figure 17.10). Flea infestations are most common in the warm weather months of the year, but they can be found year round even in climates with defined seasons and hard winters.

Foxes, raccoons, and opossums are reservoirs of infestation in these climates. Flea infestations are acquired by direct contact with another infested animal or with a contaminated environment. Flea infestations can lead to severe flea bite anemia. Young, old, and debilitated animals are typically at higher risk.

Animals that are not allergic to fleas may show no clinical signs whatsoever even though their hair coat is heavily infested with fleas. Other flea infested animals will be pruritic. Hair loss, scaling, papular eruptions with or without crusting, and areas of pyotraumatic dermatitis are common. Flea allergic animals have clinical signs out of proportion to the number of fleas found on the hair coat; no fleas may be found as flea allergic animals frequently bite, nibble, hunt, and ingest fleas. Hair loss over the lumbosacral area and hind legs is the most common presentation of flea allergy in dogs. Cats can have similar clinical signs. Cats frequently develop miliary dermatitis lesions (small red crusts consisting of serum and blood); areas of exudation and crusting, especially on their face and abdomen; ulcerated lips; and symmetrical alopecia.

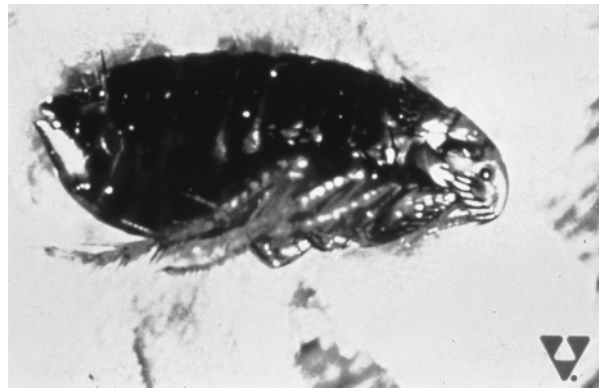

**Figure 17.10.** Cat flea.

The diagnosis of fleas or flea allergy dermatitis can be made based upon clinical signs and suspicion. Evidence of a flea infestation can be found using a flea comb. Fleas, flea eggs, and flea excreta are common findings. The finding of tapeworms in a fecal specimen is also suggestive of fleas as tapeworms may result from flea ingestion. Both cats and dogs with flea infestations and flea allergy dermatitis often have secondary bacterial infections. Treatment of flea infestations is strongly encouraged not only because of the discomfort they cause for the animal and distress for the owners, but because fleas can transmit zoonotic diseases such as *Bartonella* (cat scratch fever).

***Treatment, prevention, and control***

The only way to prevent infestation of the entire population of animals in a shelter is to practice strict flea control at the point of entry. Year-round flea control is recommended for shelter animals regardless of geographic location.

All dogs and cats should be treated with a flea control product labeled as safe for use in the target species. There

are no flea control products labeled as safe for use on ferrets and rabbits; products labeled as safe for use in kittens are usually safe.

Animals found to be infested at the time of admission can be treated with oral nitenpyram (Capstar™), 1 mg/kg orally every 24 to 48 hours for 1 to 2 weeks until no more fleas are found; however, this is expensive and may only be feasible if the drug is donated. In shelters, only products containing an adulticide (with or without growth hormone regulators or inhibitors) or spot-on treatments are recommended. Effective control with fipronil, imidocloprid, and selamectin can be achieved with topical use every 3 to 4 weeks. Regional variation in efficacy of various products is anecdotally reported, although there has been no evidence to date documenting resistance of fleas to current spot-on treatments. Concurrent systemic antibiotic for bacterial pyoderma is recommended in affected cats and dogs for at least 3 to 4 weeks. Shelter staff and veterinarians should monitor the response to all products to evaluate efficacy. Heavily infested animals may benefit from bathing.

Flea infestations of buildings should be treated using premise spray products that contain both adulticides and insect growth regulators. Flea infestations of outdoor environments are difficult to control, but measures such as keeping grass mowed short and removal of mulch from areas around the shelter are recommended.

***Other comments and/or staff and adopter information***

Fleas are a zoonotic parasite, and many people have marked allergic reactions to flea bites. Fleas can transmit *Bartonella* (cat scratch fever). Every effort should also be made to ensure that animals are not sent home with fleas. Adopters should be advised to seek professional treatment if they suspect their pet has fleas rather than use home remedies and over-the-counter products. Brewer's yeast, garlic, etc., have not been proven effective, and some homeopathic and herbal treatments may have serious side effects.

**Lice**

***Disease presentation***

Lice are host-specific parasites; almost all warm-blooded animals have their own species. Lice are contracted by direct contact with another infested host and are most common in young, old, and debilitated animals, and in situations where there is overcrowding and neglect. Dogs have a sucking louse (*Linognathus setosus*) and biting louse (*Trichodectes canis*). Cats have only one species of lice, the biting louse *Felicola subrostratus* (Figure 17.11).

**Figure 17.11.** Cat louse.

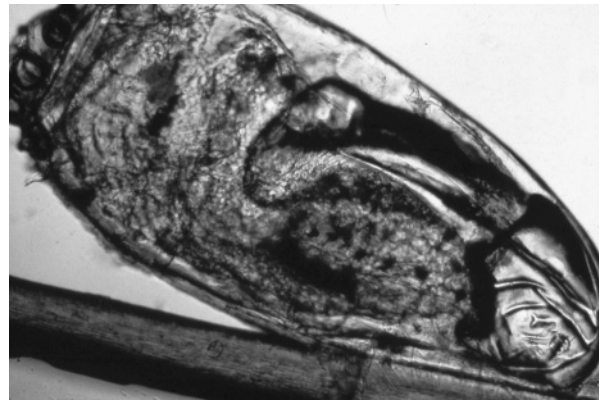

**Figure 17.12.** Louse egg attached to hair.

Infested animals may be asymptomatic or more commonly present with restlessness, pruritus, scaling, hair loss, crusts, matted hair, a "mousy odor," and anemia (dogs).

***Treatment, prevention, and control***

Lice cement their eggs on the hair coat, and treatment of louse infestations must address removal of louse eggs, commonly referred to as nits (Figure 17.12). Clipping the hair coat is the best method to remove nits and will shorten treatment time. If this is not possible, bathing infested animals in a flea shampoo will enhance removal of louse eggs. Rinsing the hair coat with a vinegar and water solution (1 part vinegar to 3 parts water) will also help loosen the attachment of louse eggs to hairs. In shelters, whole body therapy with lime sulfur (weekly), pyrethrin (weekly),

or fipronil spray (every 2 weeks) is recommended for 4 weeks. Alternative therapies using ivermectin or spot-on therapies may be effective in individual animals in pet home scenarios but are not recommended in multianimal situations. Although effective, the lag time between treatment and eradication is too long, allowing for other animals to be infested. Shelter-acquired louse infestations can be prevented or "controlled" with the administration of flea control at the point of entry. Lice do not live off the host, so no specific environmental control measures are required.

***Other comments and/or staff and adopter information***

The most important thing to stress to staff and new owners is that lice are species-specific. There is no risk of zoonosis or contagion across species.

### Fly strike in dogs and insect bite hypersensitivity in cats

***Disease presentation***

Fly strike or fly bite dermatitis is caused by flying and biting insects and is common in dogs housed outdoors. The ears are the most commonly affected areas; however, in some cases, the dorsal nose may also be affected. Dogs present with ear tips that have hemorrhagic crusts with or without ulcers and erosion on the tips or in the fold of floppy-eared dogs. The ears are intensely pruritic. Fly strike on the ears of dogs can resemble the ears of dogs with scabies, so it is important to differentiate the two diseases.

In fly strike, pruritus is limited to the ears. Cats can also develop insect bite hypersensitivity on their face (Figure 17.13). This is caused by the bites of mosquitoes or other small biting insects; it occurs exclusively in cats that go outside or have access to the outdoors via screened porches. Diagnosis is via history, clinical signs, and response to treatment. The other major differential diagnosis is scabies. Usually it is not difficult to differentiate the two diseases, as scabies is highly pruritic and involves the whole body. Skin scrapings can be performed on the ears, but negative scrapings do not necessarily rule out scabies.

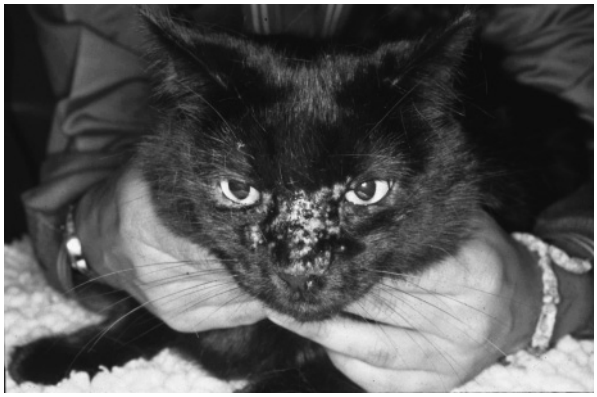

**Figure 17.13.** Cat insect bite hypersensitivity.

***Treatment, prevention, and control***

Housing of the affected animals indoors is important to prevent continued exposure. Application of a topical triple antibiotic ointment to affected areas with or without a topical steroid will usually resolve the lesions. If housing in the shelter involves exposure to flying and biting insects, control and prevention measures will be needed. Removal of the source of flies (compost heaps, manure piles) and puddles of standing water is necessary. Permethrin repellants can be used on the ear tips of dogs; permethrins are toxic to cats. Products formulated for people should not be used on animals; there have been reports of DEET toxicity. Many flying and biting insects are outside during specific times of the day, e.g., early morning and evening, and limiting the animal's exposure during this time can be helpful.

***Other comments and/or staff and adopter information***

These conditions are important to recognize because they can be confused with other skin diseases; in particular, some of the immune mediated diseases. They resolve quickly once the animal is removed from the source of the problem.

### Myiasis

***Disease presentation***

Myiasis is the infestation of living animals with fly larvae (maggots). Flies are attracted to moist areas of the skin or devitalized tissue (wounds, hair matted or wetted with feces or urine), and the larvae hatch and secrete proteolytic enzymes that destroy tissue. It is most common in weakened or paretic animals or animals with wounds that have not been properly treated. Diagnosis is made by visual examination and finding the maggots.

***Treatment, prevention, and control***

This is a disease of neglect, and prevention should be directed at the situation that precipitated the conditions that allowed the animal to become infested. This is especially true when addressing suspected cruelty and neglect cases. If cruelty is suspected, a cruelty investigator should

be contacted before treatment is rendered, photographs of the maggots should be taken, and samples collected as a minimal part of the preservation of the evidence for the cruelty investigation. [For more detailed information on this subject, consult a textbook on veterinary forensics or forensic entomology, or visit the ASPCA Web site (www.aspca.org.)]

Treatment requires clipping of the lesions, lavage of the wound, and mechanical removal of the maggots. Ivermectin 0.2–0.4 mg/kg subcutaneous (SQ) or orally (PO), and nitenpyram 1 mg/kg PO are effective and usually kill larvae within 1 to 2 days; however, this may not always be the case. The authors are aware of cases where wounds were cleaned and found to be infested with maggots the next day when bandages were removed. Therefore, ivermectin or nitenpyram therapy should be continued daily until no new larvae are found. In most cases, maggots will die in a short period of time (24–48 hours). Affected animals are usually debilitated and may need fluid therapy, daily lavage and cleaning of wounds, bandaging, systemic or topical antibiotic therapy (or both), pain medications, and special bedding to ensure that pressure-point necrosis does not occur.

After mechanical removal and lavage of wounds or affected areas of the skin, daily or twice-daily checks should be made for maggots that have hatched, emerged, or become large enough to visualize since the last examination. Bandages should be removed and changed at least daily to allow for inspection.

When myiasis is found in a single location on an animal's body, it is also important to thoroughly evaluate the rest of the animal for other sites of infestation. The oral cavity is especially important to examine because many animals may translocate maggots to their oral cavity or face while grooming or licking affected areas.

### Venomous and stinging parasites

#### *Disease presentation*

Bees, wasps, hornets, ants, and caterpillars often bite or sting dogs or cats. Bee, wasp, and hornet stings commonly present as local areas of acute erythema, edema, and inflammation. Some animals develop angioedema and anaphylaxis. Dogs bitten on the nose often develop facial eosinophilic folliculitis and furunculosis at these sites. There is an acute onset of a papular to pustular eruption that often becomes very proliferative and exudative. Impression smears of the area reveal eosinophilic inflammation.

Fire ants are found in the southern U.S. Animals that disturb nests can suffer a large number of bites that quickly develop into erythematous papules to diffuse swellings. Caterpillar bites can also occur on the lips of dogs and cats. It is rare to make a definitive diagnosis of a caterpillar bite unless one sees the incident occur.

#### *Treatment, prevention, and control*

These sting/bite reactions are all treated similarly. If a stinger is still present in the wound, it should be removed. Immediate first aid can include cold packs until glucocorticoids (0.5 mg/kg) and diphenhydramine are administered. If there is severe angioedema or anaphylaxis, epinephrine needs to be administered. Shelters should monitor outdoor play areas and kennels for nests or ant colonies. When possible, screens should be provided for outdoor runs.

## TREATMENT PROTOCOLS AND OPTIONS FOR THE MOST COMMON ECTOPARASITE INFESTATIONS

Note: Few products have label claims for the treatment of parasites commonly encountered in shelters and/or for situations where treatment needs to be directed to the population as a whole. All products need to be used under the direct supervision of a veterinarian. Mentionin in this book of the off-label use of a product does not constitute endorsement by the authors. Many factors need to be considered when selecting parasiticidal agents, one of which is human health hazards. For example, amitraz is very effective for the treatment of a variety of parasite infestations but may not be appropriate to use in shelters because of the risk associated with exposure of handlers to the chemical. The product needs to be used in areas with good ventilation. Amitraz is an MOAI and should not be handled by people taking other MOAIs. Furthermore, amitraz can inhibit insulin release (temporarily) and should not be handled by people who are pregnant or have diabetes mellitus (type 1 or 2).

### General treatment principles for the hair coat

1. Clipping and removal of hair mats will facilitate treatment and allow better visualization of the skin. Hair mats often hide areas of superficial or deep pyoderma. Use care when removing mats. Mats often form very close to the underlying skin. Skin can become pulled and entangled by mats and can be easily lacerated during mat removal; clippers held parallel and close to the skin, not scissors, are safest. Sedation or anesthesia may be necessary when animals present with severely matted hair coats. Remember that animals with severely matted coats and/or external parasites may have been neglected in other ways, be in pain, be anemic, or have

poor underlying health. Thermal burns from clipper blades can occur and be quite severe. Constantly monitor the heat of the clipper blade while working. To avoid excessive heat, use of alternating sets of clipper works well; one clipper can cool while another is being used in rotation.

2. Removal of excessively shed hairs will also remove hairs with egg sacs attached to them and facilitate mechanical removal of some parasites. The importance of the proper hygiene of electric clippers and blades and disposal of material cannot be stressed enough.
3. Dogs with clinical or highly suspect infestations of parasites benefit from bathing with a cleansing shampoo or flea shampoo. Any product labeled for use in dogs or cats or small children can be used provided it is prediluted and rinsed thoroughly from the hair coat; never use products directly out of the bottle and do not use commercial dish soap, as these can be irritating. Bathing removes scales, debris, and hairs, and facilitates application of topical products. This is also soothing to the skin. Caretakers should wear protective clothing and gloves, as often this is the stage where they may contract zoonotic parasites such as scabies or *Cheyletiella*.
4. Cats prefer not to be bathed, but severity of skin disease may make this necessary. Cats tolerate warm water, not hot, much better than cold. Water sprayed in a stream close to the skin surface and allowed to cascade over the cat is usually better tolerated than shower spray from a distance or whole body immersion. Removal of hair mats and excessively shed hairs is recommended as discussed in previous steps.
5. Animals with skin disease are often pruritic or painful; pat the hair coat dry and do not rub.

**Flea infestations**

1. Flea infestations in adult dogs and cats can initially be treated with nitenpyram (Capstar™) at intake along with a topical spot-on product. Although label claims indicate efficacy past 30 days, in a high-exposure situation animals should be retreated every 30 days.
2. Treatment of neonates (kittens and puppies) requires aggressive removal of fleas as they can cause serious life-threatening anemia. Bathing in sudsy warm water will do two important things: warm a potentially hypothermic animal and facilitate removal of fleas. Care must be taken to keep these animals warm. After drying and combing, a thorough application of a water-based pyrethrin spray is recommended, followed by aggressive flea combing.

If the infestation is severe and/or the animal is too young to safely be sprayed directly, the following technique has been successfully used by one of the authors: saturate a paper towel with a knockdown spray and tent it over the animal, taking care that the spray is kept out of the animal's eyes and minimizing inhalation of the spray. Fleas will fall off the neonate and facilitate removal.

A spot-on topical product will need to be used. The authors have safely used selamectin in young kittens. At the time of this writing, a new low-volume topical spot-on for cats (metaflumizone ProMeris, Fort Dodge) and a chewable tablet for dogs have also recently been released (spinosad Comfortis, Lilly). The safety of these new products in neonates younger than 8 weeks of age is unknown. Information on efficacy in shelters is also unknown. At the time of writing (2008), the manufacturer issued a warning that Comfortis should not be used in conjunction with ivermectin because concurrent use can result in signs of ivermectin toxicity.

**General treatment principles for ears**

1. Ears need to be handled with great care because they may be very painful.
2. In some cases, sedation may be needed because of the severity of inflammation and discomfort. Ear cleanings need to be thorough but gentle because the ear epithelium can be damaged and bruised, leading to chronic otitis.
3. Products used for treatment may not penetrate thick crusts to reach bacteria or mites within.
4. Debris may contribute to ongoing secondary infections or irritation in the ear.
5. Removal of debris that is dried, caked, or otherwise adhered to the ear (e.g., ear mite debris) is most effectively and humanely performed by first instilling mineral oil into the ear 10 to 15 minutes before the attempt to remove the debris. This will facilitate removal of the debris and prevent damage to the ear epithelium.
6. Unless adequate restraint or sedation is possible, cotton-tipped swabs should not be used to clean ears. Use soft cloths, gauze, or other similar material. Ear swabs can bruise the ears.
7. Excess debris can be removed using a bulb syringe and warm water.
8. After ear debris has been removed, commercial ear cleaners can be used; precleaning with mineral oil will minimize the volume and cost of such ear cleaners.

Any product instilled into the ear can be ototoxic; there is no product that is completely safe.

9. Ear cleaning, no matter how gentle, is traumatic. After ear cleaning, instill several drops of a topical ear steroid into the ear. One of the authors routinely uses a compounded mixture of equal parts of dexamethasone injectable (2 or 4 mg/ml) with an equal volume of propylene glycol. This can be compounded in large volumes and is inexpensive. It is nonirritating and particularly useful after cleaning the ears of cats with ear mites.
10. Ear mite debris is filled with viable eggs and mites and needs to be removed and carefully disposed of to facilitate successful treatment and prevent disease spread.

***Treatment of ear mites***

1. Unless the safety of the caretaker staff is an issue, ear mite debris should be removed from the ears. Instill mineral oil prior to cleaning to soften the debris and minimize pain. Many products claim that removal of debris is not necessary, but topical otic products or spot-on products may not penetrate thick debris in the ear. Removal speeds resolution of the infestation and allows for humane application of a topical ear medication containing glucocorticoids (e.g., Panalog, Tresaderm).

   The pruritus from ear mite infestations is caused by a hypersensitivity reaction and can be intense. In an anecdotal report, a veterinarian intentionally infected himself with ear mites and reported intense pruritus, feeling mites moving in the ear canal and hearing them chewing. He reported that mites were clearly more active at night. Even if animals are only going to be housed for a short period of time and then euthanized, administration of an injectable glucocorticoid (triamcinolone acetate) or oral prednisone should be considered to alleviate suffering.
2. A whole-body flea control product needs to be applied to the body. Ear mites will migrate on the body and can reinfest ears if not killed.
3. Primary care veterinarians commonly report relapses of ear mite infestations in cats and kittens adopted from shelters where only one application of a spot-on miticide has been used. If possible, repeat the application of products and make sure that the new owners have this potential problem addressed by their primary care veterinarians.
4. Ear mites have a life cycle of 3 weeks, and treatment should continue for up to 4 weeks under ideal circumstances. Effective otic preparations include commercial preparations of otic ivermectin, amitraz, and pyrethrin-based products. Oral ivermectin is also effective.

**Treatment options for lice, *Cheyletiella*, fur mites, "mad itchy cats," and *Notoedres cati***

1. The above parasites can be treated similarly. The key to eradication is early detection and use of a product that can be applied to the entire hair coat; spot-on treatments are not recommended.
2. Bathe and remove debris and excessive scales from the coat. Use a flea shampoo if possible.
3. Louse nits can be loosened from the hairs with a 1 : 4 dilution of vinegar and water rinse. Apply and allow it to stay on the coat for 2–3 minutes before rinsing and then treating for lice.
4. Clipping the hair coat short may effectively remove many nits and allow animals to move on to adoption more quickly.
5. Lice, *Cheyletiella*, and other fur mites generally have a life cycle of 3 weeks; treat for at least 4 weeks. Successfully treated animals will no longer show signs of pruritus and scales in the hair coat will be rare or absent.
6. These parasites are all highly contagious. Mites are very active and can live off the host for several days, whereas lice are host-specific and rarely leave the host. A combination of systemic and topical whole body therapy is recommended to limit spread of mites.
7. Topical therapy options: Lime sulfur applied twice weekly, 4–8 oz/gallon; fipronil spray every 2 weeks; pyrethrin spray administered 1 to 2 times weekly; or amitraz every 2 weeks (not for cats) are effective. Topical therapy is strongly recommended, as the use of systemic therapy alone to manage mites is inadequate; these parasites can remain contagious on the hair coat for 1 to 2 weeks after administration of systemic drugs such as ivermectin.
8. Systemic therapy options for treatment of mites: ivermectin (test dose of 0.1 mg/kg, followed by two treatment doses at 0.2–0.4 mg/kg PO or SQ), milbemycin oxime 2 mg/kg PO weekly for 4 weeks.

**Treatment options for canine scabies**

1. This disease is highly contagious to dogs and suspect animals should be isolated. Humans can become transiently infected with scabies, so precautions (gloves, disposable gowns) should be taken when handling or treating these animals.

2. All in-contact dogs should be treated. This includes animals in direct contact and those housed nearby.
3. In cases where mites have actually been found and positively identified, it is acceptable to prescribe oral prednisone (0.5 mg/kg PO daily) to improve comfort. If treatment is being used as a diagnostic test, i.e., a response to therapy, administration of oral prednisone can make it difficult to interpret the response.
4. Mites can be contagious for 1 to 2 weeks after the administration of a systemic therapy. Therefore, concurrent treatment with a whole body topical parasiticidal agent is strongly recommended even if just for two or three applications.
5. Effective whole body treatments include lime sulfur administered weekly, amitraz every 2 weeks, and fipronil spray (see below).
6. Selamectin and fipronil spray have a label claim for treatment of scabies, but clinical experience has shown that current label recommendations are not always effective. See below.
7. Selamectin is recommended in dogs with known infestations or for treatment of collies, herding breeds, or dogs with known sensitivity to ivermectin. One of the authors has successfully used it at twice the label recommendation every 2 weeks for three treatments.
8. Fipronil spray has been reported to be effective when used at 3 ml/kg at 2- to 3-week intervals in puppies. In adult dogs, it has been successfully used at 6 ml/kg once weekly for at least 2 weeks.
9. The most commonly used treatment protocol by the authors is ivermectin 0.2–0.4 mg/kg PO every 2 weeks combined with weekly lime sulfur whole-body rinses. Fipronil spray would be an acceptable alternative.
10. Moxidectin and doramectin have been anecdotally reported to be effective systemic therapies but have not been used by the authors.

## APPENDIX 17.1. ECTOPARASITICIDES

Acarexx
- Idexx Pharmaceuticals
- Ivermectin
- FDA approved
- Labeled for
  - Treatment of adult ear mite infestations (*Otodectes cynotis*); effectiveness against eggs and immature stages not proven
  - Cats over 4 weeks of age
- Precautions and toxicities
  - Reproductive safety not established
  - Local pain and vomiting possible side effects
  - No adverse effects seen in cats administered 5X dose on up to 6 consecutive days

Advantage
- Bayer Health Care
- Imidacloprid
- EPA approved
- Labeled for
  - Treatment and prevention of fleas (*Ctenocephalides* spp.) on dogs, cats, rabbits, ferrets
  - Lasts a month on dogs and up to a month on cats
  - Larval flea stages are killed in the surroundings of treated pets
  - Reduces incidence of flea allergy dermatitis
  - Control of lice (*Trichodectes canis*, *Linognathus setosus*) on dogs for up to 6 weeks
- Precautions and toxicities
  - Bitter tasting; excessive oral salivation
  - Irritating to eyes
  - Limited data on overdosage; however, animals administered 5X dose showed no adverse effects
  - Safe for use on pregnant and lactating animals

Advantix
- Bayer Health Care
- Imidacloprid, Permethrin, N-methylpyrrolidone
- EPA approved
- Labeled for
  - Dogs ONLY
  - For dogs over 7 weeks of age
  - Control of ticks including *Ixodes holocyclus*, *Rhipicephalus sanguineus*, *Haemaphysalis longicornis*; repels and kills ticks
  - Treatment and prevention of fleas (*Ctenocephalides* spp.)
  - Reduces incidence of flea allergy dermatitis
  - Larval flea stages are killed in the surroundings of treated pets
  - Control of lice *Trichodectes canis*, *Linognathus setosus* for up to 6 weeks
  - Repelling and killing of mosquitoes (*Anopheles*, *Culex*, *Aedes* sp) and biting midges (*Phlebotomus*, *Culicoides* sp) in dogs and puppies
  - Lasts for one month (2 weeks for *Ixodes holocyclus*)
- Precautions and toxicities
  - DO NOT USE ON CATS
  - Do not use on animals other than dogs
  - Do not allow cats to groom excessively or have close contact with a recently treated dog
  - Bitter tasting; excessive salivation
  - Irritating to eyes
  - Safe for use on pregnant or lactating bitches

Capstar
- Novartis
- Nitenpyram
- FDA approved
- Labeled for
  - Rapid kill of adult fleas
  - Dogs and cats over 4 weeks or age and over 2 pounds of body weight
- Precautions and toxicities
  - As fleas die, animal will begin to itch; reaction to fleas, not the medication
  - Safe for use in pregnant or lactating animals
  - No adverse effects seen in dogs or cats administered 10X normal dose

Cerumite 3x
- Evsco
- Pyrethrins, Piperonyl butoxide, n-Octyl bicycloheptene dicarboxamide
- EPA approved
- Labeled for
  - Treatment of ear mites
  - Dogs, cats, and puppies and kittens over 12 weeks of age
- Precautions and toxicities
  - Harmful if absorbed through the skin
  - Caution in debilitated, aged, medicated, pregnant, or nursing animals
  - Individual sensitivities a possibility

Comfortis
- Lilly Pharmaceuticals
- Spinosad
- FDA-approved chewable tablet for flea control
- Labeled for
  - Treatment and prevention of flea infestations in dogs
  - Dogs and puppies over 14 weeks of age
  - Once monthly product; starts to kill fleas within 30 minutes
- Precautions and toxicities
  - Use with caution in pregnant/breeding animals
  - Most commonly reported adverse reaction was vomiting, less commonly lethargy, decreased activity, diarrhea, cough, increased thirst, vocalization, increased appetite, redness of skin, hyperactivity, and excessive salivation

Eradimite
- Fort Dodge
- Pyrethrins, Piperonyl butoxide
- EPA approved
- Labeled for
  - Kills ear mites and ear ticks
  - Aids in ear wax removal
  - Dogs, cats, and rabbits over 12 weeks of age
- Precautions and toxicities
  - Harmful if swallowed or inhaled
  - Avoid contact with skin and eyes
  - Caution in debilitated, medicated, aged, pregnant, or nursing animals

Frontline (Top Spot, Spray)
- Merial
- Fipronil
- EPA approved
- Labeled for
  - Kills adult fleas before they lay eggs and prevents reinfestation
  - Controls fleas that may cause flea allergy dermatitis
  - Kills all stages of brown dog ticks, American dog ticks, lone star ticks, and deer ticks
  - Eliminated infestations with chewing lice
  - Aids in control of sarcoptic mange infestations in dogs
  - Top Spot is waterproof, fast-acting, and long-lasting; spray is fast-acting
  - Dogs over 10 weeks of age; cats over 8 weeks of age
- Precautions and toxicities
  - Caution for use on debilitated, aged, pregnant, or nursing animals
  - Harmful if swallowed or absorbed through the skin in humans
  - Spray may cause severe eye irritation
  - Rare individual sensitivities
  - Local irritation at site of application possible

Frontline Plus
- Merial
- Fipronil, (S)-methoprene
- EPA approved
- Labeled for
  - Kills adults fleas, flea eggs, and larvae; prevents all flea stages from developing
  - Kills fleas that may cause flea allergy dermatitis
  - Kills all stages of deer ticks, brown dog ticks, American dog ticks, lone star ticks; prevents and controls reinfestations
  - Eliminates infestations with chewing lice
  - Aids in control of sarcoptic mange infestations in dogs
  - Waterproof, fast-acting, long-lasting, convenient to use
  - Dogs and cats over 8 weeks of age
- Precautions and toxicities
  - Safe for use on breeding, pregnant, and lactating animals
  - DO NOT use on rabbits
  - Harmful if swallowed and may cause eye irritation in humans

- ○ Rare individual sensitivities
- ○ Local irritation at site of application possible
- ○ Caution for use on debilitated, medicated, or aged animals

Hartz Advanced Care 2 in 1
- – Hartz Mountain
- – Tetrachlorvinphos
- – EPA approved
- – Available in spray, collar, powder
- – Labeled for
  - ○ Spray: Kills the deer tick
  - ○ Collar: Kills fleas and ticks common to dogs and cats, including Rocky Mountain wood tick and deer tick
  - ○ Powder: Kills fleas and ticks, including the deer tick
- – Precautions and toxicities
  - ○ Do not use on kittens under 12 weeks of age; do not use collar or spray on puppies less than 6 weeks of age, powder not for use on puppies less than 12 weeks of age
  - ○ Do not use spray near birds, fish, water, or foodstuffs
  - ○ Spray and powder may cause eye irritation
  - ○ Contains organophosphate; may cause cholinesterase inhibition
  - ○ Individual sensitivities may occur

Hartz Advanced Care 3 in 1 Flea and Tick drops
- – Hartz Mountain
- – Phenothrin
- – EPA approved
- – Labeled for
  - ○ Controls flea and tick infestations
  - ○ Kills and prevents adult fleas, ticks, and mosquitoes
  - ○ Waterproof
  - ○ Dogs and cats over 12 weeks of age
- – Precautions and toxicities
  - ○ May cause eye irritation
  - ○ Caution in debilitated, medicated, aged, pregnant, or nursing animals
  - ○ Individual sensitivities possible
  - ○ Toxic to fish

Hartz Advanced Care 4 in 1 Flea and Tick Drops Plus
- – Hartz Mountain
- – Phenothrin, (S)-methoprene
- – EPA approved
- – Labeled for
  - ○ Kills adult fleas, ticks, and mosquitoes
  - ○ Kills flea eggs and larvae
  - ○ Dogs and cats over 12 weeks of age
- – Precautions and toxicities
  - ○ May cause eye irritation
  - ○ Caution in debilitated, medicated, aged, pregnant, or nursing animals
  - ○ Local skin irritation or alopecia, salivation, twitches possible side effects in cats
  - ○ Toxic to fish

Interceptor
- – Novartis
- – Milbemycin oxime
- – FDA approved
- – Labeled for
  - ○ Prevention of heartworm disease caused by *Dirofilaria immitis* in dogs and cats
  - ○ Control of adult hookworm (*Ancylostoma caninum*) in the dog and removal in the cat
  - ○ Removal of adult roundworm (*Toxocara cati*) in the cat
  - ○ Removal and control of roundworms (*Toxocara canis, Toxascaris leonina*) and whipworms (*Trichurus vulpis*) in the dog
  - ○ Dogs over 4 weeks of age and over 2 pounds body weight; cats over 6 weeks of age and over 1.5 pounds body weight
- – Precautions and toxicities
  - ○ Caution in face of preexisting heartworm infection; transient shocklike syndrome (labored respiration, vomiting, salivation, lethargy) may occur due to microfilaria dying. Safety in heartworm-positive cats not established
  - ○ Depression, lethargy, vomiting, ataxia, anorexia, diarrhea, convulsions, weakness, hypersalivation are possible side effects
  - ○ Safe for pregnant or lactating dogs when used at labeled dose; overdosage to nursing puppies caused transient tremors/vocalization/ataxia in one study; safety in pregnant, lactating, or breeding cats not established
  - ○ Safe for use in collies up to 20X labeled dose; 25X dose caused ataxia, pyrexia, periodic recumbancy; beagles tolerated a single 200X dose without adverse effects
  - ○ No adverse signs seen in cats administered 10X dose

Lime-sulfur dip
- – Various veterinary products
- – For treatment of *Sarcoptes scabiei*, *Notoedres cati*, *Otodectes cynotis*, *Chyletiella* spp., *Demodex* spp. in dogs and cats
- – Precautions and toxicities
  - ○ Irritation, discomfort, blistering possible; rarely death

Milbemite otic solution
- – Novartis
- – Milbemycin oxime
- – FDA approved
- – Labeled for
  - ○ Treatment of ear mite infestations (*Otodectes cynotis*); effectiveness maintained throughout life cycle of ear mite
  - ○ Cats and kittens over 4 weeks of age

- Precautions and toxicities
  - Reproductive safety has not been evaluated
  - No adverse reactions seen in controlled effectiveness studies
  - One kitten receiving 5X otic dose was lethargic 8 hours post administration; no adverse effects seen in adult cats administered 5X otic dose

Mitaban liquid concentrate
- Pharmacia & Upjohn
- Amitraz
- FDA approved
- Labeled for
  - Treatment of generalized demodicosis in dogs (*Demodex canis*)
- Precautions and toxicities
  - Reproductive safety has not been determined
  - May be harmful if swallowed by humans
  - May alter the animal's ability to maintain homeostasis; do not stress for 24 hours post administration
  - Sedation, pruritis (mite death) are possible side effects; low incidence of convulsions, ataxia, hyperexcitability, behavioral change, hypothermia, appetite stimulation, bloat, polyuria, vomiting, diarrhea, edema, skin irritation, and death
  - Transient sedation in topical overdose, single oral overdose of 100 mg/kg caused death in one animal; transient CNS depression; hypothermia; bradycardia; muscular weakness; vomiting noted with oral administration
  - This product should be applied under the direct supervision of a veterinarian and after careful screening of those applying the product. People taking monoamine oxidase inhibitors, people with diabetes, or pregnant women should not contact this product
  - The authors recommend using it with CAUTION in a shelter situation

Mitaclear
- Pfizer Animal Health
- Pyrethrins, Piperonyl butoxide, N-octyl bicycloheptene dicarboxamide, Di-n-propyl isocinchomeronate
- EPA approved
- Labeled for
  - Kills ear mites
  - Dogs, cats, puppies, and kittens over 12 weeks of age
- Precautions and toxicities
  - Harmful if swallowed in humans
  - Avoid contact with eyes
  - Caution in debilitated, medicated, aged, pregnant, or nursing animals
  - Individual sensitivities possible
  - Toxic to fish

Otomite Plus
- Virbac
- Pyrethrins, Technical piperonyl butoxide, N-octyl bicycloheptene, Di-n-propyl isocinchomeronate
- EPA approved
- Labeled for
  - Ear mite treatment
  - Dogs, cats, puppies and kittens
- Precautions and toxicities
  - Harmful if swallowed
  - Avoid contact with eyes

