UPDATE ON THE DIAGNOSIS AND TREATMENT OF *MYCOPLASMA HAEMOFELIS* AND *M. HAEMOMINUTUM* INFECTIONS OF CATS

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The large and small forms of *Haemobartonella felis* are gram-negative, epicellular parasite of feline erythrocytes. The organisms are classified as mycoplasmas. The new name for large form (Ohio isolate) is *Mycoplasma haemofelis*. The proposed name for the small form (California isolate) *Mycoplasma haemominutum*. In at least two studies of experimentally infected cats, *M. haemofelis* is apparently more pathogenic than *M. haemominutum*; all *M. haemofelis* inoculated cats became clinical ill whereas *M. haemominutum* inoculated cats were subclinically infected. Cats with chronic *M. haemominutum* infection had more severe anemia and longer duration of anemia when experimentally infected with *M. haemofelis* when compared to cats infected with *M. haemofelis* alone. The clinical syndromes associated with infection associated with either organism are now known as haemoplasmosis.

It was recently shown that naturally infected cats and fleas can be infected by *M. haemominutum*. In addition, cats with experimentally induced *M. haemominutum* infections transfer the infection mechanically to fleas. We have just shown fleas to be competent vectors for *M. haemofelis* (unpublished data). Haemoplasmas have been transmitted experimentally by IV, IP, and oral inoculation of blood. Clinically ill queens can infect kittens; whether transmission occurs *in utero*, during parturition, or from nursing has not been determined. Transmission by biting has been hypothesized. Red blood cell destruction is due primarily to immune-mediated events; direct injury to red blood cells induced by the organism is minimal.

Clinical signs of disease depend on the degree of anemia, the stage of infection, and the immune status of infected cats. It appears that *M. haemominutum* infections are potentiated by feline leukemia virus coinfection. Clinical signs and physical examination abnormalities associated with anemia are most common and include pale mucous membranes, depression, inappetence, weakness, and occasionally, icterus and splenomegaly. Fever occurs in some acutely infected cats and may be intermittent in chronically infected cats. Evidence of coexisting disease may be present. Weight loss is common in chronically infected cats. Cats in the chronic phase can be subclinically infected only to have recurrence of clinical disease following periods of stress. A greater percentage of cats with fever are infected with *M. haemofelis* than cats without fever suggesting the organism can be associated with fever of unknown origin.

The anemia associated with haemoplasmosis is generally macrocytic, normochromic but may be macrocytic, hypochromic if coinfections leading to chronic inflammation exist. Chronic non-regenerative anemia is unusual in haemoplasmosis. Neutrophilia and monocytosis have been reported in some haemoplasma-infected cats. Diagnosis is based on demonstration of the organism on the surface of erythrocytes on examination of a thin blood film or polymerase chain reaction (PCR). 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, the PCR is the test of choice due to sensitivity. Primers are available that amplify a segment of the 16S rRNA gene common to both haemoplasmas (Jensen et al, 2001).

Since haemoplasmosis and primary immune hemolytic anemia are difficult to differentiate, cats with severe, regenerative hemolytic anemia should be treated with glucocorticoids and antibiotics. Doxycycline has less side effects than other tetracyclines in cats and so is preferred. Doxycycline should be given at 10 mg/kg, PO, every 24 hours for 28 days. Generic tablets have been associated with esophageal strictures and should be liquefied or water should be given after pilling. If autoagglutination is evident, prednisolone is usually prescribed at 1 mg/kg, PO, every 12 hours for the first 7 days or until autoagglutination is no longer evident. Tetracyclines utilized to date appear to lessen parasitemia and clinical signs of disease but probably do not clear the organism from the body. In one study, experimentally infected cats treated with doxycycline have apparent clinical response but the organism could still be detected by PCR when the cats were given methylprednisolone acetate.
In cats intolerant of doxycycline, quinolones should be considered. Enrofloxacin given at 5 mg/kg, PO, every 24 hours or at 10 mg/kg, PO, every 24 hours for 14 days is tolerated by cats and is equally effective or more effective than doxycycline. Azithromycin was not effective for the treatment of hemoplasmosis in one study. Imidocarb dipropriate administered at 5 mg/kg, IM, every 2 weeks for at least 2 injections was used successfully in the management of five naturally-infected cats that had failed treatment with other drugs. Blood transfusion should be given if clinically indicated. Potential arthropod vectors should be controlled. Cats should be housed indoors to avoid vectors and fighting. Clinic blood donor cats should be screened for *H. felis* infection by polymerase chain reaction. In a recent national prevalence study, it was shown that 9.8% of the cats used as blood donors were PCR positive for haemoplasmas.

UPDATE ON THE DIAGNOSIS AND TREATMENT OF *BARTONELLA* INFECTIONS OF CATS

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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*, and *B. weissii*. *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.

The link to uveitis was first made in an individual case with uveitis that ultimately responded to doxycycline therapy (Lappin and Black, 1999). We subsequently found *Bartonella* antibody production and DNA in the aqueous humor of cats previously presumed to have idiopathic uveitis (Lappin et al, 200). However, it is still unclear as to why some cats develop *Bartonella* uveitis and others do not. We failed to induce *Toxoplasma* or *Bartonella* uveitis when we inoculated *Bartonella* IV into cats with chronic toxoplasmosis (Powell et al, 2002).

Seroprevalence in cats varies by region but as many as 54.6%-81% of cats in some geographical areas of the United States are *Bartonella* spp. seropositive. The organism is transmitted between cats by fleas (Chomel et al, 1996) and so prevalence is greatest in cats from states where fleas are common. Infection of humans is often associated with contact with kittens. We recently documented *B. henselae* and *B. clarridgeaie* in cats and their fleas. Live *B. henselae* can be grown from flea feces and so direct contact with flea excrement may play a role in infection of people. It is also possible that people are infected when fed on by fleas carrying *B. henselae*.

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 assess individual cats for *Bartonella* 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 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. 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. Testing should be reserved for cats with suspected clinical

bartonellosis. If the results of *Bartonella* tests are negative in a clinically ill cat, the organism is not likely the cause of the clinical syndrome. If the results of *Bartonella* tests are positive, the agent remains on the differential list, but other causes of the clinical syndrome must also be excluded.

Administration of doxycycline, tetracycline, erythromycin, amoxicillin-clavulanate, 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. Azithromycin led to partial clinical responses in some children with cat scratch disease and so has been promoted by some as being effective for clinical bartonellosis in cats. Since no drug has convincing been shown to eliminate bacteremia, antibiotic treatment of healthy, culture positive or PCR positive cats is controversial. Treatment should be reserved for cats with suspected clinical bartonellosis. Strict flea control should be maintained. Kittens of unknown health status should be avoided by immunodeficient people. Cat claws should be kept clipped or claw covers used and cats should never be teased. Cat-induced wounds should immediately be cleansed and medical advice sought.

FELINE *EHRLICHIA, NEORICKETTSIA, AND ANAPLASMA* UPDATE

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Cats can be infected by a number of arthropod-borne agents previously thought only to infect dogs. However, to date, there have only been a small number of experimental infection studies in cats. Cats experimentally infected with *Neorickettia risticii* (previously *E. risticii*) develop morulae in mononuclear cells and occasionally develop clinical signs of disease including fever, depression, lymphadenopathy, anorexia, and diarrhea. Cats experimentally infected with *Anaplasma phagocytophilum* (previously *E. equi*, human granulocytic ehrlichial agent, *E. phagocytophila*, and granulocytic ehrlichial agent of dogs), developed morulae in neutrophils and eosinophils, not mononuclear cells. Attempts to transmit *E. canis* to cats by SQ inoculation of cultured morulae have failed to date. When cats were inoculated SQ with an *Ehrlichia canis* strain (North Carolina State University canine isolate) maintained in cell culture, organismal DNA or antibodies that reacted to *E. canis* morulae were not detected in an eight week follow-up period (Lappin and Breitschwerdt, unpublished data, 2003). These results could be interpreted in the following manner: the *E. canis*-like DNA amplified from naturally infected cats may be a different *Ehrlichia* spp. more infective to cats, not all *E. canis* stains will infect cats, not all cats are susceptible to infection by *E. canis*, or SQ inoculation is not an effective method for infecting cats with *E. canis* (Breitschwerdt et al, 2002).

Ehrlichia canis-like DNA (3 cats in North America and 2 cats in France) and *A. phagocytophilum* (5 cats in North America; several cats in Sweden, Denmark, and the United Kingdom) have been amplified from naturally exposed cats by use of PCR assays. *Ehrlichia*-like morula have been detected in mononuclear cells or neutrophils of naturally-exposed cats in the United States, Kenya, Brazil, France, Sweden, and Thailand. Clinical diagnosis has been also been based on the combination of either positive *E canis* or *N. risticii* serology, clinical or laboratory findings consistent with ehrlichial infection, exclusion of other causes, and response to an anti-rickettsial drug. Exposure to arthropods has been reported in about 30% of the cases. *Ixodes* spp. ticks were associated with several cases with *A. phagocytophilum* infection.

Most cats from which age was reported were greater than 2 years of age, most cats were domestic short haired, and both males and females have been affected. Anorexia, fever, inappetence, lethargy, weight loss, hyperesthesia or joint pain, pale mucous membranes, splenomegaly, dyspnea, and lymphadenomegaly were the most common historical and physical examination abnormalities. Concurrent diseases are rarely reported but included *Mycoplasma haemofelis* or *M. haemominutum* infection (previously *Haemobartonella felis*) and lymphosarcoma. Anemia is a common laboratory abnormality and is usually non-regenerative. Leukopenia, leukocytosis characterized by neutrophilia, lymphocytosis, monocytosis, pancytopenia, and intermittent thrombocytopenia were reported for some cats. Hyperglobulinemia was reported for many cats; protein electrophoresis documents polyclonal gammopathy in most cats assayed. However, an epidemiological link has been made between presence of *Ehrlichia* spp. antibodies in serum and monoclonal gammopathy.

Some cats with suspected clinical ehrlichiosis had antibodies against *E. canis* and *N. risticii* and some had antibodies against *N. risticii* alone or *E. canis* alone. The five cats in the United States with *A. phagacytophilum* DNA in blood were positive for antibodies against *A. phagocytophilum*, but not *E. canis*. Positive serologic test results occur in healthy cats as well as clinically ill cats and so a diagnosis of clinical ehrlichiosis should not be based on serologic test results alone. Since there is variable cross-reactivity in antibodies against different species, antibody negative test results against one species does not exclude infection by other ehrlichial agents. Additionally, *E. canis* antibodies were not detected in 3 cats with *E. canis*-like DNA in blood and so serologic test results can also be falsely negative. Clinical signs of disease can occur prior to detection of antibodies and so serological tests can be negative in acute cases.

