Feline Medicine

with

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UPDATE ON THE DIAGNOSIS AND MANAGEMENT OF FELINE STOMATITIS

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Stomatitis is a common and often debilitating disease of cats. Lesions can range from mild inflammation to severe deep ulcerations and proliferative tissue affecting the gingiva, fauces, buccal mucosa and tongue. Treatments are primarily symptomatic with variable success rates. Most cats must be treated life-long and many undergo multiple tooth extractions in an attempt to maintain the cat’s appetite and control the oral pain. Despite aggressive therapy, some cats with severe caudal stomatitis do not respond and are euthanized due to weight loss, pain and poor quality of life.

Histological evaluation of affected tissues generally reveals infiltrations of lymphocytes and plasma cells. The cause of the syndrome is unknown in most individual cats, but most likely is a combination of a precipitating infectious agent or agents and an abnormal, hyperactive, immune response. Autoimmune reactions and dietary hypersensitivities are also proposed causes. It is likely different forms of the syndrome have different causes.

Feline calicivirus is the viral agent that has been implicated most frequently; feline herpesvirus 1 may also be associated with the syndrome in some cats. In one of our recent studies, we could amplify the RNA of calicivirus from approximately 40% of biopsies obtained from cats with chronic lymphocytic plasmacytic stomatitis (Dowers et al, 2009). However, FCV reverse transcriptase PCR results on oral swabs obtained from cats with and without stomatitis did not correlate to the presence of disease in one small study (Quimby et al, 2007). Stomatitis is more common in cats infected with feline leukemia virus or feline immunodeficiency virus and may relate to activation of other infections as immune suppression develops.

Bartonella henselae is a gram-negative organism that causes cat scratch disease in people. Up to 80% of the cats in serologic surveys have serum antibodies suggesting previous or current infection. Approximately 40% of cats tested are blood culture positive and the infection can be persistent. When first discovered in the blood of cats, the organism was felt to cause subclinical infection. However, recently B. henselae has been associated with fever, uveitis, neurologic disease, gingivitis, and lymphadenopathy in some experimentally infected or naturally infected cats. The organism is harbored inside erythrocytes and endothelial cells of cats where it is likely to partially evade the immune response, possibly explaining persistence of infection. It is possible that this persistent infection induces aberrant immune responses resulting in the clinical manifestations. Cat scratch disease in people is associated with a multitude of possible immune-mediated manifestations like fever, uveitis, and lymphadenopathy.

There is conflicted evidence linking Bartonella spp. exposure to gingivostomatitis in cats. Serum antibodies can persist for months to years after infection is eliminated and so do not denote current Bartonella spp. infection. In a study of cats with caudal stomatitis in our laboratory, the positive and negative predictive value of Bartonella spp. antibodies in cats with and without stomatitis was poor (Quimby et al, 2007). Use of culture to grow the organism from blood or polymerase chain reaction (PCR) to amplify Bartonella spp. DNA from blood can be used to document infection. Documentation of infection by culture or PCR versus documentation of exposure by detection of serum antibodies is likely to be superior for use in epidemiologic studies as it confirms infection. However, healthy cats can be positive as well limiting the positive predictive value in cats with stomatitis or other clinical manifestations of potential bartonellosis.
A complete blood cell count, serum biochemical panel, urinalysis, FeLV antigen test, and FIV antibody test should be completed to evaluate for systemic diseases associated with stomatitis. A dental examination should be performed and abnormal teeth repaired or removed. Biopsy for histopathological examination should be performed, particularly if a mass is present. Squamous cell carcinoma can sometimes appear similar to severe proliferative stomatitis. As mentioned previously, diagnostic tests for feline calicivirus, feline herpesvirus 1, and *Bartonella* spp. have low predictive value and so whether to perform these tests are controversial.

There is no one therapeutic protocol that is effective for every cat (Table 1). After abnormal teeth are repaired or removed during the initial diagnostic workup, antibiotics are generally used to control secondary infections, and potentially disease from *B. henselae*. Clindamycin is an excellent antibiotic for stomatitis owing to effects against anaerobes and penetration into bone. If administered cold, the liquid formulation available in the United States is often well-tolerated. I use doxycycline frequently in mild cases of feline gingivostomatitis because of efficacy against normal flora, effect against *B. henselae*, and an anti-inflammatory effect. Doxycycline can be liquefied in tuna flavoring and administered once daily. For those owners that cannot afford the formulation fee, doxycycline tablets or capsules can be administered followed by water or other liquids, administered coated in butter, or administered within pill delivery treats to avoid esophageal retention, esophagitis, and potential for strictures. Azithromycin is an alternate drug with effect against bartonellosis that is also anti-inflammatory. This antibiotic is expensive but can be administered q72hr which is beneficial for cats with extremely painful mouths. Long-term or pulse antibiotic therapy are required in some cats.

Analgesic therapy is indicated for most cats. Those with mild disease are usually administered buprenorphine for the first three days after the initial diagnostic workup. Those with severe disease may benefit from the administration of non-steroidal anti-inflammatory agents (NSAIDS).

Anti-inflammatory therapy is often used non-specifically. If used, oral administration of prednisolone is preferred, but injectable projects are often needed because of the difficulty associated with administering oral drugs. For some cats, NSAIDS are more effective in controlling pain and also the inflammation. I generally use meloxicam in cats with this syndrome. If used chronically, I follow both renal tests as well as the PCV as gastrointestinal bleeding can occur without vomiting.

Resistant cases may respond to administration of cyclosporine at up to 7.5 mg/kg, PO, daily or every other day but controlled data is lacking. Trough blood levels should be checked 2 weeks after starting cyclosporine to make sure that excessive blood levels are not achieved which may activate infectious diseases. The cytotoxic agent, chlorambucil has been tried with variable responses in some cats but can be difficult to administer. Some cats respond to gold salts; 8-10 weeks of an induction period are required, followed by monthly maintenance therapy.

In the United States, human interferon alpha products are commonly available. In one recent study, low dose oral interferon therapy (30U/kg, PO, daily) improved quality of life in cats with FIV infections. The effect of oral interferon is thought to be from mediation of inflammatory cytokines and the cytokine may have beneficial effects in cats with other causes of stomatitis as well. Feline omega interferon injected into the affected tissues has been effective in some cats and is available in some countries.

Coating the affected tissues with bovine lactoferrin by mixing with milk has about a 15% positive response rate. Bovine lactoferrin can be purchased from Emerson Ecologics in the United States by calling 800-654-4432. Use of a hypoallergenic diet and omega 3/omega 6 fatty acid supplements is beneficial for some cats since the syndrome may result from a dietary hypersensitivity.
CO2 laser ablation has been effective for the treatment of some cats but this form of therapy does not have universal acceptance by veterinary dentists in the United States. Up to 80% of affected cats have a positive response to extraction of all teeth in the area of the inflammation. Care should be taken to make sure all dental tissues are removed. It is the opinion of many veterinary dentists in the United States that this form of therapy should be considered early in the course of the syndrome in severely affected cats. The concern is that ineffective medical management prior to tooth extractions can lessen the efficacy of this therapy.

**Medical treatments frequently attempted for feline idiopathic stomatitis:**

<table>
<thead>
<tr>
<th>Drug</th>
<th>Dosage</th>
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<tbody>
<tr>
<td>Azithromycin</td>
<td>10 mg/kg, PO, q24hr</td>
</tr>
<tr>
<td>AZT</td>
<td>5 mg/kg, PO, q12hr (FIV cats only)</td>
</tr>
<tr>
<td>Bovine lactoferrin</td>
<td>175 mg, PO mixed with milk q12-24hr</td>
</tr>
<tr>
<td>Buprenorphine</td>
<td>0.01 – 0.03 mcg/kg, sublingual, q 6-8hr</td>
</tr>
<tr>
<td>Chlorambucil</td>
<td>2 mg/cat, PO, twice weekly</td>
</tr>
<tr>
<td>Cyclosporine</td>
<td>2-7.5 mg/kg, PO, q24-48hr</td>
</tr>
<tr>
<td>Dexamethasone</td>
<td>0.5-1 mg/cat, PO, q48-72</td>
</tr>
<tr>
<td>Doxycycline</td>
<td>10 mg/kg, PO, q24hr</td>
</tr>
<tr>
<td>Gold salts</td>
<td>1 mg/kg, IM, weekly for 8-10 weeks and then monthly</td>
</tr>
<tr>
<td>Interferon alpha</td>
<td>10 U/kg, PO, daily</td>
</tr>
<tr>
<td>Meloxicam</td>
<td>0.1 mg/cat, PO, q24-72hr based on effect</td>
</tr>
<tr>
<td>Methylprednisolone acetate</td>
<td>7.5-20 mg/cat, SQ, q3-4 weeks</td>
</tr>
<tr>
<td>Metronidazole</td>
<td>10 mg/kg, PO, q8-12hr</td>
</tr>
<tr>
<td>Omega interferon</td>
<td>Intralesional</td>
</tr>
<tr>
<td>Prednisolone</td>
<td>0.5-2 mg/kg, PO, q12-48hr</td>
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**Suggested Readings**


