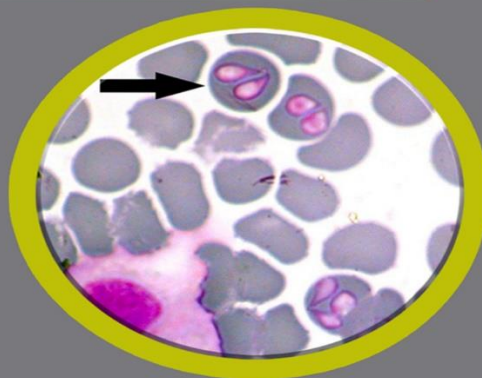
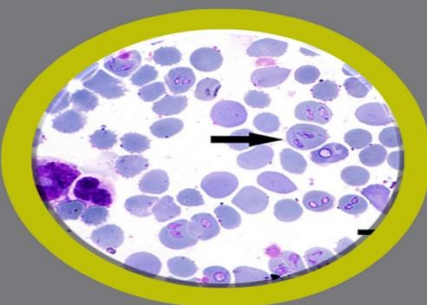


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Blood Parasites in domestic animals



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بسم الله الرحمن الرحيم

الحمد لله الذي اخرجنا من ظلمات الجهل والوهم الى انوار العلم والمعرفة والصلاة والسلام على سيد الخلق وحبیب الحق رسول الله محمد صلى الله عليه وعلى آله وصحبه أجمعين.

إن هذا الكتاب يشرح الطفيليات الدموية التي تصيب العديد من الحيوانات وتم تجميع المعلومات من عدة مصادر و مراجع في كتاب واحد.

ولقد راعيت أن يكون أسلوب المادة العلمية سهلا وبسيطا وفي نفس الوقت شاملا أحدث ما وصل إليه العلم في هذا المجال. أيضا حاولت أن تكون لغة الكتاب تصلح للطالب الجامعي وكذلك للممارس البيطري.

واتقدم بالشكر الجزيل الى كل من د. بان حمزة ، د. ايمان عبد الكريم و د عمار احمد لمساهماتهم في تلخيص بعض الامراض واظهار الكتاب بشكله الحالي.

أسأل الله أن ينفع بهذا الكتاب كل من يطلع عليه ويعود عليه بالخير والفائدة. كما أسأله سبحانه وتعالى أن يجعله خالصا لوجهه الكريم إنه نعم المولى ونعم المجيب.

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Veterinary Medicine

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Blood protozoa in Cattle and Sheep

1

Babesiosis

2

Theileriosis

3

Trypanosomiasis

4

Anaplasmosis

5

Eperythrozoonosis

Babesiosis

Etiology:

The nomenclature of these intraerythrocytic parasites is still subject to change; species in livestock include the following:

- Cattle: species include *Babesia bovis* (*B. argentina*), *B. bigemina*, , and *B. divergens*
- Sheep and goats: *B. motasi*, *B. ovis*

Age Resistance:

- In cattle, there is a variation in susceptibility to infection according to age, and the severity of babesiosis increases with age.
- Calves and foals from naïve dams are highly susceptible to infection and clinical illness from birth to 2 months of age, at which time they develop resistance that persists to approximately 6 months of age.
- Calves and foals from immune dams receive antibodies via the colostrum, and this passive immunity persists for 3 to 4 months after birth.
- The highest infection rate is in animals between 6 to 12 months of age; infection is uncommon in animals of greater than 5 years of age.
- Animals of less than 1 year of age are infected predominantly with *B. bigemina* and those of greater than 2 years of age by *B. bovis*.
- Calves of up to 1 year of age, although fully susceptible to infection, are resistant to disease.
- The average age at which calves in endemic areas become infected is 11 weeks (2 to 34 weeks), but clinical signs and pathologic changes are mild and relatively short-lived at this early age.
- After 6 months of age the number of infected animals in enzootic areas increases.

Origin of Infection and Transmission:

Viable stages of Babesia are present in the bloodstream of animals in the active phase of the infection.

Ticks are the natural vectors of babesiosis; the causative parasites persist and pass through part of their life cycle in the invertebrate host. Both *B. bovis* and *B. bigemina* pass through part of their life cycle in the tick *Rhipicephalus australis* (previously *Boophilus microplus*).

Other species of *Boophilus* and *Rhipicephalus* are major vectors of babesiosis, but other ticks of the genera *Haemaphysalis*, *Hyalomma*, *Ixodes*, and *Dermacentor* can be involved in transmission.

Rhipicephalus and Haemaphysalis spp. are common ticks of sheep and/or goat.

Life Cycle and Development:

The development of *B. bovis* and *B. bigemina* follows similar patterns. *Babesia* spp. do not parasitize any vertebrate host cell other than erythrocytes. Each sporozoite penetrates the erythrocyte membrane with the aid of a specialized structure called the apical complex. Once inside, it transforms into a trophozoite from which two merozoites develop by a process of merogony or schizogony (binary fission) (see Fig. 1).

The tick becomes infected when ingesting erythrocytes containing piroplasms (gametocytes). They develop into male and female gametes in the tick gut. The microgametes fuse with macrogametes to produce motile zygotes. The zygotes then multiply, and the resultant “vermicules” invade numerous organs of the tick, including the ovaries. Therefore the infection passes through the ovary and the egg to the next

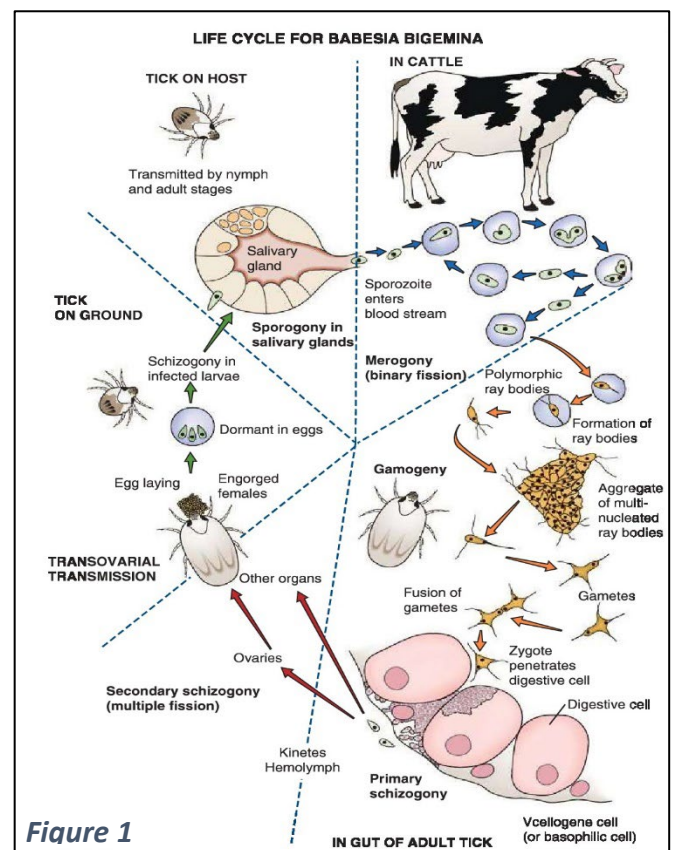


Figure 1

tick generation (called transovarial transmission). Usually the female tick becomes infected, and sporogony takes place in the salivary glands of larval, nymphal, and/or adult ticks of the next generation. When the tick attaches to a new host, sporozoites mature. In *B. bigemina*, for example, some development occurs in the feeding larvae, but infective sporozoites take about 9 days to appear, and they therefore only occur in the nymphal and adult stages of the tick.

Clinical findings:

Cattle: *Babesia Bovis*

- The acute disease generally runs a course of 3 to 7 days, and a fever of greater than 40°C (104°F) is usually present for several days
- depression, polypnea, weakness, and a reluctance to move.
- Hemoglobinuria is often present (known as “redwater” in some countries); urine is dark red to brown in color and produces a very stable froth.
- Anemia and jaundice develop, particularly in prolonged and severe cases.
- Diarrhea may occur. Muscle wasting, tremors, and recumbency develop in advanced cases, followed terminally by coma
- Many severely affected animals die precipitately at this point, after an illness of only 24 hours.
- During the fever stage, pregnant cattle can abort, and bulls may become sterile for 6 to 8 weeks.
- **A Subacute:** Syndrome also occurs, particularly in young calves, in which fever is mild and hemoglobinuria is absent.
- The syndrome associated with *B. divergens* is similar to that of *B. bovis*, except that, in addition, there is spasm of the anal sphincter, causing the passage of feces with great force in a long, thin stream, even in the absence of diarrhea; this sign is referred to as “pipe-stem” feces.

Cattle: Babesia Bigemina:

- Hemoglobinuria is present earlier and more consistently
- And fever is less of a feature. Acutely affected animals are usually not as severely affected as those with *B. bovis* infection.
- There is no cerebral involvement, and recovery in nonfatal cases is usually rapid and complete
- However, in some cases, disease can develop very rapidly, with sudden and severe anemia, jaundice, and death. Animals that recover from *B. bigemina* remain infective to ticks for 4 to 7 weeks and remain as carriers for only a few months

Sheep:

- Anemia, fever, icterus, and hemoglobinuria are common.

Clinical pathology:

Hematology:

Severe anemia with erythrocyte counts as low as 2 million/ μ L and hemoglobin levels down to 3g/dL occur in clinical cases in cattle, with anemia peaking 9 to 16 days following infection. Significant reduction in platelet numbers and a depression in the fibrinogen content of blood also occur.

Demonstration of the Presence of Babesia:

Direct Examination of Blood Smears A diagnosis of babesiosis in clinically affected animals depends on the detection of piroplasms (merozoites) in Giemsa-stained smears of capillary blood; venous blood may give a false negative result for *B. bovis* infection.

There is no exact correlation between the percentage of erythrocytes containing protozoa and the severity of the clinical signs. Also in *B. bigemina* infection, piroplasms are numerous in peripheral capillaries; *B. bovis* is less readily found. This difficulty can be largely overcome by using thick blood smears for detection. Microscopic examination can detect parasitemia of approximately 10⁵ in thin blood films and 10⁶ in thick blood smears.

Transmission Test:

The inoculation of blood from a potentially infected bovine to susceptible splenectomized calves is a highly sensitive technique for the direct detection of Babesia.

For this test, 50 to 100 mL of blood is injected into the recipient either SC or IV. In the latter case, the incubation period will be shorter.

The recipient cattle are examined daily, and the blood is examined for protozoa at the peak of the febrile reaction.

Carrier cattle infected with *B. bovis* and/ or *B. bigemina* are difficult to detect because of the small number of piroplasms in peripheral blood. Microscopic examination of stained blood smears is not a reliable technique for the detection of Babesia-carrier animals.

Culture of Babesia:

Some Babesia spp. can be cultured in vitro. For instance, *B. divergens* from the blood of carrier cattle can be isolated using an in vitro culture technique in sheep erythrocytes.

Babesia stages can be isolated 9 months after the acute babesiosis phase and can be successfully subcultured, cryopreserved, and resuscitated using culture medium. This culturing approach allows for detailed studies of the parasite.