A tentative diagnosis of feline clinical ehrlichiosis or anaplasmosis can be based on the combination of positive serologic test results, clinical signs of disease consistent with *Ehrlichia* or *Anaplasma* infection, exclusion of other causes of the disease syndrome, and response to anti-rickettsial drugs. Polymerase chain reaction and gene sequencing can also be used to confirm infection and will be indicated for some cats with *E. canis* infection since antibodies were not detected in some.

Clinical improvement after therapy with tetracycline, doxycycline (10 mg/kg, PO, q24hr, for 28 days), or imidocarb dipropionate (5 mg/kg, IM, q14 days, for at least 2-4 injections) was reported for most cats.

There are currently no known direct public health risks associated *Ehrlichia* or *Anaplasma* infected cats. However, since some species of *Ehrlichia* and *Anaplasma* cross-infect, it is possible that cats could be a reservoir for species that infect people. Thus, it seems prudent to recommend arthropod control for cats.

FELINE INFECTIOUS GASTROINTESTINAL DISEASES

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Clinical problem. Vomiting is the forceful ejection of stomach and proximal duodenal contents through the mouth. Vomiting can be induced by vestibular, vagal, chemoreceptor trigger zone, or direct input to the emetic center. Regurgitation is the passive expulsion of food or fluid from the oral cavity, pharyngeal cavity, or esophagus. Diarrhea is a characterized by increased frequency of defecation, increased fluid content of the stool, or increased volume of stool. Markedly increased frequency of defecation, small volume stools, tenesmus, urgency, hematochezia, and mucus are consistent with large bowel diarrhea. Slight increase in frequency of defecation, large volume, melena, steatorrhea, and polysystemic clinical signs are more consistent with small bowel diarrhea. Mixed bowel diarrhea is a combination of characteristics or clinical signs.

Differential diagnoses for vomiting or small bowel diarrhea

1. Secondary GI diseases
    a. Renal disease
    b. Hepatic disease
    c. Pancreatitis
    d. Endocrine: hypoadrenocorticism; diabetic ketoacidosis; hyperthyroidism (cats)
    e. Peritonitis
    f. CNS/vestibular disease
    g. Pancreatic exocrine insufficiency
2. Primary GI diseases
    a. Obstruction. Masses, foreign body, intussusception, hiatal hernia
    b. Dietary intolerance
    c. Drugs/toxins (garbage gut)
    d. Inflammatory gastric and bowel diseases
    e. Neoplastic
    f. **INFECTIOUS DISEASES**

Differential diagnoses for large bowel diarrhea

1. Inflammatory
2. Neoplastic
3. Obstructive
4. Secondary GI (rare)
5. Spastic/idiopathic
6. Dietary intolerance
7. **INFECTIOUS DISEASES**

Primary clinical signs associated with infectious causes of gastrointestinal tract diseases are abbreviated as follows: S = small bowel; M = mixed bowel; L = large bowel; V = vomiting. Any of the following agents that induce diarrhea potentially can induce vomiting as well. The primary bacteria associated with gastrointestinal tract disease in cats include *Salmonella* spp. (S,M,L), *Campylobacter jejuni* (M,L), *Clostridium perfringens* (L,rare), *Helicobacter* spp. (V), bacterial overgrowth syndrome (S), bacterial peritonitis (S), and bacterial cholangiohepatitis (S). The primary viral agents include feline coronaviruses (S), feline leukemia virus (FeLV; V,S,M,L), feline immunodeficiency virus (FIV; V,S,M,L), and feline panleukopenia virus (V only frequently, S). The primary nematodes are *Ancylostoma*/*Uncinaria* (S,M), *Strongyloides cati* (S,M, rare), *Dirofilaria immitis* (V), *Toxocara cati* (V), *Toxascaris leonina* (V), *Ollulanus tricuspis* (V), and *Physaloptera* spp. (V). Enteric protozoans include *Giardia* spp. (S,M), *Cystoisospora* spp. (*Isospora*; M,L), *Cryptosporidium* spp. (S,M), *Entamoeba histolytica* (L, rare), and *Tritrichomonas foetus* (L). The cestodes *Taenia*, *Dipylidium*, and *Echinococcus* generally cause subclinical infection. Common feline parasites are listed in Table 1. The primary fungal agent associated with gastrointestinal disease in cats is *Histoplasma capsulatum* (L).

Diagnostic plan. Occasionally, otherwise healthy cats with acute vomiting and normal physical examination findings can be handled conservatively by withholding food for 24 hours followed by introduction of a bland food for several days. For all cats with vomiting or small bowel diarrhea, I will perform a fecal flotation, complete blood cell count (CBC), and rectal cytology if diarrhea is present. While the CBC generally does not lead to a specific diagnosis, the presence of eosinophilia makes inflammatory bowel diseases and parasitism more likely.

I perform acid-fast staining of a fecal smear on all cats with diarrhea to assess for the presence of *Cryptosporidium parvum* oocysts. A wet mount will aid in identifying trophozoites of *Tritrichomonas* and *Giardia*. If neutrophils or spirochetes are evident on rectal cytology I recommend fecal culture for *Salmonella* spp. and *Campylobacter* spp.. If spore-forming rods consistent with *Clostridium perfringens* are present in large numbers, fecal enterotoxin assay can be performed to help confirm the diagnosis.

A biochemical profile, urinalysis, FeLV antigen assay, and FIV antibody assay are indicated if secondary GI diseases are on the differential list or if dehydration is present. I generally perform a total T4 on all cats with vomiting or small bowel diarrhea that are greater than 5 years of age. While amylase and lipase are poor predictors of pancreatitis in cats, a pancreatic lipase immunoreactivity assay has now been validated. It can be used to diagnose pancreatitis (increased) in cats. The positive predictive value is better for acute pancreatitis than chronic pancreatitis. If a cat with suspected pancreatitis has abdominal effusion, assay lipase concentrations in the serum and effusion; if pancreatitis is occurring the effusion lipase is usually greater than serum.

Fecal fat assessment with Sudan IV stain can help confirm malabsorption/maldigestion but is not specific for a single disease. If the MCV is low, chronic iron deficiency should be suspected; this occurs almost exclusively with gastrointestinal diseases. A serum iron panel can be used to confirm iron deficiency. Panhypoproteinemia is almost always associated with gastrointestinal tract disease.

Imaging techniques include radiographs, contrast radiographs, and ultrasound. I commonly perform abdominal radiographs in cats to support my palpation findings. I use contrast radiographs occasionally; often I perform endoscopy or exploratory laparotomy based on abdominal radiographic findings. Ultrasound of the intestinal tract can be hard to interpret and is operator dependent.

Diagnosis of gastric foreign bodies and diffuse inflammatory diseases can be made by endoscopy. Endoscopically obtained biopsies are small; I generally take at least 8-10 biopsies from stomach, duodenum, colon, and ileum if possible. Even if a lesion is present, endoscopically obtained biopsies can be falsely negative requiring full thickness biopsies. Gastric biopsies should be placed on urea slants to assess for urease which is found in the cell wall of *Helicobacter* spp..

DIAGNOSTIC PROCEDURES FOR INFECTIOUS DISEASES

Infectious diseases are common causes of vomiting and diarrhea in cats. The following is a brief discussion of the commonly used procedures.

Direct smear. Liquid feces or feces that contains large quantities of mucus should be microscopically examined immediately for the presence of protozoal trophozoites, including those of *Giardia* spp. and *Tritrichomonas foetus*. A direct saline smear can be made to potentiate observation of these motile organisms. The amount of feces required to cover the head of a match is mixed thoroughly with one drop of 0.9% NaCl. Following application of a coverslip, the smear is evaluated for motile organisms by examining it under 100X magnification. The sample should be fresh. The material for evaluation should be collected from the surface of the fecal material. Alternately, a rectal scraping can be used.

Stained smear. A thin smear of feces should be made from all cats with large or small bowel diarrhea. Material should be collected by rectal swab if possible to increase chances of finding white blood cells. A cotton swab is gently introduced 3-4 cm through the anus into the terminal rectum, directed to the wall of the rectum, and gently rotated several times. Placing a drop of 0.9% NaCl on the cotton swab will facilitate passage through the anus, but not adversely affect cell morphology. The cotton swab is rolled on a microscope slide gently multiple times to give areas with varying smear thickness. Following air drying, the slide can be stained.

White blood cells and bacteria morphologically consistent with *Campylobacter jejuni* or *Clostridium perfringens* can be observed after staining with Diff-Quick or Wright's-Giemsa stains. *Histoplasma capsulatum* or *Prototheca* may be observed in the cytoplasm of mononuclear cells. Methylene blue in acetate buffer (pH 3.6) stains trophozoites of the enteric protozoans. Iodine stains and acid methyl green are also used for the demonstration of protozoans. Acid-fast or monoclonal antibody staining of a fecal smear should be performed in cats with diarrhea to aid in the diagnosis of cryptosporidiosis. *Cryptosporidium parvum* is the only enteric organism of approximately 4 to 6 μ in diameter that will stain pink to red with acid-fast stain. Presence of neutrophils on rectal cytology can suggest inflammation induced by *Salmonella* spp., *Campylobacter* spp., or *Clostridium perfringens*; fecal culture is indicated in

these cases. Fecal enterotoxin measurement should be considered for cats with spore-forming rods morphologically consistent with *C. perfringens*.

Fecal flotation. Cysts, oocysts, and eggs in feces can be concentrated to increase sensitivity of detection. Most eggs, oocysts, and cysts are easily identified after zinc sulfate centrifugal flotation (Table 2). This procedure is considered by many to be optimal for the demonstration of protozoan cysts, in particular, *Giardia* spp. and so is a good choice for a routine flotation technique in practice. Sugar centrifugation can be used for routine parasite evaluation and may be superior to many techniques for the demonstration of oocysts of *Toxoplasma gondii* and *Cryptosporidium* spp.. *Giardia* cysts are distorted by sugar centrifugation but can still be easily identified. Fecal sedimentation will recover most cysts and ova, but will also contain debris. This technique may be superior to flotation procedures for the documentation of *Eurytrema procyonis*, the pancreatic fluke. *Strongyloides cati* larva may be easier to identify after concentration using the Baerman funnel technique.