MANAGEMENT OF FELINE INFLAMMATORY BOWEL DISEASE

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Idiopathic inflammatory bowel disease in cats can present with either vomiting (most common) or diarrhea. Prior to performing endoscopy to obtain biopsies I generally perform a number of therapeutic trials for infectious agents. See the other sections of the proceedings for a discussion of the diagnostic plan for GI diseases. Pyrantel (vomiting) or fenbendazole (diarrhea) are often prescribed to lower parasites on my differential list. A metronidazole challenge if often tried because of efficacy against Giardia, some gastrointestinal bacteria (anaerobes, Clostridium perfringens, Helicobacter spp.), and a potential anti-inflammatory effect. However, I do not use metronidazole long term because it is a potential cumulative neurotoxin. A tylosin challenge should be considered, especially if bacterial overgrowth, Campylobacter spp. or Cryptosporidium spp. infections are possible. Some cats have dietary intolerance and just changing food may resolve vomiting and diarrhea.

Those cats that have true dietary hypersensitivity will ultimately require a novel antigen or hydrolyzed antigen diet. Effects may take 4-6 weeks to maximize and so I personally generally use anti-inflammatory agents concurrently to achieve remission.

If the owner can afford the drug, I will often use budesonide (0.5 mg/cat, q24hr) as my first glucocorticoid. This drug has less systemic side-effects than other glucocorticoids. However, it is not completely metabolized in the GI tract and so some systemic side-effects do occur. In cases resistant to budesonide or if the owner cannot afford the drug I use prednisolone in cats. I always start with oral drugs. However, some cats require methylprednisolone acetate injections because it is impossible for the owners to treat orally. In cats, different glucocorticoids (dexamethasone or triamcinolone) are sometimes more effective in cases resistant to prednisolone. I generally try a second glucocorticoid in resistant feline cases before trying cytotoxic drugs. Most cats can tolerate prednisolone at 0.5 mg/kg, PO, q48hr and so this is my ultimate target dose. Other than the risk of developing diabetes mellitus, cats are fairly resistant to the development of glucocorticoids induced side-effects.

In cats resistant to glucocorticoid therapy, I use chlorambucil followed by cyclosporine (if chorambucil is ineffective). Many cats with presumed inflammatory bowel disease truly had small cell lymphoma which may explain the response to chlorambucil.

Resistant cases may respond to administration of cyclosporine at up to 7.5 mg/kg, PO, daily or every other day but controlled data is lacking. Trough blood levels should be checked 2 weeks after starting cyclosporine to make sure that excessive blood levels are not achieved which may activate infectious diseases. In recent studies in my laboratory, we have shown that Toxoplasma gondii and feline herpesvirus 1 infections are only activated in cats that develop extremely high blood levels of cyclosporine.

Use of omega 3/omega 6 fatty acid supplemental may allow for lower doses of glucocorticoids. Weekly cobalamin injections may also be indicated until the malabsorption resolves. After 6 weeks of anti-inflammatory therapy and a novel antigen diet, some cats can be maintained on the diet alone.
USE OF MOLECULAR ASSAYS FOR THE DIAGNOSIS OF FELINE INFECTION DISEASES

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Clinical syndromes induced by infectious agents are common in cats. Documenting current infection is still present is the best way to make a definitive diagnosis. Commonly used techniques vary by the body system but include fecal flotation, cytology, histopathology, immunohistochemistry, culture, antigen tests, and molecular diagnostic assays. For some agents, antibody test results are also used to help make a clinical diagnosis. However, presence of antibodies may only document prior exposure, not current infection.

Sensitivity is the ability of an assay to detect a positive sample; specificity is the ability of an assay to detect a negative sample. Sensitivity and specificity vary with each assay. Positive predictive value (PPV) is the ability of a test result to predict presence of disease; negative predictive value (NPV) is the ability of a test result to predict absence of disease. Many of the infectious agents encountered in feline practice infect a large percentage of the population, resulting in positive organism detection techniques or serum antibody production. However, they only induce disease in a small number of cats in the infected group. Classic examples include coronaviruses, Toxoplasma gondii, and Bartonella spp.. For these agents, even though assays with good sensitivity and specificity are available, the predictive value of a positive test is actually very low.

One of the newest organism demonstration techniques used in practice is the polymerase chain reaction (PCR) assay. This reaction amplifies small quantities of DNA to detectable levels. By use of a reverse transcriptase step, RNA is converted to DNA; therefore the technique can also be used to detect RNA (RT-PCR). PCR assays are of great value for documentation of infections, particularly if the organism in question is difficult to culture (e.g., Ehrlichia spp., Mycoplasma spp.) or cannot be cultured (e.g., hemoplasmas). Specificity can be very high, depending on the primers used in the reaction. For example, primers can be designed to detect one genus but not others. Primers can also be designed to identify only one species. For example a PCR assay can be developed to detect all haemoplasmas or just one species such as Mycoplasma hemofelis.

Because of the inherent sensitivity of the reaction, PCR can give false-positive results if sample contamination occurs during collection or at the laboratory performing the procedure. False-negative results can occur if the sample is handled inappropriately. Results may also be affected by treatment. For example, many cats with hemoplasmosis become negative by PCR assay of blood while on doxycycline or fluoroquinolone therapy and so should be sampled prior to treatment. Other potential problems are that minimal standardization exists among commercial laboratories offering PCR assays and minimal external quality control exists.

Although PCR assays can be one of the most sensitive for documentation of infections, positive test results do not always prove that the infection is resulting in clinical illness. For example, because the technique detects DNA of both live and dead organisms, positive test results may be achieved even if the infection has been controlled. When the organism being tested for commonly infects the background population of healthy cats, interpretation of results for a single animal can be difficult. For example, Bartonella henselae frequently infects up to 20% of healthy cats in some environments and so detection of a positive test result in a clinically ill cat does not prove a disease association. In addition, for some agents the currently available PCR assays cannot discriminate between vaccine strains and field strains. For example, currently available PCR assays for feline herpesvirus 1 (FHV-1) and feline calicivirus
(FCV) also amplify modified live vaccine strains, so a positive result does not indicate presence of a pathogenic strain. Real-time PCR can be used to determine the amount of microbial DNA in a sample. It is possible that the DNA load will correlate to the presence of disease for some agents. However, some agents are very host adapted and can have large amounts of DNA present in samples from healthy carrier cats. For example, the number of ‘Candidatus M. haemominutum’ copy numbers/µl of blood does not correlate to the PCV. Based on these findings, it is very important that small animal practitioners carefully assess the predictive values of currently available PCR and the expertise and reliability of the laboratory that will be performing the assays. New PCR assays are being developed almost daily. The purpose of this lecture is to use several common infectious disease agents to emphasize important points concerning molecular assays in the diagnosis of feline infectious diseases.

**Respiratory agents.** FCV is a common differential diagnosis for cats with clinical evidence of rhinitis and stomatitis. Less commonly, FCV is associated with conjunctivitis, polyarthritis, and lower airway disease in kittens. Virus isolation can be used to document current infection but takes at least several days for results to return. Because of wide-spread exposure and vaccination, the positive predictive value of serological tests is poor. Reverse transcriptase (RT) PCR assays can be used to amplify the RNA of FCV and results can be returned quickly. However, these assays also amplify vaccine strains of FCV. FCV RNA can be amplified from samples collected from normal carrier cats as well as clinically ill cats and so have poor positive predictive value. For example, in one study in our laboratory, presence of FCV RNA failed to correlate to the presence or absence of stomatitis in cats (1). In addition, amplification of FCV RNA cannot be used to prove virulent systemic calicivirus infection. Results of FCV RT PCR can also be falsely negative and so can have poor negative predictive value.

