Canine Distemper

Etiology

Distemper is caused by a paramyxovirus that causes a severe multisystemic fatal disease including respiratory, enteric and CNS signs. It is closely related to human measles virus and a number of other multisystemic severe diseases of animals such as herbivores, pinnipeds, and cetaceans.

Pathogenesis

As a multisystemic disease, virus must spread to many tissues as the course of infection. Serum antibody is protective against viral spread and the level at the time of infection is critical in determining the course of illness. Systemic spread can infect epithelial tissues causing severe multisystemic illness and this occurs with the lowest level of immunity. During the systemic spread, virus can enter the CNS when there is no protection or partial protection by serum antibody. CNS infection occurs after this systemic illness; however the course of infection within the CNS can either be directly caused by the virus or be a result of the body’s immune response to the presence of virus. In the latter case, dogs have an intermediate level of immunity, and the subsequent involvement of the CNS can develop months to years later.
Clinical Signs

The clinical signs of systemic CDV infection usually proceed the development of neurologic signs. However, neurologic signs can occur in the absence of other systemic manifestations. Old dog encephalitis is a chronic persistent form of latent CDV in the CNS.

Diagnosis

Clinical suspicion—in practice is the usual means and is easiest in the multisystemic versus the neurologic form. Clinical pathologic changes include erythrocyte inclusions and a nonsuppurative CSF. Radiography of the thorax will show viral pneumonia with secondary bacterial infection.

Immunocytology should be done, only in the acute phases of illness. The direct method can be used to examine scrapings of conjunctiva, tissues, blood, CSF, or urine. The chart below shows the proper timing. This test is not as sensitive as PCR and a negative does not eliminate the disease from consideration.

<table>
<thead>
<tr>
<th>FA (Acute)</th>
<th>(Chronic)</th>
</tr>
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<tbody>
<tr>
<td>Conjunctiva</td>
<td>Foot pad</td>
</tr>
<tr>
<td>Transtracheal wash</td>
<td>CNS – encephalitis</td>
</tr>
<tr>
<td>CSF</td>
<td>Lung</td>
</tr>
<tr>
<td></td>
<td>Ocular - chorioretinitis, optic neuritis</td>
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It is important to understand the timing of direct immunofluorescence for antigen in confirming infection. Acute infections are within 1 week and have epithelial signs. Chronic persistent infections are considered to last longer than week however the persistence is hidden **only** in nervous and ocular tissues (rarely lung and foot pad). This particular hidden infection is not eliminated by systemic antibody response.

Serologic detection of antibody titers can be helpful for determining the possibility of infection.

Rising IgG titers or IgM single titers are considered for systemic disease (timing for antibody determinations is later than antigen in immunocytology). Therefore for acute disease, a single IgM or paired IgG titer can be used to detect recent or active infection. The antibody titers are also protective and can be used to measure seroprotection when the appropriate type of test is used.
For CNS infections a comparison is made between serum versus CSF IgG. Using this and another titer or measure an antibody index or ratio can be calculated. It is ideal to compare this ratio with another tested antigen.

<table>
<thead>
<tr>
<th></th>
<th>Serum</th>
<th>CSF</th>
<th>Ratio CSF/serum</th>
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<tbody>
<tr>
<td>CDV</td>
<td>280</td>
<td>28</td>
<td>1/10 (.10)</td>
</tr>
<tr>
<td>ICH</td>
<td>16</td>
<td>4</td>
<td>1/4 (.25)</td>
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Which Ratio (Fraction) is greater? That for distemper or ICH? Does this indicate distemper or not?

PCR has been used to detect viral genome in tissues and body fluids. The results are very promising for diagnosis of CNS distemper when the virus can be detected. However, when viral levels are so low, it may be undetectable.

**Prevention**

Human measles and CDV are related and measles vaccine has only been used in the 6-12 week interval. It may be substituted as the first inoculation in a series when concurrent parvoviral exposure is anticipated or postvaccinal complications are suspected. Measles and distemper products are often combined making the derived benefit in parvovirus infections less advantageous.

Vaccinations for distemper in puppies are usually started at 6 to 8 weeks of age. At this age a minimum of at least 3 vaccinations, 3 to 4 weeks apart should be given, followed by a yearly booster. If an animal presents at an older age they still need at least 2 distemper vaccines for solid primary immunity if no other vaccines have been given.

There are some important and unique features of distemper vaccination. Elevated rectal temperature has an effect on the immune response as 103.6°F rectal temperatures suppress the antibody titer. Distemper vaccine can also be given in the face of an outbreak to dogs that either have a lapse in their immunity or have been exposed. Parenteral administration of vaccine can thwart canine distemper that is incubating within 4 days of exposure. It is important to remember that we are concerned with exposure and not clinical illness!

Vaccination with MLV CDV vaccine provides the greatest chance for postvaccinal disease of any canine biologic. Concurrent diseases or immunosuppression and canine distemper vaccination pose the potential problem of postvaccinal canine distemper encephalitis. Post vaccinal systemic disease such as HOD has also been observed in some breeds. These vaccine reactions may be strain dependent.

Attempts to use inactivated distemper vaccines in the past have failed. Onset and duration of immunity has been limited with inactivated products. A recombinant distemper vaccine (Recombitek, Merial) consists of a canary pox vector.
Current strains of CDV vaccine are Rockborn, Snyder Hill, Onderstepoort, and Recombinant.