Culture. Culture of feces for *Salmonella* spp., *Campylobacter* spp., and *Clostridium perfringens* is occasionally indicated in small animal practice. Approximately 2-3 grams of fresh feces should be submitted to the laboratory immediately for optimal results, however, *Salmonella* and *Campylobacter* are often viable in refrigerated fecal specimens for 3-7 days. Appropriate transport media should be available through your laboratory. The laboratory should be notified of the suspected pathogen so appropriate culture media can be used. More than 1 culture may be needed to prove infection. *Tritrichomonas foetus* can be cultured from feces of cats in general practice using a commercially available kit (InpouchTM, Biomed Diagnostics). Some *Giardia* spp. isolated from cats will grow on culture media, but this technique is not generally performed in small animal practice.

Immunologic techniques. Parvovirus, *Cryptosporidium parvum*, and *Giardia* spp. antigen detection procedures are available for use with feces. Canine parvovirus antigen assays appear to detect feline parvovirus antigen. Minimal sensitivity and specificity results for the *C parvum* and *Giardia* spp. ELISA when used with feces from small animals are currently available. When used, results of these assays should be interpreted in conjunction with results from fecal examination techniques. IFA for detection of *C. parvum* oocysts have been validated for use with feline feces; this assay is commonly available at human hospitals. It is currently unknown whether currently available immunologic techniques for detection of *Giardia* and *Cryptosporidium* detect dog and cat isolates.

Serum antibodies against *D. immitis* can be measured in cat serum but positive test results do not prove current infection or disease induced by *D. immitis*. FeLV can cause lymphoma and induces the panleukopenia-like syndrome. FIV has been associated with lymphoma and can cause enteritis. Detection of FIV antibodies or FeLV antigen in serum documents exposure, but does not prove that clinical disease is due to the virus. The only way to document that gastrointestinal signs are due to FeLV or FIV is to exclude other known causes.

Electron microscopy. Electron microscopy can be used to detect viral particles in feces of cats with gastrointestinal signs of disease. Approximately 1-3 grams of feces without fixative should be transported to the laboratory by overnight mail on cold packs.

Endoscopy or exploratory laparotomy. *Ollulanus* and *Physaloptera* rarely pass ova in feces and so frequently are diagnosed only by endoscopy. Diagnosis of diffuse inflammatory diseases can be made by evaluation of endoscopy or surgically obtained tissue samples.

Endoscopically obtained biopsies are small; I generally take at least 8-10 biopsies from stomach, duodenum, colon, and ileum if possible. Even if a lesion is present, endoscopically obtained biopsies can be falsely negative requiring full thickness biopsies. Gastric biopsies should be placed on urea slants to assess for urease which is found in the cell wall of *Helicobacter* spp.. The combination of inflammation, exclusion of other causes of inflammation, presence of gastric spiral bacteria, and positive urease testing can be used as a presumptive diagnosis of gastric helicobacteriosis. There is no benefit to performing duodenal aspirates for quantitative bacterial cultures or *Giardia* trophozoite evaluations in cats; the normal bacterial count range is very broad in cats and *Giardia* is found in the distal small intestine. Regional enteritis due to feline infectious peritonitis can be confirmed by documenting the organism in tissue after immunohistochemical staining.

Polymerase chain reaction

Polymerase chain reaction (PCR) is currently available to detect *Giardia* spp., *Cryptosporidium* spp., and *T. foetus* in feline feces. These assays are 100 to 1,000 fold more sensitive than IFA. Reverse-transcriptase PCR can be used to detect coronavirus RNA in feces of cats but is not specific for feline infectious peritonitis.

INFECTIOUS DISEASE TREATMENT OPTIONS

There are multiple drugs used in the treatment of gastrointestinal parasitic infections. Table 3 summarizes the doses and indications for some of the common drugs.

For all kittens, the strategic deworming recommendations for the control of hookworm and roundworm infections from the Centers for Disease Control and the American Association of Veterinary Parasitologists should be followed by veterinary practitioners. (http://www.cdc.gov/ncidod/dpd/parasites/ascaris/prevention.htm). Kittens should be administered an anthelmintic at 3, 5, 7, and 9 weeks of age and then periodically monitored or treated. If the kitten is not presented to the clinic until 6-8 weeks of age, administer the anthelmintic at least 2-3 times, 2-3 weeks apart. Pyrantel pamoate and fenbendazole are usually effective drugs for use in strategic deworming programs and for the treatment of nematodes causing gastrointestinal tract disease. Albendazole is more likely to cause hematologic side-effects than fenbendazole and so should not be used in cats. Even if anthelmintics for hookworms and roundworms are administered, a fecal flotation should be performed to evaluate for other parasites.

Monthly *D. immitis* preventatives can help control or eliminate some nematode infections as well as prevent heartworm infection. Ivemectin at heartworm preventative doses is effective for control of hookworms but not roundworms. Thus, selamectin or milbemycin should be used in regions where roundworm infections are common. Selamectin has the advantage of controlling fleas as well and so may lessen the potential for *Bartonella* spp., *Rickettsia felis*, and

Haemobartonella (*Mycoplasma*) spp. infections. *Dipylidium* and *T. taeniaformis* infestations usually are eliminated by praziquantel or espiprantel; fenbendazole is effective for *Taenia taeniaformis*. Since *Echinococcus multilocularis* can be a significant zoonosis transmitted to cats by carnivorism, hunting cats in endemic areas should be treated up to monthly. Administration of a pyrantel/praziquantel combination may be effective in these cats since praziquantel is approved for the treatment of *Echinococcus* and roundworms are also transmitted by carnivorism.

Giardia and *Tritrichomonas* often respond clinically to the administration of metronidazole (Table 3) but infection is usually not eliminated. Administration of metronidazole benzoate at 25 mg/kg, q12hr, PO, for 7 days was effective in suppressing cyst shedding to below detectable limits in 26 cats (Abstract 1). This is the maximum dose of metronidazole that should be used; CNS toxicity can be induced by overdosing or as a cumulative neurotoxin. Until recently, fenbendazole has not been studied for the treatment of giardiasis in cats. In eight cats with *Cryptosporidium* spp. and *Giardia* spp. coninfection, only 50% eliminated the *Giardia* infection when treated with fenbendazole (Abstract 2). A *Giardia* spp. vaccine has been introduced for use in cats. When used in an experimental study assessing its use as an immunotherapy (3 doses) for giardiasis, there was no difference in cyst shedding between vaccinates and controls (Abstract 3).

Sequential administration of clindamycin followed by tylosin blocked oocyst shedding and resolved diarrhea in one cat with chronic, clinical cryptosporidiosis. Tylosin has been apparently successful in lessening diarrhea and oocyst shedding in multiple other cats with diarrhea. However, infection is not eliminated. Unfortunately, tylosin is very bitter and usually has to be given to cats in capsules. Paromomycin can be effective for lessening diarrhea and oocyst shedding associated with cryptosporidiosis in cats and also is an alternate anti-*Giardia* drug. However, this orally administered aminoglycoside may cross the diseased intestinal wall to induce renal insufficiency and should never be used in cats with bloody diarrhea. In cats with naturally occurring cryptosporidiosis, response to azithromycin has been variable (Lappin MR, unpublished data, 2003).

The *Toxoplasma gondii* oocyst shedding period can be shortened by administration of clindamycin or sulfadimethoxine. *Cystoisospora* spp. generally respond to the administration of sulfadimethoxine or other sulfa-containing drugs.

Since many of the gastrointestinal parasites that infect cats are transmitted by carnivorism, cats should not be allowed to hunt or be fed raw meats. Additionally, infection of cats by many feline parasites results from ingestion of contaminated water. Clinical disease in some parasitized cats can be lessened by eliminating stress and providing a quality diet and clean environment. *Clostridium perfringens* and bacterial overgrowth generally respond to treatment with tylosin, metronidazole, ampicillin, amoxicillin, or tetracyclines. The drug of choice for campylobacteriosis is erythromycin; however, oral administration of quinolones is often less likely to potentiate vomiting. Salmonellosis should only be treated parenterally due to rapid resistance that occurs following oral administration of antibiotics. Appropriate antibiotics for the empirical treatment of salmonellosis while awaiting susceptibility testing results include chloramphenicol, trimethoprim-sulfa, amoxicillin; quinolones are also effective. *Helicobacter*

spp. infections are usually treated with the combination of metronidazole and tetracycline or amoxicillin and metronidazole in dogs. Clarithromycin or azithromycin may be logical choices in cats since the species is often difficult to treat with multiple drugs. Whether to concurrently administer an antacid like famotidine is controversial but seems to lessen vomiting in some cats.

Cats with apparent bacteremia due to enteric bacteria should be treated with parenteral antibiotics with a spectrum against anaerobic and gram negative organisms. The combination of enrofloxacin with a penicillin or first generation cephalosporin is generally effective. Second generation cephalosporins or imipenem are also appropriate choices.

Cats that have hepatic infections and signs of bacteremia should be treated with antibiotics that kill gram positive, gram negative and anaerobic bacteria as discussed before. Non septic hepatic infections generally respond to amoxicillin, first-generation cephalosporins, or chloramphenicol. Decreasing numbers of enteric flora by oral administration of penicillins, metronidazole, or neomycin can lessen the clinical signs of hepatic encephalopathy.

Panleukopenia virus, feline leukemia virus, feline immunodeficiency virus, and coronaviruses are the most common viral causes of gastrointestinal tract disease in cats. Viral diseases are managed by supportive treatment. Make sure to maintain hydration, correct hypoglycemia, and maintain normal potassium concentrations. Use of jugular catheters is superior to leg veins since blood samples can be drawn and CVP can be measured.

Based on results in dogs with parvovirus infection, administration of plasma or serum (1 ml/kg) from your hyperimmune blood donor cat may lessen morbidity in cats with panleukopenia due to passive transfer of immunity. This is effective because parvoviruses induce a viremic state; virus particles are complexed by the antibodies transferred passively. Antibiotics effective against gram negative and anaerobic bacteria are commonly indicated. Vaccines are available for the prevention of parvovirus, coronaviruses, and feline leukemia virus infection.

Histoplasma capsulatum infection is the most common fungal infection of the gastrointestinal tract of cats in the United States. Treatment with itraconazole can be effective.