FHV-1 is a common differential diagnosis for cats with clinical evidence of rhinitis, stomatitis, conjunctivitis, keratitis, and facial dermatitis. Because of wide-spread exposure and vaccination, the positive predictive value of serological tests is poor. FHV-1 can be documented by direct fluorescent staining of conjunctival scrapings, virus isolation, or PCR. FHV-1 DNA can be amplified from conjunctiva, nasal discharges, and pharynx of healthy cats and so the positive predictive value of conventional PCR assays is low (2). Currently used PCR assays also detect vaccine strains of FHV-1, further lessening the positive predictive value of the assays (3). In one study in our laboratory, presence of FHV-1 DNA failed to correlate to the presence or absence of stomatitis in cats. Quantitative PCR may ultimately prove to correlate to the presence or absence of disease but failed to correlate to presence of conjunctivitis in one study (4). The negative predictive value of FHV-1 PCR assays is also in question because many cats that are likely to have FHV-1 associated disease are negative. This may relate to clearance of FHV-1 DNA from tissues by a hypersensitivity reaction. Tissue biopsies have greater sensitivity than conjunctival swabs but do not necessarily have greater predictive value. FHV-1 DNA can be amplified from aqueous humor of some cats but whether this indicates FHV-1 associated uveitis is unknown.

*Mycoplasma* spp., *Chlamydophila felis*, and *Bordetella bronchiseptica* are other common respiratory pathogens in cats. As for FHV-1 and FCV, PCR positive test results for these organisms cannot be used to distinguish a carrier from a clinically ill cat. In addition, PCR assays do not provide antimicrobial drug susceptibility testing and so for cats with potential bordetellosis, culture and sensitivity is the optimal diagnostic technique, especially if an outbreak is occurring. *Toxoplasma gondii* DNA has been amplified from airway washings of some cats with lower respiratory tract disease and so PCR is an option for evaluation of samples from diseased animals from which the organism is not identified cytologically.

**Gastrointestinal agents.** The diagnosis of *Giardia* spp. infection is generally made with the combination of fecal flotation techniques and wet mount examination. Fecal antigen tests are also accurate and there are several assays available for point of care use, included one labeled for veterinary use (5). Fecal PCR assays are often falsely negative because of PCR inhibitors in stool and so PCR should not be used as a
screening procedure for this agent. However, *Giardia* spp. PCR can be used to determine whether the infective species is a zoonotic assemblage which is the primary indication for this technique. However, it now appears that assemblage determination should be performed on more than one gene for most accurate results.

While *Cryptosporidium* spp. infection is common, it is unusual to find *C. felis* oocysts after fecal flotation in cats. Acid-fast staining of a thin fecal smear is cumbersome and insensitive. Antigen assays titrated for use with human feces are inaccurate when used with cat feces. Thus, PCR may be in the diagnosis of cryptosporidiosis in dogs and cats and has been shown to be more sensitive than IFA in cats (6). *Cryptosporidium* spp. PCR assays are indicated in IFA negative cats with unexplained small bowel diarrhea and when the genotype of *Cryptosporidium* is to be determined. However, *C. felis* infection in cats is common and so positive tests results do not always prove that the agent is the cause of the clinical disease. No drug is known to eliminate *Cryptosporidium* spp. infections and small animal strains are not considered significant zoonotic agents so PCR is never indicated in healthy animals.

PCR assays are also available for detection of DNA of *Tritrichomonas foetus*, *Salmonella* spp., *Campylobacter* spp., *Clostridium* spp., paroviruses, and *T. gondii* and a RT-PCR assay is available for coronaviruses. Trophozoites of *T. foetus* can often be detected on wet mount examination of fresh feces which can be completed as an in clinic test. DNA of *T. foetus* can be detected in healthy carrier cats and so positive results do not always prove illness from the organism (7). Cases with suspected salmonellosis or campylobacteriosis should be cultured rather than assessed by PCR to determine the anti-microbial susceptibility patterns. In dogs, the PPV of *Clostridium* spp. PCR assays on feces is low and if used, should be combined with entero-toxin assays. Information in cats is currently lacking. There is no current evidence that parovirus PCR on feces is superior to currently available antigen assays. *Toxoplasma gondii* is only shed for about 7-10 days and millions of oocysts are generally shed during this time making the organism very easy to identify. Thus, PCR assays are usually not needed to diagnosis this infection. Because virus isolation is not practical clinically, RT-PCR is used most frequently to detect coronaviruses RNA in feces. However, positive test results do not differentiate FIP inducing strains from enteric coronaviruses.

**Blood borne agents.** *Mycoplasma haemofelis* (Mhf), ‘*Candidatus Mycoplasma haemominutum*’ (Mhm), and ‘*Candidatus M. turicensis*’ (Mtc) all can be found in cats. In at least two studies of experimentally infected cats, Mhf is apparently more pathogenic than Mhm. It appears that Mtc has intermediate pathogenicity. Diagnosis is based on demonstration of the organism on the surface of erythrocytes on examination of a thin blood film or PCR assay. Organism numbers fluctuate and so blood film examination can be falsely negative up to 50% of the time. The organism may be difficult to find cytologically, particularly in the chronic phase. Thus, PCR assays are the tests of choice due to sensitivity (8). Primers are available that can amplify all three hemoplasmas. Real time PCR assays can be used to monitor copy numbers during and after treatment but do not have greater sensitivity, specificity, or predictive value than conventional PCR assays. PCR assays should be considered in the evaluation of cats with unexplained fever or anemia that are cytologically negative. In addition, the ACVIM recommends screening cats for use as blood donors by PCR assays for haemoplasmas (9). Many cats are carriers of the relatively non-pathogenic ‘*Candidatus M. haemominutum*’ and so positive test results may not always correlate to the presence of disease (poor PPV).

Cats can be infected by *E. canis* like organism (10) and *Anaplasma phagocytophilum* (11). Little is known about the other agents in these genera in regards to cats. As the organisms are in different genera, serological cross reactivity is variable. Thus, while the clinical syndromes can be similar, there is no one serological test to document infection and there is currently no standardized serology for cats. In addition, some cats with *E. canis* infection do not seroconvert and so PCR assay is superior to serology in cats.
PCR assays can be designed to amplify each organism. Alternately, primers are available to amplify all of the organisms in a single reaction and then sequencing can be used to determine the infective species.

Cats can be infected by *Rickettsia felis* and have been shown to have antibodies against *R. rickettsii*. Fever, headache, myalgia, and macular rash in humans have been attributed to *R. felis* infection in several countries around the world. In recent study in our laboratory, we assayed 92 pairs of cat blood and flea extracts from Alabama, Maryland and Texas, using PCR assays that amplify a region of the citrate synthase gene (*gltA*) and the outer membrane protein B gene (*ompB*). Of the 92 pairs, 62 of 92 (67.4%) flea extracts and none of the cat blood samples were positive for *R. felis* DNA (12). In another study, we showed *R. felis* and *R. rickettsii* antibody prevalence rates in cats with fever to be 5.6% and 6.6%, respectively but neither organism was amplified from blood (13). These results prove that cats are sometimes exposed but further data are needed to determine significance of diseases associations. Whether *Rickettsia* spp. PCR assays are indicated for use in cats at this time is unknown.

Blood culture, PCR assay on blood, and serologic testing can be used to assess individual cats for *Bartonella* spp. infection. Cats that are culture-negative or PCR-negative and antibody-negative and cats that are culture-negative or PCR-negative and antibody-positive are probably not a source of flea, cat, or human infection. However, bacteremia can be intermittent and false-negative culture or PCR results can occur, limiting the predictive value of a single battery of tests. While serologic testing can be used to determine whether an individual cat has been exposed, both seropositive and seronegative cats can be bacteremic, limiting the diagnostic utility of serologic testing. Thus, testing healthy cats for *Bartonella* species infection is not currently recommended (14). Testing should be reserved for cats with suspected clinical bartonellosis. Because *Bartonella* spp. infection in cats is so common in healthy cats, even culture or PCR positive results does not prove clinical bartonellosis. For example, while we detected *Bartonella* spp. DNA in more cats with fever than pair matched cats without fever, the healthy cats were still commonly positive (15). I currently recommend combined serology with PCR in evaluation of cats with suspected bartonellosis.

*Cytauxzoon felis* in clinically affected cats is usually easily identified on cytological examination of blood smears or splenic aspirates. Serologic testing is not commercially available. PCR can be used to amplify organism DNA from blood from cats that are cytologically negative (16).