Preservation of live protozoa can be effected by cryopreservation, by culture in a medium containing infected bovine erythrocytes, and in simple culture media in special apparatus for long periods and in large numbers.

Necropsy findings:**Acute cases:**

- babesiosis in all species, in which patients die after a brief illness and during an anemic crisis, the typical findings are jaundice; thin
- Watery blood; pale tissues; enlargement of the spleen, which has a soft, pulpy consistency; and gross enlargement and dark-brown discoloration of the liver.

- The gallbladder is distended, with thick, granular bile; the kidneys are enlarged and dark; and the bladder contains red–brown urine.
- Ecchymotic hemorrhages are present under the epicardium and endocardium, and the pericardial sac contains an increased quantity of blood-stained fluid
- In cattle, a characteristic manifestation is severe intravascular clotting

Subacute or chronic cases:

- In subacute or chronic cases of relatively long duration, the carcass is emaciated but hemoglobinuria is absent; the other changes observed in acute cases are present but are less pronounced.
- The microscopic examination of blood smears taken from peripheral blood, from kidney and heart muscle, and, in the case of suspected *B. bovis* infection, from the brain, is mandatory for clinching the diagnosis
- Smears from blood and most tissues must be made within 8 hours of death, within 28 hours for the brain, and stained with Giemsa for the detection of *B. bovis*.

Differential diagnosis:

A syndrome of acute hemolytic anemia should suggest the following alternative diagnoses:

- Theileriosis
- Postparturient hemoglobinuria
- Bacillary hemoglobinuria
- S-methyl-L-cysteine-sulfoxide (SMCO) poisoning
- Leptospirosis

Treatment and Control:

A variety of drugs have been used to treat babesiosis in the past, but only diminazene aceturate and imidocarb dipropionate are still in common use.

These drugs are not available in all endemic countries, or their use may be restricted. Manufacturers' recommendations for use should be followed.

For treating cattle:

- diminazene is given IM at 3.5 mg/kg. For treatment, imidocarb is given SC at 1.2 mg/kg. At a dosage of 3 mg/kg.

- imidocarb provides protection from babesiosis for ~4 wk and will also eliminate *B. bovis* and *B. bigemina* from carrier animals.
- Supportive treatment is advisable, particularly in valuable animals, and may include the use of anti-inflammatory drugs, corticosteroids, and fluid therapy. Blood transfusions may be life-saving in very anemic animals.

Sheep

- Diminazene aceturate is effective as a treatment in sheep (3.5 mg/kg BW on two successive days, or 12 mg/kg BW as a single dose).

Control and Prevention:

Prevention

Preventing the introduction of the disease into a nonenzootic area depends on effective quarantine to prevent the introduction of the vector tick and laboratory testing to ensure freedom of the importee from infection with the pathogen(s).¹

Control

The control of bovine babesiosis in an area depends on the control the tick vector. Eradication is usually not achievable/practical because of the high cost to local wildlife, some of which can be hosts to ticks.

Other challenges encountered include the following:

- The difficulty of getting a complete muster of all cattle on every dipping day
- Multihost ticks, which can be infective but temporarily not resident on an animal on dipping day
- The spread of ticks or infested cattle as a result of environmental issues, such as floods or windstorms
- Illegal movement of cattle without a permit

Other issues include the persistence of *Babesia* through successive generations of the tick vector and the resistance of ticks to acaricides, which is also a factor relating to the infestation level of cattle.

Theileriosis

Theilerioses are those tick-borne protozoan diseases associated with *Theileria* spp. in cattle, sheep, goats, and horses and in wild and captive ungulates.

The genus *Theileria* belongs to the Apicomplexa group, which includes *Babesia*, *Toxoplasma*, *Neospora*, and *Plasmodium*, among others.

The life cycle of *Theileria* spp. involves cyclical development in ticks to form sporozoites; on being injected with tick saliva into the mammalian host, sporozoites develop into schizonts in leukocytes and then piroplasms (merozoites) in erythrocytes.

The important pathogens of cattle is East Coast fever (ECF), caused by *Theileria parva*, and tropical theileriosis (or Mediterranean Coast fever), caused by *T. annulata*, are the two most important theilerioses and are dealt with separately in the following discussion.

East Coast fever (ECF)

Etiology:

East Coast fever is caused by *Theileria parva* transmitted by ticks. The genus *Theileria* belongs to the apicomplex group.

Epidemiology:

- ECF affects mainly cattle but also buffalo.
- All susceptible cattle in endemic areas are at the risk of contracting ECF unless they are vaccinated or the tick population is under stringent control.
- The morbidity and casefatality rates are very high, approaching 90% to 100% in recently introduced exotic (*Bos taurus*) breeds and in previously unexposed or naive indigenous cattle.
- However, indigenous zebu cattle (*Bos indicus*) and African buffalo in endemic areas have a strong resistance to the disease, and calfhood mortality is around 5%.

Methods of Transmission:

- The vector of ECF is *Rhipicephalus appendiculatus*; in the field, the disease occurs only where this tick is found, except for corridor disease, which may be transmitted by *R. zambeziensis*.
- Other species of *Rhipicephalus* and *Hyalomma* spp. can transmit ECF experimentally, but they are not significant. Developmental stages of the parasite occur in the tick, and they pass transstadially through the stages of larva, nymph, and adult, but there is no transovarian transmission.
- Consequently, larvae or nymphs become infected and transmit infection as nymphs or adults, respectively.
- Adults are more efficient vectors than nymphs but each developmental stage results in amplification of the vector's competence in parasite transmission and the ability to infect more than one host during the life cycle of the tick.
- Infected ticks start transmission of the parasite from 72 hours postattachment, and mechanical transmission is of no significance.
- The epidemiology of the disease is thus largely dependent on the distribution and habitat of the tick and its ability to complete development to the adult stage, usually during the rainy season.
- Ticks may live for 1 to 2 years, but they lose their infection within 11 months.

Clinical findings:

- The basic syndrome caused by *T. parva* infection lasts for a few weeks.
- The incubation period is 1 to 3 weeks, depending on the virulence of the strain and the size of the infecting dose.
- Experimentally, the first clinical sign is enlargement of lymph nodes in the area draining the site of tick attachment (i.e., 8 to 16 days after attachment).
- One or 2 days later, there is fever, depression, anorexia, and a drop in milk in dairy animals.
- In later stages, there may be nasal and ocular discharges, dyspnea, generalized lymph node enlargement, and splenomegaly.
- In severe cases, diarrhea occurs, sometimes with dysentery, but usually only late in the course of the disease.
- Emaciation, weakness, and recumbency lead to death from asphyxia in 7 to 10 days.

- Terminally, there is often a frothy nasal discharge. Occasional cases of brain involvement occur and are characterized by circling, hence “turning sickness,” or cerebral theileriosis.
- In southern Africa, cerebral theileriosis is associated with an aberrant form of *T. taurotragi* originating from the eland. There are localized nervous signs and convulsions, tremor, profuse salivation, and head pressing.
- Infection with the strain of *T. parva* (formerly *T. parva lawrencei*) responsible for corridor disease causes a similar acute syndrome, with the additional lesion of keratitis and accompanying blepharospasm.

Clinical pathology:

- The parasites are evident as schizonts, sometimes in circulating lymphocytes, but mainly in biopsy smears of enlarged lymph nodes stained with Giemsa.
- Piroplasms are also easily visible in erythrocytes from day 16 after tick attachment, and they increase in number until death.
- Over 30% of the red cells may be infected, but the level of intraerythrocytic piroplasms is not correlated with the severity of the disease.
- *T. parva* piroplasms are difficult to differentiate from other piroplasms— hence the necessity to find schizonts.
- Blood counts will reveal a panleukopenia and thrombocytopenia with little or no anemia.
- The protozoa can be grown on a tissue culture of lymphoblastoid cells.

Necropsy findings:

- The most striking lesion is massive pulmonary edema, hyperemia, and emphysema, along with hydrothorax and hydropericardium.
- Copious froth is present in the airways.
- The carcass is emaciated, and hemorrhages are evident in a variety of tissues and organs.
- There is enlargement of the liver, lymph nodes, and spleen and ulceration of abomasum and intestines.
- Small lymphoid nodules (the so-called pseudoinfarcts) are present in liver, kidney, and alimentary tract.
- In protracted cases, animals may have small, exhausted lymphoid organs.

Differential diagnosis:

- Heartwater
- Trypanosomosis
- Babesiosis
- Anaplasmosis
- Malignant catarrhal fever
- Contagious bovine pleuropneumoniae
- The parasites must also be differentiated from other species of Theileria.

Treatment and control:

Treatment

- **Buparvaquone** (2.5 mg/kg IM, 2 doses 48 hours apart) (R-1)
- **Parvaquone** (10 mg/kg IM 2 doses 48 hours apart) (R-1)
- **Halofuginone** lactate (1.2 mg/kg PO) (R-1)
- **Oxytetracycline** (20 mg/kg IM) (R-2)

Cure rates are even higher if the animals are also treated for pulmonary edema with dexamethasone or the diuretic furosemide. A recovery rate of 95.2% was reported in field cases in Tanzania treated with buparvaquone alone.

Control

- Vaccination by infection and treatment method using tetracycline or parvaquone (R-1)
- Vaccination by infection with lowpathogenicity isolate (R-2)

Tropical theileriosis

Etiology:

Theileria annulata is a member of the Apicomplexa group, like *T. parva*, the cause of East Coast fever.

Methods of Transmission and Fatality rate

- *T. annulata* affects cattle and is transmitted transstadially by the three-host tick *Hyalomma anatolicum* in central-western Asia and northeastern Africa, and by the two-host tick *H. detritum* in the Mediterranean basin.
- In endemic areas, virtually all adult cattle are infected, but infection rates vary with the method of examination.
- Case fatality is approximately 10% to 20% and is confined mainly to calves. Exotic animals recently introduced may have 20% to 90% mortality.
- The disease occurs when there is much tick activity, mainly in summer and the rainy seasons, and in crossbred animals.
- A single tick can cause fatal infection because its salivary glands usually contain numerous sporozoites.

Clinical findings:

- In a stable endemic situation, there may be only mild or no clinical disease in local zebu cattle.
- Clinical signs are acute and severe in exotic cattle and less severe in crossbreeds and are similar to those in ECF. However, the course is longer in tropical theileriosis and may last for weeks before death.
- Clinical signs include marked fever, swelling of superficial lymph nodes, inappetence, tachycardia, dyspnea, pale mucous membranes, and icterus.
- Others are diarrhea, weight loss, convulsions, torticollis, and other nervous signs.

- In chronic cases, there may be small subcutaneous nodules, from which schizonts can be demonstrated in smears.
- In Egypt, affected cattle and buffaloes also showed ocular signs, including severe lacrimation, bilateral conjunctivitis, photophobia, and corneal opacity, whereas in Spain, there were coalescing skin nodules similar to multicentric malignant lymphoma.