ZOONOTIC CONSIDERATIONS

Parasites. While enteric zoonoses are common in cats (Table 4), direct contact with cats is an usual way for people to acquire enteric parasitic infections. *Toxoplasma gondii*, *A. tubaeforme*, and *T. cati* require a period of time outside the host to become infectious. Since cats are fastidious, feces is generally not present on the fur of the cats for a long enough period of time to become infectious. *Dirofilaria immitis* and *D. caninum* will infect cats and people but are shared vector zoonoses. While *S. cati* and *E. histolytica* are infectious when passed into the environment, infection of cats is extremely rare and so the risk of individual cats to humans is likely very small. *Giardia* spp. and *Cryptosporidium* spp. infections are common in both cats and people and both parasites are immediately infectious when passed in feces. However, documented cases of infections of people by contact with cats or their excrement are extremely rare. This may relate to the relatively small amounts of feces passed by cats. Additionally, it is becoming more apparent that not all species of *Giardia* or *Cryptosporidium* cross infect multiple

species. For example, *C. hominis* of people did not infect cats (Morgan-Ryan, 2002) and *C. felis* of cats has only been detected in extremely immunocompromised people. Additionally, a *Giardia* specific to cats has now been identified. However, the zoonotic potential of individual *Giardia* or *Cryptosporidium* cannot be determined microscopically and so all isolates should be considered potentially infectious to people.

Bacteria. *Salmonella* spp., *Campylobacter* spp., *E. coli*, *Yersinia enterocolitica*, and *Helicobacter* spp. each infect cats and can cause disease in humans. Transmission from cats to people is by fecal-oral contact. While *Helicobacter pylori* was isolated from a colony of cats. While it is unclear whether cats are a common source of *Helicobacter* infection for people, based on epidemiologic studies, it is unlikely. In 2 recent enteric zoonoses prevalence studies, *Salmonella* spp., *Campylobacter* spp. infections were extremely uncommon in pet cats. Prevalence of *Salmonella* and *Campylobacter* infections is greater in animals housed in unsanitary or crowded environments.

Gastroenteritis can occur in 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 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. 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 is indicated, particularly if the animal is owned by an immunodeficient individual.

Antibiotic therapy can control clinical signs of disease from infection by *Salmonella* spp., *Campylobacter* spp., but should not be administered orally to animals that are subclinical carriers of *Salmonella* due to risk of antibiotic resistance. Multiple antibiotic resistant strains of *Salmonella* 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.

Infection of people by feline enteric agents is usually from contact with feces in the environment, by ingestion of contaminated food or water, or by ingestion of undercooked meat (*T. gondii*). Contact with infected cats is an unlikely way for humans to acquire infection. The following guidelines may lessen the risk of transfer of feline enteric zoonotic agents to people.

- Perform a thorough physical examination and zoonoses risk assessment on all new cats.
- Perform a physical examination and fecal examination at least once or twice yearly.
- Take all cats with vomiting or diarrhea to a veterinarian for evaluation.
- Fecal material produced in the home environment should be removed daily, preferably by someone other than an immunocompromised individual.

- Use litterbox liners and periodically clean the litterbox with scalding water and detergent.
- Do not allow cats to drink from the toilet.
- Follow the CDC strategic deworming guidelines.
- Wear gloves when gardening and wash hands thoroughly when finished.
- Filter or boil water from sources in the environment.
- Wash your hands after handling cats.
- Maintain cats within the home environment to lessen exposure to other animals and their feces.
- Feed cats only commercially processed food.
- Do not share food utensils with cats.
- Avoid being licked by cats.
- Control potential transport hosts like flies, rodents, and cockroaches.
- 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.

Table 1. Common gastrointestinal parasites of cats.

Classification	1° clinical signs	Zoonoses
Amoeba		
Entamoeba histolytica	LBD	Yes
Cestodes		
Taenia taeniaformis	Subclinical	No
Dipylidium caninum	Subclinical	Yes (vector-associated)
Echinococcus multilocularis	Subclinical	Yes
Coccidians		
Cystoisospora spp.	MBD, LBD	No
Cryptosporidium spp.	SBD	Yes
Toxoplasma gondii	Polysystemic	Yes
Flagellates		
Giardia spp.	SBD	Yes
Tritrichomonas foetus	MBD, LBD	No
Fluke		
Eurytrema procyonis	V	No
Nematodes		
Ancylostoma tubaeforme	V, MBD	Yes
Strongyloides cati	V, MBD	Yes
Dirofilaria immitis	V	Yes (vector-associated)
Toxocara cati	V	Yes
Toxascaris leonina	V	No
Ollulanus tricuspis	V	No
Physaloptera spp.	V	No

V = vomiting; SBD = small bowel diarrhea; MBD (mixed bowel diarrhea); LBD (large bowl diarrhea)

Table 2. Zinc sulfate centrifugation technique

1. Place 1 gram fecal material in a 15 ml conical centrifuge tube
2. Add 8 drops of Lugol iodine and mix well
3. Add 7 to 8 ml of $ZnSO_4$ (1.18 specific gravity)* solution and mix well
4. Add $ZnSO_4$ solution until there is a slight positive meniscus
5. Cover the top of the tube with a coverslip
6. Centrifuge at 1500-2000 rpm for 5 minutes
7. Remove the coverslip and place on a clean microscope slide for microscopic examination
8. Examine the entire area under the coverslip for the presence of eggs, cysts, oocysts, or larvae at 100X.

*Add 330 g $ZnSO_4$ to 670 ml of distilled water
Fisher Scientific, Hanover Park, Illinois

Table 3. Drugs used in the management feline gastrointestinal diseases

Generic drug name	Common dosage	Primary disease/organisms
Amoxicillin	22 mg/kg, daily, for 5 days, PO	*C. perfringens*, bacterial overgrowth, *Salmonella*
Ampicillin	22 mg/kg, q8hr, for 3-7 days, IV	Anaerobic sepsis
Azithromycin	7-15 mg/kg, q12hr, for 5-7 days, PO	*C. parvum*, *T. gondii*
Budesonide	1 mg, q12-24 hr	Inflammatory bowel disease
Cefazolin	22 mg/kg, q8hr, for 3-7 days, IV	Gram positive and anaerobic sepsis
Cefoxitin	22 mg/kg, q8hr, for 3-7 days, IV	Gram positive, gram negative, and anaerobic sepsis
Cephalexin	10-30 mg/kg, q8-12hr, for 3-6 wks, PO	Bacterial cholangiohepatitis
Clarithromycin	5-10 mg/kg, q12hr, for 7 days, PO	*T. gondii, Helicobacter* spp.
Clindamycin	12.5 mg/kg, q12hr, for 28 days PO, IM	*T. gondii*
Chlorambucil	2 mg/cat, q48-72hr	Inflammatory bowel disease
Doxycycline	5-10 mg/kg, q12-24hr, 4 weeks, PO	*T. gondii*, *E. histolytica*
Erythromycin	15-25 mg/kg, q12hr, for 7-10 days, PO	*C. jejuni*
Enrofloxacin	5-15 mg/kg, q8-12hr, for 3-7 days, IV, IM	Gram negative sepsis
Enrofloxacin	5-15 mg/kg, q8-12hr, for 3-7 days, PO	*Tritrichomonas foetus*
Epsiprantel	2.75 mg/kg, once, PO	*Dipylidium*, *Taenia*
Pyrantel/praziquantel	< 6 months, 15 mg/kg (F) + 1.5 mg/kg (P), daily for 3 days	Helminths, cestodes
	> 6 months, 10 mg/kg (F) + 1.0 mg/kg (P), daily for 3 days	Helminths, cestodes
Fenbendazole	50 mg/kg, q24hr, for 3-7 days, PO	Nematodes, *Giardia*, *Taenia* spp.
	30 mg/kg, q24hr, for 6 days	*Eurytrema procyonis*
Furazolidone	4 mg/kg, q12hr, for 7 days, PO	*Giardia*
	8-20 mg/kg, q24hr, for 7 days, PO	*Cystoisospora* spp.
Ivermectin	24 micrograms/kg, monthly, PO	*D. immitis*, hookworms
Itraconazole	5-10 mg/kg, q12hr, for weeks, PO	*Histoplasma capsulatum*
Metronidazole	10-25 mg/kg, q12hr, for 7 days, PO	*Giardia, E. histolytica, T. foetus* (?), bacterial overgrowth, *C. perfringens*
Milbemycin	2 mg/kg, monthly, PO	*D. immitis*, hookworms, roundworms
Neomycin	10-15 mg/kg, q6-24hr, for < 14 days, PO	Hepatic encephalopathy

Table 3 cont. **Drugs used in the management feline gastrointestinal diseases**

Paromomycin	150 mg/kg, q12-24hr, for 5 days,	*Cryptosporidium* spp., *Giardia, E. histolytica* (?)
Praziquantel	< 1.8 kg, 6.3 mg/kg, once, PO	Cestodes
	> 1.8 kg, 5.0 mg/kg, once, PO	Cestodes
Pyrantel pamoate	5-20 mg/kg, q 14-21 days, PO	Nematodes
Prednisolone	2-4 mg/kg, PO, divided q12hr	Inflammatory bowel disease
Pyrantel/praziquantel	1 tablet per 4 kg bodyweight	Nematodes, cestodes
Selamectin	6 mg/kg, monthly, topically	*D. immitis*, hookworms, roundworms, fleas, earmites
Sulfadimethoxine	50-60 mg/kg, daily, for 5-20 days, PO	*Cystoisospora* spp.
Trimethoprim-sulfa	15 mg/kg, q12hr, for 5 days, PO	*Cystoisospora* spp., *T. gondii*
Tylosin	10-40 mg/kg, q8-12hr, for 21 days, PO	Bacterial overgrowth, *C. perfringens*, *C. parvum*

Table 4. Prevalence of enteric zoonoses in cats and kittens

	Adult cats[a] (n =206)	Cats < 1yr[b] (n = 263)
Ancylostoma spp.	0.0%	0.0%
Campylobacter spp.	1.0%	0.8%
Cryptosporidium spp.	5.4%	3.8%
Giardia spp.	2.4%	7.2%
Salmonella spp.	1.0%	0.8%
Toxocara canis	0.0%	0.0%
Toxocara cati	3.9%	32.7%
Toxoplasma gondii	0.0%	1.1%
Any zoonotic agent	13.1%	40.7%

[a]Colorado cats; Hill et al, 2000
[b]New York State kittens, Spain et al, 2001

UDDATE ON FELINE INFECIOUS RESPIRATORY DISEASES

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Management of common infectious upper respiratory tract diseases in the cat

Viral diseases. Herpesvirus 1 (rhinotracheitis) and calicivirus are the most common viral causes of sneezing and nasal discharge in the cat. If oral ulcers are present, calicivirus is most likely. If corneal ulcers are present, herpesvirus 1 is most likely.