Antibodies against feline immunodeficiency virus (FIV) are detected in serum in clinical practice most frequently by enzyme-linked immunosorbent assay (ELISA). Comparisons between different tests have shown the results of most assays are comparable (17). Results of virus isolation or RT-PCR on blood are positive in some antibody-negative cats. False-positive reactions can occur using ELISA; hence, positive ELISA results in healthy or low-risk cats should be confirmed using Western blot immunoassay. Kittens can have detectable, colostrum-derived antibodies for several months. Kittens less than 6 months of age that are FIV seropositive should be tested every 60 days until the result is negative. If antibodies persist at 6 months of age, the kitten is likely infected. Virus isolation or RT-PCR on blood can also be performed to confirm infection. However, FIV is not present in the blood in high levels and so false negative results are common. Thus, the assay is not very accurate for distinguishing a vaccinated cat from a naturally exposed cat (18).

Most cats with feline leukemia virus infection are viremic and so molecular diagnostic assays are not usually needed in clinical practice. However, newer sensitive real time PCR assays have been used to accurately characterize the stages of infection (19). However, these assays are not commonly available commercially.

RNA of both FIPV and FECV can be amplified from the blood of cats and so positive test results do not always correlate with the development of FIP. Amplification of the mRNA of the M gene by RT-PCR
had mixed results in two studies performed to date. In the one study, 13 of 26 apparently normal cats were positive for FECV mRNA in blood suggesting that the positive predictive value of this assay for the diagnosis of FIP was low (20).

Ocular agents. *Toxoplasma gondii, Bartonella* spp., FHV-1 and coronavirus are the organisms for which DNA or RNA has been amplified most frequently from the aqueous humor of cats with endogenous uveitis. While little is know about the predictive value of these assays when used with aqueous humor, the combination of molecular assays with local antibody production indices may aid in the diagnosis of some cases.

References

Zoonotic diseases are defined as being common to, shared by, or naturally transmitted between humans and other vertebrate animals. Humans are infected with zoonotic agents from direct contact with the infected pet, contact via contaminated food or water, from shared vectors, and from the shared environment. Direct contact with animal feces (enteric zoonoses), respiratory secretions, urogenital secretions, or infected skin and exudates, as well as bites and scratches can result in human infections.

Most of the agents discussed in these proceedings can infect and cause disease in anyone that is exposed, but disease is generally more prevalent or more severe in those that are immunodeficient. Immunosuppression is common in humans. Humans with AIDS are discussed most frequently, but there are many more immunodeficient individuals including the very old, the very young, and those receiving chemotherapy for immune-mediated diseases, organ transplantation, or neoplasia. Humans are unlikely to contract zoonotic diseases from contact with their pets and so in most cases do not need to relinquish their animals. The Centers for Disease Control of the United States online publication, Preventing Infections from Pets; A Guide for People with HIV Infection, states ‘You do not have to give up your pet’. The American Association of Feline Practitioner’s Zoonoses Guidelines states ‘All human or animal care providers should provide accurate information to pet owners concerning the risks and benefits of pet ownership so that an informed decision about acquiring and keeping pets can be made’ (Brown et al, 2003).

Veterinary health care providers are at increased risk for some zoonoses since they commonly handle animals; these agents will be discussed in depth in this article. Since some enteric zoonotic agents are infectious when passed with feces, direct contact with infected animals can result in human infections. However, it is felt that most enteric zoonoses result from ingestion of the infectious agent in contaminated food, water, or other environmental sources. Giardia spp., Cryptosporidium spp., and Toxoplasma gondii are notable examples. Some zoonotic agents are transmitted between animals and man by shared vectors like fleas, ticks, or mosquitoes. Rickettsia rickettsii (ticks), Ehrlichia spp. (ticks), Borrelia burgdorferi (ticks), Rickettsia felis (fleas), Bartonella spp. (fleas), Dirofilaria immitis (mosquitoes), Dipylidium caninum (mosquitoes), and West Nile virus (mosquitoes) are examples of vector borne zoonoses. The pet brings the vector of the organism into the environment resulting in exposure of the human. There could be a slight increased risk of exposure to veterinary health care providers since we handle many animals infested with fleas and ticks. However, it is the vector, not direct contact with the infected animal that results with infection of the human. Flea and tick control should always be maintained on our client’s animals and infested animals that are seen in the clinic should be treated immediately. Some zoonotic agents including Histoplasma capsulatum, Coccidioides immitis, Blastomyces dermatitidis, Cryptococcus neoformans, and Aspergillus spp do not usually infect humans from direct with the infected pet but are acquired from the same environmental source.

The following is a brief description of the more common canine and feline zoonoses that are encountered in small animal practice that can be direct contact zoonoses. General guidelines for the avoidance of zoonotic transfer of disease for veterinarians and pet owners are listed in Tables 1 and 2, respectively.

**Enteric zoonoses.** There are multiple infectious agents of the gastrointestinal tract that can be shared between animals and humans and infection rates are as high as 40% in dogs or cats with diarrhea. These findings emphasize that diagnostic workups for enteric infections are indicated due to potential human
health risks. The minimal diagnostic plan to assess for enteric zoonoses in pets with diarrhea includes a fecal flotation, *Cryptosporidium* spp. screening procedure, fecal wet mount, and rectal cytology. Fecal culture should be considered if *Salmonella* spp. or *Campylobacter* spp. are on the list of differential diagnoses.

**Nematodes.** Visceral larva migrans can be induced by infection of humans with *Toxocara cati*, *Toxocara canis*, or *Baylisascaris procyonosis*. These common roundworms are passed as eggs in feces. The eggs larvate and become infectious after 1 to 3 weeks, and can survive in the environment for months. Thus, these are not direct contact zoonoses; humans are infected after ingesting larvated eggs in the contaminated environment. Dogs are considered more important than cats for the spread of eggs. However, areas such as children's sandboxes may be contaminated with *T cati* because of the defecation habits of cats. It is extremely unlikely that human infection will develop following direct contact with dogs or cats since the eggs are not immediately infectious. Dogs and cats can be subclinically affected or may develop poor haircoats, poor weight gain, and gastrointestinal signs. Following ingestion of infectious eggs, larvae penetrate the intestinal wall and migrate through the tissues. Eosinophilic granulomatous reactions involving the skin, lungs, central nervous system (CNS), or eyes then occur, potentially leading to clinical signs of disease. Clinical signs and physical examination abnormalities in humans include skin rash, fever, failure to thrive, CNS signs, cough, pulmonary infiltrates, and hepatosplenomegaly. Peripheral eosinophilia is common. Ocular larva migrans most commonly involves the retina and can cause reduced vision; uveitis and endophthalmitis can also occur. Visceral larva migrans is most common in children between 1 and 4 years of age, while ocular larva migrans is most common in older children. Diagnosis in people is confirmed by biopsy or can be presumed in cases with classic clinical manifestations, eosinophilia, and positive serology.

*Ancylostoma caninum*, *A braziliense*, *A tubaeforme*, *Uncinaria stenocephala*, and *Strongyloides stercoralis* have been associated with cutaneous larva migrans in the United States. Eosinophilic enteritis in humans was reported following ingestion of larvated *A caninum* eggs. Following the passage of hookworm eggs into the environment in feces, infectious larvae are released after incubating for 1 to 3 days; humans are infected by skin penetration. Thus, these infectious are not direct contact zoonoses but occur from contact with the organisms in the contaminated environment. Animals are either subclinically ill or have nonspecific signs such as poor haircoats, failure to gain weight, vomiting, or diarrhea. Heavily infested puppies and kittens can present with pale mucous membranes from blood loss anemia. In humans, the larvae cannot penetrate the dermoepidermal junction and so usually die in the epidermis. Clinical signs are related to migration of the larvae which results in an erythematos, pruritic cutaneous tunnel. Cutaneous signs usually resolve within several weeks. Abdominal pain was the most common clinical sign in humans with *A. caninum* intestinal infection.