The Rockborn is the most immunogenic but has a risk of postvaccinal disease. Onderstepoort is an intermediate potency. The recombinant is relatively safe and recent studies have shown a strong protective response. It was comparable to MLV in previously vaccinated dogs and shelters. The long-term duration of immunity is currently being studied.

**Prognosis**

The prognosis for treating dogs with distemper is relative to the presence or absence of neurologic signs and the type of neurologic signs that they exhibit. Seizures, myoclonus, encephalitis and myelitis can all develop. Seizures and myoclonus, both signs of the inflammatory condition can be allowable without causing problems in many cases; however seizures often require anticonvulsant therapy. If the CNS damage progresses with continual inflammation, then the prognosis will worsen. Euthanasia is based upon neurologic signs and their incompatibility with life. The immune process is important in the progression of chronic distemper and vaccine-induced encephalitis. A vitamin P deficiency has been established for the chronic progressive inflammatory forms of CDV encephalomyelitis.

**Canine Viral Enteritis**

**Canine Parvovirus (CPV-2) Infection**

Studies on pound dogs, family dogs, and samples submitted to state diagnostic laboratories have shown that parvoviral diarrhea is more severe and prevalent than all other cause of viral diarrhea. Bloody diarrhea, fever, leukopenia and death are much more likely to be associated with parvoviral diarrhea than coronaviral or parasitic diarrheas. ELISAs have been developed to measure serum antibody to, and fecal presence of parvovirus. The fecal antibody tests measure viral antigen in the feces. Modified-live canine vaccine strains shed in the feces and can cause weak positive reactions. Currently available products licensed through veterinarians are usually potentiated, which means they break through maternal immunity more effectively. Vaccines available through other sources and over the counter may still contain conventional parvoviral antigen.

Two types of vaccines are available for parvovirus: killed and modified-live virus.

<table>
<thead>
<tr>
<th></th>
<th>Killed-canine</th>
<th>MLV-canine</th>
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<tbody>
<tr>
<td>Shed virulent after exposed</td>
<td>+</td>
<td>-</td>
</tr>
<tr>
<td>Shed vaccine virus</td>
<td>-</td>
<td>+</td>
</tr>
<tr>
<td>One vaccine protects without maternal Ab.</td>
<td>-</td>
<td>+</td>
</tr>
</tbody>
</table>
Relative maternal antibody breakthrough  +  ++
Relative duration of immunity  +  ++

Conventional products: In the past vaccine manufacturers have claimed that their (conventional) vaccines “broke through” maternal immunity as early as 6 weeks of age. Although it is difficult to compare parvoviral titers between laboratories, the titers shown in the litters protected by such vaccination programs were low. For this reason, a complete series, with vaccines given every three weeks until the dogs are 16 weeks old, has been recommended. For safety sake with certain breeds that have notoriously poor responses, vaccines can be used out to 18 weeks of age. These breeds include Dobermans, Rottweilers, (some studies also suggest increased susceptibility for English springers, Dalmatians, Siberian huskies, German shepherds, Labradors, and greyhounds). Conventional products are still sold at feed stores and in catalogs.

Potentiated products: high titer, lower passage (“potentiated”) vaccines are now in use by most major manufacturers. They provide protection as early as 12 weeks of age in most puppies. The use of potentiated Parvo products has been associated with a greater prevalence of allergic (Big Head) reactions.

Some manufacturers have products containing newer parvoviral strains (CPV-2b). A shifting of antigenic determinants and genetic composition of canine parvovirus has taken place at least twice. Cross-protection still exists between the old strains in the vaccine and the new field strains. Vaccine breaks that occur in dogs that seemingly went through a "good" vaccine schedule are probably accounted for by maternal antibody blockade. Increased virulence of the new parvoviral strains might explain more severe illness that is detected in some dogs that become infected. The CPV-2b strain may infect cats. What relationship this has to the resurgence of FPV is uncertain. Gross protection exists between FPV vaccines and virulent CPV-2b strains.

CPV-1 outbreaks have been associated with neonatal or in utero mortality and may be responsible for diarrhea and reported vaccine breaks in very young puppies. CPV-2 immunodiagnostic tests do not cross-react with CPV-2. Since the CPV-1 disease looks grossly and microscopically like CPV-2 infection, cultural diagnosis is impractical but essential to separate them.

Canine Coronaviral Infection

Infection with CCV is less severe than that with canine parvovirus (CPV). Viremia and generalized tissue infections seen with CPV are not found with CCV infection because the latter infection is localized to the intestinal tract. Nevertheless, CCV infection can increase the severity of that seen with CPV infection alone. Most recently, a more virulent disease-producing strain of canine coronavirus has been reported. More severe morbidity, and in some cases mortality, has been reported. There are several products licensed for protection against canine coronavirus (CCV) infection. These are inactivated strains, either of canine (Fort Dodge, Pfizer, and
Greene, Chicago VMA 2006

others) or feline-strain origin (Schering Plough), and one modified-live product from Merial. Further work needs to be done to see if these vaccines protect against the more virulent strain of coronavirus. It is recommended that at least 2 vaccines be given at an interval of 2 to 3 weeks, beginning at 6-8 weeks of age. However, puppies <12 weeks of age should be given an additional dose between 12 and 16 weeks of age. There are few adverse reactions with these products and they do not interfere with other biologics. Combinations of inactivated coronavirus vaccine with leptospirosis fraction have resulted in increased allergenicity. This has been overcome by reducing excessive protein fractions in the leptospirosis bacterins. Still combination of leptospiral and inactivated coronaviral vaccines in the youngest of pups may potentiate allergic reactions. I do not recommend this combination in pups less than 9 weeks unless the MLV coronaviral vaccine is used.