Clinical pathology:

- As with ECF, examination of smears of blood and lymph node biopsy will reveal piroplasms in erythrocytes and schizonts in lymphocytes.
- Schizonts of *T. annulata* tend to be more common in the liver than in lymph node smears, but they are otherwise indistinguishable from those of *T. parva*. Furthermore, the piroplasms are predominantly round and oval, as opposed to *T. parva*, which has comma- and rod-shaped piroplasms.

Necropsy findings:

- Apart from pallor of mucous membranes and yellowish discoloration of tissues, the postmortem lesions in animals dying from tropical theileriosis are similar to those of ECF.
- Lymphoid proliferation can resemble multicentric malignant lymphoma.
- Liver, spleen, and lymph nodes should be submitted for laboratory examination to detect schizonts, whereas merozoites are detected in blood smears.

Differential diagnosis:

- Other theilerioses
- Babesiosis
- Anaplasmosis
- Trypanosomosis
- Malignant catarrhal fever

Treatment and control:

Treatment

- Buparvaquone 2.5 mg/kg IM, 2 doses 48 hours apart) (R-1)
- Halofuginone lactate (1.2 mg/kg PO) (R-1)
- Oxytetracycline (20 mg/kg IM) (R-2)

Buparvaquone is the most effective agent available, and the recommended dose is 2.5 mg/kg BW. In calves, supportive treatment for anemia is indicated. Halofuginone at 1.2 mg/kg is also effective, but tetracycline at 20 mg/kg is less so.

Control

- Vaccination by infection and treatment method using tetracycline (R-1 for exotic animals)
- Vaccination with attenuated schizont vaccine (R-2)

In Sheep

The important pathogen of sheep and goats is *T. hirci* (synonym *T. lestoquardi*), the cause of malignant ovine theileriosis.

Malignant theileriosis in sheep and goats:

Is similar to bovine tropical theileriosis as a result of *T. annulata*. Like the latter, it is also transmitted by *Hyalomma* spp.

The disease can be acute, subacute, or chronic, depending on the resistance of the sheep or goats, and is seasonal, depending on availability of ticks.

The acute disease is characterized by:

- Fever and very high mortality in 3 to 6 days.
- Anemia, jaundice, and enlargement of lymph nodes are characteristic, and both piroplasms and schizonts can be demonstrated in smears of blood and tissues, respectively.
- The anemia is severe, progressive, and hemolytic and is associated with oxidative damage.

In subacute and chronic cases:

- Signs are generally less marked except for anemia and emaciation.

Parvaquone and buparvaquone may be used to treat early cases.

Trypanosomiasis

(Nagana, samore, african , tsetse fly disease)

Etiology:

Trypanosoma congolense, *T. vivax*, *T. brucei brucei*, and *T. simiae*, all salivarian trypanosomes. Tsetse flies (*Glossina* spp.) serve as biological vector, other biting flies

Transmission and Epidemiology:

- Most tsetse transmission is cyclic and begins when blood from a trypanosome-infected animal is ingested by the fly.
- The trypanosome alters its surface coat, multiplies in the fly, then alters its surface coat again, and becomes infective.
- *T brucei* spp migrate within the tsetse from the gut and eventually to the salivary glands; the cycle for *T congolense* stops at the hypopharynx, and the salivary glands are not invaded; the entire cycle for *T vivax* occurs in the proboscis. Therefore, the location within the tsetse can be useful in identifying the parasite species.
- The animal-infective form in the tsetse salivary gland is referred to as the metacyclic form.
- The life cycle in the tsetse may be as short as 1 wk with *T vivax* or extend to a few weeks for *T brucei* spp.
- The three main species inhabit relatively distinct environments: *G morsitans* usually is found in savanna country, *G palpalis* prefers areas around rivers and lakes, and *G fusca* lives in high forest areas. All three species transmit trypanosomes, and all feed on various mammals.
- Mechanical transmission can occur through tsetse or other biting flies. In the case of *T vivax*, *Tabanus* spp and other biting flies seem to be the primary mechanical vectors outside tsetse-endemic areas, as in Central and South America.
- Mechanical transmission requires only that blood containing infectious trypanosomes be transferred by bite from one animal to another.

Clinical findings:

- Although anemia is the cardinal feature, there are no pathognomonic signs that would help in pinpointing a diagnosis of trypanosomosis in farm animals. The general clinical picture is as follows, but there are many variations determined by the level of tsetse challenge, the species and strain of the trypanosome, and the breed and management of the host.
 - Acute episodes last for a few days to a few weeks, from which the animal dies or lapses into a subacute to chronic stage, or the illness may be chronic from the beginning.
 - Chronic cases may run a steady course, may be interrupted by periodic incidents of severe illness, or may undergo spontaneous recovery.
 - The basic clinical syndrome appears after an incubation period of 8 to 20 days following the infective tsetse fly bite. Chancre is not readily noticed under field conditions. There is fever, which is likely to be intermittent or cyclic for weeks.
-
- Affected animals are dull, anorexic, and apathetic; have a watery ocular discharge; and lose condition.
 - Superficial lymph nodes become visibly swollen, mucous membranes are pale, diarrhea occasionally occurs, and some animals have edema of the throat and underline.
 - Estrus cycles become irregular, pregnant animals may abort, and semen quality progressively deteriorates.
 - The animal becomes very emaciated and cachectic and dies within 2 to 4 months or longer. Thin, rough-coated, anemic, lethargic cattle with generalized lymph node enlargement are reported to have a “fly struck” appearance.
-
- Mixed infections with more than one species of trypanosomes are common and are usually more severe. Furthermore, intercurrent bacterial, viral, or other parasitic infections may mask or complicate the basic clinical syndrome. Immune response to bacterial and some viral vaccines is also depressed unless trypanocidal therapy is given at the time of vaccination.

Clinical findings peculiar to the individual trypanosome are as follows:

- *T. vivax* affects all agricultural species except pigs. Acute and chronic outbreaks occur, anemia is severe, and fever is usually associated with high parasitemia. A chronic form of the disease is more usual in East Africa, but an acute hemorrhagic form can occur with exotic cattle. Furthermore, outbreaks in Brazil have been associated with nervous signs in cattle and in sheep, characterized by head pressing, lateral recumbency, paddling movements, and muscle tremors. *T. vivax* is less commonly seen in trypanotolerant cattle breeds.
- *T. congolense* affects all species, usually with an acute disease lasting 4 to 6 weeks, but some chronic cases occur, especially in West Africa. Anemia and emaciation are severe. The savannah subspecies is more pathogenic than the other subspecies.
- *T. brucei brucei* affects all species with a subacute to chronic disease. In addition to fever and anemia, there is often marked subcutaneous edema and keratoconjunctivitis. Nervous signs are manifested in horses, pigs, and small ruminants by ataxia, circling, head pressing, and paralysis. Cattle show chronic clinical signs, and they can act as carriers.

Clinical pathology:

- A progressive drop in packed cell volume is a nonspecific but useful indicator of trypanosomosis in endemic areas.
- The classic method of confirming nagana diagnosis is to demonstrate parasites in a wet blood film and in a thin or thick blood smear stained with Giemsa.
- This is fairly reliable in the early stages of the disease when parasitemia is usually high and parasitemic peaks correspond with fever. As the disease progresses, parasitemias become infrequent and the intervals between peaks grow longer, even though the animal is still sick.
- To increase the accuracy of parasitologic diagnosis, it is now routine to concentrate the parasites in the buffy-coat layer of a microhematocrit capillary tube.
- The buffy layer is then examined directly at low power (Woo's method) or in a wet preparation with a dark-ground/phasecontrast microscope (Murray's method). Both tests are simple, sensitive, and applicable to field use on individual animals and in herds. Blood should be examined fresh but may be refrigerated for up to 24 hours, beyond which most parasites will die and disappear from the sample.

Necropsy findings:

- The postmortem lesions are, like the clinical findings, not definitive.
- The carcass is marked by anemia, emaciation, and enlargement of the liver, spleen, and lymph nodes.
- Body-fat stores are depleted or show marked serous atrophy, especially around the heart and in bone marrow.
- The bone marrow may be red (active) in the acute stage, but it becomes pale and gelatinous (unresponsive) in the chronic stage.
- Subcutaneous edema, corneal opacity, and testicular degeneration may be present. Thickening of the meninges and softening of the brain have been reported in some cattle naturally infected with the South American *T. vivax*.
- In acute cases, there will be a general congestion of the viscera and extensive hemorrhages in all tissues.
- Chronic cases show cachexia, often complicated with secondary bacterial pneumonia or other parasitic diseases.

Differential diagnosis:

Diagnosis is based on detecting parasites in blood. Because parasitemias fluctuate, multiple samples from a herd or repeated sampling of a suspected case may be required before a specific diagnosis can be made. Furthermore, an infected animal may be suffering from a concurrent disease. Emaciation and anemia can also be associated with the following:

- Malnutrition
- Helminthosis
- Babesiosis
- Anaplasmosis
- East coast fever

Acute trypanosomosis may be confused with hemorrhagic septicemia and anthrax. Laboratory examination of blood, feces, and other tissues is required to confirm diagnosis.

Treatment and control:

Treatment

The common drugs in use against trypanosomes are set out in the following discussion. The specific dose rates vary with animal species, the specific trypanosome, and the specific purpose (curative, prophylactic, or sanative).

- Diminazene aceturate (Berenil) is used widely against *T. vivax* and *T. congolense* as a curative and sanative drug at 3.5 to 7 mg/kg BW IM. It is well tolerated by ruminants, and it is one of the two recommended drugs for bovine trypanosomosis. It is not well tolerated by horses.
- Isometamidium (Samorin or Trypamidium) is the other preferred drug against *T. vivax* and *T. congolense* in ruminants. It is used as a curative and prophylactic drug at 0.25 to 1 mg/kg BW IM. At much higher doses (12.5 to 35 mg/kg BW) it can be used prophylactically against *T. simiae* in pigs but not without the risk of death from acute cardiovascular collapse.
- Homidium bromide (ethidium) and homidium chloride (novidium) are also widely used against *T. congolense* and *T. vivax* as curative and sanative drugs at 1 mg/kg BW IM.
- Pyrithidium bromide (prothridium) is less widely used against *T. congolense* and *T. vivax* as prophylaxis at 2 mg/kg BW IM.
- Quinapyramine sulfate (Antrycide) is no longer used extensively in cattle. It is the preferred curative drug against *T. brucei brucei* in horses at 5 mg/kg BW IM.
- Quinapyramine sulfate and chloride (Antrycide prosalt) is used prophylactically at 7.4 mg/kg BW SC.
- Suramin (naganol) may also be used against *T. brucei* as a curative and prophylactic drug at 10 mg/kg BW in horses and camels.
- Antrycide–Suramin complex is the only other drug effective against *T. simiae* in pigs, and it is used prophylactically at 40 mg/kg BW.