Prevention of hookworm and roundworm infection is achieved by control of animal excrement in human environments. All puppies and kittens should have a fecal flotation performed and should be routinely treated with an anthelmintic such as pyrantel pamoate at least three times. Some veterinarians administer the drugs at 21 days apart during their initial vaccination period. Roundworm and hookworm infections are occasionally occult and so all puppies or kittens should receive an anthelmintic whether or not eggs are detected on microscopic examination of feces. In puppies with high worm burdens, deworming with pyrantel pamoate can be initiated at 1-2 weeks of age and repeated at 2 week intervals. In heavily infected kittens, deworming with pyrantel can begin at 3 weeks of age and repeated at 2 week intervals. The bitch and queen should be dewormed as well as patent infections may exist. Feces of adult dogs and cats should be periodically screened for roundworms and hookworms and anthelmintics should be administered periodically. An effective way of providing strategic deworming year round is to administration of heartworm preventatives that also control or eliminate hookworms and roundworms.
**Cestodes.** Dipylidium caninum, Echinococcus granulosa, and Echinococcus multilocularis are cestodes that can infect humans. Wild carnivores are more common definitive hosts of Echinococcus spp. and shed infective eggs into the environment. Echinococcus granulosa eggs can be transmitted in feces of dogs following ingestion of infected sheep tissues; Echinococcus multilocularis can be transmitted in feces of dogs or cats after ingestion of infected vole. Transmission to humans occurs following ingestion of the intermediate host (flea, Dipylidium) or by the ingestion of eggs (Echinococcus spp.). Infection of dogs and cats with cestodes is generally subclinical. Dipylidium infection is most common in children and can lead to diarrhea and pruritis ani. In people following ingestion of eggs, which are immediately infectious, Echinococcus enters the portal circulation and spreads throughout the liver and other tissues. Echinococcus multilocularis is most common in the northern and central parts of North America but seems to be spreading with the fox population (most common definitive host). Prevention or control of cestodes is based on sanitation procedures and use of taeniacides. Dogs and cats should not be allowed to hunt and should only be fed commercial foods.

**Coccidians.** Cryptosporidium spp. inhabit the respiratory and intestinal epithelium of many vertebrates including birds, mammals, reptiles, and fish. Once thought to be commensal agents, Cryptosporidium spp. are now known to cause gastrointestinal tract disease in a number of mammalian species including rodents, dogs, cats, calves, and humans. Cryptosporidium spp. have an enteric life cycle similar to other coccidians; it culminates in the production of environmentally resistant oocysts that are passed in feces. Oocysts (4 to 6 microns in diameter) are passed sporulated and are immediately infectious to other hosts. It is now apparent that there are multiple strains of Cryptosporidium spp. including C. parvum, C. hominis, C. felis and C. canis. While some isolates infect multiple species, others have a limited host range. For example, C. hominis of people does not infect dogs, cats, or rodents. However, strains that infect both pets and people cannot be differentiated from those that only infect pets by light microscopy and so all Cryptosporidium spp. should be considered potentially zoonotic. The prevalence of Cryptosporidium spp. oocysts or antigens in dog and cat feces approximates that of Giardia leading to the recommendation that all dogs or cats with diarrhea in the homes of immunosuppressed people be assessed for this infection. Person-to-person contact with oocysts by fecal-oral contamination or by ingesting contaminated water are the most likely routes of exposure. Cryptosporidium spp. infection of people following exposure to infected calves has been recognized for years. Human infection associated with contact with infected dogs and cats has been reported but is thought to be unusual. In one study, cat or dog ownership was not statistically associated with cryptosporidiosis in HIV-infected people. Infection of dogs and cats by Cryptosporidium spp. is usually subclinical, but small bowel diarrhea occurs in some cases. Immunosuppression may potentiate disease; several dogs and cats had concurrent feline leukemia virus infection, canine distemper virus infection, or intestinal lymphoma. Clinical cryptosporidiosis is characterized by small bowel diarrhea and is generally self-limiting in immunocompetent humans, but fatal infection can occur in humans with AIDS. The small size (approximately 4 to 6 microns in diameter) of Cryptosporidium spp. oocysts lead to difficulty in diagnosis. Routine salt solution flotation and microscopic examination at 100X will commonly lead to false-negative results. The combination of concentration techniques with fluorescent antibody staining or acid fast staining appears to be more sensitive. Enzyme-linked immunosorbent assays for the detection of C parvum antigen in feces and immunofluorescent assay for detection of C parvum oocysts in feces are commercially available but do not consistently detect C felis or C canis. Polymerase chain reaction is the most sensitive test to date, but assays are not routinely available and are not standardized between laboratories. No drug has been shown to eliminate Cryptosporidium spp. from the gastrointestinal tract. However, clinical signs often resolve after administration of paromomycin at 150 mg/kg, q24hr, PO for 5 days, tylosin at 10-15 mg/kg, q12hr, PO for 14 to 21 days, or azithromycin at 10 mg/kg. q24hr, PO for 10 days. Avoiding exposure is the most effective prevention. Routine disinfectants require extremely long contact with the organism to be effective. Drying, freeze-thawing, and steam-cleaning can inactivate the organism. Surface water collected in the field for drinking should be boiled or filtered.
**Toxoplasma gondii** is an ubiquitous coccidian with worldwide distribution. Most seroprevalence studies performed in the United States suggest that approximately 30% of cats have been exposed. Human prevalence rates have been declining which may relate to food production changes over time. Cats are the only known definitive host of the organism and complete the enteroepithelial cycle (sexual phase) that results in the passage of environmentally resistant unsporulated oocysts in feces. Oocyst sporulation occurs in 1-5 days in the presence of oxygen; sporulated oocysts are infectious to most warm-blooded vertebrates. Following infection by *T. gondii*, an extraintestinal phase develops which ultimately leads to the formation of tissue cysts containing the organism. Infection by *T. gondii* occurs after ingesting sporulated oocysts, after ingesting tissue cysts, or transplacentally. Transplacental infection of humans and cats usually only occurs if the mother is infected for the first time during gestation.

In dogs and cats, clinical disease from *T. gondii* infection occurs occasionally and is manifested most commonly by fever, uveitis, pulmonary disease, hepatic disease, and CNS disease. Infected immunocompetent humans are generally asymptomatic; self-limiting fever, lymphadenopathy, and malaise occur occasionally. Transplacental infection of humans results in clinical manifestations including stillbirth, hydrocephalus, hepatosplenomegaly, and retinochoroiditis. Chronic tissue infection in humans can be reactivated by immunosuppression leading to dissemination and severe clinical illness; this has been commonly associated with drug-induced immunosuppression as well as AIDS. Approximately 10% of humans with AIDS will develop toxoplasmic encephalitis. Oocysts are most effectively demonstrated in cat feces following sugar solution centrifugation. Clinical toxoplasmosis is difficult to diagnose in humans, dogs, and cats but usually involves the combination of clinical signs, serologic test results, organism demonstration techniques, and response to anti-*Toxoplasma* drugs.

*Toxoplasma gondii* is recognized as one of the most common zoonoses. However, humans are usually not infected by direct contact with cats. The oocyst shedding period usually lasts several days to several weeks (approximately 7-10 days if the cat was infected by tissue cyst ingestion). Since oocysts have to sporulate to be infectious, contact with fresh feces cannot cause infection. Cats are very fastidious and usually do not allow feces to remain on their skin for time periods long enough to lead to oocyst sporulation; oocysts were not isolated from the fur of cats 7 days after completing the oocyst shedding period. There was no association between cat ownership and *T. gondii* seroprevalence in a group of HIV-infected humans. Veterinary health care providers generally do not have increased incidence of toxoplasmosis when compared to the general population. Thus, cats do not need to be removed from households with immunodeficient or pregnant humans due to the risk of acquiring toxoplasmosis. *Toxoplasma gondii* infection can be avoided by avoiding the ingestion of sporulated oocysts in old feline feces and avoiding ingestion of tissue cysts in undercooked meats.

**Flagellates, ameoba, and ciliates.** *Giardia* spp. (flagellate), *Entamoeba histolytica* (amoeba), and *Balantidium coli* (ciliate) are enteric protozoans that can be transmitted to humans by contact with feces; the cysts do not require an incubation period to become infectious. *Entamoeba histolytica* infection extremely rare in dogs and cats; *Balantidium coli* infection of dogs is rare and has not been reported in cats. *Giardia* spp. infection of dogs and cats is common and can be detected in feces of normal dogs and cats or those with small bowel diarrhea (and occasionally mixed bowel diarrhea in cats). Clinical signs of disease are generally more severe in immunodeficient individuals. Because the organism is immediately infectious when passed as cysts in stool, there is potential for direct zoonotic transfer. While it is known that some *Giardia* spp. will infect humans, dogs, and cats that may not be the case with all species. In 1 study, cats were relatively resistant to infection by a *Giardia* spp. isolated from humans. Based on genetic studies, it is now known that there are multiple *Giardia* spp.. Assemblage A has been found in infected humans and many other mammals including dogs and cats. Assemblage B has been found in infected humans and dogs, but not cats. Dogs (C and D) and cats (F) have there own genotypes. However, as for
Cryptosporidium, since it is impossible to determine zoonotic strains of Giardia spp. by microscopic examination, it seems prudent to assume feces from all dogs and cats infected with Giardia spp. are a potential human health risk. Fecal examination should be performed on all dogs and cats at least yearly and treatment with drugs with anti-Giardia activity like fenbendazole, metronidazole, or febantel/praziquantel/pyrantel should be administered if indicated. Zinc sulfate centrifugation is considered the optimal fecal flotation technique by most parasitologists to demonstrate cysts. If fresh stool is available from dogs or cats with diarrhea, examination of a wet mount to detect the motile trophozoites may improve sensitivity. Monoclonal antibody based immunofluorescent antibody tests, fecal antigen tests, can PCR are available for use as adjunct tests. These techniques should be used in addition to, not in lieu of fecal flotation that can also reveal other parasites. Giardia vaccines for SQ administration are now available for both dogs; the feline vaccine has been discontinued. The vaccines were considered generally not recommended by the American Association of Feline Practitioners and American Animal Hospital Association vaccine guidelines committees. Vaccination against Giardia could be considered in dogs with recurrent infection and has been evaluated as a therapeutic agent with variable results. Prevention of zoonotic giardiasis includes boiling or filtering surface water for drinking and washing hands that have handled material contaminated by feces, even if gloves were worn. It is unknown whether treated dogs and cats are cured and it is likely that if a treated dog or cat is exposed again it will be reinfected.