Although duration of immunity to challenge with CCV has not been established for longer than 2 to 3 weeks, protection is probably of longer duration. During challenge studies, vaccinates had reduced intensity of viral replication in their intestinal epithelial cells. Because of the additional cost to clients for coronaviral protection, vaccination may not be recommended routinely but rather when clients desire all possible disease prevention in areas where endemics occur with CCV. If the vaccines are shown to protect against the new virulent strains, then more widespread and routine vaccination will be recommended.

Tracheobronchitis

Etiology

Kennel cough in dogs is a clinical syndrome with several and often combined causative agents. Experimental studies have shown that concurrent *Bordetella* and canine parainfluenza virus (CPIV-2) infections in dogs cause more severe disease than with infections caused by either organism alone. Furthermore, combined infections produced predominantly lower airway disease. Other viruses such as canine adenovirus-2 and avian influenza viruses have been documented to cause respiratory infections in dogs.

Treatment

Kennel cough usually resolves on its own. Severe or persistent infections are caused by secondary invading bacteria such as *Bordetella bronchiseptica*.

Prevention

Lipopolysaccharide (LPS) has been responsible for the allergic reactions produced by some of the early parenteral bacterins for bordetellosis. Several methods have been used by manufacturers to eliminate the LPS from these products and this may affect their efficacy and side effects. Most are composed of purified extracted antigen from
bacterial cell. This modification allows for reduced local allergic reaction following 
injection and vaccination can begin at 6 weeks of age and is safe for pregnant animals. 
It is recommended that animals receive at least 2 doses, 2 to 4 weeks apart.

Intranasal vaccines for tracheobronchitis produce more rapid and effective secretory 
antibody production as compared to inactivated parenteral products. They can provide 
protection within a short time interval after a single administration which is not the case 
with inactivated parenteral products.

Recent studies show that a combination of both intranasal and parenteral vaccines may 
provide the best protection following the neonatal period.

Boostering with intranasal products can precede hospitalization or kenneling when 
upper respiratory disease is known to be a problem. In some cases the intranasal 
products can produce postvaccinal upper airway infections in dogs.
LEPTOSPIROSIS: EMERGING OR SURGING?
Craig E. Greene, University of Georgia

Etiology and Epidemiology

Leptospirosis, a zoonotic disease of worldwide importance, is caused by infection with antigenically distinct serovars of the parasitic species *Leptospira*. Leptospires are thin filamentous motile bacteria made up of fine spirals. Their central core is a protoplasmic cylinder wound about an axial filament that produces their motion. The outer envelope is an antigenic mucopeptide, which is responsible for the immune response. Much confusion about the classification of leptospires is based upon the fact that serogrouping has been used in the past, while this overlaps with the newer classifications based upon genetic methodologies. Based upon genetic analysis, *Leptospira interrogans sensu lato* includes at least eight species. For those serovars of pathogenic importance, the species *L. kirschneri* contains serovar *grippotyphosa*, while species *L. interrogans sensu stricto* contains serovars *hardjo*, *bataviae*, *canicola*, *pomona*, *icterohaemorrhagiae*, *autumnalis*, and *bratislava*. Serovars are maintained in nature by numerous subclinically infected wild and domestic animal reservoir hosts that serve as a potential source of infection and illness for humans and other incidental animal hosts. The organism and its maintenance hosts appear to undergo adaptation to their environment, and these host preferences and pathogenicity can change with time and geographic region. Due to vaccination, the prevalence of disease caused by *L. canicola* and *L. icterohaemorrhagiae* has decreased, while there is increasing evidence that the other serovars are becoming more prevalent in producing disease. Encroachment of domestic dogs on the environment of wildlife reservoir hosts in rural or suburban environments is another factor increasing prevalence.

Leptospirosis was first recognized as a cause of acute fatal illness in dogs in Europe in the 1930’s. Subsequent reports were confirmed in North America. Manifestations of both hepatic and renal failure were recognized and the disease was rapid and progressively fatal because of the lack of effective chemotherapeutic agents or vaccines. Since the advent of antibiotics and leptospiral vaccines, the disease became less common and severe, and many veterinarians have discontinued their use of the vaccines. In the last two decades, there have been increasing reports of leptospirosis in dogs caused by strains other than used in vaccines and the clinical syndrome is more of an insidious onset of chronic renal or hepatic failure. The disease caused by *grippotyphosa* has been present in kenneled hunting dogs in the southeastern United States. In the northeastern states, *pomona* has predominated and in the western coast *bratislava* and *pomona*. *L. australis* has been documented as the cause of chronic hepatitis in dogs in France. In Southern Germany, the predominant serovars in decreasing order have *grippotyphosa*, *saxkoebing*, *bratislava*, and *seroje*. The awareness of leptospirosis has expanded as the range of tested serovars has...
increased. Data gathered since the early 1980's suggests that this disease is not an expanding epidemic but an endemic problem that is now being recognized.