Preventef Flea and Tick collar
- Virbac
- Diazinon
- EPA approved
- Labeled for
  - Kills fleas and ticks for 5 months
  - Dogs and cats over 5 weeks of age
- Precautions and toxicities
  - Do not allow children to handle or play with collar
  - May cause contact skin sensitization in humans or animals.
  - Do not ingest
  - Do not use with other cholinesterase-inhibiting drugs, pesticides, or chemicals
  - Do not use on Persian cats

Preventic collar
- Virbac
- Amitraz
- EPA approved
- Labeled for
  - Kills ticks for 3 months in dogs
  - Dogs over 12 weeks of age
- Precautions and toxicities
  - DO NOT use in cats
  - Harmful if absorbed through the skin in humans
  - Do not allow children to handle or play with collar
  - Caution in debilitated, aged, medicated, pregnant, or nursing animals
  - Do not use in conjunction with other monoamine oxidase inhibitors, tricyclic antidepressants, selective serotonin reuptake inhibitors, or pressor agents
  - Ingestion may cause severe depression
  - Remove before bathing

Program flavor tabs (and oral suspension for cats)
- Novartis
- Lufenuron
- FDA approved
- Labeled for
  - Prevention and control of flea populations; prevents development of flea eggs, does not kill adult fleas
  - Dogs and cats over 4 weeks of age

- Precautions and toxicities
  - No effect on adult fleas; use with adulticide if preexisting flea infestation
  - Vomiting, depression, lethargy, anorexia, diarrhea, hyperactivity, dyspnea (cats), pruritus, urticaria (dogs), erythema (dogs), skin eruptions (cats) possible side effects
  - Excreted in high concentration in the milk; however, no adverse effects noted
  - No adverse effects noted in dogs given 30X dose or cats given 17X dose

Promeris
- Fort Dodge
- Metaflumizone
- EPA approved
- Labeled for
  - Control of existing flea infestations
  - Protects against flea infestations for up to 7 weeks
  - Reduces flea egg production within 24 hours
  - Dogs, cats, puppies, and kittens over 8 weeks of age (low-volume application)
- Precautions and toxicities
  - 5x the recommended dose was safe on kittens 8 weeks of age
  - Hair at site of application may become matted
  - Cats administered high doses and allowed to groom product showed head shaking and salivation, signs resolved within 45 minutes
  - Not approved for use in pregnant or nursing animals, but preliminary studies found no impact on reproduction or kittens being nursed by queens
  - Clients exposed to product should wash hands if exposed
  - Product safety has not been studied in geriatric cats or cats with chronic diseases; manufacturer recommends geriatric cats and cats with chronic diseases be treated with caution pending more studies

Revolution
- Pfizer
- Selamectin
- FDA approved
- Labeled for
  - Prevention and control of flea infestations (*Ctenocephalides felis*); kills adult fleas and prevents flea eggs from hatching for 1 month
  - Prevention of heartworm disease (*Dirofilaria immitis*)
  - Treatment and control of ear mite infestations (*Otodectes cyanotis*)
  - Treatment and control of roundworm (*Toxocara cati*) and intestinal hookworm (*Ancylostoma tubaeforme*) infections in cats
  - Treatment and control of sarcoptic mange (*Sarcoptes scabiei*) in dogs
  - Control of tick infestations (*Dermacentor variabilis*) in dogs
  - Dogs over 6 weeks of age; cats over 8 weeks of age
- Precautions and toxicities
  - Caution for use in dogs with patent heartworm infestations; although not tested at a higher dose, no hypersensitivity response noted when administered 3X normal dose
  - Localized alopecia or inflammation, vomiting, diarrhea, anorexia, lethargy, salivation, tachypnea, muscle tremors, pruritis, urticaria, erythema, ataxia, fever possible side effects
  - Rare reports of seizures and death
  - Do not use in sick, debilitated, or underweight animals
  - Topical administration of 10X dose in dogs and cats over 6 weeks of age did not cause adverse effects
  - Oral ingestion may cause salivation and vomiting
  - Caution in ivermectin-sensitive collies (oral administration of 5 mg/kg dose caused ataxia in one collie)
  - Safe for use in pregnant and lactating animals

Sentinel
- Novartis
- Milbemycin oxime, Lufenuron
- FDA approved
- Labeled for
  - Dogs only
  - Prevention of heartworm disease
  - Prevention and control of flea populations; prevents development of eggs, does not kill adult fleas
  - Control of adult hookworms (*Ancylostoma caninum*)
  - Removal and control of adult roundworms (*Toxascaris leonine*) and whipworms (*Trichuris vulpis*)
  - Dogs over 4 weeks of age and over 2 pounds of body weight
- Precautions and toxicities
  - Caution in face of preexisting heartworm infection; transient shocklike syndrome (labored respiration, vomiting, salivation, lethargy) may occur due to microfilaria dying (milbemycin oxime)
  - No effect on adult fleas; use with adulticide if preexisting flea infestation
  - Safe for pregnant or lactating dogs when used at labeled dose; overdosage to nursing puppies caused transient tremors/vocalization/ataxia in one study (milbemycin oxime)
  - Safe for use in collies up to 20X labeled dose; 25X dose caused ataxia, pyrexia, periodic recumbancy; beagles tolerated a single 200X dose without adverse effects (milbemycin oxime)
  - At 30X monthly labeled dose (lufenuron) in breeding bitches, puppies had lower birth weights, higher incidences of nasal discharge, pulmonary congestion,

diarrhea/dehydration, and sluggishness when compared to a control group in one study; no adverse signs seen when administered 5X dose

Vectra 3d
- Summit Vet Pharm
- dinotefuran, pyroproxyfen, permethrin
- EPA approved
- Labeled for
  - Use in dogs and puppies as young as 7 weeks of age
  - Prevention and treatment of flea infestations for up to 1 month
  - Prevention of tick infestations
  - Repels and kills fleas, ticks, and mosquitoes
- Precautions and toxicities
  - DO NOT USE ON CATS: can be fatal
  - Do not use in sick, debilitated, aged, pregnant, or nursing animals

Tresaderm
- Merial
- Thiabendazole, Dexamethasone, Neomycin sulfate
- FDA approved
- Labeled for
  - Topical use in dogs and cats
  - No efficacy against ear mites (*Otodectes cynotis*); however, may treat opportunistic or concurrent pathogens (i.e., bacteria, fungal, inflammation)
- Precautions and toxicities
  - May cause hypersensitivity in dogs resulting in erythema of exposed area (neomycin)
  - May cause transient discomfort when applied to fissured areas

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# Section 5
# Other Diseases

# 18
# Rabies

*James C. Wright*

## EPIDEMIOLOGY/COURSE OF THE DISEASE

### Prevalence and distribution in the United States

Rabies is a disease of warm-blooded animals that is caused by an enveloped RNA virus of the *Lyssavirus* genus and rhabdovirus family. The disease almost always follows a fatal course that usually involves behavioral change and other neurological signs in affected animals (Acha and Szyfres 2003). Veterinarians, animal shelters, and animal control agencies have played a key role in the near eradication of rabies in dogs and cats in the U.S. This has decreased the likelihood of human exposure to the point where only a small number of human cases occur yearly in the U.S. In countries where dog rabies still is prevalent, large numbers of human cases continue to occur. See Chapter 23 on zoonosis for more information about rabies.

Rabies most often is detected in certain wildlife species in the U.S.; the risk for wild animals varies by geographic region (Krebs, Mandel et al. 2001; Krebs, Noll et al. 2002; Krebs, Wheeling, Childs 2003; Krebs, Mandel et al. 2004; Krebs, Mandel et al. 2005). From 2000 through 2004, 92% of 36,774 reported animal rabies cases in the U.S. were in wild animals. During this time, species most frequently detected with rabies were raccoons (37%), followed by skunks (30%), bats (18%), and foxes (6%). Rabies also is sporadically reported in other wildlife such as coyotes, badgers, a rare opossum, and even rabbits and at least one unfortunate chipmunk. Rabies in rodents is rare because the bite that transmits the disease usually results in the death of the rodent. The compartmentalization of rabies in the U.S. is related to genetic variants of the virus that circulate within primary wild animal reservoirs, occasionally spilling over into domestic animals. Raccoon rabies is found primarily in the southeastern U.S. and on the eastern seaboard. Skunk rabies is present in the central states, and fox and coyote rabies occur near the Canadian and Mexican borders.

The prevalence of rabies in cats and dogs in the U.S. is much lower than the prevalence in wild animals. From 2000 through 2004, there were 1,420 cases (4% of all animal cases) reported in cats and 513 cases (1% of all animal cases) of rabies in dogs (Krebs, Mandel et al. 2001; Krebs, Noll et al. 2002; Krebs, Wheeling, Childs 2003; Krebs, Mandel et al. 2004; Krebs, Mandel et al. 2005). For many years, the number of cases in cats has exceeded that reported in dogs. This has important public health implications because cats are more likely to exhibit the "furious" form of the disease, thereby exposing many people. Cats are also often not included in rabies licensing laws, and owners may be less likely to have them vaccinated.

Since many cases of rabies probably never reach the reporting system, the true prevalence of the disease in animals in the U.S. is unknown. Wildlife that die of the disease may never be observed, and the probability of a wild animal being submitted to a laboratory for testing is low unless there is human contact or injury. Stray animals are at higher risk from the disease than owned pets because of an increased possibility of prior contact with wild animals, lack of immunization, and possible immunosuppression.

### Transmission and disease course

With rare exceptions, transmission of rabies is through bite wounds from animals shedding virus in the saliva or through saliva contact with broken skin or mucous membranes. Transmission may rarely occur in animals through ingestion of an animal that died of rabies (Beran 1981).

There have been rare occurrences of human transmission of rabies by aerosol. This has occurred in the laboratory and in a cave inhabited by a large number of bats where individuals were exposed to the aerosol for a long period of time. Indirect transmission of rabies in humans also has occurred through corneal transplant from an infected individual and, more recently, from transplant of a kidney and liver from a person who died of rabies (CDC 2004). After a bite from an infected animal, the virus replicates in the wound and then travels centrally from the bite site to the brain through neural tissues and then distally from the brain to the salivary glands and possibly other tissues.

The incubation period for rabies in animals is highly variable (Beran 1981). Most dogs and cats exposed to the virus probably exhibit signs of disease within 3 to 8 weeks of exposure; however, rare instances of prolonged incubation (up to a year or perhaps more) have been reported. Incubation is more likely to be prolonged if the bite occurs at a site more distant from the brain such as an extremity. Although the incubation period may be prolonged, in dogs and cats the period of shedding – and thus the time during which the virus may be transmitted through a bite – is relatively short. Although the possibility exists that a dog or cat will be euthanized at a shelter during incubation but prior to development of clinical signs, the likelihood of the animal being contagious during this period fortunately is small.

Unless postexposure prophylaxis is instituted, rabies in cats and dogs infected with the disease is usually fatal. There are reports of titers in unimmunized and healthy animals, but this has rarely been investigated. However, these reports indicate that rare instances of natural infection and immunization do occur. Clinical disease in dogs and cats occurs at or shortly after replication of the virus in the salivary glands and shedding in the saliva. Except in very rare instances, clinical signs will occur within 10 days of initial virus shedding. This is the basis of the 10-day quarantine requirement for dogs and cats that bite humans. The period from shedding to first clinical signs was unknown in ferrets until recently; a 10-day quarantine period now applies to ferret bites. Less is known concerning rabies virus incubation and shedding in naturally infected wild animals. Raccoons, skunks, and foxes have higher susceptibility to the virus than dogs or cats. Incubation in some wild animals may be prolonged, and at least one case of in utero transmission has been described in the skunk. The incubation of rabies in bats may be prolonged because of sequestration of the virus in the brown fat. Even though in utero transmission has never been reported in dogs and cats, they can be infected at an early age. There are reports of rabies in very young puppies and kittens and, in one case, a rabid puppy exposed 31 people (CDC 1996). In a similar case, over 600 people received postexposure prophylaxis following exposure to a rabid kitten (CDC 1995). This is the largest number of people exposed to a single source of rabies in the U.S.

**Clinical signs**

A wide range of clinical signs may be exhibited by animals infected with rabies virus. Most notable are neurological signs that may result in behavior changes such as unusual aggression (“furious” form of the disease) or somnolence (“dumb” rabies). Dogs that are normally friendly may become withdrawn, and those that are normally withdrawn may become friendlier. Other neurological signs may include aggression, extreme excitation, and exaggerated responses to external stimuli. Pruritis (intense itching) may occur at the site of exposure. Rarely, in dogs, this may lead to self-mutilation at the site of exposure. Wildlife infected with the virus are more likely to be out during the day, approach humans, and get hit by cars. Cats are more likely to exhibit the “furious” form of the disease. Early signs of moderate fever and loss of appetite are vague, which means rabies may not always be included on a differential diagnosis list. An aberrant appetite (pica) also may be exhibited, with dogs attempting to eat wood, stones, or other foreign objects. The hydrophobia exhibited by human patients is not seen in animals, and rabid dogs may show an increased thirst. Dogs typically also exhibit excessive salivation and drooling and will hold their heads down for this reason. In dogs and raccoons, the neurological signs associated with distemper and pseudorabies virus may be confused with rabies; however, distemper generally occurs in larger numbers of animals, and rabies tends to be more sporadic in nature. Foxes infected with canine distemper or infectious canine hepatitis virus also can appear to be rabid. Changes in behavior in dogs and cats placed in a shelter environment may be difficult to distinguish from early behavior changes caused by rabies. Animals exhibiting the “dumb” form of rabies may be especially difficult to distinguish from those that are withdrawn due to the shelter environment.

**Diagnosis**

There is no reliable antemortem test available for the diagnosis of rabies at this time. The head of the animal must be removed and submitted to the appropriate laboratory for testing of the brain tissue. In the case of bats, the entire body can be submitted. Samples should not be frozen, but placed in ice. Complete guidelines for sample submission should be obtained from the laboratory.

## PREVENTION AND CONTROL/RISK ASSESSMENT

### Role of shelters

Shelters play an important role in protecting the public from rabies by removing stray animals and feral dogs and cats from high population density areas. This reduces public contact with animals that have an increased risk from exposure to rabid wild animals. Additionally, rabies vaccine clinics for dogs and cats may sometimes be conducted at shelters. Care must be taken that this activity is conducted only with appropriate veterinary support. Practice acts in different states vary concerning restrictions placed on the conduct of rabies clinics. For instance, some states require that a veterinarian–client–patient relationship exist before a vaccination can be given. Before a clinic is conducted, the state veterinary board should be consulted. Care should be taken to provide enough space for people waiting to have their animals vaccinated. Provisions also should be made to keep the vaccine properly refrigerated prior to use. In locations where people other than veterinarians can administer the vaccine, there should be training on proper vaccine administration. Animals must be kept safely restrained both in the waiting area and for the actual injections.

Some shelters with animal control responsibilities may be involved in dealing with wild animals that are ill, injured, or make nuisances of themselves. Shelter personnel must be aware of the presence of rabies in wildlife in their area. State departments of public health are a good resource for information on rabies in specific areas.

### Management in animals

Dog and cat rabies is rare in the U.S. due to vaccination of owned animals; however, animals presented to shelters likely are at increased risk from exposure to the disease when compared to owned pets. Recognition of the behavioral signs of rabies in a shelter setting may be difficult because many of the animals in shelters will be fearful or aggressive when first admitted to the shelter. Animals with non-specific signs of illness are sometimes euthanized without testing for rabies.

The *Compendium of Animal Rabies Prevention and Control* is published yearly in the *Journal of the American Veterinary Medical Association* and provides guidelines for prevention and control of the disease in animals along with licensed vaccines in the U.S. These guidelines are also available at the website of the National Association of State Public Health Veterinarians (http://www.nasphv.org). The *Compendium* provides basic guidelines for rabies prevention and control. Specific rabies laws for each state, and in some cases each county, may vary greatly; therefore, shelters should be familiar with all local laws that affect them. In general, local rabies laws may be more stringent than state laws, but not more lenient. Some states recognize rabies vaccination in ferrets while others do not. There also is a great deal of controversy concerning wolf hybrids. Most states do not consider rabies vaccines in wolf hybrids to be valid in the event of a bite or exposure by a known or suspected rabid animal. The best source for state and county rabies laws is the office of the state public health veterinarian.

Recommendations in the *Compendium for Animal Rabies Control* for dogs and cats currently vaccinated and exposed to rabies through contact with a known or suspected rabid animal are that a single booster rabies vaccination should be administered immediately, and then dogs should be restricted to leash walking by the owner for 45 days. (The type of confinement may vary from state to state.) If the dog or cat is not current on rabies vaccination or is unvaccinated, the first recommendation in the event of an exposure is euthanasia. If this is unacceptable, the dog or cat can be confined by strict isolation for six months, meaning confinement in an enclosure that precludes direct contact with people and other animals, or as otherwise defined by local regulations. Revaccination can be administered immediately at the beginning of the isolation period or 30 days before its end. Public health departments are responsible for enforcement of local rabies laws in the event of owner noncompliance, though this may be delegated to law enforcement or animal control authorities.

Dogs and cats that are shedding rabies virus at the time of a bite should demonstrate clinical signs within 10 days. For this reason, healthy dogs and cats that bite humans are quarantined and observed for 10 days. If signs suggestive of rabies develop during this time, the animal is humanely euthanized and tested for rabies. Shelters may become involved in the quarantine of animals that bite humans. This can be problematic because of limited space available for quarantine or lack of veterinary support. If animals are quarantined in a shelter for rabies observation, clear lines of communication must be established in order to prevent unnecessary contact with humans or animals, euthanasia, or destruction of an animal carcass so that it is then not available for rabies testing. Requirements for veterinary observation of an animal under quarantine vary in different states; however, the safest approach for shelters is to seek consultation with a veterinarian and the public health department.

Rabies virus does not survive long in the environment, and is inactivated by sunlight, dessication, or commonly

used disinfectants, including quaternary ammonium, sodium hypochlorite, and alcohol. Fomite transmission is considered very unlikely, but it is recommended that staff wear protective garments and minimize handling of suspect or quarantined animals.

**Rabies vaccination in shelters**

Shelter vaccination guidelines by both the American Animal Hospital Association (AAHA) and the American Association of Feline Practitioners (AAFP) do not recommend administration of rabies vaccine to animals entering shelters unless they are going to be held for an extended period of time (AAHA Canine Vaccine Task Force 2006; AAFP Advisory Panel 2006). Adoptable dogs and cats may or may not be vaccinated at the shelter prior to adoption depending on local regulations and the availability of a veterinarian for supervision. If dogs and cats with unknown vaccination status are not vaccinated prior to adoption, new owners should be required to visit a veterinarian as soon as possible so the vaccination may be administered. Some shelters collect a deposit that then is redeemed by the veterinarian or adopter after the vaccine has been administered.

Rabies vaccination of dogs, cats, and ferrets is recommended beginning at 3 to 4 months of age, with a booster at 1 year of age. A booster is given 1 year after initial vaccination regardless of the age of the animal. Boosters then are given either yearly or every 3 years depending on the legal requirements of the state or territory. Fifteen rabies vaccines are licensed for use in cats and dogs in the U.S. (NASPHV 2006). Nine of these vaccines (60%) are licensed for the 1-year booster vaccination and six (40%) are licensed for the 3-year booster use (NASPHV 2006). Vaccines licensed for 1 year have been tested for efficacy at 1 year through a challenge study (inoculation of vaccinated dogs and unvaccinated controls in the masseter muscle with field virus). Vaccines licensed for 3 years are tested for efficacy with a challenge study 3 years following vaccination. Care must be taken that a 1-year vaccine not be used when booster immunization is not going to be given for 3 years. However, a "3-year" vaccine may be given to an animal requiring a booster in 1 year, provided the rabies certificate indicates the correct required time for a booster.

For cats, several recombinant vaccines are available that contain rabies glycoprotein with a live canarypox vector. These vaccines can be given to cats as young as 8 weeks of age and may reduce the risk of sarcomas that have been associated with adjuvanted rabies vaccines in cats (FTSF 2005). Recombinant canary pox vaccines may be valuable for use in shelter and community trap–neuter–return programs where 8-week-old kittens may be sterilized, vaccinated and released; however, they must be given yearly.

Most states require rabies boosters for dogs and cats every 3 years. Following initial vaccination, animals are considered to be immunized approximately 1 month postvaccination. Animals receiving a booster vaccination should develop an adequate immune response within 2 to 3 days. For more information on rabies vaccination of shelter dogs and cats, see Chapter 5.

An oral recombinant rabies vaccine using a live vaccinia vector is licensed for restricted use in federal control programs for raccoon and coyote rabies in the U.S. This vaccine is packaged as a plastic packet in a rectangular fishmeal polymer bait the size of a matchbox that either is distributed by hand or dropped from a plane. Oral baiting is now being used to control raccoon rabies in the eastern U.S. in a distribution area from Canada to the Gulf of Mexico along the western face of the Allegheny Mountains and to control coyote rabies in west central Texas. Shelters in areas where bait control programs are being conducted may become involved in educating the public about this vaccine. The baits are clearly marked and people should leave them alone. They are not harmful to domestic animals.

**Rabies preexposure and postexposure in humans**

Pet vaccination programs have reduced the prevalence of rabies in dogs and cats in the U.S.; however, the disease is still a public health concern following animal bites. Each year, thousands of people in the U.S. receive postexposure rabies prophylaxis following dog or cat bites. Rabies postexposure prophylaxis consists of the administration of rabies immune globulin and five doses of rabies vaccine given in the deltoid or upper arm on days 0, 3, 7, 14, and 28 (CDC 2006).

Preexposure rabies immunization is recommended for individuals who are at higher risk from exposure to rabies than the general public. This includes veterinarians and shelter workers with direct animal contact in rabies-endemic and epizootic areas. Preexposure rabies prophylaxis consists of three doses of rabies vaccine given on days 0, 7, and 21–28. Virtually all persons receiving the three-dose series of rabies vaccine develop an acceptable titer (1:5). There are both medical and psychological benefits to preexposure immunization. Previously immunized people who are exposed to rabies require only two doses of rabies vaccine, which reduces the likelihood of reaction to the vaccine. In addition, preexposure immunization provides a degree of

protection from rabies in the event of an unknown exposure. An obvious psychological benefit is an increased sense of protection after an animal bite. This helps to reduce emotional overreaction if a rabies exposure occurs. People who have received rabies preexposure immunization should have their titers checked every 2 years. An acceptable rabies antibody titer in the U.S. is 1:5.

Clear protocols should be established concerning rabies and animal bites. Ideally, a shelter should have access to a physician who fully understands rabies pre- and postexposure needs and proper procedures following an animal bite. See Chapter 23 for more information on bite wound management and rabies. If an animal in a shelter is diagnosed with rabies, staff members who have had contact with the rabid animal should be interviewed in order to determine whether other exposures have occurred. This also may involve determining whether there has been exposure among the general public visiting the shelter. It will also be necessary to identify any other animals with which the rabid animal may have had direct contact. The state public health department will determine how these cases are managed.

## CLIENT EDUCATION/IMPLICATIONS FOR ADOPTION

Shelters can play an important role in educating the public about rabies prevention and control. Brochures from the American Veterinary Medical Association, the Centers for Disease Control and Prevention, and state Departments of Public Health can be made available along with other educational materials. People who adopt dogs and cats must be educated about the importance of regular rabies immunization for their new pets.

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# 19
# Feline Leukemia Virus and Feline Immunodeficiency Virus

*Julie K. Levy*

## INTRODUCTION

Although the prevalence of feline leukemia virus (FeLV) and feline immunodeficiency virus (FIV) in shelters mirrors the relatively low rates found in pet cats (Levy, Scott et al. 2006), because of the sheer numbers that enter shelters several hundred thousand infected cats are likely to pass through shelters each year. Shelters should have policies in place for testing, prevention, and dealing with positive test results.

Identification and segregation of infected cats is considered the most effective method for preventing new infections with FeLV and FIV. Despite the availability of point-of-care testing and vaccines, less than one-quarter of all cats have ever been tested, and infections with these viruses are still common. Although characteristics such as sex, age, lifestyle, and health status can be used to assess the likely risk of FeLV and FIV infections, cats in all categories are at risk.

## EPIDEMIOLOGY AND COURSE OF DISEASE

### Etiologic agent and susceptible species

FeLV (oncornavirus) and FIV (lentivirus) are both in the family *Retroviridae*. The primary host species for FeLV and FIV is the domestic cat.

FeLV is also enzootic in some populations of the European wildcat but is only rarely reported in other nondomestic felids such as the bobcat, sand cat, and puma (Sleeman, Keane et al. 2001; Ostrowski, Van Vuuren et al. 2003).

Domestic cat FIV can infect nondomestic felids, but many felid species have their own distinct FIV strains that are genetically distinct from domestic cat FIV. This indicates that evolutionarily domestic and nondomestic FIV strains diverged long ago and that transmission between species is infrequent (Olmsted, Langley et al. 1992; Brown, Yuhki et al. 1994). At least 27 felid species have been shown to harbor FIV, including the lion, cheetah, and puma. In many species, the prevalence of infection is higher than that in domestic cats and may reach up to 90% (Brown, Yuhki et al. 1994; Evermann, Foreyt et al. 1997; Roelke, Forrester et al. 1993). It is generally believed that the nondomestic felid lentiviruses are less pathogenic in their natural hosts than FIV is in the domestic cat, but virus-associated immune alterations have been documented in multiple species (Roelke, Pecon-Slattery et al. 2006).

### Zoonotic potential

FeLV and FIV are not believed to be zoonotic. Both viruses have been shown to replicate in human cell lines, and FIV infection has been experimentally induced in nonhuman primates, but there is no conclusive evidence that either virus is capable of infecting humans under natural conditions (Sordillo, Markovich, Hardy 1982; Loar 1987; Morgan, Dornsife et al. 1993; Butera, Brown et al. 2000; Johnston, Olson et al. 2001).

### Prevalence

In the United States, seroprevalences of FeLV and FIV are less than 2% in healthy cats, and 6% to 33% in high-risk cats and cats that are tested during illness (Levy, Scott et al. 2006; O'Connor, Tonelli, Scarlett 1991; Moore, Ward et al. 2004). Risk factors for seropositivity include male sex, adulthood, and outdoor access, whereas indoor lifestyle and sterilization are associated with reduced infection risks (Levy, Scott et al. 2006; O'Connor, Tonelli et

al. 1991). This protection is likely to be due to the reduced risk of encountering and fighting with infected cats, events that are risk factors for transmission (Hoover and Mullins, et al. 1991; Levy 2000; Levy and Crawford 2005).

The prevalence of FeLV infection has reportedly decreased during the past 20 years, presumably as a result of implementation of widespread testing programs and development of effective vaccines (Levy and Crawford 2005; Cotter 1998). In contrast, testing for FIV infection is less widespread, and a vaccine against FIV has only recently been introduced. Thus, whether the prevalence of FIV infection is also changing is unknown.

In a study of more than 18,000 cats tested in 2004, 2.3% were seropositive for the FeLV antigen and 2.5% were seropositive for FIV antibody (Levy, Scott et al. 2006). For both viruses, seroprevalence was higher among cats tested at veterinary clinics (FeLV, 2.9%; FIV, 3.1%) than among cats tested at animal shelters (FeLV, 1.5%; FIV, 1.7%), and higher in pet cats that were allowed outdoors (FeLV 3.6%; FIV 4.3%) than in pet cats that were kept strictly indoors (FeLV, 1.5%; FIV, 0.9%). For cats tested at animal shelters, the source (stray, relinquished, or feral) was not significantly associated with FeLV seropositivity, but feral cats had a higher risk of FIV seropositivity (3.9%) than did stray cats (1.6%) and relinquished pet cats (1.4%). Seropositivity was higher among sick cats than healthy cats and was highest in sick feral cats (FeLV, 15.2%; FIV, 18.2%), followed by sick pet cats allowed outdoors (FeLV, 7.3%; FIV, 8.0%). In contrast, seropositivity in healthy feral cats (FeLV, 1.0%; FIV, 3.3%) was lower than in healthy pet cats allowed outdoors (FeLV, 2.6%; FIV, 3.2%). Specific diseases are associated with a very high rate of retroviral infections, including cutaneous abscesses (FeLV, 8.8%; FIV 12.7%) (Goldkamp, Levy et al. 2007), and oral diseases (FeLV, 7.3%; FIV, 7.9%) (J Bellows, unpublished data).

### Morbidity, mortality, and prognosis

FeLV and FIV cause chronic infections with a generally low transmission rate, so outbreaks are not expected. Although infected cats may experience a prolonged period of clinical latency, a variety of disease conditions are associated with retroviral infections, including anemia, lymphoma, chronic inflammatory conditions, and susceptibility to opportunistic infections (O'Connor, Tonelli, Scarlett 1991; Hoover and Mullins 1991; Levy 2000).

Both FIV- and FeLV-infected cats can live many years with proper care and may die at older ages from causes unrelated to their retrovirus infections. Long-term monitoring of a 26-cat household with endemic FeLV and FIV revealed that all FeLV-infected cats died within 5 years, but FIV infection did not affect survival in this household (Addie, Dennis et al. 2000).

A large study compared the survival of more than 1,000 FIV-infected cats to more than 8,000 age- and sex-matched uninfected control cats (Levy, Lorentzen et al. 2006). Of cats that were not euthanized around the time of diagnosis, the median survival rate of the FIV-infected cats was 4.9 years compared to 6.0 years for control cats. A similar comparison was made between more than 800 FeLV-infected cats and more than 7,000 controls. The cats represented a mix of healthy cats presented for well-care visits and those presented for evaluation of health problems. Median survival of FeLV-infected cats was 2.4 years compared to 6.3 years for controls. With proper care, many retrovirus-infected cats may live for several years with a good quality of life. Thus, a decision for treatment or for euthanasia should never be based solely on the presence of a retrovirus infection.

In animal shelters, the most common cause of death in FeLV- and FIV-infected cats is likely to be euthanasia for infection control purposes or because infected cats may be less readily adopted than uninfected cats. Thus, the prognosis for individual infected cats often depends more on shelter policy and circumstances than on the diseases associated with viral infection.

### Mode of transmission

FeLV infection is primarily a concern for cats that are friendly with other cats, as close, intimate contact between cats is required for transmission. Cats typically acquire FeLV via the oronasal route by nursing, mutual grooming, or sharing dishes, but also through bites. Viremic cats act as a source of infection since FeLV is shed in saliva, nasal secretions, feces, milk, and urine (Hardy, McClelland et al. 1976; Pacitti, Jarrett, Hay 1986). It has been reported that the susceptibility of cats to FeLV is age dependent. In one study, all newborn kittens and the majority of cats up to 2 months of age developed progressive infection, compared to only 15% of the cats that were inoculated when they were 4 months or older (Hoover, Olsen et al. 1976). Although cats become increasingly resistant to FeLV infection with age (Grant, Essex et al. 1980), recent studies evaluating the duration of immunity for FeLV vaccines have demonstrated that unvaccinated adult cats are readily infected (Lehmann, Franchini et al. 1991).

FIV infection is primarily a concern for cats that are unfriendly with other cats, as the major mode of transmission is through bite wounds. Transmission of FIV from infected queens to their kittens has been reported in

laboratory-reared cats, but it appears to be an uncommon event in nature. Although transmission among household cats that do not fight is uncommon, it is possible. In one household of 26 cats that were not observed to fight, FIV infection was originally diagnosed in nine cats, but spread to six other cats during the 10-year observation period (Addie, Dennis et al. 2000).

Both viruses are efficiently transmitted by fomites, during invasive procedures or by blood transfusions, so universal precautions are essential to prevent spread of the diseases.

**Incubation period and persistence of infection**

Acute infection with either virus is rarely associated with any observable clinical signs and is likely to go unnoticed by shelter staff and cat owners. In laboratory-infected cats, transient leukopenia, fever, and malaise have been reported during the first few weeks of infection.

The development of the polymerase chain reaction (PCR) and its ability to detect minute amounts of virus has recently challenged the long-held belief that a substantial proportion of cats eliminate FeLV after transient infection. Although new information is still emerging, it is now believed that most cats remain infected for life, even if circulating antigen tests become negative. PCR for FeLV provirus has demonstrated that most cats experience either "progressive infection," in which inadequate FeLV-specific immunity is associated with persistent antigenemia, viremia, and development of FeLV-associated diseases within a few years; or "regressive infection," in which an effective immune response contains virus replication prior to bone marrow infection and clinical disease is unlikely to result (Hofmann-Lehmann, Cattori et al. 2007a; Hofmann-Lehmann, Cattori et al. 2007b; Torres, Mathiason, Hoover 2005; Flynn, Hanlon et al. 2000; Flynn, Dunham et al. 2002; Lutz, Pedersen, Theilen 1983; Pedersen, Theilen et al. 1997). Progressive and regressive infections have been distinguished by repeated testing of peripheral blood. Following effective exposure to FeLV, most cats become PCR positive for FeLV provirus within 1 week and antigen positive within 3 weeks of virus exposure (Hofmann-Lehmann, Huder et al. 2001). Progressive infections are associated with persistence of antigenemia, viremia, and provirus for more than 16 weeks, whereas regressive infections are characterized by persistence of provirus but loss of circulating antigens and virus. The clinical relevance of PCR-positive, antigen-negative cats is not yet clear, but as the provirus is integrated into the cat's genome, it is unlikely to be completely eliminated over time (Cattori, Tandon et al. 2006).

In contrast to FeLV, FIV is well accepted to cause persistent viremia from which few cats are ever expected to recover.

In summary, the data available at this time indicate that both FeLV and FIV represent lifelong infections. Cats with regressive FeLV infections are not viremic, are unlikely to develop FeLV-associated diseases, are at low risk for transmitting infection, and may be immune to superinfection following subsequent FeLV reexposure. Cats with FIV infections are expected to remain viremic and infectious to other cats for life.

**Shedding**

Viral shedding in saliva begins as early as 1 week postinfection in FIV and a few weeks later in FeLV (Matteucci, Baldinotti et al. 1993; Lutz and Jarrett 1987). Both viruses are subsequently shed in high concentrations in saliva and milk throughout viremic infections, with lesser amounts found in other body secretions. Interestingly, the infectivity of FIV in milk is counteracted by the concurrent shedding of FIV antibodies, which protect most nursing neonates from infection (Pu, Okada et al. 1995). This protection does not occur with FeLV, for which nursing is considered to be a major mode of transmission.

**Clinical signs**

There are no typical clinical signs for retroviral infections in cats. FeLV can contribute to fading kitten syndrome in neonatal cats, but most clinical signs are associated with the effects of chronic retroviral infections leading to anemia, chronic inflammatory conditions such as stomatitis, neoplasia, and opportunistic secondary infections.

**Diagnosis**

***Diagnosis of FeLV***

Routine diagnosis of FeLV relies on detection of viral antigen p27 in peripheral blood. In-clinic enzyme-linked immunosorbent assay (ELISA) and other immunochromatographic test kits detect soluble circulating antigen. These tests may be more reliable when serum or plasma is tested, rather than whole blood (Barr 1996). Antigen tests should not be performed on tears or saliva as these are prone to more erroneous results (Lutz and Jarrett 1987; Hawkins 1991; Hawkins, Johnson et al. 1986). Most infected cats test positive on soluble antigen tests within 28 days of exposure (Jarrett, Golder, Stewart 1982); however, development of antigenemia is extremely variable and may take considerably longer in some cats. When soluble antigen testing is negative and recent infection

cannot be ruled out, testing should be repeated a minimum of 28 days after the last potential exposure. Kittens may be tested at any time, as passively acquired maternal antibodies do not interfere with testing for viral antigen. However, some kittens infected by maternal transmission may not test positive for weeks to months after birth.