Viral rhinitis with or without secondary bacterial infection can be recurrent. Herpesvirus can be documented by direct fluorescent staining of conjunctival scrapings, virus isolation, or polymerase chain reaction. Since herpesvirus can be detected in conjunctival cells of approximately 25% of healthy cats, the positive predictive value of these tests in diseased cats is low.

There are no consistently effective primary therapies. I generally only use the following therapies if chronic disease is present. Lysine at 250-500 mg, PO, BID may be helpful in some cats and has been shown to be safe. Administration of alpha interferon at 30 U, PO, daily may help some cats with suspected herpesvirus 1 infection. Topical administration of alpha interferon in saline to the eyes of cats with conjunctivitis or the nose may aid in the management of some cats. Lysine and alpha interferon are unlikely to lead to a cure, but hopefully will lessen clinical signs of disease. Intranasal administration of modified live, intranasal herpesvirus 1 and calicivirus vaccines may lessen disease in some chronically infected cats. In kittens with acute life-threatening infection, use of alpha interferon at 10,000 U/kg, SQ, daily for up to 3 weeks can be beneficial.

Acyclovir is an anti-herpesvirus drugs for use in people but can be toxic to cats. I would start with 10-25 mg/kg, PO, BID and monitor the CBC every 2-3 weeks. I never prescribe acyclovir until the diagnostic evaluation has been completed. Famciclovir at 31.25 mg, PO, BID has also been used for up to 2 weeks for ocular herpesvirus infections but no data is currently available for the treatment of feline herpesvirus-associated rhinitis.

Kittens presented at less that 12 weeks of age should receive a modified live or killed FVRCR with boosters given every 3-4 weeks until 12 weeks of age. Kittens presented at > 12 weeks of age should receive 2 killed or modified live FVRCP 3-4 weeks apart. One should not overvaccinate with modified live products in cats. At 1 year of age booster FVRCP and rabies virus vaccines should be administered. After 1 year of age risk of infection by herpesvirus 1, calicivirus, and panleukopenia should be assessed. In low risk cats, FVRCP vaccines can be administered every third year. Administration of parenteral FVRCP vaccines have been associated with the development of antibodies that react with feline renal tissues in the United States. Thus, the longest interval possible should be used between booster vaccines.

Bacterial diseases. Almost all cats with mucopurulent or purulent nasal discharge have a bacterial component to their disease. Primary bacterial disease is rare but may be associated with

Bordetella bronchiseptica, Mycoplasma spp. and Chlamydophila felis. Chlamydiosis in general, is a mild infection resulting only in conjunctivitis. If primary infections are suspected, doxycycline 10 mg/kg, PO, once daily or topical administration of tetracyclines are usually effective. L-form bacteria also occasionally infect the nasal cavity and usually respond to doxycycline or quinolones. Cats with acute disease only need to be treated for 7 to 10 days. Most cases of bacterial rhinitis are secondary to other diseases including trauma, neoplasia, inflammation induced by viral infection, foreign bodies, inflammatory polps, and tooth root abscessation. Thus, if routine antibiotic therapy fails, a diagnostic workup should be performed.

Due to the large number of normal flora in the nasal cavity, culture and sensitivity results from nasal discharges are hard to interpret. Since bacterial rhinitis leads to chondritis and osteomyelitis, antibiotic therapy should be continued for weeks in cats with chronic disease. I generally use drugs with an anaerobic spectrum that also penetrate bone and cartilage. Amoxicillin, clavamox, metronidazole, and clindamycin are good first choices. Clavamox has the advantage of killing most Bordetella isoloates. Clindamycin has the advantage of effective against Mycoplasma spp. and the drug can be used once daily for bacterial infections in cats. Doxycycline and metronidazole may be superior to other drugs for the treatment of chronic infections since they may modulate the immune reaction, lessening inflammation. Azithromycin (5.0-15.0 mg/kg, PO, q 12-72 hr) can be used for cats with chronic disease.

Feline leukemia virus and feline immunodeficiency virus can induce immunosuppression predisposing to bacterial rhinitis. In addition, both viruses have been linked to an increased incidence of lymphoma in cats.

Chlamydophila infection in cats generally only results in mild conjunctivitis, and so whether vaccination is ever required is controversial. The use of this vaccine should be reserved for cats with a high risk of exposure to other cats and in catteries with endemic disease. Duration of immunity for Chlamydophila vaccines may be short-lived, so high-risk cats should be immunized prior to a potential exposure.

Many cats have antibodies against Bordetella bronchiseptica and there are sporadic reports of severe lower respiratory disease due to bordetellosis, primarily in young, stressed kittens. Most cases are from crowded environments like shelters and catteries. However, in pet cats, significance of the problem is undefined and for now Bordetella vaccination should be considered primarily for use in cats at high risk for exposure. In a 7-year period at the Diagnostic Laboratory at Colorado State University, B. bronchiseptica was isolated from 1 of 109 (0.9%) lower airway cultures and 4 of 81 (4.9%) nasal cultures from clinically ill, client-owned cats. During this time period, of the 15,000 cat admissions approximately 1500 had respiratory disease. Since the disease is apparently not life-threatening in adult cats, is uncommon, and responds to a variety of antibiotics, routine use of the vaccine in client-owned cats seemed unnecessary in this population.

Cryptococcosis

Etiology and epidemiology. Cryptococcus neoformans is a 3.5-7.0 *u*m yeast-like organism with worldwide distribution. It has a thick polysaccharide capsule and reproduces by narrow-based budding. The route of transmission for Cryptococcus neoformans is thought to be inhalation; nasal and pulmonary disease manifestations are common. Cryptococcosis is the most common systemic fungal infection of cats and should be considered a differential diagnosis for cats with respiratory tract disease, subcutaneous nodules, lymphadenopathy, intraocular inflammation, fever, and CNS disease. Infected cats range from 6 months to 16 years of age, and male cats are over represented in most studies. Infection of the nasal cavity is reported most frequently (56.3 to 83.0% of cases) and commonly results in sneezing and nasal discharge. The nasal discharge can be unilateral or bilateral, ranges from serous to mucopurulent, and often contains blood. Granulomatous lesions extruding from the external nares, facial deformity over the bridge of the nose, and ulcerative lesions on the nasal planum are common. Submandibular lymphadenopathy is detected in most cats with rhinitis.

Single or multiple, small (< 1 cm), cutaneous or subcutaneous masses occur in approximately 30% to 50% of cats infected with Cryptococcus neoformans. The masses can be either firm or fluctuant, and if ulcerated, have a serous discharge. Anterior uveitis, chorioretinitis, or optic neuritis occur in association with ocular infection; lens luxations and glaucoma are common sequelae. Chorioretinitis lesions can be punctate or large; suppurative retinal detachment occurs in some infected cats. Central nervous system signs of disease result from diffuse or focal meningoencephalitis or a focal granuloma formation. Manifestations include depression, behavioral change, seizures, blindness, circling, ataxia, loss of sense of smell, and paresis, depending on the location of the lesion. Non-specific signs of anorexia, weight loss, and fever occur in some infected cats.

Definitive diagnosis of cryptococcosis is based on cytologic, histopathologic, or culture demonstration of the organism. The organism is found during cytologic evaluation of nasal lesions, cutaneous lesions, lymph node aspirates, CSF, and bronchoalveolar lavage fluid in most affected animals. The organism can be cultured from CSF in animals with neurologic involvement.

Cryptococcal antigen is detected in serum, aqueous humor, or CSF using latex agglutination (LA); serum antigen tests are positive in most cats with cryptococcosis. Animals with acute disease, chronic low grade infections, chemotherapy-induced remission, or in nondisseminated disease can be LA- negative. The LA performed on CSF is positive in almost all cats with CNS cryptococcosis. Serum and CSF LA antigen titers can diminish with therapy and have been used to monitor response. Antigen titers fail to decrease in some cats without clinical evidence of disease suggesting persistence of the organism in tissues or false-positive results.

Cats with cryptococcosis have been treated with amphotericin B, ketoconazole, itraconazole, fluconazole, and 5-flucytosine alone and in varying combinations. Good to excellent treatment responses in cats were seen with fluconazole (96.6%), itraconazole (57.1%), and ketoconazole (34.6%). Ketoconazole commonly leads to inappetence, vomiting, diarrhea, weight loss, and

increases in liver enzyme activities in some dogs and cats and suppresses testosterone and cortisol production in dogs. Cats treated with 100 mg/day of itraconazole occasionally (7/21 cats) developed anorexia, depression, and increase activity of ALT; only 1/13 cats receiving 50 mg/day developed toxicity. If toxicity develops, drug therapy should be stopped and then reinstituted at 50% the original dose after signs of toxicity abate. Inappetence in a few cats was the only adverse effect attributed to fluconazole.

Flucytosine crosses the blood-brain barrier better than ketoconazole or amphotericin B, so it has been used for the treatment of CNS cryptococcosis. Flucytosine has to be used in combination with other anti-fungal drugs and has many adverse effects including vomiting, diarrhea, hepato-toxicity, cutaneous reactions, and bone marrow suppression. Fluconazole and itraconazole are very lipid- soluble and so they are also effective for the treatment of CNS disease.

If life-threatening infection is occurring or the cat is failing to respond to the azole drugs amphotericin B should be used. Liposomal or lipid encapsulated amphotericin B are safer than regular amphotericin B but are expensive. If the client cannot afford lipid or liposomal encapsulated products, regular amphotericin B can be given safely SQ to most cats. Dilute 0.5 to 0.8 mg/kg regular amphotericin B in 400 ml of 2.5% dextrose and 0.45 % NaCl and administer SQ in 1 site. This can be given twice weekly to most cats with approximately a 10% chance for sloughing or scarring. Give at least a 12 mg/kg cumulative dose. Continue azole therapy during the amphotericin B treatment. I generally treat cats a minimum of 8 weeks or 4 weeks past resolution of measurable disease. Preferably, serum antigen titers should be measured. Optimally, the titer should go to negative. However, some clinically normal cats maintain positive antigen titers. If the antigen titer drops 16-32 fold and the cat is clinically normal, recurrence is uncommon.