Leptospires can potentially spread directly between hosts in close contact through urine, venereal routes, bites, or ingestion of infected tissues. Indirect transmission, involves exposure of susceptible animals to contaminated soil, food, or bedding. Water contact is the most prevalent means of spread, and habitats with stagnant warm water and alkaline pH favor leptospire survival. Ambient temperatures between 0 to 25°C maintain the organism, and freezing decreases survival.

**Clinical Signs**

Clinical signs depend on the immunity of the host and virulence and quantity of the serovar to which they are exposed. Young animals are more severely affected. Acutely, elevated rectal temperature, stiffness and discomfort are noted. Subsequently, vomiting, dehydration, and shock may ensue. Coagulation defects have also been noted. In subacute cases, anorexia, dehydration, and thirst may be noted. Reluctance to move and paraspinal hyperesthesia can be noted. Respiratory signs of conjunctivitis, rhinitis, and tonsillitis may be observed. In more chronically infected animals, progressive deterioration in renal function may be manifest by weight loss, polyuria and polydipsia, anorexia, and vomiting. Signs of acute or chronic hepatic dysfunction also include icterus from acute necrosis or chronic fibrosis. Overt signs of liver failure such as inappetence, weight loss, ascites, icterus, or hepatoencephalopathy may also be observed. Signs in cats are often mild or inapparent despite histologic evidence of a chronic inflammatory process in renal and hepatic tissues.

**Diagnosis**

Clinical laboratory abnormalities usually include leukocytosis, thrombocytopenia, high serum urea and creatinine, electrolyte disturbances. Dogs with hepatic dysfunction frequently have bilirubinemia, and high serum hepatic enzyme activities. Urinalysis abnormalities are often glycosuria, proteinuria, and bilirubinuria with increased numbers of granular casts, leukocytes, and sometimes erythrocytes in the sediment. Coagulation parameters may be altered in severely affected animals.

Serologic testing usually involves the microscopic agglutination (MA) test, however other methods such as immunofluorescence (FA) or enzyme immunoassay (ELISA) have been used, especially in Europe. Dogs with positive titers generally have cross-reactive sera with a variety of serovars. The highest titer is generally interpreted as the infecting one, however this cross reaction may relate to differing genotypes that overlap. The pattern of serologic reactivity is generally variable to a given geographic area with adaptation of particular strains to reservoir and domestic hosts. With the MA test, titers greater than 1:800 are considered presumptive for recent or active infection with *Leptospira*. In animals that are seronegative or have lower titers, a four-fold or greater rising titer should be demonstrated with a follow-up in 2 to 3 weeks. Vaccine titers using
bacterins do not usually increase above 1:400 titer range, and the duration of their increase is generally transient for not more than 1 to 2 months.

Organisms are difficult to isolate because of their fastidious growth requirements and susceptibility to pH and other environmental factors. Immunohistochemical methods are helpful in specific determination for tissue sections. Genetic detection using PCR has been helpful in determining specific leptospires in body fluids or tissues such as blood, CSF, aqueous humor, and urine. Genetic methods will likely improve our understanding of this disease in the future.

**Treatment**

Supportive treatment depends on the severity of infection and whether renal or hepatic dysfunction exists. Antimicrobial therapy is essential in the treatment of leptospirosis to terminate the bacteremia. Penicillin and its derivatives are the treatment of choice, however, they do not eliminate the renal carrier state. Initially penicillin or ampicillin are given parenterally to animals with gastrointestinal disturbances from uremia or visceral inflammation. Amoxicillin is preferred for oral use in animals that are alimenting normally. Other drugs such as tetracyclines, aminoglycosides, or macrolides should be used to eliminate the carrier state. Doxycycline can be given regardless of the degree of renal dysfunction; however, aminoglycosides must be strictly avoided. Newer erythromycin derivatives can be used to clear the renal carrier state should doxycycline cause toxicity.

**Prevention**

Prevention of leptospirosis involves clearing the renal carrier state of infected animals. This may prevent the risk of infecting people; however, it does nothing to eliminate the contamination of water from wildlife reservoirs. Prevention of contact of dogs and cats with wildlife reservoirs may help reduce the risk of contact but most infections are contracted from drinking or immersion in water rather than via direct urinary spread. Inactivated bacterins were developed against the serovars *icterohemorrhagiae* and *canicola*, and this strategy has reduced the prevalence of these highly virulent forms of illness in countries where vaccination is practiced. Bivalent bacterins have been available for many years that offer protection against *L. canicola* and *L. icterohemorrhagiae*. These are not cross protective against those serovars that are responsible for the majority of recent infections in dogs. A recent bacterin contains serovars *grippotyphosa* and *pomona*, either as a bivalent or quadrivalent product with the other two agents. As inactivated bacterins, leptospiral vaccines have always had the tendency to cause allergenic reactions, especially when they have been combined with other adjuvanted agents. Many manufacturers have improved and purified their leptospiral vaccines to allow them to put this product in combination with coronavirus vaccines.