**Bacteria.** Salmonella spp., Campylobacter spp., Clostridium difficile, E. coli, Yersinia enterocolitica, and Helicobacter spp. each infect dogs and cats and can cause disease in humans. Transmission from animals to people is by fecal-oral contact. Dogs can be subclinical carriers of Shigella spp. but humans are the natural hosts. While Helicobacter pylori was isolated from a colony of cats, it is unclear whether dogs and cats are a common source of Helicobacter infection for people. Based on epidemiologic studies, it is unlikely. In 3 recent enteric zoonoses prevalence studies, Salmonella spp. and Campylobacter spp. infections were uncommon in pet dogs and cats. Prevalence of Salmonella and Campylobacter infections is greater in young animals housed in unsanitary or crowded environments.

Gastroenteritis can occur in dogs or cats following infection by Salmonella spp., Campylobacter spp., or E. coli; Yersinia enterocolitica is probably commensal agents in animals but cause fever, abdominal pain, polyarthritis, and bacteremia in humans. Helicobacter infections cause gastritis which is commonly manifested as vomiting, belching, and pica. Salmonella spp. infection in dogs and cats is often subclinical. Approximately 50% of clinically affected cats have gastroenteritis; many are presented with signs of bacteremia. Salmonellosis of cats and people has been associated with songbirds (Songbird fever). Abortion, stillbirth, and neonatal death can result from in utero infection. Diagnosis of Salmonella spp., Campylobacter jejuni, E. coli, and Yersinia enterocolitica is based on culture of feces. Clostridium difficile enterotoxins can be measured in feces. A single negative culture may not rule out infection. Rectal cytology should be performed on all animals with diarrhea. If neutrophils are noted, culture for enteric bacteria should be considered, particularly if the animal is owned by an immunodeficient individual. Culture is preferred to PCR for Salmonella spp. and Campylobacter spp. to allow for determination of the antimicrobial sensitivity pattern. Antibiotic therapy can control clinical signs of disease from infection by Salmonella spp. or Campylobacter spp., but should not be administered orally to animals that are subclinical carriers of Salmonella due to risk of antibiotic resistance. Strains of Salmonella that were resistant to most antibiotics have been detected in several cats. Prevention of enteric bacterial zoonoses is based on sanitation and control of exposure to feces. Immunodeficient humans should avoid young animals and animals from crowded or unsanitary housing, particularly if clinical signs of gastrointestinal tract disease are occurring. Dog used for visitation can acquire and carry zoonotic agents like C. difficile (Lefebvre et al, 2009).

**Bite, scratch, or exudate exposure zoonoses**
Bacteria. Bartonella henselae is the most common cause of cat scratch disease as well as bacillary angiomatosis, and bacillary peliosis, common disorders in humans with AIDS. Cats can also be infected with B clarridgeiae, B koehlerae, B bovis, and B weissii (Brunt et al, 2006). Bartonella henselae has been isolated from the blood of subclinically ill, seropositive cats and also from some cats with a variety of clinical manifestations like fever, lethargy, lymphadenopathy, uveitis, gingivitis, and neurologic diseases. Seroprevalence in cats varies by region but as many as 93% of cats in some geographical areas of the United States are Bartonella spp. seropositive. The organism is transmitted between cats by fleas and so prevalence is greatest in cats from states where fleas are common. Transmission to humans commonly occurs after cat bites or scratches; the disease appears to be transmitted most commonly from kittens. Humans with cat scratch disease develop a variety of clinical signs such as lymphadenopathy, fever, malaise, weight loss, myalgia, headache, conjunctivitis, skin eruptions, and arthralgia. Bacillary angiomatosis is a diffuse disease resulting in vascular cutaneous eruptions. Bacillary peliosis is a diffuse systemic vasculitis of parenchymal organs, particularly the liver. The incubation period for cat scratch disease is approximately 3 weeks. Most cases of cat scratch disease are self-limiting but may take several months to completely resolve. Blood culture, blood PCR, and serologic testing can be used to determine risk of individual cats.

Cats that are culture-negative or PCR-negative and antibody-negative, and cats that are culture-negative or PCR-negative and antibody-positive are probably not shedding Bartonella into the human environment. However, bacteremia can be intermittent and false-negative culture or PCR results may occur. With PCR, false-positive results can occur and positive results do not necessarily indicate that the organism is alive. While serologic testing can be used to determine whether an individual cat has been exposed, both seropositive and seronegative cats can be bacteremic, limiting the diagnostic utility of serologic testing. Thus, testing healthy cats for Bartonella spp. infection is not currently recommended (Brunt et al, 2006). Testing should be reserved for cats with suspected clinical bartonellosis. Administration of doxycycline, tetracycline, erythromycin, amoxicillin-clavulanate, azithromycin, or enrofloxacin can limit bacteremia but does not cure infection in all cats and has not been shown to lessen the risk of cat scratch disease. Thus, antibiotic treatment of healthy bacteremic cats is controversial. Bartonella spp. infection is more common in flea-infested cats from catteries. Bartonella henselae replicates in fleas and can survive in flea feces for days. Thus, it is possible that flea feces contaminate our wounds, resulting in infection. Strict flea control should be maintained. Use of imidacloprid-moxidectin monthly was just shown to block transmission of B. henselae amongst experimental cats. Kittens should be avoided by immunodeficient people. Cat claws should be kept clipped and cats should never be teased. Cat-induced wounds should immediately be cleansed and medical advice sought.

Dogs and cats can have methicillin resistant S. aureus and S. pseudintermedius infections. Dogs and cats with infected wounds should always be cultured. Dog used for visitation can acquire methicillin resistant organisms from human patients (LeFebvre et al, 2009).

Feline plague is caused by Yersinia pestis, a gram-negative coccobacillus found most commonly in mid- and far-western states, particularly New Mexico and Colorado. Rodents are the natural hosts for this bacterium; cats are most commonly infected by ingesting bacteremic rodents or lagomorphs or by being bitten by Yersinia infected rodent fleas. Dogs are more resistant to infection and have not been associated with zoonotic transfer. Humans are most commonly infected by rodent flea bites, but there have been many documented cases of transmission by exposure to wild animals and infected domestic cats. From 1977 to 1998, 23 cases of human plague (7.7% of the total cases) resulted from contact with infected cats. Infection can be induced by inhalation of respiratory secretions of cats with pneumonic plague, bite wounds, or by contaminating mucous membranes or abraded skin with secretions or exudates. Bubonic, septicemic, and pneumonic plague can develop in cats and humans; each form has accompanying fever, headache, weakness, and malaise. Since cats are most commonly infected by ingestion of bacteremic rodents, suppurative lymphadenitis (buboes) of the cervical and submandibular lymph nodes is the most
common clinical manifestation. Exudates from cats with lymphadenopathy should be examined cytologically for the presence of large numbers of the characteristic bipolar rods. The diagnosis is confirmed by fluorescent antibody staining of exudates; culture of exudates, tonsillar area, and saliva; as well as by documenting increasing antibody titers. People that are exposed to infected cats should be urgently referred to physicians for antimicrobial therapy and public health officials alerted. Doxycycline, enrofloxacin, chloramphenicol, and aminoglycosides can be used successfully for the treatment of plague. Parenteral antibiotics should be used during the bacteremic phase. Drainage of lymph nodes may be required. Cats with suppurrative lymphadenitis should be considered plague suspects, and extreme caution should be exercised when handling exudates or treating draining wounds. Suspect animals should be treated for fleas and housed in isolation. Cats are not infectious to humans after 4 days of antibiotic treatment.