Since the consequences of a positive test are significant, confirmatory testing is recommended, especially in low-risk and asymptomatic patients where the risk of a false-positive result is higher (Barr 1996; Jacobson 1991; Gerstman and Cappucci 1986). Positive test results can be confirmed immediately by repeating the antigen testing using a test from a different manufacturer. Alternatively, an immunofluorescent antibody (IFA) test can be performed (Barr 1996; Hartmann, Werner et al. 2001). A positive IFA on a blood or bone marrow test at any time indicates a cat likely to remain persistently viremic. Antigen tests can also be repeated 1 to 2 months after the initial positive test to identify cats with regressive versus progressive infections. Negative test results are highly reliable due to the low prevalence of infection in most populations (Barr 1996; Jacobson 1991; Gerstman and Cappucci 1986).

Discordant test results occur when results of two different antigen tests disagree or when antigen test results disagree with other test modalities such as IFA and PCR. This situation makes it difficult to determine the true FeLV status of a cat, since it is not possible to determine which of the conflicting results is correct. Discordant results may be due to the stage of infection, the variability of host response, or technical problems with testing. The status of the cat with discordant results may eventually become clear by repeat testing in 60 days and yearly thereafter until the test results agree. Cats with discordant test results are best considered as potential sources of infection for other cats until their status is clarified.

PCR testing is offered by a number of commercial laboratories for the diagnosis of FeLV. PCR detects viral nucleic acids instead of antigen and can be performed on blood or tissues. When performed under well-controlled conditions, PCR is a highly sensitive test methodology for FeLV and may help resolve cases with discordant test results. PCR testing of saliva has been shown to have very high correlation with blood antigen tests (Gomes-Keller, Gonczi et al. 2006; Gomes-Keller, Tandon et al. 2006). PCR is usually positive within 1 week of infection. It should be noted that provirus PCR is likely to be positive in both cats with progressive infection (likely to be shedding virus and at risk for virus-associated disease) and with regressive infection (not likely to shed virus or to develop disease).

### *Diagnosis of FIV*

In contrast to FeLV, the amount of circulating FIV protein (antigen) is too low to be useful for diagnosis. Since FIV produces a persistent, lifelong infection, the detection of antibodies in peripheral blood is a sufficient surrogate diagnosis if the cat has not been previously vaccinated against FIV (Levy, Crawford et al. 2004; Hartmann 1998). In-clinic test kits use colorimetric techniques, such as ELISA, for detection of antibodies to viral antigen p24. Most cats will produce antibodies to FIV within 60 days of exposure, but time to seroconversion may be considerably longer in some cats (Barr 1996). A recent study showed that the performance of a patient-side FIV/FeLV test kit for the detection of FIV antibodies was excellent (Levy, Crawford et al. 2004). When the results of antibody testing are negative, but recent infection cannot be ruled out, testing should be repeated a minimum of 60 days after the last potential exposure. Western blot detects antibodies against a range of viral antigens and is used as a confirmatory test. Since the consequences of a positive test are significant, confirmatory testing is recommended, especially in low-risk and asymptomatic patients where the risk of a false-positive result is higher (Barr 1996; Jacobson 1991; Gerstman and Cappucci 1986). Negative test results are highly reliable due to the high sensitivity of the tests and the low prevalence of infection in most populations. Similar to FeLV, when discordant serological test results occur (positive on one test and negative on another test), it is not possible to know the true infection status of the cat.

The release of the first FIV vaccine (Fel-O-Vax FIV®, Fort Dodge Animal Health) has complicated the ability to diagnose FIV infections. Vaccinated cats produce antibodies that cannot be distinguished from antibodies due to natural infection (Levy, Crawford et al. 2004). In some cats, it may be difficult to determine whether a positive FIV antibody test means the cat is truly infected with FIV, is vaccinated against FIV but not infected, or is vaccinated against FIV and also infected. Recently, an experimental method of ELISA testing that detects antibodies to multiple FIV antigens has been described (Kusuhara, Hohdatsu et al. 2007). Using this method, researchers were able to distinguish uninfected cats from infected cats, regardless of whether they were vaccinated (Levy, Crawford et al. 2008b).

PCR has been promoted as a method to determine a cat's true FIV status, but investigation of the sensitivity and specificity of FIV PCR tests offered by commercial laboratories has shown a wide range of accuracy (Bienzle, Reggeti et al. 2004). In one study, test sensitivities (the

ability to detect true positives) ranged from 41% to 93%, and test specificities (the ability to detect true negatives) ranged from 81% to 100% (Crawford, Slater, Levy 2005). False positives were higher in FIV-vaccinated cats than in unvaccinated cats.

Positive FIV antibody tests in kittens under 6 months of age must be interpreted carefully. Kittens born to infected queens or FIV-vaccinated queens may acquire FIV antibodies in colostrum (MacDonald, Levy et al. 2004). Since it is uncommon for kittens to become infected, most kittens that test positive are not truly infected and will test negative when reevaluated at 6 months of age or older. Kittens that test positive for FIV antibodies when over 6 months of age are considered to be infected. For this reason, it is a common practice to delay testing kittens for FIV until they are over 6 months of age. However, this results in many cats never being tested and allows for the possibility that FIV-infected kittens may be inadvertently housed with uninfected cats.

### *Testing in shelters*

Diagnosis of FeLV and FIV in shelter situations follows the same principles as in pet cats. Although screening tests are commonly used in shelters, confirmatory tests pose a greater challenge. Increased costs, delays, and difficulty in interpreting discordant results are reasons why many shelters do not pursue confirmatory testing. Currently, the inability to distinguish FIV-vaccinated cats from those that are infected or both vaccinated and infected is a major concern for shelters.

All cats entering shelters should be considered potentially infected, regardless of the environment from which they originate. Both viruses have a relatively low prevalence, even in healthy stray and feral cat populations, so most test results will be negative. Because the background of most shelter cats is unknown, it is advisable to retest cats 2 months after the initial test in case of recent exposure. This also applies to unweaned orphaned kittens, which may have been exposed to an infected queen or other cat, but test negative at the time of admission to the shelter. These kittens should be retested prior to adoption. Cats that are returned to the shelter following a failed adoption should also be retested, since they may have been exposed to FeLV or FIV in their adoptive homes.

Testing at admission is optional for cats that are housed in single-cat cages. It is common for some shelters to test cats at the time of adoption instead of at admission, particularly if a substantial proportion of cats are not expected to be adopted. In some situations, shelter resources do not permit testing of all cats prior to adoption. In such cases, it should be clearly explained and documented to the adopter that the American Association of Feline Practitioners (AAFP) recommends testing of all newly adopted cats (Levy, Crawford et al. 2008a). Arrangements should be made by adopters to have their new pets tested by their own veterinarians as soon as possible. The new pet should be kept separate from other cats until the test results are known, and preferably until a second test is performed 2 months later.

Limited shelter resources may dictate that not all cats can be tested for both FeLV and FIV. In such cases, shelters can place priorities on testing cats at higher risk: sick cats, adult uncastrated males, and cats suspected to have been exposed to infected cats. The testing of cats prior to treatment for diseases such as dermatophytosis or upper respiratory tract infection may be useful since these diseases may have a more protracted course in cats with retroviral infections. If limited testing is employed, it is advisable to house cats singly and to recommend testing postadoption. If one cat in a litter or group is later reported to be infected, the adopters of other cats that had contact with the infected cat should be contacted and informed.

Cats should have negative test results for both FeLV and FIV prior to being introduced to group housing. It is ideal to quarantine and retest 2 months later, prior to group housing, to avoid the risk of admitting a cat that has been recently infected but has not yet seroconverted. Since the actual risk is low, and because quarantine is often not practical in a shelter setting, many shelters place cats into group housing immediately following a single negative test result. Resident cats in foster homes should be tested before foster cats are added to the household.

In shelters that group house cats long term, cats should be retested at least annually since cats held in multi-cat environments constitute a high-risk population even if all of the cats are tested when they are first added to the group. This is especially true if cats are not retested 2 months after the initial test or if there is a high rate of turnover within the group.

Although testing all cats for retroviral infection is generally recommended, an exception exists for feral cats in trap–neuter–return (TNR) programs. The prevalence of infection is similar in outdoor pet cats and feral cats, so feral cats do not represent an increased threat of transmission compared to pet cats. Additionally, neutering reduces the two most common modes of transmission: queen to kitten for FeLV and fighting among males for FIV; neutering may be a more cost-effective method for reducing viral transmission than testing. Since population control of feral cats requires commitment to neutering the largest number

of cats possible, many TNR programs do not routinely test feral cats (Wallace and Levy 2006).

The presence of infection varies within litters, feral cat colonies, and households. Some shelters attempt to conserve resources by testing only a queen and not her kittens, or test only a few members of a litter or household, but it is inappropriate to test one cat as a surrogate for another. Because the prevalence of retroviruses is low, even among feral cats, it is also inappropriate to test a small number of cats within a colony if the intent is to determine whether FeLV or FIV is present in the group. Medical records of shelter cats should accurately reflect the actual testing procedures performed for each cat.

Test procedures must be performed as indicated by the manufacturer to maintain accuracy. Procedures such as pooling multiple samples for use in a single antigen test reduce the sensitivity for each sample and should not be performed.

*Specific shelter testing recommendations*

- Testing at admission is optional for singly housed cats.
- Testing is highly recommended for group-housed cats.
- If not performed prior to adoption, the new owner should be advised to have the cat tested before exposure to other cats.
- Testing should be repeated 2 months after the initial test and at least annually for cats kept in long-term care.
- Each cat should be individually tested.
- Both foster families and adopters should have their own resident cats tested prior to fostering or adopting a new cat.
- Testing is not routinely performed in most large-scale feral cat TNR programs.

## PREVENTION AND CONTROL

Infected cats should be housed in individual cages and may be maintained in this manner in the general population. While FeLV and FIV are not easily transmitted via fomites, other pathogens are, including calicivirus, herpesvirus, coronavirus, panleukopenia virus, and dermatophytes. Since cats with retroviral infection may be immunosuppressed and at increased risk of infection and transmission of these pathogens, it would be ideal to house cats with FeLV or FIV infection in an area of the shelter without other cats. Animal caretakers should always wash their hands after handling animals and cleaning cages. Both FeLV and FIV can be transmitted in blood transfusions; therefore, all blood donors should be confirmed free of infection (Wardrop, Reine et al. 2005).

Dental and surgical instruments, needles, tattoo equipment, endotracheal tubes, and other items potentially contaminated with body fluids should be thoroughly cleaned and sterilized between uses. Fluid lines, multidose medication containers, and food can become contaminated with body fluids (especially blood or saliva) and should not be shared among patients.

### Vaccination

#### *FeLV vaccination*

Several FeLV vaccines are available. A review of independent studies of vaccine efficacy indicates that the ability of any particular vaccine brand to induce an immune response sufficient to prevent persistent viremia varies considerably between studies (Sparkes 1997). Results of several studies indicate that FeLV vaccine-induced immunity persists for at least 12 months following vaccination, although the actual duration of immunity is unknown (Harbour, Gunn-Moore et al. 2002; Hoover, Mullins et al. 1996; Hofmann-Lehmann, Holznagel et al. 1995).

Because protection is not induced in all vaccinates, vaccination against FeLV does not diminish the importance of testing cats to identify and isolate those that are viremic. Therefore, the FeLV infection status of all cats should be determined prior to beginning FeLV vaccinations. There is no value in administering FeLV vaccines to individuals confirmed to be infected.

FeLV vaccines are considered noncore vaccines and are recommended for cats at risk of exposure (e.g., cats permitted outdoors, residing in multiple-cat environments in which incoming cats are not tested prior to entry, residing in homes with frequent cat turnover such as foster homes, living with FeLV-infected cats, or residing with cats in which FeLV infection status is not known or in which introduction of new cats is common). However, vaccination of all kittens is highly recommended because they may subsequently be at risk of FeLV exposure even if not currently at risk. Kittens are also more likely than adult cats to become persistently viremic if exposed.

When FeLV vaccination is determined to be appropriate, a two-dose primary series is recommended, with the first dose administered as early as 8 weeks of age followed by a second dose administered 3 to 4 weeks later. Annual booster vaccinations should be administered thereafter as long as the risk of exposure remains.

Of note, although FeLV vaccination may protect cats against persistent viremia, it may not always protect against regressive infection. Vaccinated cats were found to be provirus positive as well as plasma viral RNA positive subsequent to FeLV exposure, even when antigenemia and

viremia were absent (Hofmann-Lehmann et al. 2007a; Hofmann-Lehmann, Tandon et al. 2006). Thus, FeLV vaccination does not necessarily induce sterilizing immunity. Nonetheless, efficacious FeLV vaccines are of great clinical importance. They protect cats from persistent viremia and subsequent FeLV-associated fatal diseases.

### *FIV vaccination*

As is the case for other lentiviruses, it has been difficult to develop a vaccine against FIV that protects against the broad range of virus subtypes that are found in the field (Dunham 2006). Only a single vaccine is currently available for prevention of FIV infection in the U.S. and Canada. The vaccine is a whole-virus, dual-subtype (subtypes A and D), inactivated product combined with an adjuvant. The vaccine is licensed for the vaccination of healthy cats 8 weeks old or older as an aid in the prevention of infection with FIV. Published studies have reported preventable fractions (defined as the proportion of cats protected by vaccination in excess of the proportion that is naturally resistant) of 0% to 100% (Kusuhara, Hohdatsu et al. 2005; Pu, Coleman et al. 2005; Dunham, Bruce et al. 2006). Each of these studies utilized different challenge models and different FIV strains, so it is not currently possible to estimate what level of protection cats in the field would receive from vaccination.

FIV vaccines are considered noncore vaccines, with use restricted to cats at high risk of exposure, such as those that fight or live with FIV-infected cats. An initial series of three doses is administered subcutaneously (SQ) 2 to 3 weeks apart; annual revaccination is recommended subsequent to the initial series as long as the risk of exposure continues.

Vaccinated cats will develop antibodies that cause false-positive FIV test results on currently available serological assays, and the decision to vaccinate should be reached only after careful consideration of this implication. If the decision falls in favor of vaccination, cats should test negative immediately prior to vaccination. Permanent identification of vaccinated cats (e.g., by use of a microchip) may help clarify vaccination status but will not indicate that such cats are free of infection. It will also increase the likelihood that a lost cat will be returned home if taken to a shelter and lessen the risk that a positive FIV antibody test result will lead to euthanasia.

### *Vaccination in shelters*

Vaccination against FeLV is generally not recommended in shelters in which cats are individually housed because of the low risk of viral transmission (Richards, Elston et al. 2006). In such shelters, resources are generally better spent on testing, and the decision to vaccinate is best left to the adopter based on the cat's risk profile in its new home. In facilities in which cats are group housed, such as in shelters and foster homes, FeLV vaccination is highly recommended. The high turnover of cats from multiple unknown backgrounds makes group housing and foster homes a higher risk for FeLV transmission, especially when quarantine and retesting at a later time is not possible. Caution should be used when adding newly vaccinated cats to group housing because the time to the development of optimal immunity following vaccination is variable. Maximal immunity is likely to follow at least a few weeks after completion of the two-dose primary vaccination series.

For the same reason, vaccination against FIV is not generally recommended because of the low risk of FIV transmission in typical single-cat housing (Richards, Elston et al. 2006). In addition, vaccine-induced false-positive serological test results make it difficult for shelters to confirm the FIV infection status of vaccinated cats in the future.

#### *Specific shelter FeLV and FIV vaccination recommendations*

- FeLV vaccination is optional for singly housed cats.
- FeLV vaccination is highly recommended for all cats housed in groups and for both foster cats and permanent residents in foster homes.
- Cats should be tested negative for FeLV prior to vaccination.
- Vaccination is not 100% effective and should never be used in place of a test-and-segregate program.
- In contrast to the case for feline panleukopenia, herpesvirus, and calicivirus vaccines (Fischer, Quest et al. 2007), the value of a single FeLV vaccine has not been determined. Therefore, FeLV vaccination is not recommended for feral cat TNR programs if program resources are needed for higher priorities.
- FIV vaccination in shelters is not generally recommended.

## Disinfection (environmental control)

Retroviruses are unstable outside their hosts and can be inactivated by detergents and common hospital disinfectants such as isopropyl alcohol and quaternary ammonium solutions (Francis, Essex, Gayzagian 1979; August 1991; Kramer, Schwebke, Kampf 2006; Moorer 2003; Terpstra, van den Blink et al. 2007; van Engelenberg, Terpstra et al. 2002). However, retroviruses in dried biological deposits

can remain viable for more than a week. Simple precautions and routine cleaning procedures will prevent transmission of these agents in shelters and veterinary hospitals. Items used for invasive procedures should be thoroughly cleaned and sterilized between uses.

### Euthanasia guidelines

The AAFP recommends against routine euthanasia of healthy retrovirus-infected cats and urges diagnostic evaluation and treatment of sick infected cats (Levy, Crawford et al. 2008a). This may not be practical in the shelter environment, where resource limitations prevent extensive clinical interventions or where space availability limits the length of time cats may be kept. The sheltering industry is currently in a state of flux as growing support for "no-kill" policies stimulates discussion about what constitutes an "untreatable" or "unsavable" animal. Using the strictest definition of euthanasia as an act of mercy for alleviating unremitting suffering, a growing number of shelters are classifying healthy FeLV- and FIV-infected cats as adoptable (treatable or manageable) or savable. This has created new challenges for shelters, as it often takes longer to find homes for infected cats. When shelter space is limited, longer resident times may lead to lower overall adoption success and lower numbers of animals saved. Sanctuaries devoted to long-term care of infected cats have been developed as an alternative and present their own set of challenges for optimal lifelong care and environmental enrichment.

If cats infected with FeLV or FIV are maintained long term in shelters, they should be isolated from uninfected cats. This protects both populations from cross-contamination with retroviruses and other infectious diseases that are commonly found in sheltered cats. Some infectious agents are more likely to remain active and to be shed in high quantities in cats that are immunosuppressed by retroviruses. Thus cats with FeLV and FIV may not only be more susceptible to secondary infections but may also serve as a chronic source of infection to the negative population if they are not adequately isolated. Most retrovirus-infected cats can be safely neutered and should receive routine vaccinations as described below. At this time, there is little information validating treatments to improve the outcomes of cats with FeLV or FIV infection.

## CLIENT EDUCATION/IMPLICATIONS FOR ADOPTION

Although the risk of transmission of FeLV and FIV within a household of adult cats that do not fight is relatively low, casual transmission of both viruses has been reported (Addie, Dennis et al. 2000). Therefore, it is never recommended to add an infected cat to a household of negative cats. When a cat owner already has an infected cat, adoption of another cat carrying the same virus offers an ideal opportunity for placement of difficult-to-adopt cats and for companionship for the resident cat.

Both FeLV- and FIV-infected cats can live many years with proper care, and, in fact, may die at an advanced age from causes unrelated to their retrovirus infections (Levy, Lorentzen et al. 2006). Thus, a decision for treatment or for euthanasia should never be based solely on the presence of a retrovirus infection.

Cats infected with FIV, FeLV, or both should be confined indoors to prevent spread to other cats in the neighborhood and exposure of affected cats to infectious agents carried by other animals. Good nutrition, husbandry, and an enriched lifestyle are essential to maintaining good health (August 1991; Overall, Rodan et al. 2005). Raw meat and dairy products should be avoided because the risk of foodborne bacterial and parasitic infections is greater in immunosuppressed individuals. Infected cats should receive a thorough physical examination twice a year, with special attention paid to the oral cavity and eyes, which are common sites of inflammation in affected cats. A program for routine control of gastrointestinal parasites, ectoparasites, and heartworms, where applicable, should be implemented (Companion Animal Parasite Council 2007). Vaccinations are administered as for uninfected cats, with the exception that inactivated vaccines are recommended to avoid the theoretical possibility of reversion to virulence in immunocompromised cats (Richards, Elston et al. 2006).

There are few studies that have investigated the effects of immunemodulators or antiviral drugs in controlled clinical trials with FeLV- and FIV-infected cats (Hartmann, Block et al. 1998; Hartmann, Donath et al. 1995a; Hartmann, Donath et al. 1995b; Hartmann 2005; McCaw, Boon et al. 2001; de Mari, Maynard et al. 2004). In most cases, anecdotal reports of beneficial treatment outcomes cannot be confirmed in controlled trials, but some promising treatments deserve further investigation (de Mari, Maynard et al. 2004). At this time, the best methods for optimizing long-term heath in asymptomatic and diseased retrovirus-infected cats are unknown.

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# 20
# Feline Infectious Peritonitis

*Catherine H. Mullin*

## BACKGROUND

Feline infectious peritonitis (FIP) is a sporadic yet highly feared fatal infectious disease of cats. Cases most commonly occur in multi-cat homes and in cats originating from densely housed cat populations such as breeding facilities, rescue homes, shelters, and sanctuaries. FIP was not reported before the 1950s, indicating that it is either a relatively new condition or that the causative agent has been present for years but changes in feline husbandry have contributed to emergence of the disease (Holzworth 1963/1). The disease was first described more than 40 years ago and is now one of the leading causes of kitten mortality (Cave, Thompson et al. 2002). Although it is known that the etiological agent is a feline coronavirus (FCoV), the pathogenesis of the disease FIP is still not fully understood. The vast majority of cats infected with FCoV do not develop FIP, and the diagnosis of the disease remains problematic.

This chapter will provide an overview of the basic biological properties of FCoV and will discuss the factors that appear to be important for the development of disease in individual cats. The chapter will also address the development and progression of FIP in cats and the management of FIP in shelters.

## ETIOLOGY

Coronaviruses belong to the order *Nidovirales* and family *Coronaviridae* that comprise one of the largest groups of viruses in nature. Their nucleic acid is RNA, not DNA, and they contain approximately 30,000 RNA bases in their genome. The RNA is plus-oriented, meaning it can function directly in protein synthesis without the requirement of being copied first from negative-strand RNA. Many RNA viruses mutate frequently and rapidly, in part because many mechanisms that DNA viruses and higher organisms have for repairing DNA when it is incorrectly copied are absent in RNA viruses such as coronaviruses. The high mutation rates characteristic of RNA viruses often are responsible for the evolution of new, sometimes highly pathogenic, strains of viruses.

Coronaviruses tend to infect epithelia primarily, such as the lining of the lungs or intestines. They interact with host cells after attaching via antigens on the virus surface. On electron micrographs, these antigens give coronaviruses a characteristic shape, where little rays extend out from the surface (thus the “corona”).

There are many different coronaviruses that specifically infect various species, including humans. Other coronaviruses include the transmissible gastroenteritis virus of pigs, mouse hepatitis virus, and canine coronavirus. The feline coronavirus mainly infects wild and domestic felines. Although recent studies of coronavirus infections in shelters have suggested that feline coronaviruses may infect dogs, resulting in frequent recombinations between feline and canine coronaviruses, the clinical relevance of these events is unclear (Benetka et al. 2006). There is no evidence that FCoV can infect humans. Why some cats that are infected with FCoV develop FIP whereas others do not is still largely unknown.

FCoV infects cats very easily, and it is possible to find up to 90% of cats with positive antibody titers at any time in some dense cat housing situations (Addie and Jarrett 1992a; Pedersen 1976; Horzinek and Osterhaus 1979). One study showed that 33% of cats and kittens entering a shelter were shedding virus at the time of intake, which increased to more than 60% after only 1 week (Pedersen, Sato et al. 2004).

The majority of cats infected with FCoV show no signs of clinical disease; on rare occasions, infection can be associated with transient, mild gastrointestinal signs. Most infected cats do not develop FIP.

## PREVALENCE OF FCoV IN DIFFERENT POPULATIONS OF CATS

The prevalence of exposure to FCoV in cats will depend on the population studied. The number of antibody-positive cats in a given population can range from 10% to 90% (Pedersen 1976; Horzinek and Osterhaus 1979). High prevalence of FCoV infection is generally associated with cats that have been densely housed, e.g., in catteries, shelters, and rescue facilities. Such cat-dense situations favor the transmission of FCoV, resulting in almost ubiquitous infection in these populations. By contrast, FCoV prevalence is lower among stray and feral cats that are not likely to live in close contact with one another; only 12% of these cats were found to be seropositive for FCoV in one study (Luria, Levy et al. 2004). However, even among densely housed populations there is substantial variability, probably dependent on housing and husbandry factors. One study found an average of 25.6% of cats in 14 shelters in the United Kingdom were seropositive for FCoV, with a range of seropositivity of 9% to 38%. Even in cats that had been in the shelter greater than 60 days, only 55% were seropositive, showing that FCoV transmission, though common, is not inevitable in the shelter environment (Cave, Golder et al. 2004).

Shedding of FCoV in feces is also more likely in multiple-cat housing situations, presumably due to stress. Whereas only one-third of cats entering a California shelter were shedding FCoV at intake, more than two-thirds were shedding virus after just 1 week, and the level of shedding from individual cats increased up to a millionfold (Pedersen, Sato et al. 2004). Kittens and juvenile cats were more likely to shed virus and shed higher amounts of FCoV than older cats in this study.

Although it is known that the majority of FCoV-infected cats do not develop FIP, some risk factors have been documented. FIP is a disease of younger cats; studies have shown that FIP is the second most common infectious cause of death in postweaning kittens, although it causes no deaths in the preweaning and neonatal periods (Cave, Thompson et al. 2002). Kittens are at greatest risk of developing FIP 6 to 18 months after FCoV infection, with risk falling to 4% at 36 months (Addie, Toth et al. 1995). The incidence of FIP in cats 3 to 9 years old is low. The risk of cats developing FIP is also higher in cats with very high FCoV titers, cats with immunosuppressive conditions such as FIV (Poland, Vennema et al. 1996), and in cats housed in endemic catteries in which the overall frequency of FCoV shedding or the proportion of cats in the cattery that are chronic FCoV shedders is increased (Foley, Poland et al. 1997a).

The frequency of FIP in "coronavirus endemic" catteries, multiple-cat homes, rescue, or hoarder homes is reportedly about 5% to 10% most of the time (Addie, Toth et al. 1995; Foley, Poland et al. 1997a). "Outbreaks" of FIP in over 10% of cats occurred in four of seven catteries followed over 5 years. However, these are all environments where cats are housed long term in a high-risk multiple-cat environment. In a research cattery, the rate of FIP was only 0.8% of 1,000 exposed cats following the introduction of coronavirus (Hickman, Morris et al. 1995), and in a study of cats adopted from an open-intake shelter where cats were only in the environment relatively briefly, the rate of FIP was similarly low at less than 0.6% (Spain, Scarlett et al. 2004). Therefore, rates higher than approximately 1% in a shelter are cause for concern (Addie, Toth et al. 1995; Hickman, Morris et al. 1995).

## TRANSMISSION AND SHEDDING OF FCoV

Transmission is typically by oral contact with contaminated feces. This means that the litter box is a major culprit when it comes to infection. However, transmission need not be direct, as virus on fur and litter dust can be moved from cat to cat in the house/colony or by human caretakers' clothes and hands during handling and cleaning. FCoV is one of the easiest viruses to transmit and therefore one of the most difficult to control. Keeping cats in separate cages or even separate rooms often fails to prevent transmission, though good sanitation may lower the dose and thus theoretically decrease the risk of FIP.

Virus can be shed in feces from 2 days postinfection. This shedding can be prolonged without any clinical signs, resulting in a "silent" source of infection for other cats. Some cats may shed virus for up to 10 months, while others shed chronically for years (Herrewegh, de Groot et al. 1995). Antibody-negative cats most likely do not shed virus; approximately one in three seropositive cats will shed virus at any given time (Addie and Jarrett 1992b).

The amount of virus that cats shed in their feces can also depend on the strain of coronavirus (i.e., its ability to multiply and be shed) and the cat's immune system. Immune system health is impacted by many factors including genetics, age, crowding, stress, and concurrent illnesses. Shedding will likely also be increased in cats with any concurrent gastrointestinal condition (e.g., internal parasites), as this leads to increased turnover of gastrointestinal cells.

Once a cat is infected with FCoV, it can remain so for several weeks to a few months. Virus is shed in the infected cat's stool during this period. Many cats will eventually eliminate the infection. However, the cat is not immune to

reinfection. The cat can be easily reinfected if exposed to the virus from another cat or via indirect exposure. With each new infection, the cat can shed infective virus again for weeks to months.

Without costly testing such as repeated fecal reverse transcriptase-polymerase chain reaction (RT-PCR) analysis, it is impossible to determine which cat is actively shedding since most have no clinical signs of infection.

Households of six cats or fewer will often clear the virus spontaneously (D Addie, personal communication, 2008), but households of more than six cats often maintain coronavirus infection by cycles of infection, virus elimination, and reinfection (Foley, Poland et al. 1997b; Addie, Schaap et al. 2003).

## PATHOGENESIS OF FCoV INFECTION AND FIP

There is still controversy regarding whether to consider FIP as contagious per se. It does not appear to be so in the classical way infectious agents are contagious, yet FIP does occur in sporadic outbreaks as well as isolated cases.

FCoV normally replicates in intestinal cells (enterocytes), resulting in mild or unapparent disease. Research has suggested that the disease FIP is caused by FCoV when it mutates in a susceptible cat. These presumed mutations frequently occur during FCoV infection, most of which probably do nothing to change the virus phenotype. Even within a single cat, there may be numerous strains (quasispecies) of FCoV. However, mutations may occur in the 3c, 7b, and spike reading frames, which change the viral phenotype into one that can induce FIP (Poland, Vennema et al. 1996; Vennema, Poland et al. 1998). FCoV is usually not culturable in tissue culture and replicates only in intestinal epithelia, but FIP-causing FCoVs usually are culturable in tissue culture and may acquire the ability to infect and replicate within feline macrophages. When accompanied by a particular feline immune response, infection of macrophages by a mutated FCoV can produce FIP. FIP is thus an immune-mediated, type III hypersensitivity reaction by the cat to the infection: Immune complexes of antibody and virus are formed, deposited in blood vessel linings and other tissues, and induce further immunological reactions that lead to vasculitis and the characteristic pathological and clinical abnormalities of FIP. Infection of the macrophage and the feline response result in complement activation, deposition of complement component C3, disseminated intravascular coagulation (DIC), blood vessel necrosis, and effusion. Antibodies against the spike protein help opsonize the viral antigen and, in theory, can enhance viral uptake and cause more severe disease (antibody-dependent enhancement).

In one case, two kittens exposed to an experimental dose of FCoV, and subsequently diagnosed with FIP, had different mutations of the FCoV within their bodies (Vennema 1999). Therefore, it seems the mutation of the virus to a form that causes FIP must usually occur within a cat; however, some viral strains may be more likely to undergo these mutations.

It is also unknown when the mutation from FCoV to FIP occurs after infection; this almost certainly will depend on the immune system of the individual cat. The disease becomes apparent a few weeks to 2 years after infection and/or mutation. This unpredictability is one aspect of FIP that makes control so difficult.

### Outbreaks of FIP

Given that FIP appears to arise as a mutation within individual cats, it is rarely directly infectious. It is commonly agreed that cats remaining in a household from which a cat developed FIP or those cats casually exposed to a cat with FIP (for instance, at a veterinary clinic) are not at appreciably increased risk of developing infection themselves (Addie, Toth et al. 1995). However, the risk of maintaining cats with FIP in a shelter or foster home in which they expose an ongoing parade of vulnerable new intakes to a potentially virulent FCoV is unknown.

In spite of the fact that FIP is not generally considered directly infectious per se, occasional outbreaks do occur. Studies that have documented FIP in "coronavirus endemic" multi-cat housing conditions report a disease frequency of about 5% to 10% (Addie, Toth et al. 1995; Foley, Poland et al. 1997a). "Outbreaks" of FIP were defined as greater than 10% of cats in these high-risk situations. However, in many other environments where the risk of exposure to coronavirus is likely to be lower, the rate of FIP is reported to be less than 1% (Hickman, Morris et al. 1995; Spain, Scarlett et al. 2004).

There are several possible factors that could increase the likelihood of FIP developing within a population of cats.

1. *Increased genetic susceptibility.* Development of FIP occurs more frequently in certain lineages of cats, and littermates of kittens that developed FIP are at increased risk of developing the disease themselves (Foley and Pedersen 1996). Although genetic susceptibility is unlikely to play a role in shelter outbreaks as cats are not generally closely related, the role of genetics must

be considered when making decisions for littermates of kittens with FIP.

2. *Increased infective dose.* There is speculation that an increased infective dose may be one of the causes for outbreaks of FIP. Dose increases when there is more FCoV virus in the environment owing to a larger number of shedding cats and/or more replication within individual cats. Each time the virus replicates, there is a chance that a mutation can occur to induce FIP. An increase in viral replication can be caused by several factors, including viral factors (e.g., efficiency in replication, shedding, and transmission), host factors (e.g., concurrent gastrointestinal infections, stress, young age, or immunosuppressive conditions such as FIV), and environmental factors (e.g., overcrowding, poor sanitation, use of high-tracking litter). Correcting the risk factors under the shelter's control, such as treating concurrent infections, reducing crowding, and improving husbandry, may help bring an outbreak under control.
3. *Increased tendency of an infecting strain of coronavirus to mutate into an FIP-causing virus.* Some strains of FCoV are much more likely than others to induce FIP when given experimentally to cats. Although this has not been specifically documented in the field, if one such strain should become established in a feline population, more cases of FIP would be expected as long as the strain was present. It may be that some FIP outbreaks are associated with temporary establishment of such strains and that resolution may occur when the more virulent strain dies out through removal of affected cats, development of immunity of resident cats, or continued evolution of the virus to a less virulent form.

## CLINICAL SIGNS OF FCoV INFECTION

Clinical signs of coronavirus infection can range from mild, transient to chronic diarrhea, or respiratory illness. However, most cats show no signs at all, and a cat that is seropositive for FCoV and has chronic diarrhea is very likely to have another cause for the diarrhea.

## THE FIP DISEASE SYNDROME

The FIP disease syndrome is mainly due to the deposition of virus and antibody complexes into various tissues including the lining of blood vessels. For ease of discussion, FIP has often been divided into two classical types: "wet" and "dry." In reality, the actual disease is a combination of these two presentations with one or the other being dominant.

The wet form occurs when virus/antibody complexes are deposited in the walls of blood vessels, rendering them leaky. As blood, fluid, and protein escape into the surrounding spaces, the result is the classical chest or abdomen full of fluid. The fluid tends to be very high in protein and low in blood cells.

The dry form is similar, but instead of causing widespread leakage of fluid, the complexes are deposited more in organs, especially kidneys, gastrointestinal tract, eyes, and brain. This results in a wide variety of clinical signs. It is not known why a particular cat develops one form over another; one theory is that a slightly better immune system might prevent the destruction of blood vessels but still allow for complex deposition in organs (Pedersen 1995).

### Clinical signs of FIP

The clinical signs of FIP can be strikingly obvious or frustratingly vague and will depend on what form of FIP develops. However, a diagnosis cannot be made by laboratory tests alone in the absence of clinical signs. Although the clinical manifestation of FIP can be varied, there are certain signs that are common. The most common signs of FIP in young cats are cyclic, antibiotic-non-responsive fever, lethargy, unexplained weight loss, and failure to grow. Effusion in the abdomen (ascites) or chest is also common. Fluid (effusions) that is yellowish, sticky or mucinous, high in protein, and contains numerous neutrophils and macrophages is characteristic of wet FIP infection. These effusions can occur in the thoracic, abdominal (most common), and/or pericardial cavities. However, studies have shown that only about two-thirds of cats with ascites actually have FIP (Hirschberger, Hartmann et al. 1995). It is important to consider the cat's signalment (such as age and background) when evaluating the likelihood that an effusion is associated with FIP or another cause.