**Public Heath Risks**
The majority of leptospiral infections in people are among those engaging in water-related activities, either in work or leisure. Contact with urine can produce disease when it contacts mucosal surfaces or a break in the epidermal barrier. Gloves should always be worn in cleaning kennels and when cleaning urine-contaminated areas. Facemasks and goggles are essential in people spraying down housing environments for animals. Disinfectants can be sprayed on the surface of areas before generating aerosols to reduce the chance of inadvertent transmission.
EMERGING PROTOZOONOSES: BABESIOSIS AND NEOSPOROSIS

Craig E. Greene, University of Georgia

Babesiosis

Etiology
Babesia canis and B. gibsoni are the two species causing canine disease. Various subtypes for each species exist. Other species exist that infect people and they arise from rodent reservoirs. B. gibsoni is usually found individually within erythrocytes and is predominant in northern Africa and southern Asia and is being recognized in the USA. The vectors are Haemaphysalis bispinosa and Rhipicephalus sanguineus, although this varies geographically. B. canis is larger and piriform shaped. Its range is more ubiquitous with many other vectors. Subspecies exist based upon geographic and pathogenic differences, and different vectors vary with geographic locale. In nonendemic regions without suitable vectors, such as Europe, animals will be imported as carriers that may subsequently develop clinical illness.

Epidemiology
In the U.S.A., babesiosis occurs in the southern states with highest prevalence in Florida greyhounds. Immunity is not complete and despite treatment, those dogs that become infected remain chronic carriers. Infection can be transmitted transplacentally. In Australia, the disease is more prevalent in the more tropical regions such as Queensland. In Europe, most dogs with babesiosis are imported from endemic regions in the Mediterranean basin.

Clinical Findings
Many infected dogs are subclinical carriers. In diseased dogs, fever and hemolytic anemia are most common. A hyperacute syndrome, characterized by shock, hypotension, and tissue necrosis occurs rarely or with the most pathogenic strains. Infected dogs often show additional features of thrombocytopenia, lymphadenomegaly, and splenomegaly. Young pups are most severely affected. Red or brown urine and icterus may be noted, especially in B. canis-infected dogs. CNS signs may be seen in some dogs, and with coinfections, many other manifestations are possible. Concurrent stress or immunosuppression may make subclinically infected dogs symptomatic. B. gibsoni infections are difficult to distinguish on a clinical basis from those of B. canis.

Diagnosis
Regenerative anemia is predominant with reticulocytosis being proportional to the degree of anemia. Autoagglutination and Coombs’ positive anemias are frequent. Hyperbilirubinemia may be seen with hemolysis and B. canis infections and serum liver
enzyme activities may be increased in all dogs during acute hemolysis. Other serum chemistry values are usually normal; however, some dogs may have hyperglobulinemia which may relate to a co-infection with *Ehrlichia*. Azotemia and metabolic acidosis may develop with DIC and contribute to morbidity and mortality. Bilirubinuria, hemoglobinuria, proteinuria, and granular casts may be seen on urinalysis. *B. gibsoni* strains are much more difficult to see on stained blood smears.

Definitive diagnosis is made by serologic testing. The IFA test is probably the most reliable and most commonly used test for detection of babesial antibody. A titer of 80 or greater to *B. canis*, or 640 or greater to *B. gibsoni*, has been used previously to document infection. These values may differ depending on the laboratory used. Cross reactivity between strains exists and some young or immune suppressed dogs test seronegative. Antibody titers decline within 3 to 6 months following therapy and suppression of parasitemia. PCR appears to be the most accurate way to document active infection with these organisms and to determine which species is responsible. Since the organisms are rarely cleared following treatment, this test will remain positive for extended periods, despite clinical recovery in the animal.

**Treatment**
Dogs generally show clinical improvement within 24 hours of treatment with antibabesial drugs such as diminazene aceturate or imidocarb dipropionate. Other drugs have been used but their efficacy is questionable. Whether glucocorticoids are indicated is controversial because of known immunosuppression. Preventative measures are important because treatment and clearance of the parasite is so difficult once infection is established. Tick control measures of all types should be practiced. Once carrier dogs have been identified by serologic means, a single IM dose of imidocarb dipropionate at 7.5 mg/kg should be given in an attempt to clear the carrier state. Diminazene may also have to be used in dogs with *B. gibsoni* infection as many strains have become resistant. A combination therapy using atovaquone and azithromycin has been the most effective in treating *B. gibsoni* infections. Unfortunately, some subclinical carriers may develop CNS complications within 2 weeks of treatment, attributed to the death of parasites in cerebral vasculature. Babesia species infecting humans do not appear to infect dogs however the same ticks may transmit multiple pathogens.

**Prevention**
A vaccine exists for *B. canis* disease in Europe. This is very important in a disease in which treatment is so difficult.

**Neosporosis**

**Etiology**
*Neospora caninum* is a closely-related protozoan that has been confused with *T. gondii* because of the resemblance of its tachyzoites and tissue cysts. Dogs appear to be the definitive hosts of this parasite, and herbivores, especially cattle are intermediate hosts. In dogs, tachyzoites are found within neural and muscle tissues of chronically infected
animals but dissemination to many organs may occur in the acute illness. Within neural tissue, the organism exists within cysts that may rupture eliciting a granulomatous inflammatory response. The predominant clinical sign in the intermediate herbivore host is abortion. Natural infections have not been found in cats but they can be infected experimentally.