Summary

- **Diminazene aceturate** (Berenil) (3.5–7 mg/kg IM) (R1 for ruminants, R-3 for equines)
- **Homidium chloride**/bromide (Ethidium/
- **Novidium** (1 mg/kg IM) (R-1 for ruminants and equines)
- **Isometamedium chloride** (Samorin) (0.25–1 mg/kg IM) (R-1 for ruminants)
- **Quinapyramine sulfate** (Antrycide) (5 mg/kg SC) (R1 for equines)
- **Suramin** (Antrypol) (10 mg/kg IV) (R-2 for equines, camelids, 2–3 times weekly)

Control:

The control of trypanosomosis in endemic countries involves control of tsetse fly population, prophylactic treatment of animals at risk, good husbandry of animals, and use of trypanotolerant animals.

There is no vaccine against the disease, and in spite of intensive research, vaccines appear unlikely in the near future because of the ability of trypanosomes to readily change their glycoprotein surface coat through the process of antigenic variation.

- Isometamedium chloride (2 mg/kg IM) (R-1)
- Homidium chloride/bromide (1 mg/kg IM) (R-2)
- Prothridium (2 mg/kg IM) (R-2)
- Antrycide prosalt (7.4 mg/kg SC) (R-2)
- Antrycide/Suramin complex (35 mg/kg SC) (R-2 for *T. simae* in pigs)

Anaplasmosis

Etiology:

Anaplasmosis in cattle is usually caused by *A.marginale*. An *A.marginale* with an appendage has been called *A.caudatum*, but it is not considered to be a separate species. Cattle are also infected with *A.centrale*, which generally results in mild disease.

A.ovis may cause mild to severe disease in sheep, deer, and goats. *A.phagocytophilum* has recently been reported to infect cattle; however, natural infection is rare and it does not cause clinical disease.

Transmission:

Anaplasmosis is transmitted through tick bites Spread from animal to animal occurs chiefly by insect vectors. A variety of arthropods may act as vectors, but significant natural vectors are ticks in the family Ixodidae and flies in the family Tabanidae.

Or by the mechanical transfer of fresh blood from infected to susceptible cattle from biting flies or by bloodcontaminated fomites, including needles, ear-tagging, dehorning, and castration equipment.

Pathogenesis:

Anaplasma are obligate intraerythrocytic bacteria. They infect mature erythrocytes by an endocytic process that possibly involves the twin-arginine translocation (Tat) pathway, which exports fully folded proteins out of the cytoplasm of the bacteria with the type IV secretion system (T4SS). Inside the erythrocyte, bacterial reproduction occurs by binary fission to produce two to eight infective initial bodies that leave by exocytosis to infect other erythrocytes.

The number of infected erythrocytes doubles every 24 to 48 hours, and the infection becomes patent 2 to 6 weeks after infection, with the time frame influenced by the initial challenge dose. Depending on the strain and the susceptibility of the host, from 10% to 90% of erythrocytes may be infected in the acute stage of the disease. At least 15% have to be infected before there is clinical disease.

Infected erythrocytes are removed by phagocytosis in the reticular endothelial system, with release of acute-phase inflammatory reactants and the consequent development of fever.

Continued erythrocyte destruction occurs, resulting in the development of mild to severe anemia and icterus without hemoglobinemia or hemoglobinuria.

Clinical findings:

Cattle

There are few recent reports on clinical findings during outbreaks of bovine anaplasmosis. The incubation period varies with the challenge dose but is generally several weeks with tick-borne infection and 1 to 5 weeks with the inoculation of blood.

In most cases the disease is subacute, especially in young animals:

- Rectal temperature rises rather slowly and rarely to above 40.5° C (105° F). It may remain elevated or fluctuate with irregular periods of fever and normal temperature alternating for several days to 2 weeks.
- Anorexia is seldom complete.
- Death can occur at this stage, but many survive in an emaciated condition, and their fertility is impaired.
- The mucous membranes are jaundiced and show marked pallor, particularly after the acute stage is passed, but there is no hemoglobinuria.

Peracute cases:

- Sudden onset of high fever, anemia, icterus, severe dyspnea, and death, often within 24 hours, are not uncommon in adult dairy cows.
- Affected animals are often hyperexcitable and tend to attack attendants just before death.
- Pregnant cows frequently abort.
- In convalescent bulls there may be depressed testicular function for several months.

Sheep and Goats

- In sheep and goats, infection is usually **subclinical**, but in some cases, particularly in goats, a severe anemia may occur, and a clinical picture similar to that found in cattle may be seen.
- Severe reactions of this type in goats are most frequent when the animals are suffering from concurrent disease.
- Goats may show hyperexcitability and may bite at inanimate objects.
- The experimental disease in lambs includes fever, constipation or diarrhea, pale and icteric conjunctivae, and severe anemia 15 to 20 days after inoculation.
- The anemia is not completely resolved in 3 to 4 months.

Necropsy findings:

- The most obvious findings are emaciation, pallor of the tissues, and thin, watery blood.
- There is mild jaundice, and the liver is enlarged and orange.
- The kidneys are congested, and there may be myocardial hemorrhages.
- The spleen is enlarged, with a soft pulp.
- The bone-marrow cavity may be reddened by increased hematopoietic tissue in acute cases, but there may be serous atrophy of marrow fat in chronic cases.
- Postmortem identification of *A. marginale* can be established by staining blood smears with Giemsa or with direct fluorescent stains. Peripheral blood is superior to organ smears.
- Brain smears are unsatisfactory. The technique is applicable to fetuses suspected of being aborted as a result of infection with *Anaplasma* spp.
- Nucleic acid-based tests may be used but are rarely needed for routine diagnosis at necropsy.

Clinical pathology:

Anaplasmosis in cattle, sheep, and goats is characterized initially by normocytic normochromic anemia, which becomes macrocytic normochromic as the disease develops.

Erythrocyte destruction may be so severe that the erythrocyte count is reduced to 1.5 million/ μ L. Immature red cells are common at this stage, and their presence is considered to be a favorable sign.

The small dot-like bacteria are discernible at the periphery of up to 10% of the red cells in subacute cases, but in peracute cases more than 50% of the cells may be infected.

A. ovis are usually situated at the periphery of erythrocytes, but as many as 40% of infested cells may show submarginal organisms.

Reticulocytosis and basophilic stippling are usually evident. Packed cell volume and red blood cell count were found to be the most informative parameters in the routine clinical practice for *A. ovis* infection in sheep.

Diff-Quik staining of blood smears is as accurate as Giemsa in the detection of *A. marginale* and can be completed in 15 seconds compared with nearly an hour for Giemsa.

There are no diagnostic clinical chemistry findings, but as evidence of oxidative stress, levels of erythrocyte lipid peroxidation (LPO) and plasma nitrate (NO) may be elevated during the acute phase. Concentrations of acute phase proteins (Hp, SAA, ceruloplasmin, and fibrinogen) may also be elevated.

Differential diagnosis:

Other causes of haemolytic anaemia may need to be considered. These include:

- Babesiosis
- Leptospirosis
- Bacillary haemaglobinuria
- Rapeseed poisoning
- Eperythrozoonosis
- Chronic copper poisoning

Treatment and control:

Treatment

Treatment is with tetracyclines, imidocarb, or enrofloxacin:

- Treatment of clinical disease can be with oxytetracycline, 6 to 10 mg/kg BW daily for 3 days, or a single injection of long-acting oxytetracycline at a dose of 20 mg/kg intramuscularly (IM). The convalescent period is long, and animals remain persistently infected.
- Concurrent administration of estradiol cypionate (14.3 mg/kg BW IM) appears to improve the rate of recovery by reducing rickettsemia during treatment.
- Blood transfusions are indicated in animals with a PCV less than 15%. Rough handling must be avoided.
- Imidocarb (5 mg/kg BW IM twice, 7 days apart) is also an effective treatment for clinical cases but does not eliminate persistence. The drug is not approved for use in the United States and Europe because it is a suspected carcinogen.
- Enrofloxacin (12.5 mg/kg BW SC twice, 48 hours apart) is effective, but it also results in persistent infection. At 7.5 mg/kg BW it provided faster reduction of rickettsemia and PCV recuperation compared with long-acting oxytetracycline at 20 mg/kg BW.
- The risk for infection in the rest of the herd should be assessed and, if necessary, temporary or prolonged protection should be provided. Protection can be provided by tetracyclines or by vaccination.
- Prolonged protection can be achieved by intramuscular injection at 20 mg/kg BW of long-acting tetracycline every 28 days or by chlortetracycline in the feed at 1.1 mg/kg BW daily.
- Elimination of infection is difficult but not impossible. A trial testing the ability of chlortetracycline therapy to eliminate the carrier state examined three doses (4.4 mg/kg per day, 11 mg/kg per day, and 22 mg/kg per day) of oral chlortetracycline fed for 80 days.

Treatment

Oxytetracycline (6 to 10 mg/kg IM daily for 3 days, or 20 mg/kg IM single dose) (R-1)
 Imidocarb (5 mg/kg IM twice, 7 days apart) (R-2)
 Enrofloxacin (12.5 mg/kg SC twice, 48 hours apart) (R-1)

Control

Killed *A. marginale* vaccine (2 doses 4 weeks apart, then a booster) (R-1)
 Live *A. centrale* vaccine (single dose, preferably in yearlings) (R-2)
 Live *A. marginale* vaccine (single dose, yearlings only) (R-3)
 Attenuated *A. marginale* vaccine (R-4)
 Cell-culture live *A. marginale* vaccine (R-2)

Control:

Methods for the control of anaplasmosis have not changed greatly over the past several decades.

Basically, the control and prevention measures include:

- Maintenance of Anaplasma-free herds through import and movement control, testing, and elimination of carrier cattle.
- Vector control.
- Prevention of iatrogenic transmission.
- Administration of antibiotics.
- preimmunization with live vaccines and immunization with killed vaccines.

Eperythrozoonosis

Etiology:

- The disease is associated with hemotrophic mycoplasmas, formerly thought to be rickettsial parasites and classified as Eperythrozoon.
- They infect a range of mammalian species and cannot be grown in culture.
- Species in farm livestock that have been associated with disease are Mycoplasma (Eperythrozoon) ovis in sheep, M. suis in swine, and M. wenyonii in cattle.
- Additional forms have been identified in sheep and cattle, designated Candidatus Mycoplasma haemobovis and Candidatus Mycoplasma haemovis, respectively, and the taxonomy of the hemotrophic mycoplasmas is a work in progress.

Source and Transmission:

- The reservoir of infection is the persistently infected animal, and the disease can be transmitted by any mechanism that transfers infected blood.
- In sheep it is thought that the minimal infective dose is one parasitized erythrocyte. Horizontal and vertical transmission are possible.
- Seasonal differences in disease prevalence occur, being more common in the summer and autumn.
- This corresponds to increased vector populations but also to weaning of lambs and management procedures that may encourage spread, such as the multiple use of needles for vaccination.

Pathogenesis:

- Following experimental infection there is a variable prepatent period, usually 1 to 3 weeks, which is followed by a period of intense parasitemia.
- Ring-form, coccoid, and rod-shaped organisms are evident in stained blood smears.
- The organism is epicellular, infecting the surface and periphery of erythrocytes, and is also found free in the plasma in blood examinations.