Depending on what organs are affected, FIP can mimic the signs caused by liver or kidney failure; kidney failure in a young cat should raise the suspicion of FIP. It is sometimes possible to palpate the granulomatous nodules on the surface of kidneys. Granulomatous changes in the intestines may also be felt on physical examination, mimicking intestinal tumors. Enlarged abdominal lymph nodes can also be found in cats with FIP.

Cats with FIP frequently have ocular lesions, especially of the retina and anterior chamber (Greene 2006). Cuffing of retinal vasculature appears as fuzzy grayish lines on either side of the blood vessels. Retinal hemorrhage or

detachment may also occur. Inflammation in the anterior chamber (uveitis) is common with FIP. This can be seen as cloudiness behind the cornea or simply as color changes in one or both irises. Although none of these changes are pathognomonic for FIP, a careful ocular exam is indicated in any cat in which this infection is suspected. It should be noted that similar ocular changes are seen in other diseases such as toxoplasmosis, fungal infections, FeLV, and FIV.

Neurological changes are fairly common, with more than half of cats diagnosed with inflammatory brain lesions also having FIP (Bradshaw, Pearson et al. 2004). Both profound and subtle changes in neurological function and behavior can be signs of FIP. One study found that of all cats with FIP, approximately 13% have neurological signs (Rohrer, Suter et al. 1993). The clinical manifestations can include ataxia, nystagmus, blindness, seizures, and unexplained behavior changes such as increased aggression or affection or even just a somewhat vacant expression with constant purring. Many caretakers often refer to these kittens as the "particularly sweet ones," and FIP has been called the "purring disease."

## DIAGNOSIS

As many veterinarians and frustrated shelter managers have discovered, FIP – particularly the dry form – is among the most difficult diseases to diagnose. The diagnosis of FIP must be based on a combination of clinical observations, a history of the animal, a physical examination, and laboratory findings. The diagnosis is seldom made on a single test. This is critically important because many cats have been needlessly euthanized based only on a single positive FCoV titer. A thorough physical examination, complete blood counts (CBC), and evaluation of total protein (globulin and albumin) are recommended to start the diagnostic process. Common abnormalities include elevated total protein (mainly globulin), increased numbers of total white blood cells and neutrophils, decreased numbers of lymphocytes, and anemia. However, none of these abnormalities are present in all cats with FIP, and there are other conditions that can lead to any of these findings; therefore, FIP cannot be definitely diagnosed or ruled out based on these tests alone.

There are many additional tests available, each with advantages and disadvantages. The determination of which tests to run will depend on the clinical manifestation of the disease in the patient and the resources available. Ultimately, the *only* confirmatory diagnostic test is direct visualization of the antigen by biopsy or necropsy.

### Physical exam

The importance of a thorough physical examination cannot be overemphasized. For example, finding a fluctuating fever in a kitten that is losing weight and not thriving is very common with FIP. It is unlikely that an ongoing waxing and waning fever will occur due to other diseases such as a routine upper respiratory infection (URI). Other common physical examination findings include fluid accumulation, ocular changes, neurological changes, and abdominal organ irregularities, all of which have been described under clinical signs.

### Tests on effusions

The presence of an effusion allows for some valuable diagnostic tests to be performed, hence making diagnosis of the wet form sometimes more straightforward than diagnosis of the dry form.

#### *Rivalta test*

This simple-to-run test can help identify effusions due to FIP. It identifies effusions that are not only high in protein but also high in fibrin and other inflammatory mediators that are common with FIP. A negative Rivalta test is 97% accurate in ruling out FIP. A positive test is 86% accurate in ruling in FIP. False positive tests may be due to malignant lymphoma or severe bacterial infections, both of which can usually be ruled out by simple microscopic examination of the fluid.

*Rivalta test instructions:* Fill a clear test tube three-quarters full with distilled water, add one drop 98% acetic acid (or white vinegar), and mix. Carefully place one drop of the cat's effusion on the surface of the acid. If the drop disappears, the test is negative. If the drop retains its shape, looking like a blob or jellyfish, the test is positive. The 98% acetic acid called "glacial acetic acid" can be bought at most pharmacies or photography supply stores.

#### *FCoV antibody tests on effusions*

Diagnosing FIP by measuring FCoV titers in effusions may be better than in blood (positive predictive value of 0.90) but the specificity is no better than the Rivalta test (Hartmann, Binder et al. 2003).

#### *Immunohistochemistry (immunoflurescent assay) tests*

The immunoflurescent assay (IFA) allows for the detection of FCoV within macrophages found in effusions. The reason this is a more accurate diagnostic than just finding FCoV in the fluid is due to a key step in the development of FIP, i.e., the ability of a mutated FCoV to replicate efficiently within these specific cells. Positive staining

within macrophages indicates that the FCoV has replicated in sufficient amounts to be detected. Finding positively stained cells in effusions has a positive predictive value of 100%. Unfortunately the negative predictive value is only 57%. The reason is probably due to insufficient numbers of macrophages on the effusion smear (Hartmann, Binder et al. 2003).

#### *Reverse transcriptase-polymerase chain reaction (RT-PCR) on effusions*

Although FCoV can be readily detected via RT-PCR, it cannot be differentiated from an FIP mutation. It is likely that FCoV passes from blood into effusion during any inflammatory process, not only due to FIP (Addie, Paltrinieri et al. 2004); therefore, simple documentation of coronaviral RNA in an effusion is not necessarily diagnostic of FIP. Negative results are also not uncommon for cats with effusions due to FIP, so a negative test does not rule out the diagnosis (D Addie, personal communication, 2008).

### Routine blood tests

#### *Complete blood count*

Complete blood counts (CBCs) are always useful when evaluating any sick cat. Although the CBC is often abnormal in cats with FIP (increased numbers of total white blood cells and neutrophils, decreased numbers of lymphocytes, and anemia), none of the changes are pathognomonic nor does the absence of these findings rule out the disease.

#### *Serum profile*

Serum profiles can be helpful in diagnosing FIP. A relatively consistent finding in cats with FIP is an elevated total protein concentration caused by increased globulins. In fact, this can be found in up to 70% of FIP cats that do not have effusions (Sparkes, Gruffydd-Jones et al. 1994). This increase in globulins results in a decrease in the albumin-to-globulin ratio. Specifically, if the serum albumin-to-globulin ratio is less than 0.8, the probability of the cat having FIP is 92%. Conversely, if this ratio is greater than 0.8, the probability of the cat NOT having FIP is 61%.

Other serum chemistry parameters, such as elevations in hepatic and renal values, can reveal organ damage due to possible FIP.

#### *Other blood tests*

There are several other blood tests that can be performed that have varying degrees of FIP specificity. These include FCoV titers, α1-acid glycoprotein, and RT-PCR.

##### *FCoV titers*

The evaluation of FCoV titers by enzyme-linked immunosorbent assay (ELISA) is often subject to misinterpretation; there is no "FIP-specific ELISA." Completely healthy cats can have positive FCoV titers, and neither waxing nor waning titers predict whether a cat will develop FIP (Addie, Dennis et al. 2000). This is especially true for low or medium titers. The PPV of titers is only 44%, but truly negative titers (see below) predict that the cat does not have FIP 90% of the time (Hartmann, Binder et al. 2003). FCoV titers can be considered part of the diagnostic plan, but it is important to evaluate the laboratory running the tests. Laboratories should test the serum at dilutions starting at 1:25 or less. If it is negative at 1:25, one can assume that the cat is truly negative for FCoV and thus less likely to have FIP (except in cases of advanced FIP disease). If the titer is positive at 1:25, laboratories should further dilute the serum until it no longer tests positive. The dilution at which the antibody is still barely detectable is called the "endpoint titer." This will be expressed as a number like 1:400, 1:600, 1:3,200, etc. Unfortunately, many laboratories do not titrate serum in this manner and only report titers that are 1:400 or above as positive. Cats with lower titers will be reported as negative. High titers in cats not currently residing in a shelter or other multiple-cat populations are more likely to indicate FIP infection than the same titer in a shelter cat that is exposed to a daily assault of coronavirus.

One useful management aspect of running titers is to help determine which cats are shedding virus at high levels in their feces. It appears that cats with very high titers shed FCoV more consistently and at higher levels due to the increased replication rate in their intestines (Gut, Leutenneger et al. 2002). These cats may therefore represent a greater threat to other cats, and it may be prudent to remove them from a shelter experiencing an outbreak. Other reasons to run FCoV titers are for homes and shelter facilities that wish to maintain an FCoV-free environment and to screen a group of cats for the presence and level of FCoV infection in order to formulate a coronavirus management plan.

##### *α1-acid glycoprotein*

This is an acute-phase protein that is increased in cats with inflammatory conditions. Although it is not specific for FIP, it can assist in distinguishing this disease from other clinically similar conditions. A plasma value of greater than 1500 μg/mL is commonly seen with FIP (Duthie, Eckersall et al. 1997; Paltrinieri, Metzger et al. 2007).

*Reverse transcriptase-polymerase chain reaction (RT-PCR)*

RT-PCR tests are very sensitive and specific for FCoV. However, similar to serum antibody titer tests, RT-PCR cannot distinguish between nonpathogenic FCoVs and mutant forms that could cause FIP. Furthermore, healthy cats can be viremic with FCoV, so positive RT-PCR results from serum do not predict FIP (Gunn-Moore, Gruffydd-Jones et al. 1998), nor do negative results rule it out.

**Tests on tissue**

***Histopathology***

Necropsy and/or histopathological examination of biopsy tissue from cats suspected to have FIP is considered the "gold standard" test. In wet FIP, there is diffuse peritonitis or pleuritis (or both), characterized grossly by variable amounts of viscous abdominal or thoracic fluid, deposition of gray-white exudate, and disseminated necrotic plaques (0.5–3.0 mm) on the visceral and parietal peritoneum or pleura. Fibrinous adhesions, particularly between the liver and diaphragm and between loops of bowel, can develop in protracted cases; occasionally, the omentum may be contracted into the anterior abdomen as a thickened mass of fibrinous adhesions. Gross lesions in dry FIP consist of multiple, gray-white, raised nodules (0.5–2 cm or larger) in kidneys, visceral lymph nodes, liver, intestines, lungs, eyes, and brain. A single, obstructive, granulomatous intestinal mass is seen in some cases. These typical lesions are highly suggestive of FIP. If histology is not diagnostic, then a definitive diagnosis can be made by IFA or immunohistochemistry to detect intracellular FCoV. Only cats with FIP have the IFA-detectable FCoV antigen in tissue macrophages (positive predictive value 100%) (Kipar, Bellmann et al. 1998; Hartmann, Binder et al. 2003).

***mRNA RT-PCR tests***

As of June 2008, mRNA RT-PCR tests were only available through university laboratories. The College of Veterinary Medicine at Auburn website states: "This PCR test detects mRNA of the M gene of all known feline coronavirus strains in any sample; however, for diagnosis of FIP, only the detection of mRNA outside of the intestinal tract is indicative since active replication of the virus in circulating mononuclear cells is typical for FIP. In contrast, non-FIP feline coronavirus strains replicate in the intestinal tract, but not in blood mononuclear cells." At least three different tissue samples per cat are recommended to maximize the predictive power of these tests, which appears to be 100% (Simons, Vennema et al. 2005). Unfortunately, there is now some evidence that these tests are not highly predictive of FIP (Can-Sahna, Ataseven et al. 2007). It will require time and more research to determine how helpful these tests are in the antemortem diagnosis of FIP.

***RT-PCR on samples from affected organs***

Although RT-PCR has limited usefulness on blood or effusions, the presence of FCoV in biopsy samples or fine needle aspirates of affected organs is suggestive of a diagnosis, provided blood contamination is not present (D Addie, personal communication, 2008).

**Tests to identify FCoV-shedding cats**

It may be important to identify which cats are shedding FCoV into the environment. Cats that are infected with FCoV will intermittently shed virus in their feces for weeks to months depending on their ability to eliminate the infection.

Approximately one-third of FCoV antibody-positive cats will shed virus, and it is more likely that extremely high titered cats, young cats, and those in a shelter will shed. To identify more precisely which cats are actively shedding or which are chronic shedders, it is necessary to test feces for the presence of virus by RT-PCR. Cats that have had five consecutive negative fecal FCoV RT-PCR tests can be considered to have eliminated FCoV, whether or not they remain seropositive (Addie and Jarrett 2001).

In most cases, fecal PCR testing is less useful than antibody testing to find cats that have eliminated the virus; to show that a cat has eliminated FCoV requires only one antibody titer of less than 1 : 10 in a laboratory that follows the proper testing procedure described above, but requires five monthly negative RT-PCR tests on feces. However, RT-PCR remains the only way to detect a carrier cat; a cat that sheds FCoV continually for 9 months or more is likely to be a lifelong carrier.

**TREATMENT OF FIP**

FIP is still considered to be 100% fatal. Once a cat has developed clinical signs of the disease, any treatments are palliative, not curative. FIP kittens will need intensive nursing care so it is ill-advised to treat them in homes or shelters unless this level of care can be provided. The risk to other cats must also be considered; although not directly infectious, the risk of having an affected cat in a shelter or high-volume foster home is unknown.

Various treatment modalities have been considered, including the use of corticosteroids and immune modulators. None of these protocols have been proven to be effective. Some uncontrolled studies using feline

interferon-ω have shown possible efficacy but these were conducted on cats not proven to have FIP (Ishida, Shibanai et al. 2004).

## MANAGEMENT OF FCoV AND FIP OUTBREAKS IN SHELTERS

Because FIP is rarely, if ever, transmitted cat to cat, control measures are different from those for more classic infectious diseases such as feline panleukopenia. It is impossible to distinguish highly virulent strains of FCoV from those that pose less risk; therefore, control measures must focus on reducing overall FCoV in the environment.

Although not as straightforward as resolving other outbreaks, some of the same principles will apply even to this complex disease. An improvement in overall sanitation, treatment of concurrent disease and reduction of stress are likely to be helpful, but resolution of the outbreak may require creating a clean break between exposed/at-risk cats and newly admitted ones. Because of the prolonged latent period (up to 2 years) between infection with FCoV and development of FIP, traditional "quarantine" is not an option. If cats at relatively high risk for FIP are adopted out, communication with adopters and risk to the shelter's reputation must be weighed against the cost and risk of implementing management measures to control the outbreak.

Because little published information is available about successful measures for FIP outbreak control, shelter veterinarians must extrapolate from what is known about the virus and the underlying reasons why outbreaks are thought to occur. Increased genetic susceptibility is an issue in breeding catteries, but it is unlikely to play a significant role in most shelters except in cases of seizures of several animals from a cattery, animal hoarding, or other situation in which a high percentage of cats can be expected to be closely related. That leaves the possibility that a highly virulent strain has become established in a shelter and/or that an increased dose is present due to the many factors identified above: increased population density, problems with sanitation, stress, concurrent immunosuppressive or gastrointestinal illness, etc.

Clearly, addressing those above-listed factors under the shelter's control is likely to be helpful but may not be sufficient by itself. If some cats are chronically shedding a highly virulent strain, continuing to expose newly admitted cats to these cats (directly or via fomites) may perpetuate an outbreak. Outbreaks have been known to persist in affected shelters for at least several years. If control measures as described above prove insufficient, identifying and segregating or removing those cats that are placing the newly admitted population at greatest risk may be required to terminate an outbreak. The problem is that there is no reliable, cost-effective method to determine which cats pose the greatest threat. Sometimes kittens and sick cats are targeted for removal, yet it is at least as likely that long-term housed, healthy adult cats are the ongoing source of virus. There are several options (and non-options) for dealing with this issue.

### Continuing business as usual

In some cases, it seems that FIP outbreaks resolve on their own within a few months to a year even if no special measures are taken, although some shelters and catteries have reported increased FIP rates lasting for several years. When spontaneous resolution does occur, it may be that the virulent strain of coronavirus loses the mutation that conferred its increased propensity to cause disease, as seems to happen with some hypervirulent caliciviruses. Alternatively, it may be that the chronic shedders happen to get adopted out, that the predominant strain of coronavirus circulating in the population is replaced by a less virulent one, or that all the cats that do not develop FIP have inherent immunity. However, if the outbreak persists for greater than one season, more aggressive control measures as described below should be considered.

### Quarantine or isolation

There is no way to predict via serology, PCR, or any other means which cats from a shelter that has FIP problems are going to develop the disease, with the exception of a known increased risk for siblings of affected kittens. Even in outbreaks, often no more than 5% to 10% of cats are affected. Furthermore, the latent period between exposure to FCoV and the development of FIP can take several years from the time of exposure. This means that there is no realistic way to quarantine cats in an environment where they have been exposed to a potentially virulent coronavirus. Cats in shelter quarantine can continue to shed and be infected with FCoV, which may place other newly arrived kittens and cats at risk. Spread via fomites is very easily accomplished; it is unlikely that true quarantine can be achieved in a shelter facility, even if housed in a separate room or building from other cats. It is also unlikely that acceptable welfare can be maintained for cats quarantined long term in suitably biosecure isolation facilities. For these reasons, quarantine is not a recommended means of managing an FIP outbreak and may well exacerbate the situation.

### Segregation of longer-term and shorter-term residents

Because increased rates of FIP seem to occur most often in housing situations in which at least some cats are housed relatively long term, it may be that longer-term housed cats pose a relatively high risk to new intakes. These cats have, after all, had ample opportunity to acquire and transmit whatever viruses are present in the environment. One or more cats that chronically sheds a relatively virulent strain could explain the persistence of an outbreak. Therefore, one potential approach would be to separate these cats to the extent possible from newly admitted cats and, in particular, kittens. Kittens are both more vulnerable to the development of FIP should they become infected with a virulent FCoV, and relatively likely to be adopted quickly and thus able to escape the disease entirely. It is reasonable to hope that decreasing the dose of FCoV to which new incoming kittens are exposed will be helpful in at least some cases. This can be accomplished by having staff handle separate populations with separate clothing and equipment (or separate staff) and routing visitors through the facility in such a way that they visit the new/"clean" cats first and then the resident/exposed cats.

### Depopulation and/or decreasing the number of cats

It may be possible to slow or stop an FIP outbreak by removal of the exposed population and subsequent disinfection of the environment. The number of cats may be decreased through increased adoption efforts, foster homes, off-site sanctuary homes, temporarily decreasing intake, or euthanasia. However, the removal of only kittens or sick cats is not likely to be effective if healthy and potentially chronically shedding exposed cats remain in the shelter. Most importantly, the practice of simply testing all cats for FCoV and euthanizing them if they test positive is *not* an appropriate strategy for managing an FIP outbreak in a shelter and is strongly discouraged: Most cats will test positive, yet the vast majority will not develop FIP.

## MANAGEMENT OF FCoV AND FIP OUTBREAKS IN FOSTER HOMES

It is important to focus on decreasing the amount of FCoV in foster homes just as it is in shelters. Foster homes that have had a case of FIP should consider stopping all intakes until all current kittens are gone. A good cleaning of the house will help to decrease the amount of FCoV in the environment, after which the home could resume fostering again. The focus of cleaning should be mechanical removal of virus, which can be accomplished by cleaning carpets and furniture, and washing surfaces and all clothing and bedding. It is not necessary to sterilize the home. The aim is to minimize the amount of "old" coronavirus to which new incoming kittens will be exposed.

Occasional cases of FIP are not unusual in homes with kittens, but these should happen only sporadically. Foster homes that have repeated cases of FIP should reassess their role. Outbreak conditions may indicate that there are too many kittens rotating through the home, that cleaning protocols are not sufficient between litters, that foster kittens are subjected to excessive stress or concurrent disease, and/or that one or more cats within the household is chronically shedding a relatively dangerous strain of FCoV. It may be safer in these cases for a foster home to focus foster efforts on adult cats or to volunteer to help the shelter in another way.

## PREVENTION AND CONTROL

### Cleaning/disinfection and minimizing fomite transmission

Since most FCoV is shed in the feces, it makes sense to focus on good litter box hygiene; each piece of litter can carry millions of coronavirus particles. Simple measures such as the use of low-dust litter, frequent scooping, properly cleaning a scoop between each cage, avoiding "litter-box dust storms" while dumping pans into garbage cans, minimizing litter contamination of the floors during cleaning, and changing scrub tops or gowns after cleaning a bank of cages may help decrease the amount of FCoV in the shelter.

When developing cleaning protocols, consider (1) keeping cats in the same cage rather than subjecting them to frequent rehousing or removal for cage cleaning, (2) implementing an in-cage spot-cleaning method for daily cat cage maintenance, and (3) completely disinfecting cages only between residents. This will both reduce stress and help decrease the amount of fomite transmission on hands and clothing. Luckily, most commonly used shelter disinfectants reliably inactivate FCoV.

### Vaccination

There are inherent challenges to creating a truly reliable vaccine for FCoV. Even natural infection does not convey lasting immunity, and a vaccine is unlikely to do better. In addition, the strain variability of this RNA virus makes reliable vaccination difficult, as for other variable viruses such as calicivirus and influenza. There is currently only one vaccine available for feline coronavirus, a modified live intranasal product labeled for use in cats over 16

weeks of age, to be given as a series of two vaccines 3 to 4 weeks apart. Results of studies regarding the efficacy of this vaccine have been variable. In one study using the vaccine in an FCoV endemic environment (likely to be true of most shelters) the vaccine did not prevent FIP (Fehr, Hoznagel et al. 1995). Other studies have showed limited efficacy under certain circumstances such as for cats that were seronegative at the time of vaccination (Fehr, Hoznagel et al. 1997).

Although there may be some benefit to giving the vaccine to cats that have never before been exposed to a multi-cat environment (and are therefore relatively likely to be seronegative), most shelter cats will have long since been exposed by the time the recommended booster vaccine can be administered. Unlike with the parvoviruses, vaccination will be an adjunct tool at best and will not be sufficient by itself to control outbreaks of FIP. For these reasons, vaccination against FIP is not routinely recommended for shelter cats according to the guidelines published by the American Association of Feline Practitioners (Richards, Elston et al. 2006).

## IMPLICATIONS FOR ADOPTIONS/OTHER CONCERNS

Exposure and infection by FCoV is common in any multiple-cat housing situation, but aside from a few rare circumstances, the fact remains that FIP is a statistically unlikely outcome of FCoV infection. However, the risk is increased in cats adopted from a shelter that experiences an outbreak, or in littermates of kittens with FIP. Shelters may also worry about adopting out apparently healthy cats that have been housed long term in a shelter that is experiencing an ongoing FIP outbreak. A terrible – though improbable – consequence could be transmission of an FIP-causing coronavirus to an adopter's resident pet. On the other hand, setting special restrictions on adoption, such as only allowing adoption to single cat homes, may cause these cats to linger even longer in the shelter, thereby increasing the risk for themselves and all others in the population.

### Are adopter's own cats at risk?

It is worth repeating that if cats from an outbreak environment are adopted into homes with resident cats, the other cats in the household are unlikely to get FIP because of this exposure. This is true even if the newly adopted cat happens to be shedding a relatively virulent strain of feline coronavirus or eventually succumbs itself to FIP. Resident pets are likely to be under less stress than shelter cats, and therefore at lower risk from disease; development of FIP is even less likely if all cats in the adopter's household are over 2 years of age.

### Concerns about siblings of FIP kittens

Siblings of kittens that have developed FIP represent a difficult situation, especially if the kittens were already in foster care at the time the first case was diagnosed. As noted earlier, siblings of a kitten that developed FIP have a significantly higher risk of developing FIP themselves. However, this is by no means a guarantee; many siblings will *not* develop the disease. If the decision is made to place these kittens for adoption, the increased risk should be fully disclosed to adopters. Understandably, many people are loath to adopt these kittens and risk the heartache of losing them to this fatal disease. This can lead to the kittens being held in the shelter for prolonged periods. The risk to other cats from housing these kittens in a shelter is unknown. Although these kittens probably pose little risk to a resident healthy adult cat within a pet household, they are by definition very likely to be shedding a virus that has mutated to cause FIP in at least one kitten, and they may thus pose a higher risk of transmitting a relatively virulent strain to other kittens in the shelter.

Another option is for those in the foster home to adopt these kittens themselves. Again, since the risk of exposing a group of vulnerable kittens to a kitten that may be infected with a relatively virulent FCoV is unknown, the most prudent choice in this case would be for the foster home to discontinue fostering kittens or very carefully segregate areas devoted to foster care. Unfortunately, humane euthanasia of these siblings is sometimes the most reasonable choice when other options are not available.

### Concerns about nonsibling kittens

Since there is no evidence that nongenetically related kittens exposed to a kitten with FIP are at greater risk of developing the disease, it is reasonable to adopt them out with no special precautions unless they have a concurrent health problem that prompts particular concern.

## CONCLUSION

FIP is a complicated, devastating disease of cats caused by a combination of FCoV infection, genetic predisposition, and immune system compromise. It is a sporadic disease and is more likely to occur in multiple-cat housing situations. Occasional cases of FIP are to be expected in shelters that house cats for long periods, but a frequency of disease in more than 1% of the population is cause for concern. Shelter veterinarians should be familiar with the pathogenesis of FIP, clinical signs, the diagnostic tests

available, and management control measures that may help to decrease FIP prevalence in shelters and foster homes.

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# 21
# Vector-Borne Diseases

*Janet Foley*

## INTRODUCTION

Arthropods and arthropod-vectored diseases are important problems in animal shelters: Many represent direct threats to the cat and dog populations, some are directly zoonotic, and some may be threats primarily to humans but for which dogs and cats may serve as sentinels. Traditionally, municipal animal shelter staff have played an important role in protecting public health from zoonotic diseases spread by dogs and cats, including vector-borne disease. It is not unusual for stray and neglected animals to be presented to shelters with heavy flea and tick infestations. There are arthropod-borne disease problems in shelters where the animal would have acquired the infection before entering the shelter (including some tick-transmitted diseases), while others such as flea infestations may be spread in dense shelter populations. Tickborne rickettsial and ehrlichial infections tend to be sporadic or rare problems in shelters. Common exacerbating problems in shelters include animal density, inadequate funding and resources to manage arthropods preventively, and high animal intake and rapid turnover. Efficient strategies to manage arthropod-borne infections are necessary to protect both animal and public health. Table 21.1, on page 332, lists classes of arthropods and arthropod-transmitted diseases in shelter populations. This chapter will present an overview of these diseases to create awareness and to discuss the implications, if any, for shelters. The reader should consult other veterinary textbooks for detailed information on the epidemiology, diagnosis, and treatment of these diseases.

## WEST NILE VIRUS

West Nile virus is an emerging zoonotic pathogen that has moved steadily westward since its introduction into New York in 1998. By 2006, the virus had invaded all U.S. states except Hawaii. The virus, an arbo virus in the family *Flaviviridae*, is not directly transmitted among vertebrates but requires a mosquito vector in which it replicates; i.e., the mosquito is a biological vector. Transmission is primarily via mosquito bites; and although most disease occurs during mosquito season, it can occur year round. Other routes of natural infection are suspected to occur; these include ingestion, blood transfusion, organ transplants, and transplacental (Lichtensteiger and Greene 2006). Species of mosquito involved in the transmission of West Nile virus include *Culex* spp. Wildlife reservoirs include several bird species, including corvids (ravens, crows, jays) and probably some species of songbirds that can develop sufficient loads of virus to infect mosquitoes. The strain of West Nile virus that invaded the U.S. is relatively highly pathogenic and can cause disease in wild and pet birds, humans, horses, and to a lesser extent, smaller companion animals and even rodents. Most mammals are generally considered to be dead-end hosts because they are unlikely to develop a viremia that is high enough for mosquito transmission to occur (Lichtensteiger and Greene 2006).

The virus infects various organs and causes cell necrosis if the viremia is high enough. Disease manifestations are predominantly neurological, including high fever, neck stiffness, stupor, disorientation, coma, tremors, convulsions, muscle weakness, and paralysis, as well as fever and lethargy. Although natural infections do occur in dogs and cats, these animals usually do not develop clinical signs of the disease. Clinical signs in humans may include fever or, less commonly, neurological disease. In shelters, the significance of West Nile includes the rare case in a dog and the possibility that animals will serve as sentinels for human disease risk.

**Table 21.1.** Classes of arthropods and arthropod-transmitted diseases in shelter populations.

| Taxonomic Group | Species of Pathogen | Route of Zoonosis |
|---|---|---|
| Viruses | West Nile virus | Mosquito |
| Protozoa | *Babesia canis* and *gibsoni* | Tick |
| | *Leishmania* | Sandfly |
| Bacteria | *Anaplasma phagocytophilum* | Tick |
| | *A. platys* | Not known, suspect tick |
| | *Ehrlichia canis* | Tick |
| | *Bartonella* spp. | Bite, scratch, flea |
| | *Borrelia burgdorferi* | Tick |
| | *Coxiella burnettii* | Genital and placental tissue, tick |
| | *Francisella tularensis* | Aerosol, tick |
| | *Rickettsia felis* and *rickettsii* | Flea, tick |
| | *Yersinia pestis* | Aerosol, flea |
| Arthropods | Fleas | Direct |
| | Ticks | Direct |
| | Lice | Direct |

Diagnosis of active infection can be made through evaluation of compatible clinical signs (with rabies and canine distemper a major rule-out in stray animals), serology, and polymerase chain reaction (PCR), especially as a confirmatory test. Retrospectively, diagnosis can be confirmed based on a fourfold rise in titer over 4 weeks. Diagnosis can also be confirmed via necropsy, although there are usually no specific gross findings (Lichtensteiger and Greene 2006).

Treatment for animals affected by West Nile is supportive, including therapy for immunosuppressive disease. Shelters that undertake to treat these animals may safely adopt out recovered animals as they are considered to be dead-end hosts. Although there is a vaccine for horses, there is no vaccine to prevent the disease in dogs. Prevention is based largely upon mosquito control, including draining nearby pools of standing water that serve as breeding areas for mosquitoes, use of screens in doors and windows, and application of mosquito repellents that are safe for use around and on animals. Shelters that occasionally use dogs as blood donors should protect them from mosquitoes because the disease has been reported to be transmitted via blood transfusion in humans. Shelters may also be asked to help in West Nile surveillance programs if wild or diseased birds are turned in to the facility. Staff should wear gloves when handling dead birds (National Institute for Occupational Safety and Health 2005).

### *BABESIA CANIS, B. GIBSONI*

Babesiosis (also known as piroplasmosis) is a tick-transmitted disease attributable to one of several species of protozoa, including *B. gibsoni* and *B. canis*. Occasional cases are due to transfusion with contaminated blood products. The brown dog tick, *Rhipicephalus sanguineus*, is the vector. Most cases occur in the American southeast, Arizona, and the Midwest (especially Oklahoma and Arkansas). Clinically, the presentation may be nonspecific and variable, often manifesting mainly as a weak, depressed dog. Infected dogs may develop splenomegaly, hemolytic anemia with bilirubinuria, and thrombocytopenia, eventually resulting in disseminated intravascular coagulopathy (DIC) or immune-mediated glomerulonephritis. Clinical disease is very uncommon in cats in the U.S.; *Babesia felis* is most commonly reported in South Africa. No host-specific species of *Babesia* has been found for humans, and *B. canis* and *B. gibsoni* are not believed to be zoonotic. However, disease in humans can be caused by other *Babesia* species; most infections are mild, but they can represent a greater risk to people who have had a splenectomy, resulting in severe illness and death.

*B. gibsoni* is associated with a number of dogs that are subclinically affected and are carriers, especially in the American pit bull terrier breed (Macintire, Boudreaux et al. 2002). The prevalence of *B. canis* in apparently healthy greyhounds also is very high (Taboada, Harvey

et al. 1992). The likelihood of dogs serving as a source of infection in the shelter is low unless dogs are housed together and there is poor tick control (Taboada and Lobetti 2006). Coinfection with *B. burgdorferi*, *Anaplasma phagocytophilum*, or *Ehrlichia canis* may exacerbate clinical disease.

The diagnosis of babesiosis relies on identification of antibodies through serology, *Babesia*-specific DNA through PCR, or visualization of the parasite on thick blood smears. On evaluation of Giemsa-stained whole blood, *B. gibsoni* has a variable appearance but typically is a small (1–3 µm) piroplasm within erythrocytes. *B. canis* is a larger intraerythrocytic parasite (2–5 µm). There is serological cross-reactivity among the *Babesia* spp., although PCR testing is species specific.

Treatment options include doxycycline, metronidazole, imidocarb dipropionate, clindamycin, and prednisone. Imidocarb appears particularly effective against *B. canis*. Supportive care, including blood transfusion, may be necessary. The prognosis for elimination of *B. gibsoni* is poor. Some dogs never recover from the initial episode, and others become long-term carriers or later develop episodes of hemolysis (Birkenheuer, Levy et al. 1999).

Important control measures include the prevention of tick infestation and the screening of blood products before administering transfusions. Ticks should be removed promptly from all animals when they first enter the shelter, as it typically takes 2 to 3 days of feeding for transmission of the parasite to occur. Ensure that the entire tick is removed intact if possible and disposed of properly; wear gloves and wash hands thoroughly afterwards.

In shelters, the primary significance of babesiosis is its occurrence in weak or anemic dogs on a sporadic basis. It has been suggested that shelters consider routinely testing for the disease in debilitated or anemic American pit bull terriers, greyhounds, and anemic animals that have been in a fight with a pit bull. Although it may be difficult to eliminate the parasite completely, recovered animals can be placed for adoption with counseling.

## LEISHMANIASIS

Canine leishmaniasis is a parasitic zoonosis caused by a flagellated protozoan in the *Leishmania* genus. Disease occurs in many areas of the world and recently has been documented primarily in foxhounds in the U.S., with cases in Texas, Oklahoma, Ohio, Texas, Michigan, New York, Alabama, and Canada. Cutaneous leishmaniasis of humans is caused by *L. aethiopica*, *L. major*, and *L. tropica* in the Old World (Africa, Asia, the Middle East, the Mediterranean, and India), and *L. mexicana* and *L. braziliensis* in the New World (the U.S. border with Mexico through South America). Visceral leishmaniasis is caused by *L. donovani* and *L. infantum* in the Old World regions and *L. chagasi* in the New World. Cases of canine leishmaniasis are caused primarily by *L. infantum*. Leishmaniasis is a disease of humans in Asia and Europe, vectored by *Phlebotomus* and *Lutzomyia* spp. sand flies. In some areas, dogs are reservoirs for human infection. Occasional findings of *Leishmania* in wild carnivores suggest they also may be reservoirs. Cats may also be rarely affected with the cutaneous form.

Transmission is via sand flies that inoculate hosts with promastigote *Leishmania*. These promastigotes are phagocytosed by macrophages and transformed into amastigotes that are infectious to sand flies. Amastigotes are round or ovoid from 2–4 µm, without a flagellum. They multiply by binary fission until the host cell is destroyed, and released amastigotes are phagocytosed by new macrophages.

The disease has three different forms. Cutaneous leishmaniasis is characterized by nodules and ulcers on the skin, especially ears, elbows, tarsus, neck, paws, and near the eyes. Mange is an important rule out to keep in mind in endemic areas. Dogs with visceral leishmaniasis may have anemia; fever; nasal hemorrhage; hepatomegaly; splenomegaly; weight loss; purulent conjunctivitis; keratitis; lameness; chronic wasting; long, deformed nails (onychogryphosis); or they may die. Most affected dogs have the third form, cutaneous visceral leishmaniasis, which is characterized by a combination of cutaneous and visceral symptoms.

Canine leishmaniasis is diagnosed by clinical signs; visualization of *Leishmania* amastigotes in stained tissues including bone marrow, lymph node, spleen, skin, skeletal muscle, peripheral nerves, kidney, and synovium; and by PCR.

Treatment may be unsuccessful; it may not be possible to completely eliminate *Leishmania* from infected dogs. Therapy may include a combination of allopurinol with a pentavalent antimonial such as meglumine antimonite or sodium stibogluconate. However, many *Leishmania* parasites are resistant to the drug, and patients may experience adverse side effects associated with these compounds. Pentostam (sodium stibogluconate) distribution is regulated by the CDC.