In the definitive dog host, initial infection can be by carnivorism, but once a reproductively intact female is infected, the predominant route of infection is transplacental. Chronically infected bitches transmit the organism to their offspring and sequential litters may be affected. Oocyst transmission between dogs and herbivores occurs; however oocysts are excreted in low numbers. Unlike toxoplasmosis, direct transmission to other dogs via oocysts is not established.

Purebred dogs have been noticeably more prevalent in reported cases and certain breeds predominate. This may relate to reduced host immunity from inbreeding and maintenance in the breed by transplacental spread. While some pups show signs early, others may be subclinically affected with reactivation of infection later in life.

Clinical Signs
Neural and muscular signs predominate but any parenchymal tissue may become inflamed. Young pups often develop ascending paralysis manifest by muscle rigidity. Laboratory abnormalities include increases in serum muscle enzymes and CSF pleocytosis with mixed inflammatory cell types. Adult dogs also are affected, and as with toxoplasmosis, any tissue can be infected resulting in inflammation. Most chronic and reactivated infections involve muscle or nervous tissues. Multifocal CNS involvement, polymyositis, myocarditis, dermatitis, pneumonia, peripheral neuritis or multifocal dissemination have been observed.

Diagnosis
Hematologic and biochemical abnormalities are nonspecific. Increased muscle enzymes activities, and increased hepatic transaminase activities have been observed. CSF abnormalities include pleocytosis with a mixed inflammatory pattern. EMG abnormalities include spontaneous discharges and high frequency discharges characteristic of myopathy or peripheral neuropathy.

Serologic testing is often used to demonstrate serum antibodies to *N. caninum* IFA titers can vary between laboratories; however, in general, titers above 1:200 are considered positive. Antibodies to *T. gondii* do not cross-react with *N. caninum* at lower dilutions. *N. caninum* may be found in CSF or tissue aspirates and muscle or tissue biopsies of some dogs. Biopsy of affected muscle may yield a definitive diagnosis where organisms are detected. Although *N. caninum* tachyzoites are similar to those of *T. gondii* by light microscopy, the former have thicker walls. Nonsuppurative encephalomyelitis, polyradiculoneuritis, ganglionitis, myositis, and myofibrosis are the predominant histologic findings. Tissue cysts are present only in central or peripheral neural tissues, while tachyzoites are present in many tissues.
Treatment
Drugs used for therapy of toxoplasmosis should be tried early in the course of illness. Clindamycin, sulfadiazine, pyrimethamine alone or in combinations have been used to treat canine neosporosis. The dosages are the same used to treat toxoplasmosis (see below). All pups in an affected litter should be treated as soon as possible. Unlike toxoplasmosis, there is no known public health risk to neosporosis. Dogs should be given limited access to offal from herbivores and they should never be fed raw or uncooked meat. Once the infection has been detected in a litter, the bitch and all subsequent litters should be presumed infected. Serologic testing of these related animals should be done. Furthermore, early treatment of future offspring can be attempted. Because of the effects of antifolates on replicating cells, this cannot be done for the first 2 weeks during the neonatal period without some possible risk.
NEWLY RECOGNIZED ZOONOSES: BARTONELLOSIS AND OTHER BACTERIOSES

Craig E. Greene, University of Georgia

Introduction
Immune-compromised people are the most likely to develop infections with opportunistic bacteria. There are many acquired reasons for people to become immune deficient. Disease processes can develop that temporarily or permanently impair their immune system. Despite the perceived risks, many of these people own pets at the same prevalence rate as the general population. People with medical disabilities are often socially isolated, and pets offer them various psychological benefits including companionship and a feeling of self-worth. Immune-compromised people should not eliminate their pets but should take appropriate precautions to avoid possible disease transmission. The spread of pathogenic organisms from pets to people is actually less of a problem than the spread of infectious agents between people. In summary, with appropriate hygienic measures, pets pose minimal health risks. The discussion below will take these considerations into account with specific infections.

Bartonellosis

Etiology
*Bartonella* are vector-borne hemotropic bacteria that cause disease in people and animals. Carrión’s disease, the first characterized bartonellosis, is transmitted by sandflies and caused by *Bartonella bacilliformis*. It is a hemolytic, vasculoproliferative disorder of people in the Andes Mountains. Trench fever, a multisystemic disease, characterized by bacteremia, endocarditis, lymphadenomegaly and vasculoproliferative lesions was identified in military personnel in Europe in World War I. This same disease, caused by *B. quintana* and transmitted by the body louse, was identified in the last decade as a cause of bacillary angiomatosis in immunocompromised people with AIDS. Two other members, *B. elizabethae*, and *B. henselae* were also detected in these patients, and *B. henselae* and *B. clarridgeiae* was later identified in people with cat scratch disease. In cats, two other species were also identified, *B. clarridgeiae* and *B. koehlerae*, and the former has been shown to infect people. *B. vinsonii* subsp. *Berkhofii* was found to infect dogs and subsp. *arupensis* was identified in a person. Numerous other *Bartonella* sp. have been described in domestic and wild mammals and insect vectors and the extent of the disease causing potential of these newer isolates is unknown. The significance of bartonelloses as emerging diseases to be recognized is without question.