Nasal and cutaneous cryptococcosis generally resolve with treatment; CNS and ocular disease are less likely to respond to treatment. Treatment should be continued for at least 1 to 2 months past resolution of clinical disease. Some animals have had long-term clinical resolution of disease even though the antigen test is still positive.

People and animals can have the same environmental exposure to Cryptococcus neoformans but zoonotic transfer from contact with infected animals is unlikely. Prevention is by decreasing potential for exposure; avoiding areas with high concentrations of pigeon droppings is indicated. Application of hydrated lime solution (40 g/L water) at 1.36 L/m^2 can reduce numbers of organism in contaminated areas.

Aspergillosis

Aspergillosis (Aspergillus fumigatus) and penicillinosis are the most common fungal causes of nasal disease in the dog; they occur but are rare in cats. These agents induce mucoid discharges early in the infection. The discharge progresses to mucopurulent and ultimately to hemorrhagic. Facial deformity may be present. Itraconazole therapy can be effective. Information concerning use of topical clotrimazole or enilconazole in cats is lacking.

Parasitic diseases

While nasal mites (Pneumonyssoides) and a nasal worm (Eucoleus) occur in dogs in the United States, there are no significant nasal parasites in cats of this country.

Management of common infectious causes of cough or dyspnea in cats

Parasitic diseases. Parasites leading to cough or dyspnea in cats include Toxocara, Toxoplasma gondii, Aelurostrongylus abstrusus, and Paragonimus kellicotti. Aelurostrongylus abstrusus has an indirect life cycle with rodents as intermediate hosts; the organism occurs in Colorado. It is difficult to prove respiratory cough due to Strongyloides or roundworms; demonstration larva or ova in coughing kittens supports a presumptive diagnosis. There is no effective primary treatment for the migrating phase of the parasites.

Diagnosis of the primary respiratory parasites is based on demonstration of the organism in transtracheal aspiration samples, bronchoalveolar lavage samples, or in feces.

Most of the agents are intermittent shedders and so fecal examination techniques may have to be repeated multiple times. The Baermann funnel technique will increase the odds of finding larva.

Fecal sedimentation techniques are superior to flotation techniques for demonstration of Paragonimus kellicotti. Serologic tests are available to help support a diagnosis of toxoplasmosis. Lungworms generally respond to ivermectin at 0.4 mg/kg, SQ, once. Since eosinophilic pneumonitis occurs with these agents, prednisolone is generally administered at 1.0-2.0 mg/kg, daily, PO concurrently with ivermectin. Fenbendazole is a alternate therapy; 25 mg/kg, PO, daily for 5 days, repeated again in 5 days is often used. Praziquantel can be used for the treatment of Paragonimus kellicotti. Clindamycin administered at 10-12 mg/kg, BID, PO for 4 weeks can be effective for the treatment of toxoplasmosis.

Dirofilariasis. In general, it can be assumed that the incidence of heartworm disease in cats in a given area to be approximately 10% of the incidence in dogs. Worm burdens are usually low (1-2 worms) but morbidity and mortality tends to be greater than in dogs. Many cats have aberrant signs including sudden death, vomiting and central nervous system abnormalities. Cats are usually microfilaria negative and commonly antigen negative due to low worm burdens or single sex infections. Antibody tests are currently available (HESKA Corp., Fort Collins CO; Synbiotics Corp., San Diego, CA). These assays are thought to be more sensitive than antigen testing and do not cross react with other parasites. However, positive results only document exposure not current infection or clinical illness. In one study of cats in Florida, the sensitivity and specificity for the Synbiotics antibody test were 68% and 93%. The sensitivity and specificity for the HESKA antibody test were 89% and 77%. In contrast, the sensitivity and specificity of antigen testing were approximately 75% and 98%. Thus, it is important to test cats with both antibody and antigen tests. Demonstration of pulmonary arterial distension, tortuosity and blunting by thoracic radiography is an important diagnostic procedure. Occasionally, worms can be detected by echocardiography.

Heartworm infection in cats is generally self-limiting in 2 years and so most cats should be managed symptomatically with glucocorticoids. Infected cats should be placed on preventative

to avoid new infections. Thiacetarsamide administered using the same protocol as for dogs can be successful but commonly results in acute death. To date, melarsamine is not recommended for treatment of cats. Microfilaricides are not required in cats. Ivermectin, selamectin, and milbemycin are approved for use as preventives. Selamectin and milbemycin have the advantage of controlling roundworms and hookworms; selamectin also controls ear mites and fleas.

Bronchial diseases. Bronchial obstruction can develop due to inflammatory infiltrates (eosinophils, neutrophils, or macrophages) or hypertrophy of bronchial tissues. The result is obstructive airway disease. Obstructive airway disease is characterized by increased airway resistance with resultant expiratory dyspnea. There is no clear terminology for the bronchial obstructive diseases in the cat. Bronchitis is inflammation of the airways. Asthma generally implies a reversible bronchoconstriction related to hypertrophy of smooth muscle in airways, hypertrophy of mucous glands, and infiltrates of eosinophils. Asthma in cats is primarily due to Type I hypersensitivity reactions; the etiology is generally undetermined. Cats with bronchitis not due to asthma generally have infiltrates of neutrophils or macrophages as well as hypertrophy of mucous glands, hyperplasia of goblet cells, excessive mucous, and ultimately fibrosis secondary to chronic inflammation. Calicivirus is the most common viral disease of cats leading to acute bronchial disease. Bordetella bronchiseptica, Mycoplasma spp., and possibly, Chlamydophila felis are the bacteria capable of inducing bronchial disease. If disease occurs due to Chlamydophila occurs, it is mild.

Cats with bronchitis can be of any age; chronic bronchitis usually develops in middle-aged to older cats. There is no obvious breed or gender predilection. Primary presenting complaints include cough, dyspnea, and wheezing. Some cats will have a terminal retch following cough. Physical examination abnormalities include cough, dyspnea, and crackles, and wheezes in the pulmonary tissues. Increased bronchovesicular sounds may be the only abnormality noted on auscultation. If dyspnea occurs, it commonly has a pronounced expiratory component. Open mouth breathing or panting commonly occur during periods of stress.

CBC is generally normal with the exception of eosinophilia in some cats with asthma. Thoracic radiographs reveal primarily a bronchial pattern. Overinflation and air trapping is seen in some dyspneic cats with chronic disease. Air bronchograms are commonly seen in cats with bronchitis due to bacterial infection. Cytology of transtracheal wash samples generally reveal increased mucous with the primary cell types being eosinophils, neutrophils, or macrophages. Bacteria may or may not be visualized. Aerobic and Mycoplasma culture as well as antibiotic susceptibility testing should be performed regardless of the type of inflammatory cell and whether or not bacteria are seen.

Cats with eosinophilic TTW cytology should be assessed for dirofilariasis using adult antigen detection tests and antibody tests if from endemic areas. Fecal flotation (Toxocara), Baermann examination of feces (Aelurostrongylus), and fecal sedimentation (Paragonimus) should be performed in cats with eosinophilic TTW cytology particularly if indoor-outdoor and from parasite endemic areas.

Non-dyspneic cats are generally treated with broad spectrum antibiotics while awaitng diagnostic test results (Table 1). I generally use doxycycline initially due to efficacy for the primary

bacterial respiratory pathogens and anti-inflammatory effects. I generally do not use oral theophylline (phosphodiesterase inhibitor) or terbutaline (beta 2 agonist) unless necessary. Feline terbutaline pharmacokinetics vary from people; serum levels are extremely high in cats. This drug should be avoided in cats with cardiac disease or disease resulting in hypertension like renal failure and hyperthyroidism. Phosphodiesterase inhibitors often cause anorexia and behavior change in cats. Inhalational albuteral given via inhaler may work more quickly and oral or injectable bronchodilators in cats with dysnea. Cats with neutrophilic TTW cytologic results and positive bacterial cultures are treated with appropriate antibiotics for 4- 8 weeks depending on radiographic severity of disease and response to therapy. Some cats with acute bronchitis will have the disease resolve and not recur. Most cats with chronic bronchitis will require life-long anti-inflammatory therapy and perhaps, bronchodilator therapy. If an eosinophilic component is present on TTW cytology, glucocorticoids will likely be required. Oral, repositol, or inhalational glucocorticoids can be administered. I generally attempt oral prednisolone therapy initially. Administration of methylprednisolone acetate every 2-3 weeks adequately controls some cats with asthma or allergic bronchitis. Titrate the dosage of glucocorticoid to the lowest dose required to control clinical signs of disease. Use of inhalational steroids can be very effective and if fluticasone are used, minimal systemic side-effects occur. In dyspneic cats, delivery of glucocorticoids by inhalation may work more quickly than those delivered orally or by injection. Chambers for the delivery of inhalational drugs can be purchased at www.aerokat.com. Cyproheptadine may be effective in some cats if glucocorticoids cannot be used (ie. Diabetes mellitus). Use of omega 3 fatty acid supplementation may lessen requirements for glucocorticoids. Since allergic bronchitis can be related to dietary hypersensitivity, a hypoallergenic diet trial should be tried in cats with recurrent or persistant disease. Cats that become refractory to prednisolone will often respond to dexamethasone or triamcinolone. Some cats with asthma will have seasonal exacerbations. Removal of potential irritants in the environment including clay litter, cigarette smoke, hairspray, and carpet cleaners should be considered in all cases of bronchial inflammation.

Pneumonia. Pneumonia is inflammation of the lung parenchyma; bronchopneumonia is pneumonia that has begun in the terminal bronchioles. Bacterial pneumonia is rarely a primary disease. Occasionally, Bordetella bronchiseptica or Mycoplasma spp. will induce pneumonia directly due to their adverse effects on mucociliary apparatus function. Yersinia pestis can cause pneumonia in infected cats and is directly zoonotic. Febrile cats with cough in the Southwestern states should be handled carefully.

Most cases of bacterial bronchopneumonia are secondary to immunosuppressive diseases or previous inflammatory insults including viral infection, aspiration, and irritant inhalation. Owners should be carefully questioned concerning potential exposure to other animals and clinical signs associated with immunosuppressive diseases or aspiration.