- There is a profound hypoglycemia during the parasitemic phase, which is believed to be a result of direct consumption of glucose by the parasite.
- The period of intense parasitemia lasts for a period of 5 to 10 days, following which visible organisms in the blood become much less frequent and anemia develops.
- Parasitized erythrocytes are removed from the circulation by the spleen. It is believed that the parasite alters the erythrocyte membrane, exposing new antigenic determinants antierythrocyte antibodies.
- The severity and duration of the anemia vary between individuals, but the disease commonly lasts from 1 to 2 months. Upon recovery there may be further cycles of parasitemia and anemia, which are less severe.
- Sheep that develop a high antibody titer tend to rapidly clear the Parasitemia, whereas sheep that have a poorer antibody response tend to show persistent parasitemia and recurrent episodes of anemia. Once an animal is infected, it is probably infected for life.

Clinical findings:

Sheep

- Sudden death and deaths associated with exercise, accompanied by hemoglobinuria and icterus.
- The disease is manifest with fever and depression followed by the development of anemia, exercise intolerance, and ill-thrift.
- In some cases, it may be the principal cause of ill-thrift in lambs.
- There is reduced wool growth, and in the experimental disease in lambs at pasture, a retardation of growth of up to 2 kg has been recorded 5 weeks after infection.
- Lambs suckled by infected ewes are passively immunized via the colostrum until weaning.

Cattle

Clinical disease has been considered uncommon and has largely been a problem in cattle that have been splenectomized for experimental use, with disease occurring 1 to 4 weeks after the splenectomy.

However, clinical disease is recorded in adult commercial dairy cattle manifest with:

- Lassitude, stiffness
- Pyrexia, diarrhea
- Hind limb and udder edema, and a fall in milk production.

Eperythrozoonosis has also been associated with a syndrome occurring in heifers in early to midlactation, during late summer and early autumn, in which there was:

- Fever,
- Swelling of the teats and the hindlimbs.
- Lymph node enlargement.
- Fall in milk production.

Signs of infection resolved in 7 to 10 days, regardless of treatment.

A similar transient disease occurring in the spring and summer months, and manifest with scrotal and hindlimb edema and infertility, has been associated with eperythrozoonosis in young bulls.

Clinical pathology:

- **Blood Smears and Hematology** The presence of the organism can be established by examination of a blood smear taken during a clinical episode and when the animal has fever.
- Parasitemia is most intense before the development of clinical anemia and appears as 0.5- to 1.0-mm, coccoid, rod- or ring-shaped basophilic particles on red cells or free in plasma.
- Parasitemia is difficult to detect once clinical signs of disease are evident and very difficult in chronic disease.
- It is recommended that blood samples from a number of animals in the group be examined if eperythrozoonosis is suspected.

Treatment:

- A single intramuscular injection of tetracycline or oxytetracycline (3 mg/kg BW or more) is an effective treatment in sheep, with clinical improvement occurring in 24 hours in the early stages of the disease.
- Chronic infections are less responsive.
- Treatment of affected lambs with neoarsphenamine (30 mg/kg BW) or Antimosan (6 mg/kg BW antimony) is effective in relieving clinical illness but does not completely eliminate the parasite.
- Imidocarb dipropionate also is effective in treatment, but recrudescence at 2 to 4 weeks is common.

Control:

- Control of disease in sows and neonates has been reported with the inclusion of chlortetracycline in the sow feed at 300 g/ton or by intramuscular administration of oxytetracycline to sows at 14 and 7 days before the expected farrowing date.
- Tetracyclines can also be used in feed or by in-line water medication in feeder pigs.
- With large flocks of sheep in enzootic areas, reinfection or recrudescence occurs so quickly that control by treatment.

Blood protozoa in horses

1

Trypanosomosis or Surra

2

Equine piroplasmosis

3

Equine anaplasmosis

Trypanosomosis or Surra

Etiology:

Trypanosoma evansi (synonym *T. equinum*), a subspecies of *T. brucei*, but transmitted mechanically by biting flies, mainly tabanids, and by vampire bats in Latin America.

Morbidity and Case Fatality:

- Endemic disease of mainly horses, camels, and buffaloes in the tropics and subtropics, seasonality is related to fly population.
- Infection rates in camels, horses, and buffaloes in endemic countries vary considerably and can be as high as 100% in buffalo herds in high-risk areas.

Method of Transmission:

- Several hematophagous flies can transmit *T. evansi* mechanically, but the most important is the horse fly (*Tabanus* spp.), followed by the stable fly (*Stomoxys* spp.).
- Transmission is enhanced when horses or camels congregate or are closely herded and when they have high numbers of parasites in their blood.

Immune Mechanisms:

- Immune mechanisms are related to antigenic variation of the parasite and production of antibodies by the host, as in *T. brucei* and all its subspecies.
- Infected animals are also immunosuppressed and respond poorly to vaccination.
- As with other trypanosome infections, the immunosuppressive effect is abrogated following successful antitrypanosome treatment. The disease can be reproduced experimentally by blood inoculation.

Pathogenesis:

- Trypanosomes are inoculated into the host from the contaminated mouthparts of biting insects or the saliva of vampire bats.
- Parasites multiply in blood, causing anemia and spread to serous fluids and interstitial tissue, resulting in inflammatory changes nagana.
- There is just like those seen with *T. brucei*. The anemia of surra is probably similar to that of increased erythrophagocytosis and intravascular hemolysis resulting from lipid peroxidation of erythrocytes it has been suggested that protein breakdown and lipolysis might contribute to the cachexia in infected horses.
- In horses, *T.evansi* frequently invades the central nervous system, including the spinal cord, where it is less exposed to chemotherapeutic agents.

Clinical findings:

The main clinical findings are:

- Intermittent fever
- Progressive anemia,
- Edema of dependent parts of the body
- Dullness, listlessness, loss of body condition despite a good appetite
- Nasal and ocular discharge,
- Abortion and infertility.
- In the late stages, there are marked nervous signs, including:
- Marked paraplegia,
- Paralysis
- Delirium, and convulsions.

In a recent outbreak involving horses in Brazil, the nervous signs were:

- Ataxia blindness, head tilt, circling, head pressing, and paddling movements before death.

Surra is invariably fatal in camels and horses with death occurring in days or months, but camels may exhibit chronic signs for years. These signs include:

- A reduction in milk yield and capacity for work, and a high abortion rate in pregnant females. Abortion and high neonatal mortality characterized the camel outbreak in the Canary Islands.

In endemic areas, cattle and buffalo usually have a milder disease that may be exacerbated by stress from adverse climatic conditions, work, or intercurrent disease.

Signs may include:

- A reduction in milk yield and capacity for work
- Irregular estrus
- A high rate of abortion and stillbirth
- Poor semen quality in bulls.

Outbreaks of a more severe disease in indigenous zebu cattle are reported from time to time. Nervous signs and high mortality rate.

Clinical pathology:

- As with tsetse-transmitted trypanosomosis routine parasite detection is more reliable in the acute phase.
- Examination of wet blood films and stained smears of blood and lymph node should be carried out, and this should include the buffy-coat method.
- In the chronic phase, repeated sampling for some days may be required.
- In addition, suspected blood samples may be inoculated into rats or mice both of which are highly susceptible.

Necropsy findings:

- The carcass is emaciated and pale and may be icteric but, as in *T. brucei* infections, there are no pathognomonic gross and microscopic lesions unless the parasites are detectable. Infected horses will show hindquarter muscle atrophy, splenomegaly, and lymphadenomegaly.
- Asymmetric leukomalacia has been described in naturally infected horses, but it is not clear whether or not this was a result of treatment with diminazene aceturate.

Differential diagnosis:

- Nagana
- Malnutrition
- Helminthosis
- Babesiosis
- Anaplasmosis
- Hemorrhagic septicemia

Treatment and control:

Treatment

Drugs used for treating nagana could be used for surra, but the outcome is less favorable because of their low trypanocidal activity against *T. evansi* and their specific toxicity for camels and horses.

Furthermore, the drugs are not able to cross the blood–brain barrier to reach parasites in the cerebrospinal fluid and nervous tissue. As a result, relapses are common and may present as drug resistance.

Quinapyramine sulfate (quintrycide) is used curatively for camels, and diminazene aceturate (Berenil) is used for horses.

A water-soluble arsenical, melarsomine hydrochloride (Cymerlasan), given IM is recommended for camels at 0.25 mg/kg BW and for cattle at 0.5 mg/kg BW.

For both curative and prophylactic use, quinapyramine prosalt (trypacide), suramin (naganol), and isometamedium chloride (samorin or trypamidium) are recommended.

- Quinapyramine sulfate (Quintricide) (5 mg/kg SC) (R-1 for camels)(
- Diminazene aceturate (Berenil) (3.5–7 mg/kg IM) (R-1 for ruminants, R-3 for equine
- Melarsomine (Cymerlasan) (0.25 mg/kg IM for camels and 0.5 mg/kg for cattle) (R-1)
- Isometamedium chloride (Samorin) (0.25-1 mg/kg IM) (R-1 for ruminants)
- Suramin (Antrypol) (10 mg/kg IV) (R-2 for equines, camelids, 2–3 times weekly)

Control

- Isometamedium chloride (2 mg/kg IM) (R-1)
- Antrycide prosalt (7.4 mg/kg SC) (R-2)
- Suramin (Antrypol) (10 mg/kg IV) (R-2 for equines, camelids, 2–3 times weekly)

Equine piroplasmosis

Piroplasmosis of equids is a tick-borne infectious disease caused by the hemoprotozoan parasites *Theileria equi* and *Babesia caballi*. Piroplasmosis, also known as equine babesiosis (*B. caballi*), theileriosis (*T. equi*), or “biliary fever,” affects all equids, including horses, donkeys, mules, and zebras.

Infection with either or both of these obligate intraerythrocytic organisms can cause varying degrees of hemolytic anemia and associated systemic disease.

Etiology and Mortality rates:

- *Babesia caballi* and *Theileria equi*.
- Mortality rates in outbreaks of equine piroplasmosis can be high, but the predominant losses in horses result from the interference with racing and equine competitions and meetings.

Life Cycle and Transmission:

- The life cycles of both *T. equi* and *B. caballi* involve distinct developmental stages that occur in the host and tick.
- Both parasites progress via three stages: the sporozoite (asexual transmission stage), merozoite (asexual blood stage), and gametocyte (sexual blood stage).
- Development within the tick varies, depending on the tick species involved.
- Infective sporozoites are transmitted through tick saliva to the equid host.
- Once within the equid host, *B. caballi* sporozoites directly invade erythrocytes, where they multiply and develop into trophozoites, and then into merozoites.
- After erythrocyte rupture, merozoites are released and invade other erythrocytes.
- Transmission can also occur iatrogenically through inappropriate mixing of the infected and uninfected blood. This can occur during the practice of sharing needles among different horses, but use of any bloodcontaminated equipment could result in transmission.
- Infection can also result when chronically infected horses serve as blood donors to naive horses.