*Bartonella* show a certain degree of host specificity. Although they appear to infect multiple species, each *Bartonella* has adapted to a reservoir mammalian host. The
mechanism of bacteremic persistence appears to be an adaptation to live intracellularly. Intracellular persistence allows the reservoir host to develop high levels of bacteremia in the absence of clinical disease. The heightened bacteremia facilitates the transmission of infection to the insect vector thus maintaining the disease in nature.

Any means of mechanical or biologic transmission of blood allows for spread of Bartonella infection. Fleas, ticks, and lice have all been incriminated in the transmission of infection among various hosts and species of Bartonella. In the absence of arthropods, transmission is limited, unless iatrogenically through blood transfusion. Thus all blood donors should be screened for these infections.

Epidemiology
The geographic distribution of feline bartonellosis is worldwide, however in given continents; prevalence of infection is highest with increasing temperature and humidity. This corresponds to the distribution of the flea vector. Other prevalence studies of feline bartonellosis have shown greater risk for young, stray cats and those in multiple cattery environments. Canine bartonellosis, caused by B. vinsonii, subsp berkhoffii has been highest in dogs from rural environments, those exposed to cattle, and those heavily infested with ticks.

Clinical Signs
Cats
In cats, the pathogenic nature of Bartonella is still in question; however there is convincing evidence that certain strains of B. henselae produce clinical illness in experimentally infected cats. Cats infected with some strains have developed anorexia, lymphadenomegaly, fever, transient neurologic dysfunction. Reproductive failure, with lack of transmission to offspring has been described in experimentally infected queens. Uveitis was suspected to be caused by Bartonella in a naturally infected cat. Based upon antibody seroreactivity, bartonella infection has been questionably associated with stomatitis in cats. In general B. henselae is a subtle feline pathogen and its disease causing potential will be difficult to assess because of the widespread level of subclinical bacteremia in cats.

Dogs
B. vinsonii subsp berkhoffii is a cause of endocarditis and bacteremia in dogs and may cause substantial clinical illness. Signs have related to systemic bacterial infection and include lethargy, anorexia, shifting leg lameness, and heart murmur. Some of the infected dogs develop granulomatous inflammation in many organs leading to lymphadenomegaly, myocarditis, hepatomegaly or splenomegaly. A very similar syndrome has been caused by closely related members of alpha proteobacteria. Unlike the situation in the reservoir cat host, dogs become infected with B. henselae and develop very similar clinical signs as seen in people.
People
Immunocompetent people infected with *B. henselae* develop so called “cat scratch disease” which is characterized by localized lymph node enlargement with eventual clearing of the organism. Immune deficient people that become infected develop bacillary angiomatosis, bacteremia or meningitis. Testing of cats in households with immunocompromised people is advised. Since fleas appear to be important in the acquisition and transmission of infection between cats, control measures should be instituted. Although scratch or bite injuries have been related to human infections, fleas may be involved in transmitting infection to people through their bites or by contaminating the animals hair-coat or local environment with organisms in their excreta.

Diagnosis
Serologic testing provides useful epidemiologic information with regard to organism exposure; however, it gives inaccurate information with regard to the exact prevalence of infection. High serologic titers generally correlate with recent or active infection; however seropositivity cannot be correlated with bacteremia in all cases. Blood or tissue culture provides the best indicator of infection in cats. PCR gives similar information in a more rapid fashion; however false-negative results are possible. Since cats are the reservoir hosts for *B. henselae* and *B. clarridgeiae*, high levels of bacteremia make it relatively easy to isolate the organism from blood. In contrast, definitive diagnosis in people or dogs with *B. henselae* has relied primarily on demonstration of organisms in tissues or body fluids by immunologic or genetic means, respectively. Species identification and strain recognition frequently requires genetic methods. Genetic detection has also been used as it provides a more rapid means of determining infection.

Gross pathologic changes are not usually observed in infected cats with exception of lymphadenomegaly. Reactive follicular hyperplasia is often the histologic appearance. In severe inflammatory states, multifocal granulomatous lesions are observed in cats and dogs. Organisms may be visualized in lesions with immunohistochemical or silver staining methods. In a dog with *B. henselae* infection, vascular lesions identical to visceral peliosis were found in the liver. Dogs with *B. vinsonii* infection usually have visible vegetative lesions on the cardiac valves.

Treatment
In vitro susceptibility testing generally shows susceptibility of *Bartonella* to beta-lactams, chloramphenicol, tetracyclines, macrolides, aminoglycosides, and rifampin. In people with *B. henselae* infections, response is generally rapid with bacteremia and less dramatically improved with localized lymphadenitis or granulomatous disease. This difference may relate to antimicrobial penetration. Due to the intracellular location of *Bartonella*, dose and choice of antibiotics is a critical factor. Several choices effective in treating people have been reported to be ineffective in cats. Several drugs, such as doxycycline, cause a reduction in the bacterial count; however, there is a rebound in the
bacteremia once treatment is discontinued. Culture- or PCR-positive cats can be treated and followed to determine if their infection has cleared. Cats can be treated with high doses of doxycycline given for at least 2 weeks. Azithromycin has been recommended for use in treating infected cats, although specific dosage regimens have not been studied for efficacy. If doxycycline or azithromycin are ineffective, adding rifampin in reformulated capsules may help in clearing the organism. Hepatotoxicity is a major risk with these drugs, especially when used in combination. Spontaneously infected cats may be more difficult to treat and have shown some resistance in clearing of their infection. Culture-positive cats can be treated and followed to determine if their infection has cleared, but sampling should be done at least 3 weeks after treatment is discontinued.