Cases of leishmaniasis are of public health importance because of the concern that dogs could infect local sand flies and become a threat to human health. Infected animals may still pose a disease threat despite treatment. While ownership of an infected dog does not appear to be a major

risk factor for the disease, direct transmission between dogs and people cannot be ruled out entirely. Care must be taken when handling open wounds, discharges, or other material from infected animals (Baneth 2006). Adopters should be advised about the risks if they choose to adopt an animal with the disease.

Control of sand fly vectors is important for preventing the spread of disease, but it can be difficult. Window and door screens and topical insecticides should be used to protect dogs from sand flies in shelters in endemic areas. Control of the disease through traditional methods of testing and removal is problematic because nonsymptomatic carriers and seronegative dogs can still serve as a source of transmission, and test methods do not identify all infected animals. Leishmaniasis has also been reported as a shelter concern because of international transport programs that import dogs into the U.S. from areas, particularly the Mediterranean, where *Leishmania* is prevalent, thus contributing to the potential for further spread in the U.S.

### *ANAPLASMA PHAGOCYTOPHILUM*

In some geographical areas of the U.S. such as New England, the upper Midwest, and California, anaplasmosis in dogs is far more common than monocytic ehrlichiosis. *A. phagocytophilum* is a tick-transmitted rickettsial pathogen that targets the neutrophil. It was formerly known as the causative agent of granulocytotrophic ehrlichiosis, but because of its reclassification, it is now known as the cause of canine granulocytotrophic anaplasmosis. In the U.S., *A. phagocytophilum* is vectored by the Pacific black-legged tick, *Ixodes pacificus*, or the deer tick, *I. scapularis*. Reservoirs are wild rodents. The same pathogen can infect people, horses, dogs, and wildlife. Transmission requires the tick to be attached to the host for a minimum of 24 hours; the incubation period is generally 1 to 2 weeks (Greig and Armstrong 2006).

The clinical signs in dogs, horses, and people include fever, anorexia, lethargy, muscle and joint pain, and in people, headache. Hematological and biochemical abnormalities may include thrombocytopenia, anemia, leukopenia, and elevated liver enzymes. Horses particularly are susceptible to icterus, head pressing, and lower limb edema. However, in all species, most infections do not manifest any abnormal signs and go unnoticed. There is a statistical association between *A. phagocytophilum* infection and polyarthritis as well as thrombocytopenia in dogs (Foley, Drazenovich et al. 2007).

Anaplasmosis is diagnosed by direct visualization of the organism in neutrophils, serology, and PCR. Within neutrophils, *A. phagocytophilum* (formerly *E. phagocytophila* and *E. equi*) appears within small cytoplasmic, membrane-bound vacuoles called morulae. If monocytes contain morulae, these could be *A. phagocytophilum* or *E. canis*. The sensitivity of this assay is increased if a buffy coat smear is examined. PCR of whole blood is one of the most sensitive tests available for diagnosing active anaplasmosis because acute infections often are resolved before the dog seroconverts. Serology must be interpreted carefully, as many dogs in endemic areas are seropositive, indicating prior exposure although with little clinical relevance. The finding of a fourfold increase in titer confirms recent infection. There is sometimes cross-reactivity between *A. phagocytophilum* and *E. canis*; it is best to run both titers because typically one is much higher than the other (Dumler, Asanovich et al. 1995).

Granulocytic anaplasmosis responds well to treatment with tetracycline, with resolution of the fever typically within 24 hours. Even without treatment, most cases of granulocytic anaplasmosis resolve on their own within about a week. The risk of shelter animals serving as a source of zoonosis is not known at this time, but precautions should be taken whenever a necropsy is performed on a confirmed or suspect case (Greig and Armstrong 2006).

### *ANAPLASMA PLATYS*

*Anaplasma platys* (formerly *E. platys*), is a rickettsial pathogen that infects canine platelets and is responsible for canine cyclical thrombocytopenia (otherwise known as thrombocytotrophic anaplasmosis). Little is known about the natural history, reservoirs, or arthropod vectors of *A. platys*. However, because this organism is so closely related to other anaplasmas and ehrlichias, a tick vector is strongly suspected. Recent advances in molecular diagnosis have resulted in documentation of considerably more cases than were previously identified, suggesting that many dogs are subclinically infected.

Diagnosis requires serology or PCR because affected dogs often have profound thrombocytopenia and thus few platelets are available in which to visualize the organism. Treatment includes tetracycline-class drugs, as well as steroids if the case is severe. Chronic thrombocytopenia may occur; thus prolonged treatment may be necessary.

### *EHRLICHIA CANIS*

*E. canis* is the most common ehrlichial agent found in sick dogs. It is responsible for causing canine monocytotrophic ehrlichiosis and is closely related to *E. chaffeensis*, the agent of human monocytic ehrlichiosis [although a case of

human disease was reported in Venezuela in a patient infected with *E. canis* (Perez, Rikihisa et al. 1996)]. The vector for *E. canis* infection is the peridomestic tick *Rhipicephalus sanguineus*, and the dog is the reservoir. *E. canis* targets the monocyte where it produces a morula similar to *A. phagocytophilum*. There is also a risk of transmission of the disease via blood transfusion.

Clinical signs and hematologic abnormalities include fever, lymphadenopathy, anemia, and thrombocytopenia in the early stage. If the dog remains persistently infected, canine ehrlichiosis may enter a second subclinical stage where it may remain for months to years, although the serological titer may continue to remain high or increase in this stage. Eventually, in less than 10% of dogs, ehrlichiosis may enter a third stage of systemic disease with bone marrow suppression and pancytopenia. Dogs in this stage may have vague generalized signs of systemic disease associated with immune complexes and very high titers. Clinical signs at this stage may include lethargy and weight loss; lymphadenomegaly and splenomegaly; uveitis and retinitis; and bleeding from eyes, nose, and in bowel movements. German shepherd dogs are predisposed to more severe disease. Diagnosis is based on clinical signs, cytology (identification of the morulae in leukocytes), hematology, serology, and PCR.

As with granulocytic anaplasmosis, most acute cases of *E. canis* respond well to doxycycline, showing some positive response within 48 hours of treatment. In contrast, chronic monocytic ehrlichiosis is not easily treated and has a poor prognosis. Dogs require antiehrlichial drugs (doxycycline or imidocarb); fluids and/or blood transfusions; possibly erythropoietin or granulocyte colony stimulating factor; and steroids. Because some of these animals can relapse after treatment, follow-up bloodwork is recommended 1 to 3 months after treatment, and tick-control measures, including advice about proper and safe removal of ticks, should be provided to adopters.

### *BARTONELLA* SPP.

Bartonellas are gram-negative bacterial parasites of red blood cells. Cats are the reservoirs for zoonotic *Bartonella henselae* and *B. clarridgeiae*, while dogs may be reservoirs for *B. vinsonii berkhoffii*. *B. henselae* and *B. clarridgeiae* cause cat-scratch disease, bacillary angiomatosis, relapsing fever, bacillary peliosis, and meningitis/neuroretinitis in people. Cats show few if any clinical problems with *B. henselae* and *B. clarridgeiae* infection and can remain infected for months to years. Young cats that are or have been infested with fleas are at highest risk for infection, with seroprevalence rates in some areas of over 90%. Clinical manifestations reported uncommonly include anemia, fever, and lymphadenomegaly. There have been many published reports, conference proceedings, and anecdotes regarding *Bartonella* association with uveitis, stomatitis, upper respiratory infections, chronic diarrhea, etc., but a causative association has not been clearly established, and disease has not been re-created experimentally.

People are infected by cat bite or scratch or from being bitten by cat fleas. It seems likely that the bite or scratch must be contaminated by flea dirt or otherwise by blood in some fashion as specific-pathogen-free (SPF) kittens housed with highly bacteremic kittens in the absence of fleas did not become infected (Chomel, Kasten et al. 1996). Thus flea control greatly decreases risk.

*B. vinsoni berkhoffii* causes endocarditis and granulomatous lymphadenitis in dogs; a single case of *B. clarridgeiae* endocarditis also has been reported in a dog (Chomel, Mac Donald et al. 2001). In cases of human endocarditis, *B. henselae* and *B. vinsoni berkhoffii* have been detected.

*B. henselae* and *B. clarridgeiae* are transmitted by cat fleas. The routes of spread of *B. vinsoni berkhoffii* are unknown but thought to be ticks.

Active *Bartonella* infection can be diagnosed by blood culture or PCR, although specialized techniques are required to improve culture sensitivity. Positive serology does not equate to current infection or bacteremia. Serology documents whether a cat or dog has previously been infected; often serologically positive animals are infected chronically. However, fewer than 50% of seropositive cats were bacteremic according to the American Association of Feline Practitioners (AAFP). The negative predictive value is good but not perfect (95% to 97%), so even negative cats may occasionally be bacteremic. Additional tests may be necessary to evaluate dogs for endocarditis, including cardiac ultrasound and blood culture.

It is difficult to clear *Bartonella* spp. infection in cats. Those antibiotics that are reasonably effective include tetracycline, amoxicillin-clavulanate, enrofloxacin, erythromycin, and rifampin. The main justification for treatment is to prevent human infections, but given concerns about fostering antimicrobial resistance, treatment of healthy cats should perhaps be reserved for pets of immunocompromised people or as an alternative to euthanasia. If treatment for human health reasons is performed, it should be combined with careful flea control, as this is likely to be an important component of preventing human infection. In dogs, treatment of *B. vinsoni berkhoffii* is aimed at treating endocarditis and has a poor prognosis.

It is important to match cat adoptions carefully with an appropriate home by performing an in-depth risk assessment. Although *Bartonella* infection is common in young cats, the risk of disease transmission is very low provided excellent flea control is practiced. The populations most at risk for infection include elderly people, young children, or immunocompromised individuals. Young cats with fleas should not be adopted to members of this risk group without full disclosure of the concerns. Per U.S. Public Health Service (USPHS) and Infectious Diseases Society of America (IDSA) guidelines, precautions for human immunodeficiency virus (HIV)-infected persons are limited to adopting a healthy, flea-free cat over 1 year of age. AAFP also endorses this for immunocompromised individuals in general.

Management of bartonellosis in shelters requires excellent flea control, minimization of bite and scratch wounds (primarily through staff and volunteer training), prompt washing of all wounds with soap and water, and counseling of potential owners with regard to risks.

### *BORRELIA BURGDORFERI* (LYME DISEASE)

Lyme disease or borreliosis is caused by the spirochete *B. burgdorferi*. Lyme disease is one of the most commonly diagnosed vector-borne diseases in people. Generally, borreliosis is clinically silent or mild, but severe manifestations can include fever, polyarthritis, monoarticular arthritis, chronic arthritis, and neurological and cardiac dysfunction. In dogs, particularly Labrador retrievers, *B. burgdorferi* infection can cause severe immune-complex associated nephritis with protein-losing glomerulopathy and fatal renal failure (Dambach, Smith et al. 1997). *B. burgdorferi* broadly comprises a number of closely related genospecies, including *B. burgdorferi* per se, *B. bissettii*, and others. Vectors for *B. burgdorferi* include *I. pacificus* and *I. scapularis*, as for granulocytic anaplasmosis. After a tick bite and attachment for at least 50 hours, the spirochete is inoculated into the skin and connective tissue, and eventually may disseminate to joints, heart, or other areas of connective tissue. Infection in some dogs may last months to years, but most animals that are bitten do not develop signs of clinical disease.

Infection with *B. burgdorferi* should be considered in dogs with severe or chronic arthritis or nephritis. Blood samples are screened by immunofluorescence (IFA), enzyme-linked immunosorbent assay (ELISA), or an equivalent test and the diagnosis confirmed with western blotting because IFA alone has a high rate of false positivity. Alternatively, a C6 protein ELISA is highly sensitive and specific. It is important when interpreting serology results to distinguish positive test results from vaccine reactions. A culture or PCR may be positive, especially in joint fluid.

Acutely infected animals may be treated with doxycycline, amoxicillin, or azithromycin. Treatment should be continued for 30 days. Chronic disease, particularly nephritis, has a poor prognosis. In humans, neuroborreliosis is treated with intravenous ceftriaxone, a treatment that could be useful in chronic canine borreliosis. Nephritis treatment also requires immunomodulation (to minimize Arthus-type reactions) and possibly dialysis. Adopters should be advised that animals that appear to have recovered may relapse after antibiotic therapy is discontinued. Although Lyme disease is classified as a zoonotic disease, the general public often forgets that ticks rather than dogs are the direct source of infection for people; dogs are not a reservoir for disease spread to humans, do not shed appreciable amounts of infectious organisms, and do not pose a risk of spreading disease if adopted. Even if dogs bring infected ticks into the home, once they drop off the dog, they rarely reattach to re-feed (Greene and Straubinger 2006).

There are two classes of Lyme vaccine available for dogs: whole cell preparations and recombinant outer surface protein A (OspA) vaccine. In Lyme-endemic areas, shelters might consider Lyme vaccination of sheltered dogs, although this is not part of current AAHA shelter dog vaccine recommendations. Investment in effective tick control for both the dog and the environment would be a better use of shelter resources because Lyme disease is not a disease that is likely to spread within a shelter that practices effective vermin control. Long-term sanctuary-type shelters, where dogs are out walking in the woods with staff or volunteers, might be possible exceptions, and they should consider including Lyme vaccination as a routine vaccination. It must be reiterated that the vaccine will interfere with disease testing for months to even years. If the vaccine is administered, particular care should be taken to ensure medical records documenting vaccination for Lyme disease are provided to adopters.

### *COXIELLA BURNETTII* (Q FEVER)

*C. burnettii* is a rickettsial pathogen that causes Q fever (Query fever) in sheep, goats, cats, and humans. The bacterium is transmitted by direct exposure to infectious fluids such as the vaginal discharge that accompanies abortions and live births, via exposure to the environmentally resistant spores, and by tick bite. More than 40 different tick species contribute to the maintenance of the infection in nature and transmission to animals. Sheep and goats are

particular sources of zoonotic disease because periparturient discharges contain high levels of bacteria. More information about the disease can be found in Chapter 23 on zoonosis.

The cellular targets of *C. burnettii* are epithelium and endothelium, leading to vasculitis and necrotizing pneumonitis. The incubation period is 4 to 70 days, depending on whether infection is direct or vector transmitted. People usually acquire Q fever by inhalation or ingestion of contaminated spores and develop organ failure, vasculitis, chronic endocarditis, and other problems. Immune-complex deposition may occur in joints, the anterior chamber of the eye, and kidneys. Clinical disease ranges from no signs to pneumonia to abortion. After infection, *C. burnettii* may be shed in urine, milk, feces, and especially placental fluids and tissue; in cats, shedding may last for a month or more.

Infected dogs and cats are generally without symptoms but may have lymphocytosis and thrombocytopenia. Other signs may include fever, lethargy, and anorexia. Q fever is diagnosed based on a fourfold rise in titer over 4 weeks. Both phase I and phase II antigens should be tested. Phase I antigens are those from the organism while in the host and are usually low in acutely ill patients and higher in chronic infection. Phase II antigens are present in the bacteria following repeated in vitro passage. PCR is useful in the diagnosis of acute infections.

The treatments of choice for Q fever include tetracycline, chloramphenicol, or enrofloxacin. Trimethoprim-sulfonamide and erythromycin are variably effective. On rare occasions, infected cats and dogs have been implicated in causing environmental contamination that is linked to disease spread to humans. For this reason, although the risk appears to be small, staff should use care in handling and treating infected animals.

*Coxiella burnettii* is very environmentally resistant, and animal contamination of soil is a serious problem, especially in areas where dust is transported by wind. To decontaminate an environment, bleach, ultraviolet light (UV), heat, and desiccation are NOT effective. Alcohol (70%) applied for 30 minutes and allowed to evaporate will kill the bacteria. Zoonotic disease management also includes elimination of ticks and reduction of exposure to infected hoofstock and cats, especially during parturition or abortion. Shelters that admit sheep and goats should be particularly aware of this disease. Staff should wear gloves and wash their hands after handling these animals. Q fever is a reportable disease; shelters should check with their state or local Department of Health about the management of suspected cases.

### *FRANCISELLA TULARENSIS* (TULAREMIA)

Tularemia is a highly infectious disease that affects many species, including birds, cats, less commonly dogs, and humans. It results from infection with the small gram-negative bacterium *F. tularensis* biotype A (*tularensis*) and B (*palearctica*). Biotype A (which causes rabbit fever) is maintained in the U.S. in hare reservoirs, and *Dermacentor* spp. and *Amblyomma americanum* tick vectors. Biotype B is spread among a number of hosts by ticks, mosquitoes, biting flies, in water, and by direct contact. Cats and dogs may also acquire biotype B infection by eating infected prey, although natural infection in dogs is fairly rare. Cases of human tularemia have been identified in Massachusetts after exposure to infectious material during lawn mowing; it is also transmitted to people via inhalation of contaminated dust or aerosols, or via ingestion of contaminated food and water. The bacterium persists in macrophages.

Infected animals typically have fever, purulent ocular and nasal discharge, lethargy, anorexia, possible lymphadenopathy of the nodes draining the site of inoculation, and bacteremia and abscessation of multiple internal organs. Diagnosis is made by history, clinical index of suspicion, blood or lymph node culture or PCR, serology, and histopathology. There are no good data on treatment of this disease in animals.

In people, tularemia may appear as a slow-growing ulcer and swollen lymph nodes. If the bacteria are inhaled, tularemia can present as pneumonia, while oral ingestion may lead to sore throat, abdominal pain, diarrhea, and vomiting. Effective drugs for treatment of tularemia are streptomycin, gentamicin, and doxycycline. Animals with tularemia can be a source of infection for people, particularly when bacteria are present in the oropharynx. Cases of transmission from cats have only been documented via bites; most cases of tularemia in humans are associated with ticks or contact with infected tissues, particularly those of rabbits. Rare cases of unusual transmissions have been reported; one case described a girl who contracted the disease because her infected dog licked her skin, and another by hunting dogs that shook the bacteria off their wet fur with aerosol transmission as a result. The dogs appeared clinically normal (Greene and Debey 2006). Animals with lymphadenopathy and/or pneumonia should be diagnosed promptly if possible in a shelter in order to minimize public health risks. Tularemia is considered a potential bioterrorism weapon; infections and outbreaks must be reported to public health officials. Suspected cases should be isolated immediately; treatment of unowned or stray animals with this dangerous

disease is strongly discouraged in shelters. See Chapter 23 for more information.

### *RICKETTSIA RICKETTSII* AND *R. FELIS*

Rocky Mountain spotted fever (RMSF) is caused by *Rickettsia rickettsii*, a bacterium transmitted by the ticks *Dermacentor andersoni*, *D. variabilis*, and *Rhipicephalus sanguineus*. Like other spotted fever rickettsiae, *R. rickettsii* is maintained in ticks transstadially and transovarially, which facilitates the persistence of the pathogen in nature. Mammalian reservoirs of infection include wild mammals and dogs. Several nonpathogenic species of spotted fever rickettsiae also circulate in tick–mammal epidemiological cycles including *R. canada*, *R. peacockii*, and *R. bellii*. Despite the fact that RMSF was originally observed in the western U.S., cases in humans and animals are uncommon west of the Rocky Mountains, while the disease appears to be emerging in the American southeast.

*R. rickettsii* is inoculated into a mammalian host via the bite of an infected tick. It invades endothelial cells and leads to vasculitis, causing especially severe lesions in skin, brain, heart, and kidneys. Classically, edema develops 2 to 10 days after the tick bite. Skin lesions range from vesicular, hyperemic lesions to severe necrosis. There may be mucosal, genital, and retinal petechiae and hemorrhages. Ultimately, shock and central nervous system (CNS) disease can be fatal.

If RMSF is suspected in a dog in a shelter, supporting diagnostic tests may reveal thrombocytopenia, leukopenia followed by leukocytosis, and possibly elevated protein in cerebrospinal fluid (CSF). Antibody testing (especially with a fourfold rise in titer) may retrospectively confirm the diagnosis. Positive IgG does not confirm active RMSF, however, as many animals may be seropositive after exposure to common nonpathogenic spotted fever group rickettsiae. Immunohistochemistry may be performed on biopsy samples (e.g., skin). PCR testing is a good option where available.

RMSF can be a severe to fatal disease in dogs; thus, appropriate treatment is essential and should be initiated without waiting for confirmation of diagnosis. Appropriate antibiotics include tetracycline, enrofloxacin, and chloramphenicol. Concurrent steroid therapy is recommended to reduce the inflammation and vasculitis, and supportive care of gangrene and shock are necessary. Fluids must be delivered slowly to avoid cerebellar/cerebral edema. The prognosis is fair, depending on how early disease is detected and how quickly it progresses. Tick control is important for prevention. Infected dogs are not a risk to other animals or staff in the shelter.

*Rickettsia felis* is another zoonotic rickettsia that can present problems in shelters. *Rickettsia felis* is transmitted by the cat flea (*Ctenocephalides felis*), and the opossum, *Didelphis virginiana*, is the reservoir. *R. felis* and *R. typhi* are both causes of murine typhus in humans. People acquire infection through exposure to rickettsiae in flea feces, given that fleas tend to defecate while biting. The rickettsiae then enter the body through the bite wound or when the bite area is scratched. The relationship of *R. felis* with other rickettsiae is complicated. Although *R. felis* causes a disease similar to *R. typhi* in people, and the two bacteria cross-react serologically, *R. felis* is more closely related genetically to the spotted fever group of rickettsiae than the typhus group.

*R. felis* was first identified as a human pathogen in 1994. People with clinical *R. felis* infection have fever, rash, headache, and CNS involvement, with variable nausea, vomiting, diarrhea, abdominal pain, myalgia, and conjunctivitis. There is no evidence that *R. felis* is pathogenic in cats or dogs.

Little is known about the extent and prevalence of *R. felis* infection, although it has been reported in cat flea populations in North and South America and southern Europe. Given that the reservoir of *R. felis* is the opossum, it is possible that infection in cats is improbable and that cats are most important as sentinels for human risk. Nevertheless, the presence of this pathogen in cat fleas underscores the importance of effective flea control in stray and shelter animal populations.

### *YERSINIA PESTIS* (PLAGUE)

*Y. pestis* is a non-spore-forming, facultatively anaerobic, gram-negative bacterium in the family *Enterobacteriaceae*. Infection occurs in nature primarily in rodent hosts such as prairie dogs and some ground squirrels and is spread by fleas or through aerosol discharge from heavily infected animals. Cats, and less commonly dogs, acquire the infection through direct exposure to these rodents, predation on infected animals, and via exposure to rodent fleas. Cat and dog fleas are poor vectors of plague. Humans can be infected by rodent fleas or exposure to respiratory secretions of cats or other humans infected with the pneumonic form. In the U.S., plague occurs sporadically in the eastern Sierra Nevada; transverse mountain ranges of southern California; the Four Corners areas of Colorado, New Mexico, Arizona, and Utah; and into Texas, Oklahoma, and Kansas (Chomel, Jay et al. 1994).

There are three forms of clinical disease: bubonic, septicemic, and pneumonic. Infected cats develop leukocytosis and bacteremia with high levels of infection in the oropharynx from 1 to 10 days after exposure. Mandibular and retropharyngeal lymph nodes may become enlarged and eventually abscess and drain. Infection can spread to the lungs (pneumonic plague) or other organs where abscesses may develop, or the *Y. pestis* endotoxin can cause septic shock, DIC, or death. In endemic areas, cats with fever, lymphadenomegaly, pneumonia, or nonspecific systemic illness should be evaluated for plague. If the animal has signs of respiratory tract infection with lymphadenopathy, rule-outs include plague, tularemia, and mycobacteriosis.

For diagnosis of plague and tularemia, fine needle aspirate and cytology and a culture of lymph nodes, or a culture of swabs of the throat, will often yield the diagnosis. Extreme caution should be used when obtaining these samples to avoid contact with infected tissue; wear gloves and face masks and discard appropriately, wash hands, etc. Serology is available through local health departments. Chest auscultation and radiography are important for determining whether a cat has diffuse interstitial pneumonia, which could be a sign of pneumonic plague.

If a cat is presumptively diagnosed with plague, treatment should be aggressive, but protection of human health is imperative as well, given that exposure to feline plague is an important risk for pneumonic plague in humans (Gage, Dennis et al. 2000). *Y. pestis* is extremely virulent and has been classified as a high-priority potential bioterrorism weapon. Although treatable today, plague historically has been responsible for more human deaths than any other disease and continues to present a problem because clinicians fail to recognize the signs or delay seeking treatment.

Given the human health risk and the fact that all free-roaming cats in an endemic area are probably at risk for exposure to plague, it is not unreasonable for shelters at least to consider euthanasia of suspect cases in at-risk cats to protect human and animal health. If treatment is undertaken, cats should be hospitalized in isolation, signage should be posted and treatment also initiated for flea infestation. The local health department must be notified, and any staff interacting with the cat must be trained in universal precautions, including an N-95 mask, gown, and gloves. Drug treatment is often rewarding, with cats responding clinically within a few days. Cats are considered noninfectious 48 hours after the initiation of antibiotic therapy. The bactericidal drugs gentamycin and enrofloxacin are excellent choices for treatment. Oral drugs should be avoided initially to minimize the risk of inoculating plague bacilli into caregivers' hands. All shelters in plague-endemic areas should have standard written protocols and adequate ongoing staff training to allow staff to rapidly identify prospective cases of plague and manage them safely until appropriate diagnostic and management steps can be taken.

## CONCLUSION

New information about vector-borne diseases and their zoonotic potential is constantly emerging. It is one of the fastest areas of growing interest in veterinary medicine. It is far beyond the scope of this chapter to provide detailed diagnostic or epidemiological information about these diseases or their management in shelter populations. A broad overview of some of the most common diseases that are likely to be encountered in shelter animals has been provided here. Shelters should make certain that every precaution is taken to protect both human and animal health by educating staff about disease transmission and safe flea and tick removal from animals, practicing effective general flea and tick control in the environment and implementing management protocols that will ensure both the health and well-being of the animals while in the facility, and adoption of only healthy animals from the shelter. The reader is referred to Chapter 23 on zoonosis for more information.

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# 22
# Heartworm Disease

*C. Thomas Nelson*

## INTRODUCTION

Heartworm infections are particularly challenging in a shelter setting because of the length of time needed to treat the animal and the cost of treatment. This chapter will explore the various options available for managing heartworm infections in shelter animals.

## EPIDEMIOLOGY

Heartworm disease is caused by the parasitic filarial nematode *Dirofilaria immitis*. Since its discovery in 1847, heartworm has gone from being a parasitic disease limited to the southeastern United States to being diagnosed in all 50 U.S. states. Alaska is the only state in which transmission has not been documented. The number of cases diagnosed yearly continues to rise despite the large number of chemoprophylactic drugs available. This increase has been significant in the western U.S. over the past 30 years and can be attributed to two factors: (1) heartworm-positive dog relocation as people have moved from endemic areas to the western regions, thereby establishing a reservoir of infection, and (2) creation of mosquito habitats as a result of the irrigation of developed areas and the subsequent influx of mosquito vectors. The heartworm infection rate in the coyote population is over 90% in many of these areas (Sacks 1998). Heartworm also can be found through out Central and South America, the Caribbean Islands, southern Europe, coastal regions of Africa, portions of the Middle East, India, Southeast Asia, Australia, the South Pacific Islands, and Japan. While the dog is the definitive host for heartworms, the parasite has been found in over 30 species of animals, including coyotes, foxes, wolves, and other wild canids; domestic cats and wild felids; ferrets; sea lions; and humans.

Transmission of the parasite requires a reservoir of infection, a competent mosquito vector, and favorable climatic conditions. Unprotected domestic and feral dogs, as well as wild canids, are the reservoir of infection. There are multiple mosquito vectors in every region of the U.S. (Scoles 1998). Over 70 species of mosquitoes have been shown to be capable of transmitting heartworm; 22 species have been proven to be significant vectors. Laboratory studies have determined that an average temperature of 64°F is necessary for the development of heartworm larvae to the infective L3 stage. Since the *Culex* mosquito is a competent vector frequently found indoors, transmission can continue even during cooler months in large indoor kennels (Lok and Knight 1998).

Dogs, cats, and ferrets will be the most common animals encountered in shelters that are susceptible to heartworms. Infection can occur at any age and in any breed. Since 2-inch-long immature adult worms can be found in the pulmonary arteries 3 months postinfection, it is important to place all puppies, kittens, and ferret kits on a heartworm preventive by 8 weeks of age.

The prevalence of infection varies by region, with over 90% of unprotected dogs along the Gulf Coast, lower Atlantic Coast, and Mississippi River valley being infected (McTier et al. 1992). The severity of infection also varies by region. The worm biomass in an infected dog is typically higher in dogs coming from the areas listed above, but there are pockets with higher prevalence and severity of infection throughout the U.S. Since few animals arrive in shelters with a travel or medical history, one cannot assume the worm burden of a heartworm-positive dog is low because the shelter is located in a low-prevalence area.

## PATHOGENESIS

The pathogenesis of heartworm disease is very complex, and the reader is referred to other texts or the American

Heartworm Society (www.heartwormsociety.org) for a complete description of the life cycle of *D. immitis*. A basic diagram of the life cycle of the parasite can be found in Figure 22.1.

As expected, the number of worms has an effect on the severity of disease, but of equal importance, if not greater, is the activity level of the dog. Controlled studies have shown that dogs infected by surgical transplantation with 50 heartworms and subsequently exercise restricted took longer to develop clinical disease and developed less pulmonary vascular resistance than dogs with 14 heartworms that were allowed moderate activity. This is also evident in naturally infected dogs where there was no correlation between the number of heartworms and pulmonary vascular resistance. It is an indication that the host–parasite interaction plays a significant role in the severity of disease (Dillon, Brawner et al. 1995). A subsequent study (Fukami et al. 1998) reported similar findings in dogs that were treated with melarsomine.

Whereas live heartworms can cause endarteritis and muscular hypertrophy of arteriole walls primarily of the caudal pulmonary arteries, the majority of the pathology seen in clinical disease is a result of the effects of dying heartworms. As worms die from either natural causes or as a result of administration of adulticidal drugs, they decompose, and small worm fragments lodge in the distal pulmonary arteriole and capillary beds in the caudal lung lobes, blocking blood flow. During periods of increased activity or exercise, the increased blood flow can cause capillary delamination, rupture, and subsequent fibrosis, which leads to increased pulmonary vascular resistance and potential right-sided heart failure. This illustrates again how the activity level of the dog has a direct correlation on the severity of disease and is an important factor when determining how to treat the heartworm-positive dog (Dillon, Warner, Molina 1995).

The disease process in the cat is significantly different. After infection with third-stage larvae, development continues to the fourth-stage larvae, and juvenile worms that penetrate into peripheral veins are carried via the bloodstream to the distal caudal pulmonary arteries just as in the dog. At this point, most of the worms die, leading to an

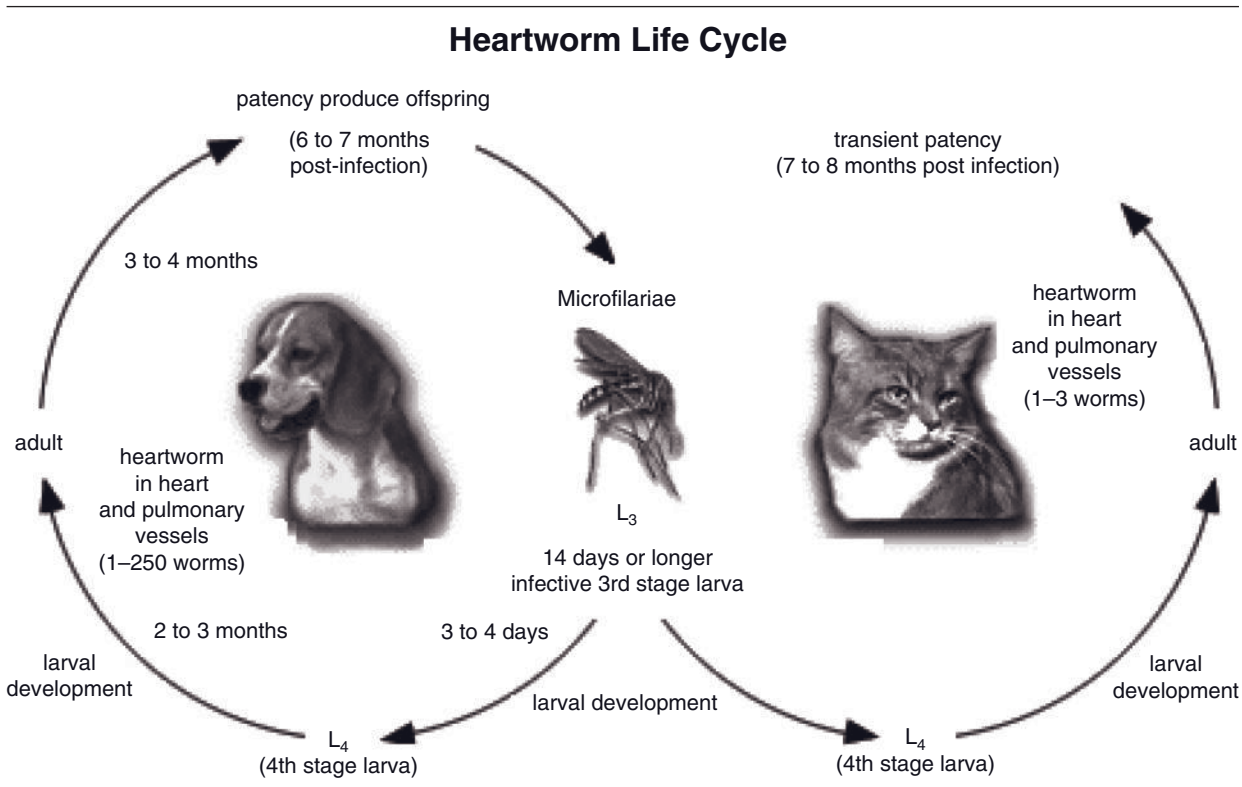


**Figure 22.1.** Heartworm life cycle (American Heartworm Society).

inflammatory process that resembles asthma or allergic bronchitis. Histopathology of the caudal lung lobes in cats that have been subject to these abbreviated heartworm larval infections have pathological lesions in their pulmonary arterioles (Browne et al. 2005), bronchioles, and alveoli similar to those found in cats whose heartworm infection had progressed to the adult stage (Blagburn et al. 2007). This phenomenon has led to the term heartworm associated respiratory disease (HARD) (Nelson et al. 2007; Blagburn et al. 2007) or pulmonary larval dirofilariasis.

In cats whose infection progresses to the adult stage, there is the added concern of a severe, acute respiratory distress-like syndrome that can lead to sudden death. This has been reported to occur in 10% to 20% of adult infections in retrospective studies (Atkins et al. 1998; Genchi, Venco et al. 2007).

## DIAGNOSTIC SCREENING IN DOGS

Diagnostic testing for heartworm disease in dogs is based on detection of microfilariae or heartworm antigen. The earliest the antigen can be detected is 5 months postinfection and may be delayed as long as 9 months in dogs with low worm burdens. Microfilariae are not detectable until approximately 6.5 months postinfection and are only generally detectable in 80% to 85% percent of positive dogs. Based on these numbers, there is no reason to test puppies less than 7 months of age.

Antigen tests are available in either a well format, more suitable to running multiple samples at one time, or as single point-of-care tests. The sensitivity and specificity for all the commercially available tests are excellent. The well test does perform better with infections with only one to two female worms, but with infections of three or more female worms, the sensitivity of all test range from 95% to 100%. The specificity is essentially 100% for all heartworm antigen tests (McCall 1998). False positives are extremely rare and are more probably due to technical error. It is recommended to retest asymptomatic antigen-positive dogs before treating or making a decision about their fate.