Most cats with bacterial pneumonia will be clinically ill. Common complaints include depression, anorexia, dyspnea, productive, moist cough with a terminal retch, and exercise intolerance. Some cats with bacterial pneumonia will present only with cough. Physical examination findings commonly include fever, crackles and wheezes, and muffled lung sounds in cases with consolidated or abscessed lung lobes. Many cats will have increased tracheal

sounds, a tracheal cough, and pharyngeal inflammation due to transport of inflammatory cells up the mucociliary apparatus to the mouth.

The initial diagnostic plan for cats with suspected bacterial pneumonia should include a CBC, biochemical panel, urinalysis, thoracic radiographs, FeLV antigen test, and FIV antibody test. Neutrophilic leucocytosis with or without a left-shift is common but not present in all cases. Monocytosis is common in chronic pneumonia. Assessment of the biochemical panel and urinalysis will often detect underlying immunosuppressive diseases. Thoracic radiographs usually reveal a mixed alveolar, bronchial, and interstitial pattern. Aspiration pneumonia generally has radiographic lesions that are most pronounced in the right middle lung lobe.

Esophageal diseases are commonly evident on evaluation of thoracic radiographs. Laryngeal paralysis commonly predisposes to aspiration pneumonia and is characterized by inspiratory stridor; this disease is rare in cats. Further diagnostic testing for cats with inspiratory stridor includes laryngeal function assessment by visualization under sedation. Intravenous administration of low-doses of ultra-short acting thiobarbiturates will enable examination of laryngeal function. Following documentation of pulmonary disease on thoracic radiographs, a TTW for cytology, aerobic bacterial and Mycoplasma culture, and antibiotic susceptibility testing should be performed. Transthoracic aspiration of consolidated lung lobes should be considered for anaerobic culture and antibiotic susceptibility testing. Bronchoscopy for bronchoalveolar lavage and biopsy is superior to TTW and is sometimes required.

The combination of increased numbers of neutrophils and macrophages on cytologic assessment of secretions obtained by TTW and positive bacterial culture confirms the diagnosis of bacterial pneumonia. Bacterial culture is commonly positive in healthy cats and so the presence of bacteria without inflammatory cells does not document pneumonia. Treatment consists of airway hydration, antibiotic therapy, physical therapy, expectorants, and bronchodilators.

Following correction of underlying conditions, the most important treatment of bacterial pneumonia is hydration. The mucociliary apparatus functions best in a well-hydrated animal and is essential for the clearance of infection. Affected cats should receive parenteral fluid therapy until able to maintain hydration orally. Airway hydration can be accentuated by nebulization or by placing the animal in a closed bathroom while running hot water through the shower.

Antibiotic therapy should be based on culture and antibiotic susceptibility testing. Septic cats should be treated initially with parenteral antibiotics. Oral antibiotics should be administered for 6-8 weeks or for at least 2 weeks following resolution of radiographic evidence of disease.

Antibiotics can be administered by nebulization. Aminoglycosides are commonly used. Renal toxicity is not a concern since serum levels of aminoglycosides remain low following nebulization. If nebulization is used, 25 mg of gentamycin is generally mixed in 3-4 ml saline. Saline has some mucolytic effects and will aid mucociliary apparatus function. Nebulization is generally administered 3-4 times daily. Mucolytic agents such as acetylcysteine are generally not used during nebulization of cats due to severe bronchoconstriction. If acetylcysteine is used, a topical beta-2 agonist like isoetharine should also be nebulized. Nebulization can be administered through most oxygen cages. Electric air pumps and hand-held nebulizers that give

a particle size of 5 microns can be rented from many human home respiratory care companies. Nebulization can be performed by attaching the nebulizer to a closed box with holes placed on the opposite side to allow escape of CO_2.

Oxygen therapy is indicated due to acute dyspnea in some cats with bronchopneumonia. If a oxygen cage is not available, oxygen can be administered via nasal tube. Positive end expiratory pressure aids in the treatment of some pulmonary conditions but is not practical in most clinical settings.

Passive physical therapy is indicated for the treatment of bacterial pneumonia. Gentle percussion using a cupped hand is the technique most commonly used but is not tolerated by many cats. Playing with the cat to encourage mild exercise may be beneficial.

Bronchodilator treatment may be of benefit in the treatment of bacterial pneumonia (Table 1). I generally use this therapy if above treatments are not rapidly resolving the disease. Phosphodiesterase inhibitors improve mucociliary apparatus function and may strengthen muscles of respiration. Bronchodilators can be indirect anti-tussives.

Cats with consolidated lung lobes should be receive antibiotics that penetrate tissue well and have a spectrum against anaerobes. Clindamycin hydrochloride or azithromycin are appropriate choices. I generally combine enrofloxacin with clindamycin for the treatment of consolidated lung lobes. Thoracic radiographs should be reassessed in all cases within 3-4 days post-treatment and then every 2-3 weeks until radiographic evidence of disease has resolved. If the consolidated lung lobes that are not starting to inflate within 7-10 days post-treatment, surgical exploration should be considered, particularly if systemic signs like fever persist.

Feline plague. 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. 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. 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 (available at Centers for Disease Control, Fort Collins, CO); culture of exudates, tonsillar area, and saliva; as well as by documenting increasing antibody titers.

Tetracycline derivatives (doxycycline, 5 mg/kg, PO, BID, for 21 days), enrofloxacin (5 mg/kg, PO, IM, or IV, BID for 21 days), 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 suppurative 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. All exposed humans should be directed to their physician for prophylactic antibiotic administration. Cats are not infectious to humans after 3-4 days of antibiotic treatment.

Pyothorax. Pyothorax is the most common infectious disease leading to dyspnea in the cat. Any bacteria can be involved, but anaerobes including Nocardia and Actinomyces are common. Unless there is an obvious foreign body, I manage pyothorax medically initially with appropriate antibiotic therapy and pleural space lavage. Unilateral or bilateral tube placement is dependent on the individual case.

The pleural space is lavaged twice daily with approximately 20 ml/kg of warmed 0.9% saline or Ringer's solution. The lavage fluid should be instilled slowly; the injection should be discontinued if respiratory distress occurs. The lavage fluid remains in the pleural space for 1 hour unless respiratory distress occurs. Approximately 25% of the initial lavage volume will be absorbed by the patient. Lavage efficacy is monitored by clinical findings, thoracic radiographs and cytology of the pleural effusion. Most animals with successful pleural lavage will have a decrease in fever and improvement in general attitude within the first 48 hours. I generally perform recheck radiographs 48 hours after tube placement. Radiographs are made following complete removal of all lavage fluid. The radiographs are assessed for pleural space fluid volume, atelectasis, and areas of encapsulated fluid. Cytology of pleural fluid is generally performed prior to lavage. Numbers of neutrophils, macrophages and bacteria as well as the percentage of degenerate neutrophils are estimated. Most cases with pyothorax will have a gradual decrease in inflammatory cells numbers over 3-5 days.

Systemic antibiotic therapy should ultimately be based on culture and sensitivity results. Success in culture of anaerobic bacteria is dependent on sample handling and the laboratory. Anaerobic bacterial culture must be requested specifically and samples must be submitted in a capped syringe within 1 hour or in appropriate transport media (Anaerobic culturette, Marion Scientific Corp.; Portacul, Bectin Dickinson) within 24 hours. Due to the high incidence of anaerobic infections, antibiotics with an anaerobic spectrum should be started immediately following diagnosis of pyothorax and continued throughout the course of disease. Many animals with pyothorax will have bacteremia or septicemia and intravenous antibiotics are indicated in the initial treatment period. I commonly use ampicillin (22 mg/kg, IV, q 6-8 hours) or cefoxitin (22 mg/kg, IV, q 6-8 hours). It was recently shown that amoxicillin-clavulanate has a better broad-spectrum anaerobic effect than ampicillin.

Aminoglycosides are only used if there is evidence of septic shock and only after dehydration and hypokalemia have been corrected. Enrofloxacin can be used parenterally to improve gram negative spectrum in septic animals. Oral antibiotic therapy should be continued for at least 4-6 weeks after initial diagnosis. Thoracic radiographs are generally suggested 7 and 28 days following tube removal. The combination of pleural lavage and antibiotic therapy have been reported to successfully resolve pyothorax in 60% of cats.

Feline infectious peritonitis. The effusive form of feline infectious peritonitis can lead to pleural effusion and resultant clinical signs of disease. Some affected cats do not have evidence for peritoneal effusion. This syndrome occurs most commonly in cats from crowded environments that are less than 2 years of age. Concurrent ocular, CNS, hepatic, and renal disease often is detected; most cats have a history of weight loss and fever.

Effusions from cats with FIP are sterile, colorless to straw-colored, may contain fibrin strands, and may clot when exposed to air. Protein concentration on fluid analysis commonly ranges from 3.5 g/dl to 12 g/dl. Mixed inflammatory cell populations of lymphocytes, macrophages, and neutrophils occur most commonly; non-degenerate neutrophils predominate in most cases but in some cats macrophages are the primary cell type seen.

Measurement of protein concentrations in effusions can aid in the diagnosis of effusive FIP. If the albumin-to-globulin ratio of the effusion is > 0.81, FIP is unlikely. If the albumin-to-globulin ratio of the effusion is < 0.81 but > 0.4, the positive predictive value for FIP is approximately 80%. If the albumin-to-globulin ratio of the effusion is < 0.4, the positive predictive value for FIP is 100%.

Serology can be falsely negative in cats with effusive disease and the presence of antibodies in serum does not confirm FIP. A test to detect the 7B protein of coronaviruses has been introduced and purported to correlate to FIP. However, not all cats that are positive develop FIP. Thus, all positive coronavirus tests should be interpreted with other clinical factors including signalment (generally young cats), appropriate clinical signs and physical examination abnormalities, and appropriate laboratory abnormalities like lymphopenia and hyperglobulinemia. Definitive diagnosis of FIP still requires documentation of characteristic histopathologic findings or the organism in inflamed tissues by immunohistochemistry or PCR.

Polymerase chain reaction for the detection of coronavirus has been evaluated for diagnostic accuracy in a limited number of cats. Positive reactions were detected in the pleural or peritoneal effusions from 13/15 cats with effusive FIP. At this time, detection of coronavirus by PCR in whole blood does not appear to correlate to the development of FIP. There is no effective treatment. Administration of alpha interferon at 10,000 U/kg, SQ, daily may lessen clinical signs of disease in some.