Clinical findings:

Horses with acute infection initially develop nonspecific signs, such as:

- High fevers, sometimes greater than 40° C (104° F),
- Lethargy
- Peripheral
- Edema
- Anorexia, and/or weight loss.
- Petechia caused by thrombocytopenia can be observed on mucous membranes, including the nictitating membrane.

Signs of hemolytic anemia follow and include:

- Icteric or pale mucous membranes, tachycardia, tachypnea, pigmenturia (linked to bilirubinuria or hemoglobinuria), and weakness.

Some horses show gastrointestinal signs, including:

- Colic or impactions, followed by diarrhea.

Other less common clinical signs include:

- A secondary development of pneumonia, pulmonary edema, cardiac arrhythmia, catarrhal enteritis, laminitis, and/or central nervous system signs, characterized by ataxia, myalgia, and/or seizures.
- Permanent or temporary infertility has been seen in stallions.
- Acute renal failure might occur as a result of hemoglobininduced pigment nephropathy.
- Systemic responses to severe inflammation (hypotension) can worsen the kidney disease.

Neonatal foals infected in utero with *T. equi* might present with severe and acute signs. Such foals can exhibit clinical signs at birth or can become ill at 2 to 3 days of age.

Clinical signs:

- Such as decreased suckling and weakness, are often nonspecific, but progress to resemble those of an infected adult horse (icterus, fever, and anemia).
- Cases of fetal and neonatal *B. caballi* infection have been reported but are rare.

Chronic *T. equi* or *B. caballi* infection usually results only in nonspecific signs, including:

- Weight loss, poor performance, partial anorexia, and/or lethargy.
- Mild anemia might be present, and the spleen might be enlarged.
- Splenomegaly appears to be caused by an increased rate of extravascular hemolysis within the spleen in less severely affected horses.
- Pregnancy in carrier mares can result in abortion or neonatal infection.

Clinical pathology:

Light microscopic examination of Giemsa stained blood smears can be used to identify piroplasms within erythrocytes.

Necropsy findings:

- Pathology might reveal jaundice, splenomegaly, haemorrhagic fluid within the pericardium, kidney degeneration, haemorrhages, and haemoglobinuria.
- Bone marrow should not be excluded as a potential reservoir site for *T. equi* and *B. caballi* in infected asymptomatic horses

Differential diagnosis:

- A syndrome of acute hemolytic anemia should suggest the following alternative diagnoses:
- Equine infectious anemia—has a much longer, recurrent course; usually occurs in sporadic cases; and is not associated with protozoa in body fluids and tissues
- Myoglobinuria—red urine is a result of myoglobinuria, always associated with elevation of serum creatine phosphokinase activity
- Foals with alloimmune hemolytic anemia detectable only upon laboratory examination for evidence of incompatibility between the serum of the dam and the foal's erythrocytes
- Other immune-mediated disorders
- Cardiac form of African horse sickness (AHS)—edematous lesions that occur are similar to those of babesiosis, but there is no evidence of hemoglobinuria or jaundice
- Equine viral arteritis virus, equine anaplasmosis, purpura hemorrhagica, and red maple leaf toxicity.

Management/Treatment:

- Management of tick-transmitted parasitic diseases relies on eradicating the vector tick and the development of effective vaccines.
- Treatment of diseased horses should include supportive treatment, especially with regard to anaemia.

There are a number of effective babesiacides:

- imidocarb dipropionate, which is often the only available drug on the market, and diminazene aceturate are the most widely used.
- For instance, diminazene aceturate has been mentioned to be effective in the chemosterilization of *B. caballi* and in the elimination of clinical signs in *T. equi* infections.
- Antitheilerial drugs such as buparvaquone have been shown to be effective in combatting disease due to *T. equi*.
- Imidocarb dipropionate (a carbanilide derivate) should be administered at a dosage of 2 mg/kg BW IM sid for 2 days in cases of *B. caballi* infection, and at a dosage of 4 mg/kg BW IM four times with a 72- hour interval in cases of *T. equi* infection.
- However, treatment with five consecutive doses of imidocarb dipropionate (4.7 mg/kg BW IM q 72 h) turned out to be unable to eliminate spontaneous *B. caballi* and *T. equi* infections from healthy carriers.
- Nevertheless, a high-dose regimen (4.0 mg/kg BW IM four times at 72-h intervals) of imidocarb dipropionate cleared *B. caballi* infection following inoculation with 105.2 *B. caballi* parasites. It should be mentioned that imidocarb dipropionate crosses the equine placenta.
- Cholinergic side effects of imidocarb may be alleviated by treatment with atropine.

Equine anaplasmosis

Etiology and Transmission:

- Equine anaplasmosis is a noncontagious infectious disease of horses caused by *Anaplasma phagocytophilum* (formerly named *Ehrlichia phagocytophila* and *Ehrlichia equi*) identified as emerging in Europe.
- Transmission and propagation of *A. phagocytophilum* occur in large mammals such as horses, cattle, sheep, goats, dogs, and cats. Small mammals and not ticks are the reservoirs of anaplasmosis.

Clinical signs:

The incubation period in experimentally infected horses varies from 1 to 9 days

Clinical signs include:

- High fever
- Depression
- inappetence
- petechiation
- Icterus, ataxia
- Rhabdomyolysis
- Distal limb oedema associated with lymphopenia, neutropenia, thrombocytopenia, and anaemia.

Extensive urticaria may also be associated with equine anaplasmosis.

The disease can be self-limiting when untreated, and the clinical signs abated and disappeared without specific treatment 7–14 days after onset of the disease.

However, infection with *A. phagocytophilum* can persist in the horse for at least 129 days although the continued presence of the organism is not associated with detectable clinical or pathological abnormalities.

It is unclear whether horses younger than 3–4 years of age generally experience less severe clinical disease. Occasionally euthanasia is required because of deterioration despite treatment.

Differential diagnosis:

Clinical signs are similar to those caused by infections with other pathogens such:

- *B. burgdorferi*, *B. caballi*, *Theileria equi*.
- Equine herpesvirus
- Equine infectious anaemia virus
- equine arteritis virus
- Viral encephalitides
- Leptospiraceae

Clinical pathology:

- Diagnosis of equine anaplasmosis is usually based on the detection of characteristic cytoplasmic inclusion bodies in peripheral blood; either morulae or elementary bodies are seen.
- In the neutrophilic and occasionally eosinophilic granulocytes on a Wright– Giemsa- or haematoxylin and eosin (H&E)-stained smear of peripheral blood obtained during days 3–5 of fever during peak ehrlichiaemia.

Necropsy findings:

Macroscopically, oedema of the ventrum and limbs may be present including subcutaneous petechiae.

Management/Treatment:

- The treatment of choice is oxytetracycline 7 mg/kg BW IV sid for 3–7 days to hasten recovery and alleviate clinical signs.
- Clinical immunity in experimental horses was shown to last 2 years.

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Babesiosis

Etiology:

- In dogs: *Babesia canis*, *Babesia gibsoni*, *Babesia conradae*.
- In cats: *Babesia felis*, *Babesia cati* (cats).
- Several other unnamed species (phylum Apicomplexa)

Mode of Transmission:

A variety of tick vector species; fighting or biting interactions; vertical transmission; blood transfusion

Clinical Findings:

In dogs:

Physical examination abnormalities in most dogs with babesiosis include:

- Fever, mucosal pallor, lethargy, splenomegaly, and bounding pulses.
- Fever is not consistently identified, because it often waxes and wanes.
- Tachycardia and tachypnea may be present in severely anemic dogs.
- Mucosal hemorrhages and/ or epistaxis may be present in dogs with *B. conradae* infection and excessive bleeding from venipuncture sites may be noted.

Dogs with severe babesiosis may show CNS signs such as:

- Incoordination, pelvic limb paresis, muscle tremors, nystagmus, anisocoria, intermittent loss of consciousness, seizures, stupor, coma, aggression, or vocalization.

Dogs with red biliary syndrome may have congested mucous membranes or icterus.

Other clinical abnormalities in dogs with severe babesiosis include:

- Tachypnea, increased lung sounds, and cardiac arrhythmias.

Occasionally owners note jaundice, mucosal pallor, or discoloration of the urine caused by bilirubinuria or hemoglobinuria.

In Cats:

Cats with Babesiosis show:

- Lethargy, anorexia, weakness, an unkempt haircoat, and/or diarrhea.
- Fever and icterus are less common.
- Anemia can be severe and is the underlying reason for the clinical signs.
- The disease is chronic, and signs may not be apparent until a later stage of illness.
- Cats usually adapt to the anemia and may have only mild clinical signs until they are stressed by handling.
- Complications of the hemolytic anemia have included hepatopathy, pulmonary edema, renal failure, CNS signs, and concurrent infections.

Diagnosis:

Initial diagnosis is made by examination of a blood smear.

- A large, clear, teardrop-shaped trophozoite organism in erythrocytes, sometimes seen in pairs, is representative of the three subtypes of *B. canis*.
- A much smaller, signet ring-shaped form occurring singularly and more frequently suggests subtypes of *B. gibsoni* or a Californian isolate genetically similar to *Theileria* species.
- An indirect fluorescent antibody (IFA) serum test is available but may be negative in early infections or display crossreactivity.
- A nested PCR test is most sensitive and can distinguish among canine babesial subtypes.
- A Coombs test is frequently positive in dogs with severe anemia related to a secondary immunemediate disease.

Differential Diagnoses:

- Hemoplasmosis
- Primary immunemediated
- Hemolytic anemia and/or thrombocytopenia,
- Other causes of hemolysis such as oxidative toxins or
- microangiopathic hemolysis (e.g., with splenic hemangiosarcoma).

- Canine monocytic ehrlichiosis,
- Rocky Mountain
- Spotted Fever
- Bacterial endocarditis should also be considered.

Treatment:

Dogs

Dogs generally show clinical improvement within 24 to 72 hours of treatment with antibabesial drugs, but some animals take as long as 7 days to respond (See Table 1).

Table 1: Selected Antibabesial Compounds Used in the Treatment of Dogs and Cats

Generic Name	Dose (mg/kg)	Route	Interval (hours)	Duration (days)	Organism			
					<i>Babesia canis</i>	<i>Babesia gibsoni</i>	<i>Babesia conradae</i>	<i>Babesia felis</i>
Imidocarb dipropionate†	5-6.6	IM	Once	Repeat in 14	+++	+	+	—
	7.5	IM	Once	NA				
Diminazene Aceturate	3.5-5	IM	Once‡	NA	+++	++	?	+
Azithromycin§ and Atovaquone	10	PO	24	10	+++	+++	+++	?
	13.3	PO	24	10				
Primaquine phosphate	0.5	PO	24	1-3	?	—	?	+++
	1 mg per cat#	IM	36	6	—	—	?	+++

+++, Very good; ++, good; +, fair to poor; —, not effective; ?, unknown.
 †For combination therapy, a dose of 3.5 mg/kg diminazene has been followed by a dose of 6.0 mg/kg imidocarb.
 ‡Not available in the United States, except by compassionate use. For *B. canis*, this dose is sufficient; for *B. gibsoni*, repeat dose in 24 hours. Total Dosages of 7 mg/kg or higher are associated with an increased risk of neural and parasympathomimetic toxicity.
 §These two drugs should be used in combination. Atovaquone must be given with a fatty meal to facilitate absorption. The suspension causes minimal gastrointestinal side effects.
 || Anecdotal evidence for activity against *B. canis*. Not effective in clearing the infection. Not recommended as sole therapy because of the potential to develop resistance. Further documentation needed to establish efficacy of this combination (see text).
 #Note that 1 mg/kg is a lethal dose.