While antigen tests are considered the gold standard for diagnosing canine heartworms, examining blood for microfilariae using a concentration technique (modified Knott's or filtration test) is an inexpensive way to screen animals admitted into a shelter. This simple test is easy to learn by anyone with basic microscopic skills. Since it can identify 80% to 85% of canine heartworm infections, it can represent a significant cost savings over the more expensive antigen test. However, a negative microfilaria test does not rule out infection and should be followed with an antigen test because 15% to 20% of dogs with heartworm disease may not be microfilaremic.

The modified Knott's test is performed by mixing 1.0 ml of blood with 9.0 ml of 2% formalin in a test tube. The tube is inverted several times to mix the blood with the formalin solution that will lyse the red blood cells, which can be noted when the mixture becomes a clear, red-wine color. The tube is then placed in a centrifuge and spun for 5 minutes. The liquid is poured off, leaving the sediment. A drop of methylene blue is added to the tube and then a drop of the stained sediment is placed on a glass slide and a coverslip applied. The slide is then examined under 100X for the presence of microfilariae. If present, the slide is then examined under 400X to observe the characteristics of the microfilariae. The microfilariae of *Dirofilaria immitis* are 295–325 µm long and have tapered heads and bodies and tails. The microfilariae of *Acanthocheilonema reconditum* are 250–288 µm long with blunt heads and curved bodies and tails. The presence of microfilariae of *Dirofilaria immitis* is considered diagnostic of heartworm infections (see Figure 22.2).

Animals that test negative on an antigen test, have not been on a preventive, and have potentially been exposed to mosquitoes carrying infective larvae should be retested in 6 months because of the lag period between infection and antigen release. The animals should be kept on preventive during this time (Nelson et al. 2005).

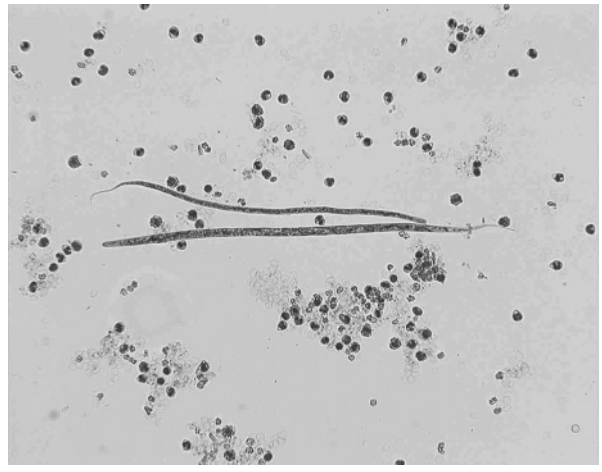

**Figure 22.2.** *A. reconditum* (top), *D. immitis* (bottom). Image courtesy B Blagburn.

## DIAGNOSTIC SCREENING IN CATS

Diagnostic screening in cats for heartworms has not been widely accepted because of ambiguities associated with the current testing procedures. The current antigen tests are capable of detecting a single mature female worm in a cat. Since the average adult worm burden is only one to two worms, approximately one-third of infections will consist of only male worms that will not be detected by the antigen test.

The heartworm antibody tests are able to detect a history of infection from both male and female adult worms, as well as late fourth-stage larvae and juvenile worms. Initial studies of experimentally infected cats indicated 97% to 98% sensitivity, but surveys of necropsy-confirmed heartworm-positive cats from shelters have indicated the sensitivity is in the 50% to 80% range (Nelson et al. 1998; Snyder et al. 2000). Furthermore, 50% of cats with confirmed HARD have seroconverted to negative within 8 months postinfection. A negative test does not rule our heartworm infection; it just lowers the index of suspicion. A positive antibody test indicates a cat was successfully infected at some point within the last 18 months but cannot confirm the cat is currently infected.

In summary, a positive test to either an antigen or antibody test is significant, whereas a negative test does not rule out current or previous heartworm infection.

With the introduction of a combination feline leukemia virus (FeLV), feline immunodeficiency virus (FIV), and heartworm antigen test (SNAP® Feline Triple™), the number of cats tested for heartworms may dramatically increase as cats routinely screened for FeLV and FIV at shelters and general veterinary practices can now also be tested for heartworm infections. Necropsy studies have shown that 5% to 10% of shelter cats in the southeast U.S. harbor adult heartworms (Nelson 1998; Snyder et al. 2000). As more cats are tested, a significant number of shelter cats are going to be found to be positive for adult worms. This will introduce a new dilemma for shelters in how to manage these cats, as there is not currently a successful adulticidal therapy available for cats.

## PREVENTION AND CONTROL

The heartworm preventives that are currently routinely used belong to the macrocyclic lactone class of drugs and have a high therapeutic/toxic ratio. Examples of this class of drugs are ivermectin, milbemycin, moxidectin, and selamectin. There are a variety of formulations, and they may be combined with other parasiticides to offer a broader spectrum against some intestinal parasites. All are extremely effective in preventing heartworms when administered properly. It is recommended by the American Heartworm Society (AHS) and the Companion Animal Parasite Council (CAPC) to give broad-spectrum heartworm preventives year round.

Some herding breed dogs such as collies, Australian shepherds, and Shetland sheepdogs may harbor a mutation of the *ABCB1* (formerly *MDR1*) gene denoted as *ABCB1-1Δ*. Dogs that express this gene can experience toxicosis to macrocyclic lactones at much lower doses than normal dogs; however, the manufacturer recommended doses of all heartworm preventives licensed in the U.S. are safe in dogs that carry this gene (Mealey 2007).

### Puppies, kittens, ferret kits, and adult cats

All puppies, kittens, and ferret kits in endemic areas should ideally be placed on a heartworm preventive as soon as they enter the shelter. If economic or management constraints render this impractical (e.g., a high-turnover facility where a significant fraction of animals are euthanized rather than adopted), priority should be given to providing a preventive for animals that will be held long term or for whom adoption is highly probable. Also, all cats should ideally be placed on preventives, with similar considerations regarding economic and management factors. Heartworm-positive cats are rarely microfilaremic, and even when microfilariae are present, they are in such low numbers that there is not a risk of precipitating a reaction to dying microfilaria.

### Dogs

Dogs 7 months and older should ideally be tested prior to the administration of heartworm preventives, as heartworm-positive dogs with high levels of circulating microfilariae have the potential for adverse effects from large numbers of dying microfilariae. These dogs are more likely to be encountered in high endemic areas such as the Gulf Coast, lower Atlantic coast, and Mississippi River Valley, where worm burdens are generally higher. However, the origin of dogs presented to shelters cannot always be determined. The risk of these adverse effects is higher with milbemycin, as this drug is a potent microfilaricide. The risk is much lower with ivermectin, moxidectin, and selamectin when used at standard preventive doses; the benefits of these products in parasite control outweighs the risk. However, when livestock preparations of ivermectin are used, the dose administered is frequently in excess of the 6µg/kg preventive dose. Ivermectin at 50µg/kg is a potent microfilaricide, and this dosage can lead to adverse reactions in heartworm-positive dogs. Signs of adverse reactions include lethargy, inappetence,

salivation, retching, pale mucous membranes, tachycardia, and in severe cases, acute circulatory collapse. Affected animals are treated with intravenous fluids and glucocorticosteroids.

There may be instances when it is prudent to suppress the microfilariae in heartworm-positive dogs to eliminate the animal as a reservoir for infection within a shelter, especially if all susceptible animals within the shelter are not on monthly preventives. The administration of monthly standard doses of ivermectin, moxidectin, or selamectin will gradually reduce microfilariae over a period of 6 to 9 months. If a more rapid decrease is desired, one dose of the previously mentioned drugs on day 1 followed by a second dose on day 15 can be administered. On day 30, administer either ivermectin at 50 µg/kg or milbemycin at standard preventive dosage. Pretreatment with diphenhydramine 2 mg/kg and prednisone 1 mg/kg immediately prior to administration of the microfilaricide will reduce the risk of adverse reactions.

Controlling mosquitoes within shelters is important for the comfort of the resident animals and workers but is a poor method of preventing the spread of heartworm disease, as one mosquito bite can potentially transmit up to eight infective larvae. Time, effort, and resources are better spent on acquiring and administering preventives than trying to eliminate mosquito exposure totally.

## ADULTICIDAL TREATMENT

The goal of heartworm treatment is to eliminate the adult worms as safely as possible. The American Heartworm Society recommends a preadulticide evaluation to include, when feasible, a physical exam, antigen test, complete blood count (CBC), blood chemistries, and thoracic radiographs to assess the patient thoroughly for coexisting disease that may affect the outcome of treatment. These diagnostic tests are not always readily accessible to many shelters, in which case one would have to rely on a thorough physical exam to assess the patient. Dogs that exhibit significant clinical signs of heartworm disease should be stabilized before administering an adulticide. There are multiple protocols currently being used to treat heartworms in dogs. The efficacy and post-treatment complications will vary between the protocols, but regardless of which protocol is chosen, exercise restriction needs to be enforced as this is the number one factor in reducing complications. The decision on which protocol to use will most likely be determined by available resources and length of time a dog can be kept in the shelter. In most cases any treatment is better than the alternative of not treating.

### Melarsomine

Administration of heartworm preventives should begin as soon as the dog is diagnosed with heartworms, in a manner as described in the previous section or as soon as can be safely accomplished if the shelter facility or staffing is not sufficient to provide safe housing or monitoring. Since melarsomine has not been shown to be effective on worms less than 4 months old, administration of two to three doses of a heartworm preventive allows the immature worm to reach an age when it is susceptible to melarsomine and prevents any third- and fourth-stage larvae from developing any further.

Pretreatment with doxycycline at 10 mg/kg before administration of melarsomine has been shown to be effective in reducing lung pathology (McCall 2007). Heartworms are host to a Rickettsial intracellular endosymbiont belonging to the genus *Wolbachia* as are most filarial nematodes. These intracellular bacteria produce metabolites that have been incriminated in the disease process associated with many filarial nematodes (Kramer et al. 2005; Kozek 2005). McCall (2007), in a study that evaluated multiple treatment protocols, found the fewest lung lesions in experimentally infected dogs that were pretreated with a macrocyclic lactone and doxycycline prior to receiving melarsomine. If doxycycline is added to a heartworm treatment regimen, it should be started before or at the same time as the first heartworm preventive dose and be administered for 4 weeks.

Melarsomine is then administered using the three-injection alternative protocol (one injection followed by two injections 1 to 2 months later, administered 24 hours apart) described on the package insert. This is the treatment of choice of the American Heartworm Society regardless of the stage of disease because of increased safety and efficacy. This protocol spreads the elimination of the adult worms over a 2-month period, reducing the risk of thromboembolsim and achieves a 98% reduction in worm mass. The two-injection protocol results in a 90% reduction in worm numbers, with only 50% seroconverting to a negative antigen test. Therefore, the three-injection treatment protocol listed above is the ideal method for treating heartworms. However, this protocol will not be practical in most shelter situations due to total length of time to complete the treatment and cost. An alternate method would be to rely on physical exam alone for preadulticide evaluation, giving 1 month of a preventive with or without doxycycline prior to starting the three-injection protocol. If time constraints will not allow for use of the three-dose protocol, then the higher-risk, two-injection protocol is

an appropriate choice if the alternatives are either not treating or euthanasia.

Exercise restriction for 6 to 8 weeks should be strictly enforced as overactivity is the number one cause for complications. Pulmonary thromboembolsim will occur as a result of dead worm particles lodging in the pulmonary arterioles and capillary beds. The complications from these embolisms can be minimized by cage resting the dog. Dogs that do exhibit signs of embolisms such as low-grade fever, coughing, and hemoptysis should be treated with reducing anti-inflammatory doses of glucocorticosteroids (Atwell et al. 1995). Dogs that have previously been symptomatic or dogs from highly endemic areas can be started prophylactically on reducing doses of prednisone during the month following melarsomine injection.

There have been anecdotal reports of veterinarians administering one injection of melarsomine once monthly for 3 consecutive months. There are no data to support this approach as safer or effective. There are data from the original studies that indicate two doses within a 24-hour period were required to kill female worms (Keister, Sol et al. 1992).

**Ivermectin**

Studies (McCall 1998, 2007) have shown that ivermectin administered at standard preventive doses of 6 µg/kg will cause a gradual reduction in adult worm burdens. Seven-month-old worms were reduced 94.9% after 29 months, and 8–month-old worms were reduced 56.3% after 16 months. It is important to note that these dogs were caged during the entire study. As discussed in the previous section on melarsomine and in the pathogenesis section, strict exercise restriction is the most important factor in minimizing the risk of pulmonary thromboembolsim associated with dying worms. In a study of naturally infected dogs administered ivermectin over a 2-year period, 21% had radiographic and echocardiographic evidence of disease progression. The overall worm burden was reduced 71% over the 2-year period. The conclusion from this study was that dogs that exhibit signs of heartworm disease or very active dogs should not be treated with this approach, and if used in asymptomatic dogs, they should be exercise-restricted and examined every 4 to 6 months until they become antigen negative (Venco et al. 2004).

The American Heartworm Society states that long-term continuous administration of ivermectin is not a substitute for conventional melarsomine-based adulticidal treatment. If this approach is elected, exercise should be restricted and owners made aware of potential consequences.

Another concern in using heartworm preventives long term in heartworm-positive dogs is the potential development of resistance to the macrocyclic lactone class of drugs. Resistance to this class of drugs has occurred in some gastrointestinal parasites found in livestock and in some human filarial nematodes (Prichard 2005). While heartworm resistance has not become apparent, there are increased reports of lack of efficacy of heartworm preventives to the Food and Drug Administration, so vigilant oversight and prudent use of the drugs is required.

**Treating cats**

Treating heartworm-positive cats is currently limited to symptomatic therapy as there has not been any study indicating that any form of medical adulticidal therapy increases the survival rate in cats. Prednisone is the cornerstone of treatments, with some evidence that antileukotrienes may be beneficial. Prevention of heartworm disease is the most effective approach for cats.

Recommendations are constantly evolving for the diagnosis, prevention, and treatment of heartworm disease in both dogs and cats. The latest updates and recommendations can be found at the American Heartworm Society's Web site (www.heartwormsociety.org).

## ELECTIVE SURGERIES ON HEARTWORM-POSITIVE DOGS

A question that has sparked considerable debate is whether to perform elective spay/neuter procedures on heartworm-positive dogs or to wait until after a heartworm treatment. In an ideal world, one would treat for heartworms and allow a 6-month period for the lungs to recover; however, in the real world this is hardly practical, and many veterinarians will perform surgery 2 months following heartworm treatment. As discussed previously in the pathogenesis section, the majority of pathology associated with heartworm infections is a result of dead worms, not live worms, and heartworm treatments cause worm death. It takes upwards of 4 to 5 months for a heavily infected dog to become antigen negative following treatment. This means it can take 4 to 5 months for all of the remnants of the dead heartworms to be removed from the pulmonary vasculature. Therefore, in heartworm-positive dogs, the risk of surgery before treatment is not higher (and may actually be lower) than if an adequate post-treatment recovery period is not allowed before surgery is performed.

A reasonable compromise is to perform spay/neuter procedures on asymptomatic dogs (Class 1) before heartworm treatment. In dogs with mild symptoms (Class 2), a

**Table 22.1.** Classes of heartworm disease.

| | | |
|---|---|---|
| Class 1 | Asymptomatic | No radiographic lesions |
| Class 2 | Mild to moderate signs | Cough, exercise intolerance, abnormal lung sounds |
| Class 3 | Severe signs | Cough, exercise intolerance, dyspnea, abnormal heart and lung sounds, enlarged liver (hepatomegaly), syncope (temporary loss of consciousness from reduced blood flow to the brain, ascites (fluid accumulation in the abdominal cavity), death |
| Class 4 | Caval syndrome | Hemoglobinemia, hemoglobinuria |

reducing-dose course of prednisone with or without doxycycline over 4 weeks should reduce the inflammatory response to the heartworm infection sufficiently enough to allow spay/neuter procedures to be performed. Dogs exhibiting moderate to severe signs of heartworm disease (Class 3) should be treated first and allowed a full 6-month recovery period. See Table 22.1 for a description of the classes of heartworm disease.

## CLIENT EDUCATION AND IMPLICATIONS FOR ADOPTION

Heartworm infections have a profound affect on the adoptability of a pet. Potential owners are reluctant to adopt heartworm-positive animals because of the added cost of treatment or from horror stories they have heard about heartworm treatment. This disease can be treated successfully in the overwhelming majority of canine cases if recommended protocols are followed.

The new challenge is going to be how to handle cats that test positive for heartworms on the FeLV, FIV, and heartworm test kit. With no specific curative treatment available and the potential for a catastrophic, life-threatening event occurring when the adult worm eventually dies, many potential owners will shy away from these cats. Not all heartworm-positive cats are going to die suddenly. In fact, the opposite is true; most will survive the infection if given the chance. Adopters who take home a heartworm-positive cat need to be instructed to seek immediate veterinary care if the cat shows any signs of respiratory distress. Cats exhibiting clinical signs of heartworm disease such as coughing or dyspnea should be treated with anti-inflammatory doses of glucocorticosteroids and bronchodilators. There is some anecdotal evidence that antileukotrienes may be beneficial in thwarting a fatal acute lung injury when the adult worm dies. Retrospective studies have indicated that between 10% and 20% of cats with adult heartworm infections will die either suddenly or as a result of complications from a dead or dying heartworm (Atkins et al. 1998; Genchi, Venco et al. 2007).

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# 23
# Zoonosis

*Jennifer Calder and Lila Miller*

## INTRODUCTION

The shelter environment presents a disease management challenge because animals of unknown medical backgrounds and unknown exposure histories must coexist in a congregate living environment. Often, asymptomatic animals are carriers of infection, and the congregate environment facilitates animal-to-animal and animal-to-human disease transmission. Zoonotic disease is strictly defined as infectious disease that is naturally transmitted from living animals to humans. Anthroponosis (also known as reverse zoonosis) refers to infections that can be transmitted from humans to animals. An exhaustive discussion of zoonotic disease is beyond the scope of this chapter; the objective here is to cover the zoonotic diseases that are most frequently encountered or that may be of interest to shelter personnel who care for dogs and cats, and to describe the special concerns of shelters when considering housing and adopting these animals to the public. The reader should refer to other veterinary and public health resources for general information and to other chapters in this textbook for information about the management of these targeted diseases in shelters.

It is unrealistic to expect that shelters can routinely ensure that animals are free of every potential zoonotic condition. Depending on the source of information, estimates are that over 250 organisms are zoonotic, and anywhere from 30 to 40 of them affect companion animals (Greene and Levy 2006). In addition, it has been shown that a higher percentage of shelter cats than client-owned cats tend to have zoonotic enteric pathogens (Hill, Cheney, Taton-Allen 2000). Although it should be stressed that the benefits of pet ownership generally outweigh the risks of contracting a zoonotic disease, shelters should be aware of the populations that are most at risk, i.e., the elderly, the immunocompromised, infants, and very young children.

Shelters should perform a risk analysis to minimize the possibility of spreading infection to the staff, volunteers, and public, and should educate adopters about precautions to prevent disease transmission from pets. The decision to release an animal from the shelter when that animal is known to have been infected with a zoonotic disease should be based on (1) the risk of transmission from the animal to the caregiver and other members in the household; (2) the risk of disease actually developing in the owner and other members of the household; and (3) the risk of fatality in humans. For example, one would not release for adoption a dog or cat that had been potentially exposed to rabies via a bite from a wild animal. However, a puppy undergoing treatment for giardiasis could be released to a nonimmunosuppressed owner as long as the owner was aware of the risks and advised of preventive measures needed to protect himself or herself.

The adoption recommendations offered in this chapter are offered only as general guidelines; they are summarized in Appendix 23.1. Whenever making medical decisions about adoptability, each veterinarian should consider the shelter's ability to treat the disease successfully and verify the cure. This may be difficult for many shelters, especially when dealing with a zoonotic disease such as brucellosis, which is difficult to cure. The handling of some of these animals may occasionally require input from the Department of Health. Regardless of the resources consulted, outside of legal restrictions, the ultimate responsibility for determining medical suitability for adoption and the need to provide adopter counseling regarding medical issues should rest with the veterinarian.

Shelter veterinarians are often asked for advice about human health when a zoonotic disease is encountered because veterinarians are frequently at the forefront with knowledge about to zoonotic diseases. Some information

about clinical signs in humans and treatment will be offered here, but veterinarians are cautioned to use their best judgment and to refrain from offering an opinion that could be interpreted as practicing human medicine. Questions about human health should always be referred to a physician.

## CONSULTING WITH THE DEPARTMENTS OF HEALTH

All shelters should establish a working relationship with their State Public Health Veterinarian or State Veterinarian. This relationship will facilitate the two-way flow of information and provide the shelter staff with the professional support they will need prior to and during events of public health concern, disasters, or emergencies.

Some diseases are nationally notifiable, and all practitioners are required to report specific conditions to the Centers for Disease Control and Prevention. Some diseases are reportable only at the state or local level; that is, each state or local health department decides what conditions, in addition to the nationally reportable conditions, they require practitioners to report. Shelter personnel should contact their local or state health departments to obtain a list of reportable diseases. The State Public Health Veterinarians and the State Veterinarians listings can be found at State Public Health Veterinarians, www.nasphv.org/Documents/StatePublicHealthVeterinariansByState.pdf (accessed August 23, 2008), and State Veterinarians, www.usaha.org/StateAnimalHealthOfficials.pdf (accessed August 23, 2008).

## GENERAL GUIDELINES FOR ZOONOTIC DISEASE PREVENTION

Shelters and veterinary practice environments can present a high risk of exposure to various infectious pathogens that can transmit disease from animals to humans (and vice versa). Infection control measures should be implemented in all animal care facilities to minimize the risk of all disease transmission. The *Compendium of Veterinary Standard Precautions – Zoonotic Disease Prevention in Veterinary Personnel* (2006) is an excellent resource for shelters to use and adapt for their special needs. The reader should also consult the Centers for Disease Control and Prevention National Center for Zoonotic, Vector-Borne, and Enteric Diseases (www.cdc.gov/nczved/) for additional advice about zoonotic disease.

The *Compendium* reports that of the 1,415 agents that cause disease in humans, 61% are zoonotic; of the 175 pathogens defined as emerging infections, 75% are zoonotic. Many of the animals that enter shelters are debilitated, immune compromised, and have vague histories about their backgrounds or previous exposure to disease. Many zoonotic diseases present no overt clinical signs in animals; it is therefore imperative that shelter personnel be ever vigilant about the possibilities regarding zoonosis. Because shelters often have limited space and resources, there is a tendency to try to reuse syringes, share storage space, limit vaccinations, crowd animals, etc. Many of these practices increase the potential for disease transmission and should be discouraged. General recommendations to limit disease transmission will be discussed in this section, but the reader is referred to other public health sites, such as the National Association of State and Public Health Veterinarian Web site, www.nasphv.org/Documents/VeterinaryPrecautions.pdf, and the Centers for Disease Control and Prevention, www.cdc.gov, for more detailed information. Basic recommendations include:

- Practice hand hygiene routinely
- Use protective gloves, sleeves, gowns, hair covers, and shoe covers, especially when handling animals with suspicious or obvious clinical signs or histories of disease
- Use facial protection to protect eyes, nose, and mouth when handling animals, performing procedures (e.g., dentals), or cleaning
- Use appropriate protective garments when cleaning, such as boots, coveralls, smocks, eye protection (goggles, glasses), etc.
- Do not reuse disposable items

Animals should be examined on intake to identify those with signs of infectious disease so they may be isolated from the general population as soon as possible and handled appropriately. Vaccinations and prophylactic deworming, especially for zoonotic internal parasites, should be administered to all animals. Exam rooms should have a sink and be supplied with soap and paper towels so that staff may wash their hands frequently. Alcohol-based (70%) hand gels may also be effective against some pathogens and compliance with their use may be higher; both alcohol hand sanitizers and hand-washing stations should be available to shelter staff and visitors.

Food for human consumption should be stored in a refrigerator separate from animal products, vaccines, etc. The consumption of food and beverages should be banned in animal holding areas. Fungal and other cultures and test

materials should be stored separately; gloves should be worn when they are handled.

Vaccines and biologics should be stored and handled appropriately, according to the manufacturer's instructions. Intranasal vaccines should not be used around immune-compromised individuals. Sharps containers should be readily available wherever needles are used. The practice of recapping or cutting needles before disposal is strongly discouraged to avoid needle sticks or aerosolization of certain pathogens. Shelters that perform surgeries, necropsies, or handle diagnostic specimens are advised to follow the same, if not higher, safety precautions than would be followed in a veterinary practice because there may be a greater degree of uncertainty about disease in stray animals. Nonessential personnel should not be permitted in the room, and protective garments should be worn. Hands should always be washed at the end of any procedure and definitely before handling other equipment, rubbing one's eyes, or consuming food.

Environmental sanitation is discussed in detail in Chapter 4. Spills, blood, urine, feces, etc. should be cleaned up promptly and surfaces disinfected with an appropriate disinfectant. Infected tissues should be handled as biohazardous waste and disposed of properly. Laundry should be machine washed using hot water, detergent, and bleach, and machine dried. Rodent and vector control is an important component of any comprehensive disease control program.

Shelters should have a written infection control plan that contains information pertinent to protection of employee health. This section may be best written by a physician in consultation with a shelter veterinarian. Shelter veterinarians are generally more knowledgeable about the zoonotic disease risks faced by shelter staff. Staff who routinely handle animals should receive rabies preexposure and tetanus vaccinations, and there should also be a risk assessment to determine if other preventive vaccinations and procedures may be warranted. The plan should be available to all staff and updated regularly. Staff training regarding zoonotic diseases, transmission of disease, and sanitation should be provided on a routine basis.

**Hand hygiene**

Hand hygiene is a key element in preventing the transmission of infections; in fact, it is probably the single most effective disease prevention method to use in a shelter. However, it must be done correctly and at the appropriate time to be effective.

Hands should be washed with plain soap, or a soap that contains antiseptic, and water. If hands are not visibly soiled, an alcohol-based rub may be used temporarily to decontaminate hands instead of hand washing with soap and water. However, alcohol-based gels do not substitute for hand washing. To minimize disease transmission, hand hygiene with soap and water or an alcohol-based product must occur:

1. Before direct contact with patients
2. Before donning gloves when inserting a central intravascular catheter
3. Before inserting indwelling urinary catheters, peripheral vascular catheters, or other invasive devices that do not require a surgical procedure
4. After direct contact with the patient's intact skin
5. After contact with mucous membranes, body fluids or excretions, nonintact skin, and wound dressings
6. After contact with inanimate objects in the immediate vicinity of the patient or contaminated by the patient
7. After emptying/cleaning litter boxes
8. After cleaning cages or runs
9. After handling known or suspected tick- or flea-infested dogs or cats
10. After removing gloves

Wash hands with soap and water in these instances:

1. When hands are visibly soiled
2. Before eating
3. After using the restroom
4. Especially after caring for patients colonized or infected with spore-forming bacteria, e.g., *Bacillus anthracis*, *Clostridium difficile*

The use of moisturizers can enhance the integrity of the skin and reduce skin breakdown. Shelters are encouraged to provide glove-compatible moisturizers for their staff to use.

***How to wash hands properly***

1. Turn the faucet on using warm, not hot water. Hot water will dry out skin and increase the risk of infections.
2. Remove rings before wetting hands.
3. Apply 1–2 oz of liquid soap. Bar soap should not be used as this increases the risk of cross-transmission of microorganisms.
4. Rub hands together to make a lather, making sure to wash the palms, the back of hands, between the fingers and under the nails.

5. Scrub vigorously for 15 seconds.
6. Rinse with water.
7. Dry hands with a disposable towel.
8. Using the disposable towel, turn the faucet off before disposing of towel in wastebasket.

## ISSUES OF CONCERN WHEN ADOPTING TO HIGH-RISK PERSONS

This chapter will refer to the immunocompromised individual in almost every section as being at high risk for contracting a zoonotic disease. Although the public often associates immunocompromise solely with human immunodeficiency virus (HIV) infection and acquired immune deficiency syndrome (AIDS), other groups of individuals should be considered at high risk. At-risk individuals include, but are not limited to, people who have chronic renal failure, diabetes mellitus, cancer, severe or extensive burns, or liver cirrhosis; are malnourished or on long-term steroid therapy, chemotherapy, or have undergone organ transplantation; pregnant women and their unborn fetuses; newborns; children under 5 years of age; the elderly; and people who have been recently hospitalized, especially if they have indwelling catheters, tubes, or synthetic implants. In general, high-risk individuals should avoid cleaning litter pans and avoid adopting pets that:

1. Are younger than 6 months of age
2. Have diarrhea (animals that are diarrheic should be tested for helminthes, bacteria, and protozoa including *Giardia*, *Cryptosporidia*, *Campylobacter* spp., and *Salmonella* spp.)
3. Have fleas or ticks
4. Have long, unclipped nails

## DISEASES ACQUIRED THROUGH A CONTACT SUCH AS A BITE, SCRATCH, OR EXPOSURE TO SALIVA

Bite-inflicted wounds are common in the shelter environment and may become infected with bacteria from either the flora on the victim's skin or the "normal flora" of the biter. The animal inflicting the bite is often clinically normal. Risk factors for dog bites include the dog's age, breed, size, reproductive status, and medical condition. It is interesting to note one reference indicates most cat bites are inflicted by unowned female cats on female adults (Greene and Goldstein 2006). Shelters should ensure that staff are properly trained to recognize the behavior signs that indicate possible aggression and how and when to use safety and restraint equipment, including tranquilizers or sedation for fractious animals.

Dog bites are more common than cat bites; however, cat bites are more likely to become infected because they tend to produce deep puncture wounds. Dog bite wounds often become infected with the dog's oral flora; they are frequently infected in descending order with *Staphylococcus aureus*, *Streptococcal* species, or *Pasteurella* species. Cat bites are more likely to become infected with *Pasteurella* species (Zurlo 2005). *Pasteurella multocida* subsp. *septica* has a greater prevalence in cats, and *P. canis biotype 1* is found only in dog bites.

Bite wounds, in general, typically include lacerations, avulsions, punctures, and scratches. Persons who wait more than 8 hours to seek treatment after a bite usually will have an infected wound. Typical signs of infection include pain at the site of the injury, a purulent discharge, gray color, and a foul odor. Approximately 2% to 30% of all bite wounds for which medical care is sought will become infected and may result in hospitalization of the patient. Puncture wounds are more likely than avulsions to become infected and result in abscess formation. Wounds in close proximity to bones and joints may cause septic arthritis, tenosynovitis, or osteomyelitis. Osteomyelitis should be considered whenever there is joint pain or limited range of motion.

### Bite wound pathogens

#### Pasteurella

*Pasteurella multocida* is a small bacillus that is frequently found as a normal inhabitant in the oropharyngeal and nasal cavity of cats and dogs as well as other animals. Cat bites are more likely to have serious consequences in humans than dog bites; more than 50% percent of all cat bite wounds are contaminated with *Pasteurella*, and cats account for more than 75% of hospital room visits associated with *Pasteurella*-infected bites. *Pasteurella multocida* subsp. *septica* is more likely to cause central nervous system infection, while *P. stomatis* and *P. dagmatis* may cause systemic infections, including respiratory, urogenital, or intra-abdominal disease. Cellulitis is often seen within 48 hours of an exposure. Immunocompromised persons are prone to more severe outcomes after a bite exposure. In addition to bites, exposure may occur through animals licking wounds.

#### Capnocytophaga

*Capnocytophaga canimorsus* and *C. cynodegmi* are normal inhabitants of the canine oral flora (Gill 2005). Most people who report infections do so after being bitten or scratched by a dog (occasionally a cat), although in some cases the only contact the patients reported was exposure

to a dog without a bite or scratch (Kullberg, Westendorp et al. 1991).

*C. canimorsus* infections are more prevalent and serious than *C. cynodegmi*. Asplenia, alcoholism, and steroid use predisposes to infection with *C. canimorsus*; however, individuals without these underlying conditions may also become infected (Gill 2005). Infection may cause disease that ranges from mild to fulminant. In splenectomized individuals, the disease tends to be fulminant and may include shock, disseminated purpura, disseminated intravascular coagulation, renal failure, bite-site gangrene, and pulmonary infiltrates. While fulminant infections can occur in healthy people, they tend to have milder infections. Physicians should initiate treatment or prophylaxis of suspected *C. canimorsus* infection promptly because confirmation through isolation and identification and in vitro susceptibility testing is slow.

### *Rabies*

No chapter on zoonoses would be complete without mention of rabies, which is covered more thoroughly in Chapter 18 in this textbook. According to the World Health Organization, at least 55,000 human deaths worldwide occur annually due to this disease (www.who.int/mediacentre/factsheets/fs099/en/). Rabies is caused by a virus belonging to the Lyssavirus genus of the *Rhabdovirus* family. Rabies occurs worldwide except in a few rabies-free countries. All warm-blooded mammals are susceptible to rabies; however, it is maintained in wildlife with spillover into domestic animals. In the United States, rabies can be found in all 50 states except Hawaii, and wildlife is the main cause of rabies transmission in the U.S. The epidemiology of rabies in domestic animals in the U.S. varies by region. While there has been a significant decrease in the number of canine rabies cases in the U.S., sporadic cases occur along the U.S.–Mexico border and in areas of enzootic rabies (CDC 2008). Rabies can be transmitted by bite, non-bite, bat, or human-to-human exposures. Rabies should be considered whenever there is a bite from a mammalian animal, especially wildlife. In general, bites from small rodents (e.g., squirrels, rats, mice, chipmunks, and hamsters) and lagomorphs (e.g., rabbits and hares) are not considered rabies exposures for humans. However, the health department should be consulted on rodent or lagomorph bites regarding the need for postexposure prophylaxis (CDC 2008). Currently, more cases of rabies are reported in cats than dogs in the U.S. (Blanton, Hanlon et al. 2007). Nonbite exposures (contamination of open wounds, abrasions, scratches, or mucous membranes) to saliva or other potentially infectious material rarely cause rabies. However, non-bite exposures associated with rabies include the transplant of corneas, solid organs, or vascular tissues from individuals who died from rabies and the inhalation of large amounts of aerosolized rabies virus (CDC 1980, 2008; Srinivasan, Burton et al. 2005). Most cases of human rabies in the U.S. are acquired from bat exposures; however, bites or scratches from bats may be difficult to document, and thus any bat exposure must be thoroughly investigated (CDC 2008). The CDC notes, however, that as rabies has decreased in the U.S. over the years, the proportion of rabies patients with no known exposure has increased (CDC 1989).

As stated previously, animals may become infected via a bite, non-bite, or bat exposure. Humans become infected similarly to animals, as well as with human-to-human exposures via organ transplants. Exposure to or accidental injection of the inactivated rabies vaccine is not considered an exposure. The incubation period in humans is usually 20 to 90 days but can be quite variable, lasting for shorter periods or longer, even for years (Acha and Szyfres 2001). Humans often experience the following symptoms at the exposure site during the early stages: fever, headache, malaise, respiratory and gastrointestinal disorders, and paresthesia. As the disease progresses, excitability, disorientation, inability to drink, excessive salivation, and convulsions may be seen, culminating in paralysis, respiratory arrest, and death. Rabies infections in people and animals are almost invariably fatal once clinical signs appear. However, the recent successful treatment of clinical rabies in a 15-year-old girl may alter the clinical outcome of future rabies cases (Willoughby, Tieves et al. 2005).