Francisella tularensis is the gram-negative bacillus found throughout the continental United States that causes tularemia. Dermacentor variabilis (American dog tick), D. andersoni (American wood tick), and Amblyomma americanum (Lone Star tick) are known vectors. Human tularemia occurs most commonly following exposure to ticks and less commonly from contact with infected animals. There have been at least 51 cases of human tularemia resulting from contact with infected cats. Dogs are not considered a source of human tularemia, but may facilitate human exposure by bringing infected ticks into the environment. Cats are infected most frequently by tick bites or by ingesting infected rabbits or rodents. Most cases of feline tularemia have been documented in the mid-Western states, particularly Oklahoma. Infected cats exhibit generalized lymphadenopathy and abscess formation in organs such as the liver and spleen, which leads to fever, anorexia, icterus, and death. Ulceroglandular, oculoglandular, lymph node aspirates from infected cats. Cultures and documentation of increasing antibody titers can be used to confirm the diagnosis in cats and humans. Most cases of tularemia in cats have been diagnosed at necropsy and so optimal treatment is unknown. Streptomycin and gentamicin are the drugs used most commonly to treat humans. Tetracycline and chloramphenicol can be used in cases not requiring hospitalization but may be associated with relapses. The disease is prevented by avoiding exposure to lagomorphs, ticks, and infected cats. All cats dying with bacteremia should be handled carefully.

Approximately 300,000 emergency room visits per year are made by people bitten by animals in the United States. Most of the aerobic and anaerobic bacteria associated with bite or scratch wounds only cause local infection in immunocompetent individuals. However, 28% to 80% of cat bites become infected and severe sequelae including meningitis, endocarditis, septic arthritis, osteoarthritis, and septic shock can occur. The majority of the aerobic and anaerobic bacteria associated with dog or cat bite or scratch wounds lead only to local infection in immunocompetent individuals. Immunodeficient humans or humans exposed to Pasteurella spp., Capnocytophaga canimorsus (DF-2), or Capnocytophaga cynodegmi more consistently develop systemic clinical illness. Splenectomized humans are at increased risk of developing bacteremia. Dogs and cats are subclinical carriers of multiple bacteria in the oral cavity. After a human is bitten or scratched, local cellulitis is noted initially, followed by evidence of deeper tissue infection. Bacteremia and the associated clinical signs of fever, malaise, and weakness are common, and death can occur in hours following infection with Capnocytophaga spp. in immunodeficient humans. Diagnosis is confirmed by culture. Treatment of carrier animals is not needed. Treatment of clinically affected humans includes local wound management and parenteral antibiotic therapy. Penicillin derivatives are very effective against most Pasteurella infections; penicillins and cephalosporins are effective against Capnocytophaga spp. in vitro.

Mycoplasma spp. infections of people secondary to cat bites, one with cellulitis and one with septic arthritis, have been reported. L-form bacteria are cell-wall deficient organisms associated with chronic draining skin wounds in cats that are commonly resistant to cell-wall inhibiting antibiotics like penicillins.
and cephalosporins. Infection of a human after a cat bite was documented. Diagnosis can only be confirmed by histologic examination of tissue. Doxycycline has been used to successfully treat cats and people. Gloves should be worn when attending cats with draining tracts, and hands should be cleansed thoroughly.

**Fungal.** Of the many fungal agents that infect both humans and animal, only *Sporothrix schenckii* and the dermatophytes have been shown to infect humans upon direct exposure. *Histoplasma, Blastomyces, Coccidioides, Aspergillus,* and *Cryptococcus* infections of humans and animals can occur in the same household, but infection of humans generally results from a common environmental exposure rather than by direct contact with an infected animal. *Sporothrix* is cosmopolitan in distribution and the soil is thought to be the natural reservoir. Infection of cats and humans usually occurs after the organism contaminates broken skin. Cats are thought to be infected by scratches from contaminated claws of other cats; infection is most common in outdoor males. Humans can be infected by contaminating cutaneous wounds with exudates from infected cats. *Sporothrix* infection in cats can be cutaneolymphatic, cutaneous, or disseminated. Chronic draining cutaneous tracts are common. Cats commonly produce large numbers of the organism in feces, tissues, and exudates, thus, veterinary care personnel are at high risk when treating infected cats. The clinical disease in humans is similar to that in cats. Dogs generally do not produce large numbers of *Sporothrix* in exudates and so are less of a zoonotic risk. The organism can be demonstrated by cytologic examination of exudates or culture. Fluconazole, itraconazole, or ketoconazole are effective treatments. Gloves should be worn when attending cats with draining tracts and hands should be cleansed thoroughly.

**Viral.** Rabies is still the only significant small animal viral zoonosis in the United States. Since 1980, more cases of rabies have been reported in cats than in dogs in the USA. Rabies is a major, potentially lethal, occupational health hazard for those commonly working with animals with unknown vaccination status including veterinary staff as well as humane shelter and rescue group employees. Pre-exposure vaccination should be offered to veterinarians and others who work with dogs and cats in rabies enzootic areas. However, in a recent survey, 85.1% of veterinary medical association members and managers of animal shelters or wildlife rehabilitation centers had been vaccinated versus only 17.5% of staff members. Some have been concerned whether the retroviruses of cats, feline leukemia virus, feline immunodeficiency virus, and feline foamy virus, can infect people because FeLV subtypes B and C can replicate in human cell lines. However, to date, humans have not been shown to be infected with any of the feline retroviruses. In the most recent study, 204 veterinarians and others potentially exposed to feline retroviruses were assessed for antibodies against FIV and FeFV, FeLV p27 antigen, and FeLV provirus; all were negative. Since both FeLV and FIV can induce immunodeficiency, infected cats should be considered more likely than retrovirus-naive cats to be carrying other potential zoonotic agents, particularly if gastrointestinal tract signs are occurring.

**Respiratory and ocular zoonoses.** *Bordetella bronchiseptica* is a bacterium that induces respiratory tract infections in dogs and cats. The classic clinical manifestation is tracheobronchitis, but the organism can also cause pneumonia, sneezing, and nasal discharge. Humans rarely develop clinical disease due to *B bronchiseptica* unless they are immune compromised. Only 39 cases of *B. bronchiseptica* infection in people had been reported by 1998; most were immunodeficient. Amoxicillin-clavulanate, chloramphenicol, enrofloxacin, and tetracycline derivatives are effective treatments. Animals with upper or lower respiratory tract inflammatory disease should be kept away from immunodeficient people until clinically normal. However, treated animals can still shed the organism.

*Chlamydophila felis* (formerly *Chlamydia psittaci*) causes mild conjunctival disease and rhinitis in cats. In Japan, the prevalence rates of antibodies against an isolate of *Chlamydophila felis* were 51.1% in stray cats, 15.0% in pet cats, 3.1% in the general human population and 5.0% in small animal clinic
veterinarians, suggesting that transfer between cats and people may occur. Conjunctivitis in humans following direct contact with ocular discharges from cats has been described but systemic disease is rare. Diagnosis is based on organism demonstration by culture, cytological documentation of characteristic inclusion bodies, polymerase chain reaction assay, or fluorescent antibody staining of conjunctival scrapings. Tetracycline or chloramphenicol-containing eye ointments generally are effective in the treatment of infection. Care should be taken to avoid direct conjunctival contact with discharges from the respiratory or ocular secretions of cats, especially by immunosuppressed persons. Employees should be directed to wear gloves or wash hands carefully when attending cats with conjunctivitis.

Humans are the principal natural hosts for Streptococcus group A bacteria, S. pyogenes and S. pneumoniae, which cause “strep throat” in people. Dogs and cats in close contact with infected humans can develop transient, subclinical colonization of pharyngeal tissues and can transmit the infection to other humans. However, this is poorly documented and thought to be unusual. The organism can be cultured from the tonsillar crypts. Culture-positive animals should be treated with penicillin derivatives. If animals are to be treated in a household with chronic recurrent “strep throat”, all humans should also be treated since they also could be chronic subclinical carriers.

Yersinia pestis and Francisella tularensis can be transmitted from cats to people in respiratory secretions (see Bite, scratch, or exudate zoonoses section). In endemic areas, cats with clinical signs or radiographic abnormalities consistent with pneumonia should be handled as plague or tularemia suspects. Gloves, mask, gown, and eye protection should be worn while performing transoral airway washings in suspect cats.