Cats

- Treatment of feline babesiosis has not been as critically evaluated, but most antibabesial drugs appear ineffective.
- Primaquine phosphate, an antimalarial compound, administered orally or as an intramuscular injection, is currently the drug of choice (See Table 1).
- However, the effective dose, 0.5 mg/kg, is very close to the lethal dose (1 mg/kg).
- In experimental studies, rifampin and trimethoprim-sulfadiazine were not as effective as primaquine.

Supportive Care

- Other supportive care measures that may be required to treat animals with babesiosis are packed red blood cell transfusions and intravenous crystalloid fluid therapy.
- The administration of the plasma component of whole blood is unnecessary in the majority of dogs with babesiosis and can place the patient at risk of volume overload.
- If rehydration is required, crystalloid replacement solutions are preferable. Whether glucocorticoids are indicated to counteract the immune-mediated complications of babesiosis is controversial.
- In most dogs that require glucocorticoids, the glucocorticoid dosage can be tapered and discontinued within a 2- to 3-week period. Continued glucocorticoid therapy may predispose the animals to other infections and has the potential to induce babesial relapse.

Hemoplasmosis

Etiology:

Hemoplasmosis or hemotrophic mycoplasmosis, previously known as hemobartonellosis, is caused by a mycoplasma organism that infects the erythrocytes of dogs (*Mycoplasma haemocanis*) and cats (*M. haemofelis* and “*Candidatus M. haemominutum*”).

It can be transmitted by ticks and fleas or by queens to their newborn kitten in the absence of blood-sucking arthropods.

Splenectomy (especially in the dog), immunosuppression caused by glucocorticoid therapy, or stress in cats with latent *M. haemofelis* infection predispose to the development of clinical disease in the animal infected by the organism.

Clinical Features:

Signs and Their Pathogenesis:

- Because only *M. haemofelis* infection is associated with significant anemia in cats, only the pathogenesis of disease induced by this species is described here.
- After experimental infection, there is a delay of 2 to 34 days before the onset of clinical signs. Anemia then occurs and persists for about 18 to 30 days (acute phase), although its severity and chronicity vary considerably between infected cats.
- Anemia predominantly results from extravascular hemolysis, and the onset of anemia is usually followed by a strong regenerative response with reticulocytosis.
- The organism resides in an indentation on the erythrocyte surface. Production of both cold and warm reactive erythrocytebound antibodies, increased osmotic fragility, and decreased erythrocyte life span have been noted in infected cats.
- The organisms can also “bridge” adjacent erythrocytes, which might promote splenic trapping and removal of red blood cells. In contrast, erythrocyte-bound antibody formation and significant reticulocytosis have not been documented in cats infected with ‘*Ca. M. haemominutum*’ or ‘*Ca. M. turicensis*’.
- Anemia can result in signs of lethargy, inappetence, pallor, and weakness.

- Some owners report that their cats eat dirt or litter or lick cement (pica). Weight loss and dehydration can occur.
- Rapid development of anemia may result in neurologic signs, vocalization, collapse, and death.

Physical Examination Findings

- Physical examination findings in cats with acute *M. haemofelis* infection include fever, weakness, mucosal pallor, tachypnea, tachycardia, and weak or bounding femoral pulse quality.
- Other physical examination abnormalities can include dehydration, cardiac murmurs, splenomegaly, and occasionally mild icterus. Moribund cats may be hypothermic. Dogs with hemoplasmosis can show lethargy and mucosal pallor. Fever is usually absent.
- Cats infected with '*Ca. M. haemominutum*' or '*Ca. M. turicensis*,' and dogs infected with '*Ca. M. haematoparvum*' generally appear healthy unless concurrent disease is present

Pathologic Findings:

Generalized pallor, splenomegaly, and, in some cats, icterus are the main gross necropsy finding in cats that die or are euthanized as a result of hemoplasmosis.

Histopathologic findings include:

extramedullary hematopoiesis, follicular hyperplasia, and erythrophagocytosis within the spleen.

Diagnosis:

Laboratory findings generally reflect a strong regenerative response in the CBC. The absence of marked anisocytosis or polychromasia in confirmed cases of feline hemoplasmosis may suggest peracute infections with too little time to respond or concurrent infection with feline leukemia virus (FeLV) or feline immunodeficiency virus (FIV).

- Thin smears, made directly without anticoagulant, assist in finding the epicellular organisms. Blood films should be well stained without precipitate to minimize any confusion in identifying the parasite.
- Cats often have coccoid or ring shapes, whereas dogs mostly have linear chain forms.
- A positive Coombs test result may be associated with feline hemoplasmosis, presumably because of erythrocyte membrane alteration.
- PCR-based assays are available for the diagnosis of hemoplasma infections in cats.

Treatment:

- Consider whole blood transfusion if the anemia is severe.
- Prednisolone (2mg/kg PO q12h) may be necessary initially to suppress the severe immune-mediated destruction of erythrocytes.
- Doxycycline (5 mg/kg PO q12h for 4 weeks) is preferred for dogs and cats.
- Enrofloxacin (5 mg/kg PO q24h for 14 days) can be used in cats intolerant of doxycycline.
- Cats who recover may become latent carriers.

Immunity and Vaccination:

- Little information is available in regard to the immune response to hemoplasma infection, and no vaccines are available.
- Because co-infections with multiple hemoplasma species occur, infection with one species does not appear to protect against infection with other species.

Cytauxzoonosis

Etiology:

- Cytauxzoonosis is an emerging, life-threatening infectious disease of domestic cats (*Felis catus*) caused by the tick-transmitted protozoan parasite *Cytauxzoon felis*. *Cytauxzoon* spp are apicomplexan parasites within the family Theileriidae along with their closest relatives of *Theileria* spp.
- *C felis* is transmitted to domestic cats by the lone star tick (*Amblyomma americanum*).
- The natural host for *C felis* is the bobcat (*Lynx rufus*); reservoir hosts of the parasite include bobcats and domestic cats that survive infection.

Transmission and Risk Factors:

- *C felis* is transmitted by the lone star tick, *A americanum*. Cytauxzoonosis is typically diagnosed during April through September, which correlates with climate-dependent seasonal tick activity.
- Cats living near heavily wooded, low-density residential areas particularly close to natural or unmanaged habitats where both ticks and bobcats may be in close proximity are at highest risk of infection.
- Oral and "cat-to-cat" transmission does not occur.
- Vertical transmission may not occur commonly, if at all.

Clinical Findings:

Onset of clinical signs for cats infected with *C felis* usually occurs 5–14 after infection by tick transmission.

Nonspecific signs such as:

- Depression, lethargy, and anorexia are the most common presenting problems.
- Pyrexia and dehydration are the most common findings on physical examination; body temperature, which increases gradually, can be as high as 106°F (41°C).
- Other findings include: icterus, lymphadenomegaly, and hepatosplenomegaly.
- In extremis, cats are often hypothermic, dyspneic, and vocalize as if in pain.

- Without treatment, death typically occurs within 2–3 days after peak in temperature.

Lesions:

- At necropsy, splenomegaly, hepatomegaly, enlarged lymph nodes, and renal edema are usually seen.
- The lungs show extensive edema and congestion with petechial hemorrhage on serosal surfaces and throughout the interstitium.
- There is progressive venous distention, especially of the mesenteric and renal veins and the posterior vena cava.
- Hydropericardium is often seen with petechial hemorrhage of the epicardium.

Clinical pathology:

- The most common abnormalities on the CBC in animals with cytauxzoonosis include leukopenia with toxic neutrophils and thrombocytopenia with a normocytic, normochromic anemia seen at later stages.
- The most common biochemical abnormalities are hyperbilirubinemia and hypoalbuminemia but may vary depending on organ systems affected by parasitic thrombosis and ischemia with tissue necrosis.
- Other, less consistently detected abnormalities include increased liver enzyme concentrations and azotemia.
- Rapid diagnosis requires microscopic observation of piroplasms or schizonts. Observation of piroplasms on blood smears is variable; they are seen in association with increasing body temperature and typically become apparent approximately 1–3 days before death.
- There are anecdotal reports of a higher level of sensitivity when blood is collected from smaller vessels (eg, ear vein prick) to prepare blood smears. On a well-prepared, well-stained (Wright-Giemsa, Giemsa, Romanowsky most commonly) blood smear, when detectable, merozoites may be seen ranging from 1%–4% on average, with extremely high percentages (ie, >10%) reported in some cases.
- They are pleomorphic and may be round, oval, anaplasmod, bipolar (binucleated), or rod-shaped; however, the round and oval piroplasm forms are most commonly seen.
- Smears must be examined carefully to exclude *Mycoplasma haemofelis*, Howell-Jolly bodies, stain precipitate, and water artifact.

Treatment and Control:

- Historically, attempts to treat cytauxzoonosis with a variety of antiparasitic drugs (parvaquone, buparvaquone, trimethoprim/sulfadiazine, sodium thiacetarsamide) have been met with little success.
- In one study, five of six cats and one additional cat were successfully treated with diminazene aceturate (not approved in the USA) and imidocarb dipropionate (2 mg/kg, IM, two injections 3–7 days apart), respectively.
- The most consistent successful treatment in a large case series resulted in survival of 64% of cats given a combination of atovaquone (15 mg/kg, PO, tid for 10 days) and azithromycin (10 mg/kg/day, PO, for 10 days) and supportive care.
- Supportive care, including IV fluid therapy and heparin (100–200 U/kg, SC, tid) should be instituted in all cases.
- Nutritional support via an esophageal or nasoesophageal feeding tube is recommended, which also facilitates administration of oral medications (eg, atovaquone and azithromycin).
- Oxygen therapy and blood transfusions should be administered when necessary.
- Anti-inflammatory drugs may be warranted in cases with unrelenting fever; however, the use of NSAIDs is contraindicated in cats with azotemia or dehydration.
- Once a diagnosis is achieved and treatments have begun, minimal stress and handling are recommended.
- Recovery, including resolution of fever, is often slow and may take as long as 5–7 days.
- Cats that survive have a complete clinical recovery, including resolution of hematologic and biochemical abnormalities within 2–3 wk.
- Some survivors remain persistently infected with piroplasms and may represent a reservoir of infection.
- In one study, dose-intense diaminazene diacetate (4 mg/kg/day, IM, for 5 consecutive days) failed to reduce the severity of parasitemia in cats chronically infected with *C. felis* and resulted in adverse drug reactions.

Prevention:

Routine application of a tick preventive is recommended to prevent cytauxzoonosis; however, disease has occurred in cats despite this treatment.