Municipal shelters are often required to hold animals that have bitten humans for observation for rabies. (See Chapter 18 for more information on the management of rabies.) Briefly, healthy dogs, cats, or ferrets that cause human exposures should be observed for 10 days for signs of illness. Any illness in an isolated or confined animal should be reported immediately to the local health department. Should the animal develop signs or symptoms suggestive of rabies, the animal should be euthanized and the head submitted for testing (NASPHV 2008). In the case of rabid or suspected rabid dogs, cats, or ferrets, the animal should be euthanized, the brain submitted for testing, and consideration given to the initiation of postexposure treatment immediately. Alternatively, in cases where animal exposure to rabies has occurred and an owner of a vaccinated or unvaccinated animal refuses euthanasia, the health department may order the animal to be held in quarantine for up to 6 months or longer in accordance with local ordinances.

Shelter personnel should utilize standard precautions whenever examining or working with animals presenting with neurological signs. This is of particular importance when handling stray animals. Gloves should be worn whenever an oral examination is performed or when attempting to remove foreign objects from an animal's mouth. Veterinary staff should wear disposable gowns, gloves, masks, face shields, or goggles when removing animal heads for rabies testing. When heads are submitted for testing, they should be submitted in a leakproof container surrounded by frozen gel packs and absorbent material to prevent leakage from the package. Do not freeze the head or brain. Although blood and urine in the carcass do not appear to be risks, all precautions for safety should be taken to avoid disease exposure. Even though rabies does not persist in the environment, cages in which known rabid animals were housed should be thoroughly cleaned and disinfected after the animal has been removed. The virus is sensitive to phenolics, halogens (sodium hypochlorite or bleach, iodine), alcohol, and many other disinfectants and heat (Greene and Rupprecht 2006).

Shelter staff, e.g., veterinarians, veterinary technicians, kennel personnel, animal control officers, and any other personnel who handle animals regularly should be vaccinated against rabies as soon as possible. The recommended schedule using the human diploid cell vaccine (HDCV), the rabies vaccine adsorbed (RVA), or the purified chick egg cell (PCEC) vaccine is days 0, 7, 21, or 28 intramuscularly (deltoid area) (CDC 2008). Personnel working in rabies-enzootic areas should receive biannual serum neutralization serologic testing. If titers are less than 1:5 on the rapid focus inhibition test (RFIT), then a booster dose of vaccine is needed (CDC 2008).

The decision to initiate rabies postexposure treatment will be determined by the department of health based on several factors: (1) the species of the animal that caused the exposure, (2) the appearance and behavior of the attacking animal, (3) whether the encounter was provoked by human presence, (4) the location and severity of the bite wound, (5) whether the animal is available for observation or testing, and (6) laboratory test results if the animal is tested. Questions and concerns about exposures should be immediately directed to the state or local health department. Both animal and human rabies are reportable to the health department.

### Wound management

Dog bite wounds that are classified as moderate or severe should be considered contaminated unless they are less than 1 day old and there is no clinical evidence of infection (Goldstein 2005). Cat bites are likely to become infected because these are often punctures to the extremities. All bite wounds and scratches should be immediately washed with soap (preferably a virucide such as povidone iodide) and water. First aid should consist of immediate irrigation with copious amounts of normal saline and soap. Puncture wounds should be irrigated under pressure using a 20-ml syringe and an 18-gauge needle. The wound should be covered with a bandage and evaluated immediately by a physician. If the hand is injured it should be elevated; it is strongly suggested that physicians administer aggressive antibiotic treatment to puncture wounds near joints, especially on the hands. One should always collect a history about the bite that will help in determining the circumstances surrounding the bite. Table 23.1 is an example of an animal bite investigation form that may be used. Animal bites are reportable to the local health department in some jurisdictions, so it is advisable to check on their regulations before a bite occurs.

## DISEASES THAT ARE ACQUIRED THROUGH CLOSE CONTACT OR A SCRATCH

### Sporotrichosis

Sporotrichosis is caused by *Sporotrix schenckii*, a dimorphic fungus that is found worldwide in the environment, commonly in soil. Dogs and cats may become infected via a puncture wound acquired from either a contaminated thorn, claw, or oral cavity of another cat (Rosser and Dunstan 2006). It is more commonly seen in outdoor male cats. Infected cats play the key role in the transmission of infection to humans because they have high numbers of organisms in their tissues, exudates, and feces. The clinical signs in cats include draining puncture wounds, abscesses, and large ulcerated and crusted lesions on the head, limbs, and tail base. The organism can spread when the cat grooms itself, resulting in multiple lesions. Diagnosis is via cytology, fungal isolation, histopathology, or immunofluorescence.

Humans may acquire infection percutaneously or by aerosol. It is believed the infection can be acquired from the claw of an infected cat or from a healthy cat that has been living with an infected cat. There has been speculation that the disease may even be spread by an infected cat rubbing its face against a human. Sporotrichosis in humans may present as several clinical syndromes. It usually begins at the site of inoculation where it produces an ulcerative nodule that is often associated with local lymphatic spread; lymphocutaneous sporotrichosis is just one form of the disease. There may be localized or widespread

**Table 23.1.** Animal bite investigation form.

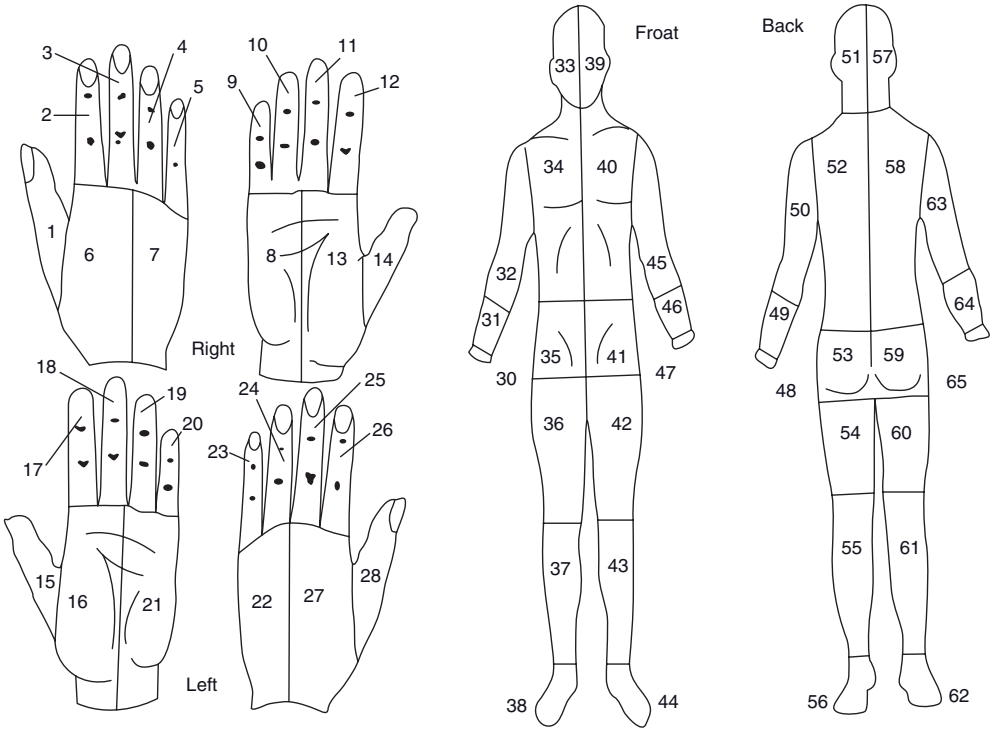
Shelter name: _____ Shelter phone number: _____
Shelter address: _____
Veterinarian in Charge of Shelter: _____
Employee last name: _____ Employee first name: _____

1. Date of Injury: ___/___/_____ (mm/dd/yyyy)
2. Time of Injury:___:___ am/pm (circle one)
3. Location where the injury occurred? (Check one box only)
   - □ Examination Room
   - □ Procedure Room *(X-ray, EKG, etc)*
   - □ Kennel
   - □ Euthanasia Room
   - □ Outside Patient Care Area *(hallway, unloading bay, etc.)*
   - □ Other, describe: _____
4. What is employee's job category? (Check one box only)
   - □ Veterinarian
   - □ Veterinary Technician
   - □ Kennel Personnel
   - □ Other: (describe):_____
5. How was employee hired at the time of the injury? □ Full time □ Part time
6. Was this the employee's regular shift? □ Yes □ No
7. Was the employee working overtime? □ Yes □ No
8. What species of animal caused the injury? □ Cat □ Dog □ Other (describe) _____
9. Animal ID #_____
10. Was the animal that caused the injury previously owned? □ Yes □ No □ Don't know
11. Was the animal vaccinated against rabies? □ Yes □ No □ Don't know
12. If yes; date of rabies vaccination___/___/_____ (mm/dd/yyyy)
13. Describe the signs and symptoms the animal had or has

    _____
    _____
    _____
    _____
    _____
14. Is the animal available for observation? □ Yes □ No
15. Date animal was placed under observation ___/___/_____ (mm/dd/yyyy) □ NA
16. Disposition of animal (Check one)
    - □ Died Date ___/___/___ (mm/dd/yyyy)
    - □ Euthanized Date ___/___/___ (mm/dd/yyyy)
    - □ Released from observation Date ___/___/___ (mm/dd/yyyy)
    - □ Other (describe) _____date ___/___/_____ (mm/dd/yyyy)
17. Was the animal tested for rabies? (Check one) □ Yes □ No □ Don't know
18. If yes; date of test _____/_____/_____ (mm/dd/yyyy)
19. Type of specimen sent (Check all) □ Brain stem □ Cerebellum
    □ Cerebrum □ Entire head
    □ Other (specify) _____
20. If yes; name of laboratory: _____

**Table 23.1.** *Continued*

21. Circle on the diagram below the location(s) of the injury(ies):




22. For each injury site identified in the figure above, indicate the type of wound obtained (A = avulsion; L = laceration; P = puncture; S = scratch)

| Injury site # | Wound type | Injury site # | Wound type |
|---|---|---|---|
| _____ | _____ | _____ | _____ |
| _____ | _____ | _____ | _____ |
| _____ | _____ | _____ | _____ |

23. Describe the circumstances leading to this bite injury: _____
_____
_____
_____
_____

| | | | |
|---|---|---|---|
| 24. Did employee complete a tetanus vaccination series? | ☐ Yes | ☐ No | ☐ Don't know |
| 25. When was the last tetanus vaccine given? ___/___/___ (mm/dd/yyyy) | | | ☐ Don't know |
| 26. Did employee complete a rabies vaccination series? | ☐ Yes | ☐ No | ☐ Don't know |
| 27. When was employee's last rabies vaccine given? ___/___/___ (mm/dd/yyyy) | | | ☐ Don't know |
| 28. When was employee's last rabies vaccination titer taken? ___/___/___(mm/dd/yyyy) | | | ☐ Don't know |
| 29. Was employee's rabies RFIT titer ≥1 : 5? | ☐ Yes | ☐ No | ☐ Don't know |
| 30. Was employee referred to a physician/ER for follow-up? | ☐ Yes | ☐ No | |

31. Physician/ER name _____
Address_____
Physician's/ER's phone number_____
32. Reported to ☐ State DOH ☐ Local DOH (Check one) on ___/___/___ (mm/dd/yyyy)
32. Follow up recommendations and other information _____
_____
_____
_____
_____

cutaneous lesions or mucosal lesions. There may also be hematogenous spread (extracutaneous sporotrichosis), resulting in osteoarthritis, central nervous system, ocular, or pulmonary lesions in the immunocompetent host or multifocal lesions in the immunosuppressed host (Rex and Okhuysen 2005). People who handle cats suspected or confirmed to have sporotrichosis should wear disposable gloves, dispose of these gloves immediately after use, and then wash their hands with a chlorhexidine or povidone-iodine scrub (Rosser and Dunstan 2006).

Sporotrichosis in companion animals can be treated with a number of drugs, including supersaturated potassium iodide in dogs and itraconazole in cats. Treatment can be prolonged, however, lasting anywhere from 16 to 80 weeks for a complete clinical cure with confirmatory negative cultures. This is a treatment regimen that would be prohibitive for many shelters due to the handling procedures that must be in place and the length of time to isolate, treat, and culture to verify cure.

Cessation of treatment prematurely can result in a relapse and return of clinical signs. If a decision to provide treatment is made, cats should be feline leukemia virus (FeLV) feline immunodeficiency virus (FIV) tested first because infection with these viruses may have an effect on the length of time of treatment and its effectiveness. Potential adopters should receive counseling; animals with this disease should not be adopted out to immunocompromised individuals. Ongoing veterinary surveillance and care may be necessary for these animals to ensure a complete clinical cure.

**Bartonellosis (cat scratch disease)**

The agent that causes cat scratch disease (CSD) is believed to be *Bartonella henselae*, although the American Association of Feline Practitioners' 2006 AAFP Bartonella Panel Report speculates there may be other agents involved as well (www.catvet.com). *B. hensalae* is a small gram-negative bacterium that is transmitted among cats, largely by the cat flea. The exact role of the flea in transmission remains undetermined, but consensus from the AAFP Panel is that exposure to fleas or flea feces is essential. There is some speculation that ticks and other blood-feeding parasites may also be involved in the transmission of *Bartonella* species between cats and possibly to humans (2006 AAFP Bartonella Panel Report; Guptill-Yoran 2006). Most cats infected with *Bartonella* are asymptomatic; those that do develop disease usually have mild or nonspecific signs that go undetected, such as transient fever, muscle pain, lethargy, etc. In most cases of human CSD, a primary cutaneous papule develops at the site of a cat scratch or bite 3 to 20 days after contact with a kitten or cat. One to seven weeks later, there is regional lymphadenopathy. Occasionally complications occur; these include Parinaud's oculargladular syndrome, encephalitis, osteolytic lesions, and thrombocytopenic purpura (Acha and Szyfres 2001).

The diagnosis and treatment of *Bartonella* in cats is covered in more depth in Chapter 21 on vector-borne diseases. Stray or feral cats less than 1 year of age with fleas are most likely to be infected (Guptill-Yoran 2006). Staff and volunteers in shelters are advised to use gloves when handling flea-infested cats, maintain good flea control both on cats and in the environment, trim cats' nails, and avoid rough play with cats to minimize the risk of bite and scratch wounds. All wounds should be promptly washed with soap and water and reported to shelter management for referral for professional care by a physician.

Some shelters have contemplated screening all adoption cats for *Bartonella*; the limits of diagnostic testing are discussed in Chapter 21, and this approach is not recommended. Instead, counseling of potential owners with regard to risks should be provided, and young cats with fleas should generally not be adopted to high-risk, immunocompromised individuals.

**Dermatophytosis (ringworm)**

Zoonotic dermatophytosis in dogs and cats is caused by *Microsporum canis* or *Trichophyton mentagrophytes* (Acha and Szyfres 2001). The disease is covered in depth in Chapter 16 on dermatophytosis. *M. canis* and *T. mentagrophytes* are found worldwide. Contact with broken hairs and associated spores, both on the animal and in the environment, plays an important role in the transmission of the disease (Kahn and Line 2005). Young kittens and puppies and debilitated animals may have persistent and widespread infection. Ringworm presents problems in shelters because of its often-subtle appearance, highly contagious nature, its tremendous environmental persistence, and the possibility that animals can act as mechanical carriers. Compared to other dermatophyte species, *M. canis* has a greater potential for zoonotic and contagious spread. Cats infected with *M. canis* thus cause shelters the most severe problems.

*Microsporum* infections in humans cause tinea capitis or tinea corporis (lesions on the scalp and body, respectively), while *T. mentagrophytes* causes infection on any part of the body. Humans become infected by exposure to the hair from infected animals. People most at risk for infection are the immune compromised, the elderly, and young children. The incubation period in humans

is 1 to 2 weeks. The lesions may resemble classic ringworm plaques. In other cases, there are red, tender, edematous draining nodules within which are pustules. The most common sites for lesions are the face, scalp, and extremities. With the exception of tinea capitis, topical antifungal medication is usually recommended to treat humans infected with zoophilic dermatophytosis (Radentz 1991). Suspected ringworm infections should be evaluated and treated by a physician or dermatologist; effective treatment of caretakers is important to prevent reverse transmission to felines, as well as for human health protection. *M. canis* is long-lived in the environment and can be a challenge to eliminate. Stringent measures must be taken to effectively treat animals affected by the disease and to rid the environment of contamination. Failure to follow established guidelines for disease management can result in disease transmission not only throughout the shelter, but also among staff, volunteers, adopters, and their homes.

Animals with ringworm may be adopted out after successful treatment is confirmed by consecutive negative cultures. The absence of visual lesions on the fur should never be used as a criterion for confirmation of a cure as animals without lesions may still be infective. More specific details on the diagnosis, treatment, management, and control of outbreaks are provided in Chapter 16 on dermatophytosis.

### *Malassezia pachydermatis* infection

*Malassezia pachydermatis* is a yeast that can colonize the skin of dogs and cats, dogs more frequently than cats (Bond 2006). Although not commonly associated with human disease, during an outbreak in a neonatal intensive care unit (NICU) in which the neonates experienced bacteremias, urinary tract infections, and meningitis, the investigation suggested a link between the health-care workers' dogs and infection of the neonates in the NICU with *M. pachydermatis* (Chang, Hilary et al. 1998). It may also affect immunocompromised individuals.

Human dermatological disease consisting of seborrheic and atopic dermatitis may be associated with other species of *Malassezia* (Rincon, Celis et al. 2005). *M. pachydermatis* affects the moist warm skin areas of the animal's body, e.g., the ear canal, interdigital skin, ventral neck, lip region, axillae, groin, and body folds (Bond 2006). It causes pruritis, erythema, and greasy exudative lesions in animals. Presumptive diagnosis is via clinical signs, detection of the yeast via microscopic examination of samples from affected skin, and response to therapy. Diagnostic rule-outs include inflammatory and seborrheic skin diseases (Bond 2006). Therapy consists of topical antifungals such as 2% miconazole–2% chlorhexidine shampoos, benzoyl peroxide shampoo, or systemic drugs such as itraconazole or ketoconazole. Because host immunity, the presence of skin folds, and concurrent disease may play a role in the development of clinical signs, treatment may be prolonged and relapses can occur if these other problems are not addressed. However, these animals can typically be treated and adopted without additional precautions.

### Acariasis–Scabies

In dogs, scabies is a highly contagious skin disease that is caused by the mange mite *Sarcoptes scabies var canis*. The disease is covered in more detail in Chapter 17 on ectoparasites. The clinical signs in dogs include intense pruritis and hair loss over the elbows, ears, ventrum, and eventually the entire body. The *Sarcoptes scabei* mite can cause infections in humans that present as pruritic, papular, or urticarial lesions. The lesions are found mainly on the trunk, arms, axillae, and breasts. The mites do not produce burrows in human skin as they do on dog skin, so they are unable to complete their life cycle on the human host (Mathieu and Wilson 2005). *Sarcoptes scabei var canis* infestation is therefore considered a self-limiting problem in humans; although eliminating the infestation on the dog should resolve the problem in humans, consultation should be scheduled with a physician or dermatologist for diagnosis and treatment.

To prevent infestation in humans, dogs with scabies infestation should be isolated and promptly treated; personnel examining and treating these animals should wear disposable gloves and gowns. Environmental control and prevention of transmission to other dogs during treatment is covered in Chapter 17 on ectoparasites. These animals can be treated and adopted.

## INFECTIONS SPREAD VIA THE FECAL–ORAL ROUTE

### Toxoplasmosis

Toxoplasmosis is caused by *Toxoplasma gondii*, an obligate coccidian parasite that infects all mammals, including humans. The definitive host is the cat and other felids. The disease is covered in more detail in Chapter 15 on gastrointestinal pathogens. Toxoplasmosis has received a great deal of publicity as a zoonotic disease because of its ability to cause fetal injury when pregnant women are infected; it also causes central nervous system disease in AIDS patients. However, most cases of toxoplasmosis in humans

in the U.S. and industrialized countries result from the consumption of raw or uncooked meat or occasionally salads contaminated with oocysts. The fear of cat ownership amongst pregnant women and immunosuppressed individuals largely ignores the fact that although cats are the only species that shed infective oocysts, the overall risk of infection from cats is very low. Cats shed infective oocysts in their feces for 2 weeks only after initial infection and then do not shed again. These environmentally resistant oocysts must then sporulate to become infective, which takes from 1 to 5 days. Sporulation does not appear to occur on the fur, so direct handling of cats is unlikely to be a cause of disease spread. Furthermore, cats that test positive on serology will not shed again and are therefore safe as pets. With attention to a few precautions listed below, cat ownership should be considered safe for the previously identified at-risk individuals.

Litter box hygiene is one of the keys to prevention because the risk of infection from cats is due to exposure to and ingestion of infective oocysts. Pregnant women should adopt cats that are healthy and at least 1 year old because these cats are less likely to be infected with *Toxoplasma gondii*. It is preferable to ask someone who is not pregnant or immunocompromised to change the litter pan during the pregnancy period. The litter pan should be changed daily before sporulation of the oocysts has a chance to take place, and the litter should be disposed of properly. If the pregnant woman must change the litter pan herself, she should wear gloves, remove the fecal waste daily, and wash her hands with soap and hot water afterward. Cats should be fed only canned or dry commercial cat food. Outdoor cats or cats that may have been eating raw meat should not be brought into the house; indoor cats should not be allowed to go outside. If serology is performed, it should be remembered that a cat that tests positive is unlikely to shed oocysts because the shedding period is transient and only lasts for 2 weeks after the initial exposure. However, cats that test negative may pose a greater risk as they have not yet been infected and could shed oocysts should exposure and infection occur. The key to safety is to prevent these cats from becoming exposed by following the aforementioned precautions. Finally, it should be remembered that cats can be treated to reduce or clear shedding, although that is usually unnecessary.

### Giardiasis

*Giardia intestinalis*, which is also known as *Giardia duodenalis* and *Giardia lamblia*, causes giardiasis in humans, most domestic animals, and other mammals (Acha and Szyfres 2001). Based on nucleic acid sequence analysis, *G. duodenalis* has been divided into seven genetic groups, A through G. Much controversy still surrounds the zoonotic risk associated with this organism. Genetic groups A and B can be found in humans in addition to animals, while genotypes C through G are animal specific (Barr 2006a). Genetic group A (also referred to as Assemblage A) has been found in dogs and cats as well as people. Assemblage B has only been found in dogs and humans. Although no cases of human giardiasis have been firmly documented or associated with cats, infected dogs and cats should still be presumed to be a potential, although very low, health risk to humans.

Giardiasis occurs worldwide. Most infections are asymptomatic; however, diarrhea occurs in puppies, kittens, and animals that are stressed, immunosuppressed, or housed in groups (Barr 2006a). When diarrhea occurs in older animals, the presentation may be quite varied, i.e., acute and of short duration, intermittent or chronic. Dogs and cats shed *Giardia* cysts intermittently. A more detailed consideration of the diagnosis, treatment, and management of giardiasis in shelter dogs and cats can be found in Chapter 16 on gastrointestinal disease.

Although it is believed that there are host-adapted strains of *Giardia* spp., humans can easily acquire giardiasis. The median infective dose is 10 cysts (Acha and Szyfres 2001). The most common mode of infection for humans is the ingestion of contaminated water. However, direct hand-to-hand and hand-to-mouth transmission from infected to susceptible persons is also common. Infections have been reported in zoo employees caring for an infected gibbon (Acha and Szyfres 2001); therefore, veterinary staff should practice good hand hygiene, i.e., wash hands after cleaning cages, runs, and handling animals (NASPHV 2006). Clinical signs in humans include watery, foul-smelling diarrhea, flatus, and abdominal distention. Individuals working in shelters who develop diarrhea should alert their physicians so that diagnostic procedures and empiric therapy for *Giardia* (and other zoonotic causes of diarrhea) can be considered. Diagnosis is commonly performed using enzyme-linked immunosorbent assay testing (ELISA).

Animals can be treated for the disease and adopted. Please refer to Chapter 15 for detailed guidelines for managing outbreaks of *Giardia* spp. infection in shelter animals. *Giardia* cysts are sensitive to drying and are inactivated by quaternary ammonium compounds, household bleach (1:32 or 1:16 dilution), steam, and boiling water (Kahn and Line 2005). Grass yards or runs contaminated with *Giardia*-infected feces should be considered

contaminated for at least 1 month after the dogs have been removed (Kahn and Line 2005). Frequent and prompt removal of feces from cages, runs, yards, and litter boxes reduces the level of environmental contamination. After removal, the area should be cleaned, disinfected, and allowed to dry. Shampooing dogs and cats to reduce cyst contamination of the hair is also recommended (Kahn and Line 2005; Barr 2006a). Shampoo should be followed by a 3- to 5-minute bath with a quaternary ammonium compound to kill cysts (Barr 2006a). Shelters should take heed of the following warnings: only antiseptic products that, unlike disinfectants, are approved for use on the skin should be used on animals (Webber, Ruptula et al. 2007). The solution *must* be thoroughly rinsed from the animals' coats and oral ingestion prevented. Exposure to improperly diluted quaternary ammonium disinfectant can cause severe oral and skin ulceration, systemic disease, and death. Human cases of giardiasis are reportable to the department of health in most states in the U.S. (CDC 2006).

**Cryptosporidiosis**

Cryptosporidiosis is caused by *Cryptosporidium* spp., a non-host-specific protozoan that infects many different species of animals, including humans. Dogs and cats can be infected by *Cryptosporidium felis*, *C. canis*, or less commonly *C. parvum*. *C. parvum* will cause diarrhea in puppies and kittens or immunocompromised dogs and cats, while infections with *C. felis* and *C. canis* are usually asymptomatic (Barr 2006b).

All three genospecies will infect humans to different degrees (Barr 2006b), but *C. parvum* is the most common cause of infection in humans; *C. felis* and *C. canis* may infect immunocompromised individuals. Infection in immunocompetent persons is often self-limiting but may also present as watery diarrhea and abdominal pain accompanied by nausea, vomiting, low-grade fever, and weight loss. In people who are immunosuppressed, especially HIV-infected individuals or those with AIDS, the infection can cause a chronic diarrheal, extraintestinal, or even fatal illness (White 2005). Humans most commonly acquire the infection from contaminated water, but human-to-human transmission also occurs. It may also be transmitted by direct contact with infected dogs or cats (Greene and Levy 2006). Infected animals with diarrhea should not be adopted until signs resolve; staff should wear appropriate protective clothing and personal protective equipment (PPE) and practice good hand hygiene when cleaning cages, runs, and handling infected animals (NASPHV 2006). Human cases of cryptosporidiosis are reportable to the department of health in most states in the U.S. (CDC 2006).

Recommendations for treatment and control of *Cryptosporidia* in shelter animals may be found in Chapter 15 on gastrointestinal disease. Adopters should be counseled as to the risks and precautions if a known-infected animal is to be adopted. It is probably best to avoid adopting these animals to individuals with a history of being immunocompromised.

**Echinococcosis (hydatid disease)**

Echinococcosis is caused by tapeworms of the genus *Echinococcus*. Echinococcosis or hydatid disease in humans is caused by the larval stage of the tapeworm. The most commonly encountered form of disease in humans, cystic echinococcosis, is caused by *E. granulosus*. Alveolar echinococcosis is caused by *E. multilocularis*, which is also discussed in Chapter 14 on internal parasites (for more information, also see www.dpd.cdc.gov).

*E. granulosus* is maintained in endemicity via a dog–sheep–dog cycle during which dogs pass infected eggs in their stool, which in turn infect sheep that develop hydatidosis (infected cysts in their viscera). The sheep are slaughtered and their infected viscera are fed uncooked back to the dog, which becomes reinfected.

*Echinococcus granulosus* is endemic in Latin America, southern Europe, the Middle East, Africa, the southwestern U.S., Australia, and New Zealand (King 2005; Acha and Szyfres 2001). While this organism is frequently found in rural areas, it can appear in urban areas if dogs are fed raw meats, especially offal (internal organs). Dogs carry the *E. granulosus* eggs on their tongues and snouts and infect humans who touch the dogs, fail to wash their hands, and ingest the eggs. Once the eggs enter the human host, the oncospheres hatch and enter the bloodstream where they invade the liver, lungs, or other organs. Once in these organs, they develop into hydatid cysts; the symptoms that develop depend on the organs that are invaded. Common signs, when seen, can include abdominal or chest pain, itching, fever, coughing, etc. If the hydatid cysts rupture, additional visceral seeding will occur, and anaphylaxis may develop (Despommier et al. 2000).

Infection is best controlled by a variety of human and animal health precautions: (1) avoid feeding dogs raw viscera; (2) provide routine treatment of dogs in endemic areas; and (3) ensure that staff use appropriate PPE and practice good hand hygiene when cleaning cages, runs, and handling animals (NASPHV 2006).

Infected animals should be treated before placement for adoption. New owners should be advised to seek follow-

up care with a veterinarian to discuss preventative health care and ongoing parasite control.

**Visceral, cutaneous, and ocular larval migrans**

Visceral larval migrans (VLM) is caused by the larvae of *Toxocara canis* and, less commonly, *Toxocara cati*. Ocular larval migrans (OLM) is caused by the larvae of *T. canis*. *Baylisascaris procyonis*, the roundworm of raccoons, has also been implicated as a cause of eosinophilic meningoencephalitis and unilateral OLM and should be of concern to shelters (Nash 2005). Human infections with *Strongyloides stercoralis* are primarily caused by the human strains of this parasite. However, occasionally humans become infected with dog and cat strains that result in cutaneous larval migrans and gastrointestinal problems (Heymann 2004). Cutaneous larval migrans is caused by the migration of the larvae of the hookworms *Ancylostoma braziliense*, *Ancylostoma caninum*, and (less commonly) *Uncinaria stenocephala* through the skin. (See Chapter 14 on internal parasites for more information about these parasites and the disease they cause in animals.) The life cycle of these parasites is described in other textbooks; only *Toxocara* will be discussed in this chapter because concerns about VLM are due largely to this parasite.

In the case of *Toxocara* spp., infective eggs are shed by both lactating bitches and puppies. Most puppies born to infected mothers are also infected and shed eggs in their feces. One-third to one-half of all bitches shed eggs in their feces after delivering a litter. After being released, eggs require 10 days to become infective; humans acquire infection as accidental hosts. Transmission to humans is not normally associated with direct animal-to-human contact; infection occurs through the fecal–oral route. Humans who are most at risk are young children who may accidentally ingest dirt contaminated with infective eggs while playing and immune-compromised individuals. Most VLM infections are asymptomatic. When symptoms occur, cough, fever, wheezing, and other generalized symptoms are seen. Hepatomegaly is common. The diagnostic hallmarks of the disease in humans are eosinophilia and leukocytosis. A definitive diagnosis is made by identifying the larvae in tissue. Eggs will not be found in the stool of humans because the larvae do not develop into adults and complete the life cycle. ELISA tests are helpful in confirming a clinical diagnosis but are of little value when the patient is asymptomatic (Nash 2005).

OLM usually presents as a unilateral eye infection. There is an eosinophilic, inflammatory posterior or peripheral subretinal mass. Eosinophilia, hepatomegaly, and the other signs and symptoms associated with VLM are often missing. The patient may have low or negative serum titers but elevated vitreous or aqueous titers. These values, along with the accompanying clinical signs and symptoms, are helpful in diagnosing disease (Nash 2005).

In the case of cutaneous larval migrans, infective hookworm larvae are acquired from soil that has been contaminated with feces from infected dogs or cats. The larvae directly penetrate a person's skin and cause a highly pruritic, "creeping eruption" with raised, red "tracks" and vesicles. Systemic eosinophilia is less common than with VLM, and lesions often regress spontaneously.

*Strongyloides stercoralis* is more readily transmitted than the other causes of visceral larva migrans because the eggs of *Strongyloides* are embryonated and can be infective as soon as they are passed. They do not require a prolonged period of development in the soil. Humans are infected by cutaneous penetration of infective larvae that then migrate to the gastrointestinal tract. Clinical symptoms in humans can include abdominal pain and nausea; diarrhea; protein-losing enteropathy; weight loss; and a skin rash, especially on the buttocks, abdomen, and thighs. Eosinophilia may be seen. The disease can be fatal in immunocompromised individuals, who may also suffer from pulmonary involvement, sepsis, and meningitis.

Methods to control these diseases in the shelter include (1) deworming animals prophylactically upon arrival at the facility and at regular intervals, particularly puppies, kittens, pregnant and nursing mothers; (2) removing animal waste promptly and regularly; (3) using gloves when changing or cleaning litter boxes, cages or runs; and (4) engaging in hand hygiene after handling animal waste or cleaning cages, litter boxes, or runs. The eggs of some of these parasites are extremely resistant and can remain infective in soil for months to years, posing an ongoing threat to susceptible animals and children who use these areas.

There is no problem adopting these animals after treatment, but new owners should be advised to seek follow-up deworming and to discuss ongoing parasite surveillance and treatment with their veterinarian. They should also discuss hygiene with young children, including telling them not to let pets lick them in the face.

**Campylobacteriosis**

Campylobacteriosis is caused by curved or spiral-shaped gram-negative rods. Several species cause infection in dogs and cats, all of which are zoonotic: *Campylobacter jejuni*, *C. coli*, *C. helveticus*, *C. upsaliensis*, and *C. lari* (Allos and David 1998; Fox 2006). Birds are also natural

reservoirs of *Campylobacter* spp. Infection in adult dogs and cats is often asymptomatic, but clinical symptoms may include vomiting or diarrhea, and are especially common in puppies and kittens. Transmission is usually fecal–oral via ingestion of contaminated food or water.

*Campylobacter* has been a leading cause of enteric infection in humans (Baker, Barton et al. 1999). Humans most commonly become infected through exposure to animals, raw or undercooked meats, unpasteurized milk or milk products, or contaminated food and water; however, transmission from cats and dogs has also been reported. Infection with *Campylobacter* typically presents as diarrhea (*C. jejuni*, *C. coli*, *C. helveticus*, *C. upsaliensis*, or *C. lari*), bacteremia or extraintestinal infections (*C. helveticus*, *C. upsaliensis*, or *C. lari*) (Allos and David 1998; Krause, Ramschak-Schwarzer et al. 2002; Morrison, Lloyd et al. 1990). *C. jejuni* is responsible for 90% of human infections (Acha and Szyfres 2001). Infection may result in Gullain-Barre syndrome (Kuwabara 2004), carditis, and encephalopathy. Diagnosis is based on a positive stool or blood culture or a rising paired titer (Allos and David 1998). Treatment is recommended for individuals who are immunosuppressed, pregnant, septic, or have extraintestinal infections (Allos and David 1998). Campylobacteriosis in humans is a reportable disease; outbreaks in shelters, although uncommon, should be reported to the health department.

Animals with diarrhea should be isolated from the general population. This is especially important in young animals. A sign should be placed on the cage of infected patients to alert staff. The following steps should also be taken: (1) wear a gown and gloves when examining animals with diarrhea; (2) wear disposable shoe covers when entering the isolation room (NASPHV 2006); (3) dedicate equipment such as thermometers, stethoscopes, etc., to the isolation room; (4) wash hands between each patient contact, after finishing tasks that involve contact with animal feces, before leaving the isolation room, and after removing PPE; (5) wear a mask when hosing or cleaning cages or runs to reduce fecal splashes to the face; and (6) prohibit the consumption of food and beverages in animal treatment or holding areas. Treatment and other control recommendations specific to *Campylobacter* infection in shelter dogs and cats may be found in Chapter 15 on gastrointestinal disease.

As with *Cryptosporidium*, adopters should be counseled as to the risks and precautions if a known-infected animal is to be adopted. It is probably best to avoid adopting these animals to individuals with a history of being immunocompromised.

**Salmonellosis**

Salmonellosis is caused by a single species of gram-negative, non-spore-forming rod, *Salmonella enterica*. More than 2,400 serotypes belong to this species. With the exception of *S. Typhi*, *S. Paratyphi A*, and *S. Paratyphi C*, all serotypes are considered zoonotic or potentially zoonotic (Acha and Szyfres 2001). *Salmonella* spp. infections occur worldwide, with *S. enteritidis* being the most prevalent (Acha and Szyfres 2001).