Genital and urinary tract zoonoses. Coxiella burnetii is a rickettsial agent found throughout the world, including North America. Many ticks, including Rhipicephalus sanguineus, are naturally infected with Coxiella burnetii. Cattle, sheep, and goats are commonly subclinically infected and pass the organism into the environment in urine, feces, milk, and parturient discharges. Seropositive dogs have been detected but zoonotic transfer to people from dogs has not been documented. Infection of cats most commonly occurs following tick exposure, ingestion of contaminated carcasses, or aerosolization from a contaminated environment. Fever, anorexia, and lethargy develop in some experimentally infected cats. Infection has been associated with abortion in cats, but the organism can also be isolated from normal parturient cats. Infection of cats appears to be common; 20% of cats from a humane society in southern California and in Maritime Canada were seropositive, and the organism was grown from the vagina of healthy cats in Japan. We have also amplified C. burnetii DNA from the uterus of healthy, client-owned cats. Human illness associated with direct contact with infected cats occurs after aerosol exposure to the organism passed by parturient or aborting cats; clinical signs develop 4 to 30 days after contact. Humans commonly develop acute clinical signs similar to those associated with other rickettsial diseases including fever, malaise, headache, pneumonitis, myalgia, and arthralgia. After primary infection, chronic Q fever develops in approximately 1% and can manifest as hepatic inflammation or valvular endocarditis. Tetracyclines, chloramphenicol, and quinolones are usually effective therapeutic agents in people. Gloves and masks should be worn when attending to parturient or aborting cats. People that develop fever or respiratory tract disease after exposure to parturient or aborting cats should seek medical attention.

There are at least 11 Leptospira serovars that infect dogs in the United States; cats are very resistant to infection. Leptospira spp. can be transmitted in urine from infected dogs and cats to humans, resulting in clinical disease. Host-adapted species cause subclinical infection; infection by non-host adapted species commonly results in clinical illness. Human clinical syndromes vary with the serovar, but are similar to those that occur in the dog. The organisms enter the body through abraded skin or intact mucous membranes. See recently published papers for a detailed discussion of the clinical manifestations of this disease and its treatment in dogs and cat. Leptospirosis should be suspected in dogs with acute nephritis or hepatitis. The infections also frequently cause fever; the infections can also induce chronic disease in
some animals. Azotemia with pyuria but no bacteriuria are also common since the organisms are usually not seen under the light microscope. Cats generally do not develop clinical leptospirosis and the role they play in human infections is unknown but thought to be minimal. Diagnosis can be made by dark field examination of urine, culture, presence of serum antibodies, and PCR amplification of organismal DNA in urine. Intravenous administration of penicillins should be used initially for treatment followed by several weeks of doxycycline treatment to clear the tissue phases. Vaccines contain 2-4 serovars and so are not 100% protective since the serovars do not cross-protect. In addition, immunity associated with vaccination may persist less than 1 year.

Animals with suspected leptospirosis should be handled while wearing gloves. Contaminated surfaces should be cleaned with detergents and disinfected with iodine-containing products.

*Brucella canis* is a bacterium that preferentially infects the testicles, prostate, uterus, and vagina of dogs. The infection is maintained in dogs primarily by venereal transmission. Humans can be infected by direct contact with vaginal and preputial discharges from dogs. Clinical syndromes in dogs are diverse but commonly include abortion, stillbirth, failure to conceive, orchitis, epididymitis, vaginal discharge, uveitis, diskospondylitis, and bacteremia. Intermittent fever, depression, and malaise are common in infected people. Diagnosis is based on serologic testing or demonstration of the organism by culture. Dogs with clinical signs of brucellosis should be evaluated serologically for *Brucella* infection using the 2-mercaptoethanol rapid slide agglutination card test. Seronegative dogs are unlikely to be harborng *Brucella* unless the clinical syndrome was peracute. Seropositive dogs should have results confirmed by tube agglutination or agar gel immunodiffusion. Long term antibiotic treatment (tetracyclines, aminoglycosides, quinolones) usually does not clear the infection. Ovariohysterectomy or castration will lessen contamination of the environment. Genital tract secretions should be avoided.

**SHARED VECTOR ZOONOSES**

Some zoonotic agents are transmitted between animals and man by shared vectors like fleas, ticks, or mosquitoes. *Rickettsia rickettsii* (ticks), *Ehrlichia* spp. (ticks), *Anaplasma phagocytophilum* (ticks), *Borrelia burgdorferi* (ticks), *Rickettsia felis* (fleas), *Bartonella* spp. (fleas and ticks), *Dipylidium caninum* (fleas), *Dirofilaria immitis* (mosquitoes), and West Nile virus (mosquitoes) are examples of vector borne zoonoses that are common in the United States. For the flea- and tick-borne zoonoses, the pet brings the vector of the organism into the environment resulting in exposure of the human. There could be a slight increased risk of exposure to veterinary health care providers since we handle many animals infested with fleas and ticks. However, it is the vector, not direct contact with the infested animal that results with infection of the human. Flea and tick control should always be maintained animals and infested animals that are seen in the clinic should be treated immediately.

**SHARED ENVIRONMENT ZOONOSES**

Some agents that infect both animals and man are not commonly transmitted between the pet and the owner by direct contact but are acquired from the same environmental source. Notable examples include *Histoplasma capsulatum, Coccidioides immitis, Blastomyces dermatitidis, Cryptococcus neoformans,* and *Aspergillus* spp.
FOOTNOTES

a http://www.cdc.gov/hiv/pubs/brochure/oi_pets.htm
b http://www.cdc.gov/ncidod/dpd/parasites/ascaris/prevention.htm
c http://www.catvets.com
d http://www.capcvet.org

SUGGESTED READINGS (a complete reference list is available on request).


Table 1. General guidelines for veterinarians to avoid zoonotic transfer of disease

- Veterinarians and their staff should familiarize themselves with zoonotic issues and take an active role in discussing the health risks and benefits of pet ownership with clients so that logical decisions concerning ownership and management of individual animals can be made.

- The veterinary clinic should make it clear that the staff understands conditions associated with immune deficiency, is discreet, and is willing to help; use of signs or posters can be effective for this purpose.

- Pet owners should be provided information concerning veterinary or public health aspects of zoonoses, but veterinarians should not diagnose diseases in humans or discuss specific treatments.

- Clinically ill pet owners should always be referred to a physician for additional information and treatment.

- Veterinarians and physicians have different experiences concerning zoonoses; veterinarians should volunteer to speak to the pet owner’s physician to clarify zoonotic issues when indicated.

- When public health related advice is offered, it should be documented in the medical record.

- When reportable zoonotic diseases are diagnosed, appropriate public health officials should be contacted.

- Diagnostic plans to assess for presence of organisms with zoonotic potential should be offered, particularly to owners with clinically ill pets.

- All dogs and cats should be vaccinated for rabies.

- Dogs and cats should be routinely dewormed with a drug that kills hookworms and roundworms.

- Flea and tick control should be maintained at all times.
Table 2. General guidelines for pet owners to avoid zoonotic transfer of disease

- If a new pet is to be adopted, the dog or cat least likely to be a zoonotic risk is a clinically normal, arthropod-free, adult animal from a private family.
- Once the animal to be adopted is identified, it should be quarantined from any immunocompromised person until a thorough physical examination and zoonoses risk assessment is performed by a veterinarian.
- Veterinary care should be sought for all clinically ill pets.
- Physical examination and fecal examination should be performed at least once or twice yearly.
- Fecal material produced in the home environment should be removed daily, preferably by someone other than an immunocompromised individual.
- Use litter box liners and periodically clean the litter box with scalding water and detergent.
- Do not allow dogs or cats to drink from the toilet.
- Wear gloves when gardening and wash hands thoroughly when finished.
- Filter or boil water from sources in the environment.
- Wash your hands after handling animals.
- Do not handle animals that you are unfamiliar with.
- Clinically ill animals should not be handled by immunocompromised people, if possible.
- Pets should be maintained within the home environment to lessen exposure to other animals that may carry zoonotic agents, exposure to excrement of other animals, and exposure to fleas and ticks.
- Pets should only be fed commercially processed food.
- People should not share food utensils with pets.
- Avoid being licked by animals.
- Claws of cats should be clipped frequently to lessen the risk of skin penetration.
- To lessen the risk of bites and scratches, do not tease or physically restrain dogs and cats.
- If bitten or scratched by a dog or cat, seek medical attention.
- Control potential transport hosts like flies and cockroaches that may bring zoonotic agents into the home.
- Cook meat for human consumption to 80°C for 15 minutes minimum (medium-well).
- Wear gloves when handling meat and wash hands thoroughly with soap and water when finished.