Ehrlichiosis and anaplasmosis

Etiology:

The brown dog tick *Rhipicephalus sanguineus* is the arthropod vector of *E. canis*. Although vector ticks do not serve as reservoirs of infection, they are able to harbor infectious organisms for over 1 year and can transmit the infection to susceptible dogs for at least 155 days following infection.

Phagocytophilum is a gram-negative obligate intracellular parasite. Subsequent to the reclassification of ehrlichiae, the term 'granulocytic ehrlichiosis' has been replaced with granulocytotropic anaplasmosis. Occurrence of infection follows the distribution of *Ixodes* spp tick vectors and is similar to that of canine Lyme borreliosis.

Pathophysiology:

Canine monocytotropic ehrlichiosis is characterized by a reduction in cellular blood elements. *E. canis* is characterized by three distinct phases of infection:

- Acute (weeks) subclinical (months to years), and chronic (months).

During the acute phase:

- The organism multiplies within circulating mononuclear cells and the mononuclear phagocytic tissues of the liver, spleen, and lymph nodes. Infected cells are transported in the blood to other tissues particularly meninges, lung, and kidney, where they attach to the vascular endothelium, causing vasculitis and infection of the subendothelial tissue.
- During this phase thrombocytopenia develops subsequent to platelet consumption, sequestration, and destruction.
- Anemia develops progressively owing to suppression of erythropoiesis and accelerated destruction of erythrocytes during the subclinical phase there is variable persistence of the thrombocytopenia, leukopenia, and anemia.

Chronic disease:

Occurs in those dogs unable to mount an effective immune response to the organism.

The actual mechanism whereby *A. phagocytophilum* causes clinical disease is unknown:

- The bacteria enter neutrophils by endocytosis, where they become incorporated into phagosomes.
- Morulae are formed within the phagosome subsequent to replication. Infection occurs only after an extended feeding time by the Ixodes tick lasting at least 24–48 hours.
- Clinical signs develop of infection are described 1-2 weeks following infection.
- Acute and chronic phases of infection are described.

Clinical signs:

- Classically, canine monocytotropic ehrlichiosis is categorized into three phases.
- **The acute phase** begins following a 1–3-week incubation period and lasts for 2–4 weeks.
- Clinical signs of illness are varied and include:
 - Fever, nasal discharge, decreased appetite, weight loss, and lymphadenomegaly.
 - Clinical signs typically resolve spontaneously.
- **During the subclinical phase**, at 40–120 days post infection, clinical signs are absent, although the infection is still established. The subclinical phase can persist for several years.
- In some dogs a chronic phase of infection will develop and is characterized by either vague signs of illness or more severe hematologic impairment associated with bone marrow suppression. Profound pancytopenia may develop.
- Spontaneous bleeding, characterized as dermal petechiae or ecchymoses, is common.
- Epistaxis is most frequently reported by owners.
- In other cases profound neurologic signs such as seizures, ataxia, vestibular dysfunction, and anisocoria, as well as hyperesthesia have been observed.
- The spectrum of clinical signs associated with ehrlichiosis is further complicated by the fact that they can vary dramatically depending on the species involved.
- Clinical findings range from polyarthritis associated with immune complex arthritis or hemarthrosis, to atrophy of skeletal muscles, enlarged peripheral lymph nodes, edema and lethargy.

Clinical signs associated with granulocytotropic anaplasmosis are vague and indistinct.

It is currently not known whether all infections lead to the development of clinical signs.

Most dogs are reported to develop fever and lethargy, with associated anorexia.

Generalized nonlocalizing pain is described in most dogs. Dogs may appear weak, stiff, or lame. Discrete joint pain is uncommon.

Thrombocytopenia and granulocytopenia are spontaneous and are infection appears shortlived and reinfection is possible.

Differential diagnosis:

Immune-mediated thrombocytopenia is an important differential diagnosis to consider when evaluating a patient suspected of having ehrlichiosis, but not granulocytotropic anaplasmosis.

Affected dogs may also have concurrent immune-mediated hemolytic anemia.

The presence of other clinical signs (neurologic signs, peripheral limb edema) and laboratory findings (leukopenia) significantly expands the list of differential diagnoses. Dogs with granulocytotropic anaplasmosis may appear to have:

- Lyme borreliosis
- Toxoplasmosis (myositis)
- Systemic lupus erythematosus
- Bacteremia sepsis
- Or any of a multitude of system disorders

Treatment/prognosis:

- Although several inexpensive drugs are available, the success of treatment of ehrlichiosis is generally dependent on the severity of disease and the ability to treat early in the course of infection.
- Dogs with chronic ehrlichiosis are particularly difficult to treat and have a commensurately poor prognosis.
- Doxycycline (5–10 mg/kg PO q12h for 10-21 days) is the preferred treatment for acute infection.
- Significant clinical improvement may be noted within 1-2 days.
- However, the treatment duration is justifiably extended to 6 weeks depending on clinical response. The cost of treatment combined with the dramatic resolution of clinical signs

justifies the empiric administration of antibiotic to treat ehrlichiosis in the absence of a confirmed diagnosis.

- In fact, a presumptive diagnosis of ehrlichiosis can be based on response to therapy alternatively, minocycline (10 mg/kg PO q12h) can be given for 10 days with similar results expected.
- Tetracycline and oxytetracycline are still considered effective but they should be given three times daily and may be associated with mild side-effects.
- Since the tetracyclines including doxycycline will produce yellow discoloration of erupting teeth, it is feasible to recommend chloramphenicol (15-25mg/kg PO, IV, or SC q8h) for at least 2 weeks in dogs less than 6 months of age.
- Failure to respond to conventional oral antimicrobial therapy may denote the presence of a resistant infection. Imidocarb dipropionate (5 mg/kg IM once, repeated in 2-3 weeks) is recommended.
- The role of short-term corticosteroid therapy in the early treatment of ehrlichiosis is controversial. In the clinical setting it may be difficult quickly to distinguish between immune-mediated thrombocytopenia and ehrlichiosis. As a result, initial empiric therapy of thrombocytopenic dogs is justified and includes both immunosuppressive levels of prednisolone (1-2 mg/kg PO q12h for 7-10 days) plus administration of an appropriate antimicrobial (e.g. doxycycline).
- The recommended treatment for canine granulocytotropic anaplasmosis is doxycycline (5-10 mg/kg PO q12h for 10 days).

Prevention:

- There is currently no vaccine available for the prevention of ehrlichiosis or anaplasmosis.
- Short-term preventive measures include oral administration of tetracycline (6.6 mg/kg/day) or doxycycline (10 mg/kg/day) for dogs living in endemic areas.
- In addition, efforts to manage tick infections using oral or topical acaricidal products are recommended.

Trypanosomiasis

Chagas' disease, or American trypanosomiasis, is a zoonotic, vectorborne disease transmitted by triatomine bugs and caused by *T. cruzi*.

All mammals are considered susceptible to infection, with infection demonstrated in >100 mammalian species. Avian species are not susceptible.

The disease is best recognized in dogs and people, with dogs serving as a major domestic reservoir.

Domestic cats can also be infected, but their role as reservoirs for human infection is limited.

Etiology:

Trypanosoma cruzi, a protozoan parasite (phylum Sarcomastigophora, family Trypanosomatidae)

Mode of Transmission:

- The nocturnal and hematophagous triatomine insects of the *Triatoma*, *Rhodnius*, and *Panstrongylus* genera serve as vectors for *T. cruzi*. Common names include the “kissing bug,” “assassin bug,” “cone-nosed bug,” “vinchuca,” “chinche,” and “barbeiro.”
- Insects take an infected blood meal ingesting extracellular *T. cruzi* trypomastigotes. These differentiate in the midgut to epimastigotes and divide.
- Epimastigotes travel to the hindgut, where they differentiate back into metacyclic trypomastigotes. Infective metacyclic trypomastigotes are shed in insect feces.
- In insectivorous animals, including dogs, consumption of infected bugs or materials contaminated with infected triatomine feces is a major mode of transmission.
- Additional methods of transmission include transplacentally or via blood transfusions and organ transplant.

Pathogenesis:

- Once metacyclic trypomastigotes enter the bloodstream, they actively invade many cell types, exiting the parasitophorous vacuole and becoming nonflagellated amastigotes. Intracellular amastigotes divide every 15–18 hr for 5–6 days.
- *T. cruzi* transforms back into trypomastigotes and lyses the cell. Released trypomastigotes invade new cells.
- *T. cruzi* has a tropism for cardiac and smooth muscle but can be found in numerous other tissues.

Clinical Findings and Lesions:

- Chagas' disease is divided into acute and chronic phases, with the chronic phase further subdivided into latent and symptomatic chronic disease.
- Incubation ranges from 5–42 days before acute disease.
- Acute infections may be asymptomatic or consist of nonspecific febrile illness with a chancre at the site of parasitic entry.
- Dogs may also present with regional or generalized lymphadenopathy, anorexia, lethargy, vomiting, diarrhea, and hepatomegaly or splenomegaly.
- Rarely, acute clinical myocarditis is seen.
- Parasitemia peaks 2–3 wk after infection and dissipates after the first month as the organism moves to predominantly tissue-borne disease.
- The latent phase can last for months to years. Chronic disease symptoms can include generalized weakness or sudden death. Symptomatic dogs commonly present with right-side congestive heart failure.
- This can progress to myocarditis, with arrhythmias and bilateral cardiac dilation.
- Death secondary to heart failure is common.

Diagnosis:

- Diagnosis of Chagas' disease can be made by visualization of the organism, detection of DNA, or antibody detection.

- Parasitemia during the acute phase allows for detection on a microscopy of a routine peripheral blood smear.
- Although samples can be tested for T cruzi DNA by PCR or cultured, these diagnostic tests are uncommon in the field.
- On Giemsa stain, T cruzi is an extracellular, C-shaped protozoan with a single flagellum.

Differential Diagnoses:

The differential diagnoses for suspected Chagas' myocarditis include:

- Dilated cardiomyopathy of large-breed dogs
- parvoviral myocarditis in puppies
- Canine monocytic ehrlichiosis
- babesiosis, and leishmaniosis

The primary differential diagnoses for suspected Chagas' meningoencephalitis in puppies are:

- Canine distemper virus infection
- neosporosis
- Other infectious and inflammatory causes of meningoencephalitis should also be considered.

Treatment:

- Benznidazole is the drug of choice for treatment, but nifurtimox can also be used.
- In dogs, benznidazole is administered at 5–10 mg/kg/day, PO, for 2 mo.
- Symptomatic treatment for heart failure and arrhythmias is also recommended.

Treatment:

- No vaccine is available; thus, control focuses on preventing disease transmission.
- Vector control methods include pesticide application to eliminate triatomine vectors and decreasing vector attraction to dwellings at night by turning off outdoor lighting.
- Breeding of positive bitches is discouraged.

- Screening of blood donors is recommended.
- To avoid iatrogenic transmission, disinfection with 10% bleach or 70% ethanol is suggested for contaminated surfaces.
- Dead infected insects can remain a source of infective *T. cruzi* for up to 6 days at 10°C or up to 2 mo at 26°–30°C.