Animals, by definition, are the reservoir of zoonotic *Salmonellae* spp. (Acha and Szyfres 2001). Other common sources of human infection are contaminated food, water, or fomites. Dogs and cats may also become infected from eating raw or undercooked meats. Dogs sometimes become infected by engaging in coprophagia (Acha and Szyfres 2001). Once infected, shedding occurs for 3 to 6 weeks; it is continual during the first week, then intermittent subsequently. Thereafter, the organism may be persistently sequestered in the intestinal lymph nodes, liver, or spleen from where shedding can be reactivated during periods of stress. Clinical signs range from no signs to diarrhea and death in young or debilitated animals. Clinical signs of the disease, diagnostic techniques, and treatment guidelines are described in Chapter 15.

Transmission to humans is via several sources, but usually via ingestion of contaminated products of animal origin, i.e., eggs, milk, other dairy products, and meat. Infections have occurred through direct and indirect contact with reptiles (CDC 1999). Case-control studies conducted from 1996 to 1997 estimate that exposure to reptiles accounts for approximately 74,000 *Salmonella* spp. infections in humans annually (Mermin, Hutwagner et al. 2004). Transmission via exposure to infected dogs and cats has also been reported, and even subclinically affected animals may transmit disease. Humans have also been infected by exposure to animal-derived pet treats (Clark, Cunningham et al. 2001). There is concern that handling raw food or the feces of dogs fed raw food diets may contribute to disease transmission, especially to young children who are more susceptible to infection, as are most immunocompromised individuals.

Clinical signs in humans include nausea, vomiting, abdominal tenderness, fever, dehydration, and headache. Outbreaks of salmonellosis have occurred in veterinary clinics and shelters after exposure to diarrheic animals (CDC 2001; Cherry, Burns et al. 2004). The increased use of antimicrobial agents contributes to the increasing incidence of multidrug-resistant *Salmonella* spp.; the elimination of inappropriate use of antimicrobial agents may help to prevent outbreaks of multidrug-resistant *Salmonella*

spp. infections in veterinary facilities (CDC 2001). When addressing ongoing transmission of nontyphoidal *Salmonella* spp. in shelters, humans should be considered as potential carriers of infections. The local health department should be notified when human cases of *Salmonella* spp. are identified or when outbreaks occur in animals.

To prevent salmonellosis, shelter staff should wash their hands after handling animals, or fomites such as beds or anything contaminated with feces. Commercially available, heat-processed foods should be fed and protected from rodent contamination, and pet treats or chews made from animal hides should be avoided (Greene 2006). Other guidelines for minimizing transmission of diseases spread in the feces can be found in the section on control at the end of this section.

Symptomatic animals should be treated judiciously with antibiotics to avoid contributing to the development of antibiotic-resistant strains and should not be adopted to households with the elderly, children under the age of 5, or other immune-compromised individuals.

### Dipylidiasis

Dipylidiasis is caused by the dog tapeworm *Dipylidium caninum*. Infection occurs when the intermediate hosts – dog or cat fleas – are ingested by humans. Most infections occur in young children (Acha and Szyfres 2001); transmission takes place when the child ingests the flea, commonly by either kissing, licking, or biting a flea-infested animal, or the flea falls into the food and is ingested.

Symptoms in humans include diarrhea, colic, irritability, erratic appetite, and insomnia. Asymptomatic infections also occur (Acha and Szyfres 2001). Prevention consists of: (1) intestinal parasite management in dogs; (2) flea control in dogs and cats, including their environment; and (3) avoidance of oral contact with pets. Parents should be advised to supervise young children around pets and to teach them to not let animals lick their faces.

These animals can be adopted after treatment for fleas and parasitic infestation; visits with a veterinarian should be advised for follow-up treatment and to devise a parasite surveillance and prevention plan.

### General guidelines for prevention of disease transmission via the fecal–oral route

Staff can further reduce potential exposure to feces by wearing utility or disposable gloves, and by removing gloves and washing their hands immediately after finishing a task that involves contact with animal feces. When reusable utility gloves are used, these must be cleaned and disinfected after each use. To reduce fecal splashes to the oral cavity, workers should wear a mask when hosing or cleaning cages or runs. Eating should not be allowed in animal treatment or holding areas. All surfaces contaminated with feces should be cleaned and then disinfected with an EPA-veterinary-approved disinfectant or household bleach diluted 1:32 (Ewart, Schott, Robison 2001). Food dishes should be cleaned and disinfected or autoclaved between uses. Cages should be cleaned and disinfected between uses by different animals.

## DISEASES THAT ARE ACQUIRED VIA CONTACT WITH URINE OR GENITAL SECRETIONS

### Canine brucellosis

Although *Brucella abortus*, *Brucella melitensis*, and *Brucella suis* have been known to cause brucellosis in dogs (Baek, Lim et al. 2003; Barr, Eilts et al. 1986), the primary cause of canine brucellosis is *Brucella canis*. *Brucella canis* is a small coccobacillary organism. Canine brucellosis occurs worldwide (Acha and Szyfres 2001). The dog is the natural reservoir for *B. canis*; cattle, goats, and pigs are the natural reservoirs for *B. abortus*, *B. melitensis*, and *B. suis*, respectively (Acha and Szyfres 2001).

Dogs become infected with *B. canis* via the genital, oronasal, or conjunctival mucosa, through contact with vaginal secretions, aborted fetuses, placenta, or lochia (Wanke 2004). Of all the potential routes of infection, the most common route is via oronasal contact with aborted materials. The bacteria may be shed for up to 6 weeks after an abortion; it may also be harbored in seminal fluid and urine. Males excrete the bacteria in semen, and both sexes excrete bacteria in their urine, with males having a higher concentration than females; as high as $10^3$–$10^6$ bacteria/ml in urine (Wanke 2004). Bacteruria starts at 4 to 8 weeks after infection; male dogs may shed the bacteria in urine for 3 months after infection, and intermittently in low levels in semen for up to 2 years (Greene and Carmichael 2006). Puppies are infected in utero; however, the milk of the bitch contains high bacterial concentrations and may be important in environmental contamination. Saliva, nasal and ocular secretions, and feces contain low concentrations of bacteria and are insignificant sources of infection. Fomites, e.g., cages, equipment, and persons in contact with infected dogs, have been reported to be sources of infection (Wanke 2004).

Although brucellosis causes a systemic infection, severe illness is uncommon in adult dogs. Clinical signs most commonly involve the reproductive system; abortion 2

weeks before term, accompanied by a greenish-gray vaginal discharge that may last for up to 6 weeks may be the only sign in females. Puppies that are carried to term may die suddenly shortly after birth. There may be breeding problems, although females with *B. canis* will have normal estrus cycles. Infections in females go largely undetected, but males may have more prominent signs, including an enlarged scrotum and scrotal dermatitis from licking. However, in chronic cases, the scrotum may actually be smaller, and males may also suffer from fertility problems. Other clinical signs include, but are not limited to, lymphadenomegaly, splenomegaly, diskospondylitis, and back pain. Ocular signs may also be seen, including uveitis, hyphema, and retinal detachment, for example.

Diagnosis is usually confirmed by serology, although test results may be negative during the first 3 to 4 weeks postinfection. False positives are not uncommon due to cross-reactivity with other bacteria. Low or intermediate titers may indicate recent infection or previous disease. Urinalyses are frequently normal. There are several diagnostic options; the reader is referred to other references on infectious disease for more information.

The treatment of brucellosis in animals is rarely recommended because no effective regimen has been established (Glynn and Lynn 2008). Treatment yields uncertain results and is costly, lengthy, and problematic because of owner noncompliance, and it could pose a possible ongoing public health problem. However, if undertaken, combination antibiotic therapy is necessary, as no single antibiotic therapy has proven successful. Follow-up evaluation after the conclusion of the initial treatment should be conducted because relapses are not uncommon; the mercaptoethanol tube agglutination test (ME-TAT) should be used at 6- and 9–month intervals post-treatment (Greene and Carmichael 2006). Infected animals should be spayed or neutered as part of the treatment protocol.

Natural and laboratory-acquired infections have been reported for *B. canis*, but of all the *Brucellae* species known to cause infection in humans, *B. canis* is the least infectious (Acha and Szyfres 2001). The disease in humans is much milder than disease caused by other *Brucella* species. Humans may become infected with *Brucellae* spp. percutaneously via contact with aborted tissue, blood, urine, or vaginal discharge; by consuming contaminated food products; or by airborne contact through laboratory exposure (Chin 2000; Wallach, Giambartolomei et al. 2004). Clinical signs range from none (most commonly) to fever, chills, fatigue, and lymphadenomegaly.

Outbreaks in breeding kennels can be very serious. Control measures often consist of quarantine, the elimination of all infected animals, restriction of entry or release of animals, and testing and retesting of all the animals until seronegativity can be established. The guidelines for control in shelters are different because shelters are not involved in breeding animals or affected by reproductive failures in long-term resident animals. In most instances, brucellosis may go undiagnosed in shelters because of the nature of the clinical signs.

*Brucella canis* does not live long outside the host. However, it can survive in the environment in the presence of organic material; disinfection of the environment and fomites with quaternary ammonia or iodophores is recommended (Wanke 2004, Greene and Carmichael 2006).

There is some controversy regarding the adoption of animals infected with *B. canis*. Some experts believe that *Brucella*-infected animals are never truly cured and that because relapses are so common, these animals should never be made available for adoption. If a decision is made to adopt out these dogs despite these recommendations, seronegativity must be verified for 6 months by a series of cultures and serology. There must be full disclosure and counseling provided about brucellosis to anyone who chooses to adopt an animal infected with this disease. The animals should not be adopted out to the immune compromised or members of the at-risk categories.

**Leptospirosis**

Leptospirosis is caused by a gram-negative, helical, motile bacterium (Faine 1998). Using a serological classification that is based on agglutination by cross-absorption, leptospires are divided into more than 200 serovars. Both pathogenic and nonpathogenic serovars have been identified. The more recent method of classifying leptospira relies on DNA hybridization, and 16 genome species have been defined (Levitt 2001).

Animals are divided into two groups in the epidemiological classification of leptospirosis: maintenance and accidental hosts. In maintenance hosts, the serovar is adapted to the host, the infection is endemic within the species, it is often acquired at an early age, it rarely causes disease, and leptospiruria is chronic. The accidental host is more resistant to infection; however, infection usually results in disease. Animals may be a maintenance host for some serovars and an accidental host for others (Levitt 2001). There are some maintenance hosts that are known to be associated with certain serogroups or serovars, e.g., rats are maintenance hosts for serogroups icterohaemorrhagiae and ballum; mice for ballum; cattle for serovars

hardjo, pomona, and gryppotyphosa; and dogs for canicola (Levitt 2001). Although the prevalence of clinical cases of leptospirosis in cats is very low, canicola, grippotyphosa, and pomona serovars have been isolated from them (Greene and Sykes et al. 2006). It is known that there are worldwide variations in the association between maintenance hosts and the serovars that they carry (Adesiyun, Hull-Jackson et al. 2006).

Animals become infected through contact of skin or mucous membranes with contaminated urine, feed or water, ingestion of infected animals, or by venereal transmission (Kahn and Line 2005). Transmission also occurs through contact with contaminated bedding. Moist soil may remain contaminated with leptospires for months (Greene and Sykes 2006). Chronic shedding for months (carrier state) may be seen in some animals that become infected and recover from illness.

Clinical signs of disease vary considerably, including an acute and subacute syndrome. Symptoms are seen more commonly in young, outdoor, and large breed animals. An in-depth description of the clinical disease will not be provided here; however, the clinical picture is multisystemic and may include fever, vomiting, diarrhea, muscle tenderness, hyperesthesia, icterus, melena, widespread petechiae, epistaxis, and renal disease. Diagnosis can be accomplished through a variety of methods. Most dogs with clinical signs of leptospirosis present with renal disease. Clinical laboratory tests may reveal several abnormalities, including leukocytosis or leukopenia (depending on the stage of the disease), thrombocytopenia, elevations in blood urea nitrogen (BUN) and creatinine, electrolyte imbalances, and other abnormalities that parallel the clinical symptoms. Serology, dark field microscopy, and organism identification are also employed as diagnostic tools.

Treatment consists largely of fluid therapy, antibiotics, and supportive care. Infected animals should be isolated and gloves worn when handling the animals or urine-contaminated objects. Special consideration should be given to the use of antibiotics that can eliminate the carrier state. Penicillin or amoxicillin are good initial drugs to use to eliminate the leptospiremia; doxycycline is effective in eliminating both the leptospiremia and carrier state.

Humans can become infected with leptospires through direct or indirect contact with the urine of infected animals or inhalation of their aerosolized urine. The portal of entry is via cuts and abrasions on the skin, the conjunctiva, and the mucous membranes. It has been established that the risk of exposure to leptospira is greater in certain occupations, e.g., rodent control workers, miners, sewage workers, fish workers, veterinarians, and dairy farmers. (Demers, Frank et al. 1985; Waitkins 1986). Pet dogs can be a common source of infection for humans (Levitt 2001). In recent years, there have been several recreation-associated outbreaks (CDC 1998; Jevon, Knudson et al. 1986; Katz, Manae et al. 1991). Most human infections are acquired through occupational or recreational exposure to contaminated animal urine or fomites, and the infections are subclinical or mild. When clinical infection occurs, patients may experience fever, chills, headache, myalgia, and abdominal pain. In humans, less than 25% of all leptospirosis cases develop aseptic meningitis, 5% to 10% of all patients have icterus, and petechial lesions may occur. Pulmonary involvement has been reported and may be severe enough to cause death. A chronic sequelae of this infection is uveitis (Levitt 2001). Treatment is dependent on the severity of the illness; some patients will require hospitalization. Human vaccines are not widely used but are available in France, Cuba, and the Far East (Levitt 2001).

Leptospirosis is not commonly seen as a serious problem in shelters, although cases may occur in individual dogs. Crowding can increase direct transmission. Leptospires survive in warm, humid environments and are sensitive to desiccation. Rodent control is important to prevent leptospirosis. Staff should ensure that cages and runs are washed and disinfected on a regular schedule to remove urine contamination. Appropriate facial protection, i.e., a mask with a face shield or goggles; rubber boots; and gloves should be worn when hosing and disinfecting the cages and runs. All cuts and abrasions on the hands should be covered with a bandage before donning gloves; wash hands with soap and water after removing gloves.

A recent outbreak of leptospirosis among workers in an animal trading company reemphasizes the need to avoid bare-hand contact with exotic species (Masuzawa, Okamoto et al. 2006).

There are vaccines available against leptospirosis for dogs, but according to the *2006 AAHA Canine Vaccine Guidelines Revised*, this vaccine is "not generally recommended for shelter animals without knowledge that infection is known to occur in the community" (Paul, Carmichael et al. 2006). The vaccine for leptospirosis is not considered a core vaccine for use in shelter animals because of the low risk of direct transmission in this environment and the limited value of vaccinating animals on intake in preventing zoonotic disease (Ford 2004). The current vaccines contains two to four of the main serovars: canicola, gryppotyphosa, icterohemorrhagiae, and pomona. Effective

immunization requires at least two injections given at least 2 to 3 weeks apart initially, and annual boosters because the immunity wanes with time.

Dogs with leptospirosis should be isolated for treatment and can be adopted if care is taken to eliminate the carrier state. If this is not done, reshedding can occur after antibiotic therapy is discontinued. This is a nationally notifiable disease for animals (NASPHV 2006). Clusters of leptospirosis in animals or humans should be reported to the department of health for investigation.

### Coxiellosis

Query fever (Q fever) is caused by *Coxiella burnetti*, an obligate, intracellular, gram-negative bacteria. Q fever is endemic worldwide except in Sweden, Norway, Iceland, and New Zealand. Most of the cases in the U.S. are reported from the west (Greene and Breitschwerdt 2006). Several species of ticks from the *Ixodidae* and *Argasidae* families have been found to be naturally infected with *C. burnetii* (Acha and Szyfres 2001). However, domestic animals frequently become infected via inhalation or ingestion of the organisms, which are environmentally resistant. Animals usually are subclinically infected and spread the bacteria via urine, feces, milk, and parturient discharges. Bitches have been shown to shed coxiellae in their milk and urine for 30 days and at least 70 days, respectively (Greene and Breitschwerdt 2006).

Humans have been known to become infected by inhalation of the organisms during contact with parturient cats or dogs, direct contact with parturient animals and their tissues and fluids, or contact with fomites contaminated by parturient fluids or aborted tissues from infected cats and dogs (Greene and Breitschwerdt 2006). Infection presents as several clinical syndromes in humans: (1) a self-limiting febrile illness that last 2 to 14 days; (2) pneumonia; (3) endocarditis; (4) hepatitis; (5) osteomyelitis; (6) Q fever in the immunocompromised host; (7) Q fever in infants; or (8) neurological syndromes: encephalitis, aseptic meningitis, toxic confusional states, dementia, or extrapyramidal disease (Marrie and Raoult 2005).

*C. burnetii* is resistant to dehydration, elevated temperatures, ultraviolet light, osmotic shock, and chemicals (Greene and Breitschwerdt 2006); therefore, if *C. burnetii* is suspected or known to be the cause of infection, animals should be removed from the environment, which should then be washed with soap and water and properly disinfected. Alcohol (70%) allowed to sit for 30 minutes will destroy *C. burnetii*; 1% Lysol or 5% hydrogen peroxide are also bactericidal (Greene and Breitschwerdt 2006; Marrie and Raoult 2005).

Shelter personnel who are assisting with deliveries or handling aborted fetuses or tissue should wear gloves, gowns, protective eyewear, and a mask. Once PPE is removed, staff must engage in proper hand hygiene.

Q fever is described in more detail in Chapter 21 on vector-borne diseases. It is considered a potential bioterrorism weapon; animals with the disease should be isolated immediately and cases in humans and animals reported immediately to the department of health. Animals with Q fever should not be adopted.

## DISEASES ACQUIRED THROUGH AIRBORNE TRANSMISSION

### Bordetellosis

Bordetellosis is caused by a gram-negative bacterium, *Bordetella bronchiseptica*, which causes respiratory illness in affected animals. *B. bronchiseptica* causes infection in dogs, cats, guinea pigs, rabbits, pigs, and primates, including humans (Kahn and Line 2005). In dogs, the infection is characterized by a honking cough, with or without emesis, pyrexia, and lethargy. It has recently been demonstrated to be a primary cause of respiratory disease in cats. See Chapters 8 and 9 on feline and canine respiratory diseases for more information about *Bordetella*, including its epidemiology and management of outbreaks.

Humans become infected via the aerosol route (NASPHV 2006). Illness has also been reported from an accidental spray to the face with the intranasal vaccine (Berkelman 2003). Therefore, young children, infants, and immunosuppressed persons should not be in the room when the modified live, intranasal vaccine is being administered (Greene and Levy 2006). Infections in humans have been shown to cause tracheobronchitis, sinusitis, pneumonia, septicemia, whooping cough, and cough (Woolfrey and Moody 1991). There has been a reported case of pneumonia in an HIV-positive animal care worker (Carter and Kahn 2004). While this is not a reportable disease in animals, all outbreaks of illness in humans are reportable to the department of health.

*B. bronchiseptica* is a component of canine and, to a lesser extent, feline upper respiratory disease in shelters. Many shelters have serious and ongoing problems with upper respiratory disease that are described in Chapters 8 and 9 and will not be described here. There are canine and feline vaccines available, but they do not prevent infection and thus are limited in their ability to prevent or stop an outbreak. Decisions to treat in house, place in foster care facilities, or euthanize animals showing clinical signs of the disease are often made based on the shelter's

resources, size, ability to isolate and treat, and availability of other healthy adoptable animals. Animals with bordetellosis can be adopted, but animals that are symptomatic or recently recovered from upper respiratory disease should not be adopted to those with respiratory or immune compromise, as shedding after recovery may persist for several weeks.

**Coxiellosis**

See under diseases that are spread via contact with urine or genital secretions.

**Plague**

Plague is caused by *Yersinia pestis*, which is maintained in the environment by small rodents and small mammals. Rodent fleas are the vectors that maintain the sylvatic cycle. Dogs and cats become infected by consuming infected rodents or lagomorphs, or by being bitten by infected fleas (Macy 2006). Cats may develop bubonic, septicemic, or pneumonic plague. Dogs are less likely to develop clinical disease (Macy 2006). Humans become infected by flea bites, direct contact with infected animals, and inhalation of respiratory secretions from infected cats. Humans can also develop bubonic, septicemic, or pneumonic plague. Occasionally, other syndromes occur such as plague meningitis or pharyngeal plague (Butler and Dennis 2005). *Y. pestis* is a potential bioterrorism agent; cases of plague in a domestic animal or human or outbreaks of plague in a shelter should be reported to the department of health. Treatment in the shelter is not recommended, nor should animals with this disease be adopted from a shelter. See Chapter 21 on vector-borne disease for more information.

**Tularemia**

See under vector-borne diseases.

**VECTOR-BORNE DISEASES**

Dogs and cats, like humans, are not the reservoir for most vector-borne diseases; they are accidental hosts. They serve as a mechanism of transmitting the infected vectors (i.e., the ticks or fleas) to humans. In the case of Lyme disease, for example, dogs develop infection from *Borrelia burgdorferi*, but do not transmit the infection to humans; they harbor the infected *Ixodes* spp. ticks that are capable of infecting humans. Rocky Mountain spotted fever, a disease affecting dogs that is caused by *Rickettsia rickettsii*, is spread by the *Dermacentor* spp., *Amblyomma* spp., and *Rhipicephalus* spp. ticks. In addition to being bitten by the infected ticks that dogs carry, people may expose themselves (via skin abrasions or the conjunctiva) to the infected hemolymph or excreta of the tick during tick removal. Ehrlichiosis or anaplasmosis caused by *Ehrlichia chafeenisis*, *E. canis*, *E. ewingii*, and *A. phagocytophilum*, depending on geographical location, are transmitted by ticks belonging to at least one of the following species: *Dermacentor* spp., *Amblyomma* spp., *Ixodes* spp., *Rhipicephalus* spp., *Haemaphysalis* spp., and *Otobius* spp. To avoid the risk of infection, exposure to ticks infected with *Ehrlichia* spp. or *Anaplasma* spp. should be minimized and care should be taken when performing necropsies on animals known or suspected to be infected with *Anaplasma* (Greig and Armstrong 2006).

In general, shelters should maintain an effective vector-control program to treat individually affected animals and ensure that tick or flea infestations are not a problem within the shelter. When handling tick-infested animals, staff should use gloves and gowns, and engage in hand hygiene after glove removal. Ticks should be removed promptly because many diseases are transmitted only after the tick has been attached to the animal for a few days. Care should be taken when removing ticks to ensure the entire tick is removed and its body disposed of properly. Gloves must be worn during tick removal and hand hygiene must be performed after glove removal. See Chapter 21 for more information about vector-borne diseases.

**Plague**

See under diseases that are acquired via airborne transmission.

**Tularemia**

Tularemia is caused by *Francisella tularensis*, a facultative intracellular pathogen that requires a low infectious dose to cause illness. It is endemic in the Northern Hemisphere. Rodents and lagomorphs maintain the sylvatic cycle; the vectors include ticks in North America, biting flies in the western U.S., and mosquitoes in Scandinavia and the areas formerly known as the Soviet Union. Various ticks that play an important role as a biological vector include *Dermacentor* spp. *andersoni, occidentalis, variabilis*, and *Ambylomma americanum*. Dogs and cats may contract the disease by ingestion of infected rabbits or rodents. The disease is discussed in Chapter 21.

Most human infections are linked to a vector bite and, to a lesser extent, contact with the tissues of infected wildlife or the contaminated environment, e.g., water. Inhalation is another route of infection. Among domestic animals, cat scratches or bites account for most human infections (Greene and DeBey 2006). Clinical signs in humans

may be typhoidal or ulceroglandular, including fever, chills, muscle pain, lymphadenomegaly, and pneumonia. Untreated tularemia can result in a 30% fatality rate.

Animals suspected of having the disease should be isolated immediately and signage posted. Tularemia has been classified as a potential bioterrorism weapon. Cases of tularemia in a domestic animal or human or outbreaks of tularemia in a shelter should be reported to the department of health. Treatment in the shelter should be avoided. The cage should be disinfected with a 10% bleach solution; bedding, toys, etc., should be similarly disinfected or discarded (Penn 2005).

## ANTHROPONOSES

Anthroponoses are diseases that are spread from humans to animals. Only a few diseases will be discussed here; most anthroponoses are unlikely to be of concern to shelters.

### *Clostridium difficile*

*Clostridium difficile*-associated diarrhea (CDAD) is associated with long-term antibiotic use. CDAD may be self-limiting or profuse. Patients often are febrile and experience leukocytosis and abdominal pain (Thielman and Wilson 2005). A newer human epidemic strain of *C. difficile*, ribotype 027, toxinotype III has been associated with more severe disease such as toxic megacolon. CDAD-afflicted patients have heavy fecal clostridial burdens of greater than $10^8$ colony-forming units per gram of feces. This facilitates environmental contamination. A recent case report of a pet therapy dog being infected with the human epidemic strain of *C. difficile* suggests that the dog became infected from the health-care environment or contact with contaminated hands (Lefebvre, Arroyo et al. 2006). Therefore, it is important during pet therapy that the animal handler ensures that (1) dogs do not visit with persons who are on isolation precautions for multidrug-resistant organisms, e.g., *C. difficile*, methicillin-resistant *Staphylococcus aureus* (MRSA), etc., and (2) attention is paid to proper hand hygiene both for the handler and the patient. Routine screening of animals is not recommended. However, screening is recommended if there is epidemiological evidence that the animal may be involved in transmission (Lefebvre, Golab et al. 2008).

### Methicillin-resistant *Staphylococcus aureus* (MRSA)

MRSA refers to a strain of *Staphylococcus aureus* that is resistant to oxacillin or nafcillin (Osterholm and Hedberg 2005). MRSA is an important health-care-associated infection that is spread by person-to-person contact and by contact with contaminated environments or equipment. MRSA may also be community-acquired (CA-MRSA). Health-care-acquired (HA-MRSA) and CA-MRSA strains of MRSA are somewhat different in phenotype and genotype. In addition, HA-MRSA occurs in immunosuppressed individuals in health-care facilities such as hospitals, nursing homes, or dialysis centers, while CA-MRSA occurs in healthy persons who, for the past year, have not been hospitalized nor had a medical procedure, e.g., surgery, dialysis, or insertion of a catheter.

*Staphylococcus aureus* organisms normally colonize the anterior nares of humans; they comprise less than 10% of the clinical isolates from dogs and cats (Cox 2006). Initially, clinical signs may just be a red bump or pimple on the skin. However, once through the skin (typically via an abrasion, cut or wound), *S. aureus* can seed any organ via hematogenous spread and cause a variety of infections (e.g., impetigo, furunculosis, abscesses, bacteremia, or endocarditis). MRSA causes the same infections as methicillin-sensitive *Staphyloccous aureus* (MSSA).

Human-to-animal transmission of MRSA is well-documented (van Duijkeren and Wolfhagen et al. 2004), and animal-to-human transmission has been suggested (Vitale, Gross, and Weese 2006). *S. aureus* is readily spread via direct contact or fomites. While routine testing is not recommended, pets living in close contact with persons who are infected or colonized with MRSA are at risk of becoming colonized with the same strain and should be tested by their veterinarian. Diagnosis is by culture and sensitivity testing or polymerase chain reaction (PCR). Screening is also recommended if there is epidemiological evidence that the animal may be involved in transmission (Lefebvre, Golab et al. 2008).

If decolonization is undertaken, both the colonized pets and the human carriers should be treated simultaneously to eliminate MRSA carriage. Pets should be treated systemically, not topically. In dogs, CA-MRSA is more responsive to oral antibiotics than HA-MRSA infections. Several antibiotics are effective against *S. aureus* normally, but MRSA is more difficult to treat. The use of antibiotics such as vancomycin or teicoplanin should be avoided in pets as they are among the only antibiotics that are effective in humans; overuse and inappropriate use of antibiotics has been linked to the development of antibiotic-resistant strains of bacteria.

Measures that can be taken to prevent disease spread include judicious use of antibiotics to avoid creating resistance, hand washing, and strict attention to sanitation. Staphyloccal organisms are resistant to drying and disinfection. After cleaning with hot water and soap, an EPA-approved disinfectant labeled to kill MRSA should be used

to disinfect the environment. As concern about MRSA increases in human medicine, the veterinary profession should also be aware and ever vigilant about this problem.

### *Mycobacterium tuberculosis* (tuberculosis)

The natural hosts of *Mycobacterium tuberculosis* include people, dogs, cats, and pigs; however, humans are the only reservoir host. *M. tuberculosis* is considered a true anthroponosis. Human-to-animal transmission of *Mycobacterium tuberculosis* has been reported in a dog whose owner was diagnosed with pulmonary tuberculosis. The dog frequently sat on the owner's lap and licked her face (Erwin, Bemis et al. 2004). While there is the potential for environmental contamination from contaminated secretions, there is no documentation that pets spread the disease back to people (Greene and Gunn-Moore 2006).

Transmission is primarily via aerosolized droplets and close contact. *M. tuberculosis* causes pulmonary and extrapulmonary tuberculosis in humans. An increase in the prevalence of the disease has been seen because of an increase in homelessness, illegal drug use, and HIV infections; more pets are now exposed.

A complete discussion of the epidemiology and management of this disease is beyond the scope of this textbook, and only a brief synopsis will be offered here. Clinical signs in dogs and cats include coughing, fever, bronchopneumonia, weight loss, anorexia, dysphagia, and retching. Dogs are more susceptible to infection from *M. tuberculosis* than cats. Cats may show more intestinal involvement, manifested as anorexia, weight loss, and enteritis. Disseminated granulomatous disease can produce a wide range of symptoms depending on the organ system affected. Mycobacterial culture is the standard for diagnosis. A variety of other tests, including tuberculin testing, are available.

Serious consideration must be given to management of these cases because of public health concerns that, if left untreated, and even though infected dogs and cats are not natural reservoirs, they can shed bacteria into the environment. Combination, rather than single, antibiotic therapy is advised for the best results, but treatment may take as long as 6 to 9 months, which is unfeasible in most shelters. Treatment is not advised in shelters, nor is adoption of affected animals.

A variety of disinfectants are effective against *Mycobacteria* spp. Phenolics have variable activity against *Mycobacteria* spp. but can be toxic to cats and thus should be avoided in the shelter environment. Aldehydes are carcinogenic and need to be utilized in a well-ventilated area. Bleach at 1,000 parts-per-million (5% household bleach diluted at 1:5, or 3 cups per gallon) is an inexpensive and effective disinfectant but irritating to skin and respiratory membranes and should not be used when animals are in the vicinity (NASPHV 2006).

### *Streptococcus*

Streptococci are anaerobic cocci that cause disease in animals and people. There is a wide range of hosts and virulence; streptococci may be commensal or pathogenic. There are several different systems of classification that are beyond the scope of this chapter to describe. Group A *Streptococcus* (otherwise known as *S. pyogenes* and GAS) colonizes the pharynx and tonsillar area of humans. Signs of disease can include pharyngitis and tonsillar enlargement in humans (also known as "strep throat"). Domestic animals that are exposed to infected humans sometimes show signs of pharyngeal colonization with Group A *Streptococcus*, but clinical signs of illness are normally not seen. In one study where Group A *Streptococcus* was cultured from human households, the prevalence in dogs was 42%; in cats it was 36%. On the other hand, random screening from urban households revealed a prevalence of about 1% to 10% in dogs and cats. In other studies using a different system of typing, there has been no correlation between streptococcal carriage in dogs and the presence of disease in humans. Although there is no convincing evidence that dogs and cats serve as a significant reservoir of infection for humans (Greene and Prescott 2006), there is still concern that failure to treat animals in households with infected owners will result in reinfection and relapse.

Diagnosis is by culture. Transmission is via direct or close contact among susceptible individuals. Individuals can harbor the organism for long periods without showing signs of disease. Treatment of both human and animals in a household with Group A *Streptococcus* should be undertaken; penicillin, amoxicillin, azithromycin, erythromycin, and chloramphenicol are effective antibiotic choices.

Although transmission of Group A streptococcal infection from dogs to people is rare, it is advisable to perform routine hand washing and not allow dogs to lick one's face or wounds.

## CONCLUSION

The purpose of this chapter is to present a broad, responsible, and balanced approach to handling diseases in shelters that have the potential to be zoonotic. While there are many diseases that are not mentioned or covered minimally in this chapter because they are uncommon, are discussed elsewhere, or do not affect or have much impact on shelter populations, many of the general disease

prevention and management principles discussed here would apply.

Many families consider pets to be members of the family, and the emotional and health benefits of pet ownership have been demonstrated repeatedly. While shelters must be vigilant about the prevention of zoonosis, it must be emphasized that the risk of contracting a zoonotic disease is fairly small for the immune-competent population if attention is paid to personal hygiene and regular veterinary care for pets to ensure their health. At-risk individuals can also enjoy pet ownership if a few precautions are taken regarding careful pet selection, regular health checks and routine preventative care.

## APPENDIX 23.1. ZOONOTIC DISEASES OF DOGS AND CATS AND THEIR MODES OF TRANSMISSION

In using this appendix, shelters must consider if they have the resources to humanely treat the animal, if a complete cure and elimination of carrier states is possible, and if treatment does not endanger the rest of the population, staff, volunteers, the public, and all others concerned. Ultimately, adoption decisions should be made by the veterinarians and staff. This appendix should be used in conjunction with the information included in the chapter and in accordance with guidelines from the shelter's local Department of Health.

| Disease | Transmission | Adoption |
|---|---|---|
| Acariasis (Mange) | Contact | Treat and adopt |
| Bartonellosis (cat scratch disease) | Contact/vector-borne | Adopt to nonimmunosuppressed persons |
| Bordetellosis | Airborne | Treat and adopt |
| Borreliosis | Vector-borne | Treat for ectoparasites (ticks) and adopt |
| Campylobacteriosis | Contact | Adopt |
| Canine brucellosis | Contact/airborne | Neuter, treat, test and prove seronegativity prior to adopting to nonimmunosuppressed persons |
| Capnocyptophagiosis | Contact | Adopt to nonimmunosuppressed persons |
| Cryptosporidiosis | Contact | Treat, adopt to nonimmunocompromised if symptomatic |
| Coxiellosis (Q fever) | Contact/airborne/ vector-borne | No |
| Dermatophytosis | Contact | Treat and adopt |
| Dipylidiasis | Vector-borne | Treat for endo- and ectoparasites (fleas) and adopt |
| Echinococcosis | Contact | Treat and adopt |
| Ehrlichiosis/anaplasmosis | Vector-borne | Treat for ectoparasites (ticks) and adopt |
| Giardiasis | Contact | Treat, adopt to nonimmunocompromised if symptomatic |
| Leptospirosis | Contact/airborne | Adopt after effective treatment to clear renal carriage |
| Malassezia pachydermatis | Contact | Treat and adopt |
| Plague | Contact/airborne/vector-borne | No |
| Pasteurellosis | Contact | Adopt to nonimmunocompromised persons |
| Rabies | Contact/airborne | No |
| Salmonellosis | Contact | Treat if symptomatic, adopt to households with children over 5 years old, and nonimmunocompromised |
| Sporotrichosis | Contact | Treat and adopt to nonimmocompromised |
| Toxocariasis | Contact | Treat and adopt |
| Toxoplasmosis | Contact | Adopt to nonpregnant or nonimmunocompromised persons |
| Tularemia | Contact/airborne/vector-borne | No |

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