Treatment of dogs with *B. vinsonii* is difficult if there has already been progression to valvular colonization. These dogs have to be managed for heart failure and the progression has been unavoidable. For all other conditions, use of the same drugs and recommendations for cats is advised.

Prevention

Vaccination of cats would be a plausible means of decreasing human exposure to *Bartonella*. Unfortunately, studies have shown protection to challenge with homologous, but not heterologous, strains. An effective vaccine would have to address all these differences. Cats and dogs should always be screened for *Bartonella* infections before they are used as donors for blood transfusions.

Streptococcal Infections

Group A. Group G streptococci are the predominant cause of streptococcal infections of dogs and cats, while Group A are the major cause of human infections. A higher percentage of group A streptococci have been cultured from pets in households where streptococcal-throat infections are present in people. Genetic or immunologic testing for streptococcal strains has not always been done when these claims have been made. Rather, the supposition has been made that pets are reinfecting children. Despite this concern, Group A streptococcal infections are most likely an inverse zoonosis. No clinical signs are evident in pets harboring Group A streptococci. Diagnosis is made with dry swab culture of the tonsillar region. Therapy includes penicillins and the response to treatment may be improved with clavulanic acid added. Erythromycin can be considered as an alternative drug but it is associated with more gastrointestinal side effects. First generation cephalosporins are similarly effective and less toxic.

Group C. Both dogs and cats may carry Group C organisms as commensal flora, in lower frequency than group G. Acute hemorrhagic and purulent pneumonia has been described, primarily in racing greyhounds or research dogs. Weakness, coughing, dyspnea, fever, hematemesis, and red urine have been the predominant clinical signs. Many of the dogs developed septicemia and some died suddenly without signs of clinical illness.
Group G Streptococcal toxic shock syndrome (STSS) and necrotizing fasciitis (NF). "Flesh-eating" bacterial infection of people has been discussed in the popular media. A similar clinical picture caused by various isolates of \textit{S. canis} or other group G streptococci has been identified in dogs and cats. Most cases involve previously healthy adult dogs. A history of mild trauma, bite wounds, or respiratory or urinary tract disease has been apparent. In a majority, treatment with fluoroquinolones has been used. High fever has been a characteristic feature. Severe, rapidly developing cellulitis, usually of a limb develops. In association the animals exhibit intense pain which may become generalized. Chains of streptococci would be readily demonstrated in fluid aspirated from the cellulitis or in underlying tissues by histopathology. Dogs develop septic shock and have extensive exudate accumulation along fascial planes and fascia that requires surgical debridement. Dogs with extensive swelling that develop shock often die while those with more localized NF may survive. All dogs had full thickness skin sloughs and required debridement of necrotic tissue, appropriate antibiotic treatment and intensive supportive fluid therapy. Indicated antibiotics are penicillin G, aminopenicillins (ampicillin, amoxicillin), erythromycin or clindamycin. The latter drug has been most effective in people with this condition.

**Staphylococcal Infections**

\textit{Staphylococcus intermedius} has also been associated with some cases of cellulitis and toxic shock in dogs. As with streptococci, staphylococci can produce bacterial exotoxins that behave as superantigens to T cells causing massive inflammatory responses. The disease is similar to toxic shock involving Lancefield group G (\textit{S. canis}) described above. In one documented case the dog had cellulitis with marked swelling and dermal inflammation. DIC and septic shock was associated with the dog’s death. Staphylococci have also been transmitted among hospital patients by visiting animals when hand washing precautions were not practiced.

**Methicillin-Resistant Staphylococcal Infections**

Antimicrobial-resistant bacterial microflora are a problem in human and veterinary medicine. People and animals treated with antimicrobial drugs develop colonization with antimicrobial-resistant organisms. Prophylactic use of antimicrobials is a controversial subject. There is a justified concern for their unnecessary use because of the increased incidence of resistant microorganisms. Antibiotics alter the patient's microbial flora and allow infection by resistant bacteria.

Methicillin-resistant staphylococci causing clinical infections have been isolated from companion animals, especially postoperative wound infections. A number of isolates have been characterized and the relationship between these organisms as human or animal isolates has not been determined. Antimicrobial susceptibility and genotyping may be needed to determine the public health significance and transmission dynamics of these strains.
A nurse became colonized at a health facility and was found to transmit an endemic MRSA from herself to her child and dog in the home environment. The dog carried the organism as a subclinical commensal in its nasal passage. Isolations of *Staphylococcus aureus*, a number of them methicillin-resistant, have also been made from hospitalized horses, ruminants, and pet animals in participating veterinary teaching hospitals. Furthermore, the organism could be isolated from environmental surfaces of hospitals where the organism was found in animal patients.

The isolates from dogs and cats can harbor the *mecA* gene. Sequence analysis shows that these genes from human and animal isolates are identical. Epidemiologic studies suggest that animals are most often infected from exposure to human reservoirs as opposed to the organism being maintained in the animal population. *Staphylococcus schleiferi* subsp. *coagulans* has emerged as a pathogen separate from *S. intermedius* that is responsible for pyoderma and otitis externa in dogs.