Table 1. Doses of drugs used in respiratory tract diseases in cats

Anthelmintics	
Fenbendazole	20 mg/kg, PO, daily for 5 days, repeat in 5 days
Ivermectin	0.4 mg/kg, SQ, once
Antibiotics	
Amoxicillin	22 mg/kg, PO, q 12 hrs
Amoxicillin-clavulonate	12.5-25 mg/kg, PO, q 12 hrs
Azithromycin	7.5-15 mg/kg, PO, q 12-24 hrs.
Cefadroxil	22 mg/kg, PO, q 24 hr
Cefoxitin	22 mg/kg, IV, q 8 hrs
Cephalexin	22 mg/kg, PO, q 8 hrs
Chloramphenicol	10-15 mg/kg, PO, q 12 hrs
Clindamycin-bacterial	10-12 mg/kg, PO, q 24 hrs
Clindamycin-Toxoplasma	10-12 mg/kg, PO, q 12 hrs
Doxycycline	5 mg/kg, PO, q 12-24 hrs
Enrofloxacin	2.5-5 mg/kg, PO, q 12-24 hrs
Imipenem	3-10 mg/kg, IV, q 6-8 hrs
Metronidazole	12.5-25 mg/kg, PO, q 12 hrs
Trimethoprim sulfonamide	15 mg/kg, PO, q 12 hrs
Antihistamine/antiserotonin/anti-leucotriene	
Chlorphenarimine	2 mg/cat, PO, q 12 hrs
Cyproheptadine	2 mg/cat, PO, q 12 hrs
Zafirlucast	5 mg/cat, PO, q 12 hrs
Bronchodilators	
Albuteral (inhalational)	As needed
Terbutaline	0.625-1.25 mg/cat, PO, q 12 hrs
Theophylline (Theodur)	25 mg/kg, PO, at night
Glucocorticoids	
Prednisolone	2.5-5 mg/cat, PO, q 12 hrs
Budesonide (inhalational)	Emergency use or 2-3 times daily
Dexamethasone SP	0.5-1 mg/kg, IV, as needed
Fluticasone (inhalational)	Emergency use or 2-3 times daily
Methylprednisolone acetate	5-15 mg, IM, q2-3 weeks as needed

Table 1 continued

Immune modulator/anti-viral	
Acyclovir (herpesvirus 1)	10-50 mg/kg, PO, q 8 hrs
Famciclovir (herpesvirus 1)	32.25 mg/cat, PO, q 12 hrs
Interferon alpha-routine infection	30U, PO, q 24 hrs; 10,000 U/kg, SQ, q 24 hrs
Internasal vaccine	Once
Lysine (herpesvirus 1)	250 mg, PO, q 12 hrs
Catecholamines	
Epinephrine	0.5 ml, 1:10,000 solution, SQ or IM

PREVENTION OF FELINE INFECTIOUS DISEASES

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It is always preferred to prevent rather than treat infections. Avoiding exposure is the most effective way to prevent infections. Most infectious agents of cats are transmitted in fecal material, respiratory secretions, reproductive tract secretions, urine; by bites or scratches; or by contact with vectors or reservoirsMany infectious agents are environmentally resistant and can be transmitted by contact with a contaminated environment. It is extremely important to avoid zoonotic transfer of infectious agents, because some of the zoonotic diseases like plague and rabies are life-threatening. Recognition of risk factors associated with infectious agents is the initial step to prevention of infectious diseases. Veterinarians should strive to understand the biology of each infectious agent so that they can counsel clients and staff on the best strategies for prevention. Vaccines available for some infectious agents can prevent infection or lessen clinical illness when infection occurs. However, vaccines are not uniformly effective and are not available for all pathogens; thus, it is paramount to develop sound biosecurity procedures to avoid exposure to infectious agents when developing a preventative medicine program.

The American Association of Feline Practitioners and the Council on Biological and Therapeutic Agents have published information concerning cat vaccination guidelines in the last several years. The AAFP guidelines are endorsed by AAHA and the American College of Veterinary Internal Medicine (ACVIM).

There are many vaccine antigens available for administration to cats. For some of the antigens, there is strong consensus nationally that all cats should be immunized ("core" vaccines). For other vaccine antigens, there are differences in regional prevalence of the disease in question or other reasons that make some antigens optional for some pets. All kittens and all adult cats with unknown vaccination history be optimally immunized with core vaccine antigens. Optional antigens and administration intervals should be individualized to each patient upon consultation with the owner and a discussion of benefits, risks, and costs. After the kitten vaccine series, each cat should be presented to the veterinary clinic for a general health examination and a vaccine needs risk assessment yearly. The following is a brief discussion of the feline vaccine antigens currently available.

Vaccination protocols for cats.

All healthy kittens and adult cats without a known vaccination history should be routinely vaccinated SQ or IM for panleukopenia, rhinotracheitis, and calicivirus (FVRCP); intranasal products can also be used. I generally only use intranasal products in cattery, shelter, and outbreak situations since the intranasal products cause mild clinical signs of disease in some cats. Most vaccine-associated soft tissue sarcomas have been associated with adjuvanted feline leukemia virus and rabies virus vaccines. However, tumors at injection sites have also been documented after both killed and modified live FVRCP vaccines. Recently, parenterally administered FVRCP vaccines have been shown to induce antibodies that recognize renal tissues

of cats (Abstract 1). However, disease causation has not been determined to date. Thus, intranasal FVRCP vaccines may be safer than injectable FVRCP vaccines.
Modified-live products should not be administered to clinically ill, debilitated, or pregnant animals, but are preferred over killed products in healthy cats, since cell-mediated immune responses are superior. Kittens presented at 6 to12 weeks of age should receive a modified live or killed FVRCR with boosters given every 3-4 weeks until 12 weeks of age. Kittens presented at > 12 weeks of age and adult cats with unknown vaccination history should receive 2 killed or 2 modified live FVRCP 3-4 weeks apart. Parenteral products should be given SQ, low on the right forelimb so vaccine reactions can be tracked.

All cats should be vaccinated against rabies. Rabies vaccine should be administered SQ in the lower right rear limb at 12 or 16 weeks of age depending on local ordinances. Use of IM injection does not lessen the risk of vaccine sarcoma development but may make it harder to feel the mass as it develops. A new canarypox vector rabies vaccine is available that has minimal tissue irritation and so it may be less likely to be associated with soft tissue sarcomas. However, this hypothesis has not been proven.

At one year of age or one year after the last vaccination, booster FVRCP and rabies virus vaccines should be administered. After one year of age, risk of infection by herpesvirus 1, calicivirus, and panleukopenia should be assessed yearly. In low risk cats, FVRCP vaccines can be administered every third year. The canarypox vector rabies vaccine is only approved for intervals of 1 year. If a rabies product with known duration of immunity of 3 years is used, it should then be administered every 3 years; more frequent vaccination is not required for immunity and only increases the risk for vaccine reactions. However, your county rabies vaccination guidelines should be followed.

Serology can be used in lieu of arbitrary vaccination with FVRCP. In a study of 72 vaccinated and control cats that assessed 2 different parenteral vaccines, the positive predictive value of antibody titers against panleukopenia, calicivirus, and herpesvirus 1 were all 100% in appropriately vaccinated cats. Results were similar using virus neutralization (New York State Veterinary Diagnostic Laboratory, Ithaca, NY) or ELISA (Heska Corporation, Fort Collins, CO). In that study, 70.7%, 92.4%, and 68.5% of randomly screened, client-owned cats had titers predictive of protection against herpesvirus 1, calicivirus, and panleukopenia virus, respectively. These results suggested that use of an arbitrary vaccine interval leads to unneeded vaccination of the majority of cats (Abstract 2).

Optional vaccines currently available for use in cats include Chlamydophyla felis (previously Chlamydia), feline leukemia virus (FeLV), feline immunodeficiency virus (FIV), feline infectious peritonitis virus, Bordetella bronchiseptica, Giardia, and ringworm.

Chlamydophila felis infection in cats generally only results in mild conjunctivitis, and so whether vaccination is ever required is controversial. The use of this vaccine should be reserved for cats with a high risk of exposure to other cats and in catteries with endemic disease. Duration of immunity for Chlamydophila vaccines may be short-lived, so high-risk cats should be immunized prior to a potential exposure.

Many cats have antibodies against Bordetella bronchiseptica and there are sporadic reports of severe lower respiratory disease due to bordetellosis in young kittens. However, since significance of the problem for pet cats is undefined, Bordetella vaccination should be considered primarily for use in cats at high risk for exposure. In an 11 year period at the Diagnostic Laboratory at Colorado State University, B. bronchiseptica was isolated from < 3% of the lower airway cultures and nasal cultures from clinically ill, client-owned cats. Since the disease is apparently not life-threatening in adult cats, is uncommon in pet cats, and responds to a variety of antibiotics, routine use of this vaccine in client-owned cats seems unnecessary.

Several FeLV vaccines are currently available. Due to difficulties in assessment of efficacy studies it is unclear which vaccine is optimal. FeLV vaccines are potentially indicated in cats allowed to go outdoors or that have other exposure to cats of unknown FeLV status. The vaccines are likely to be most helpful in kittens because as cats age, there is an acquired resistance to FeLV infection that limits usefulness of vaccination. Vaccinated cats should receive 2 vaccinations initially. Adjuvanted products should be administered SQ in the distal left rear limb due to the risk for development of soft tissue sarcomas. A non-adjuvanted product is available and induces less inflammation. Duration of immunity is unknown, so annual or biannual boosters are currently recommended. The vaccines are not effective in persistently viremic cats and so are not indicated. However, administration of the vaccine to viremic or latent cats does not have increased risk of vaccine reaction. FeLV testing should be performed prior to vaccination because the retrovirus serologic status of all cats should be known so appropriate husbandry can be maintained.

A killed vaccine containing immunogens from 2 FIV isolates was recently licensed for use in the United States. In pre-licensing studies, 689 cats received 2,051 doses of vaccine with side-effects detected in < 1%. In a challenge study performed 375 days after inoculation with 3 doses (3 weeks apart), 84%% of the vaccinates did not become FIV- infected and 90% of the controls became FIV-infected giving a preventable fraction of 82%. However, the efficacy and safety of the vaccine has not been assessed under field conditions in large numbers of cats with large multiple FIV strains. Whether the vaccine will induce vaccine sarcomas is currently unknown. The primary problem with FIV vaccination at this time is that the vaccine induces antibodies detectable by the currently available antibody test. Thus, after vaccination, the practitioner will be unable to determine whether the cat is infected by FIV. PCR for detection of FIV provirus is available in some laboratories, but standardization and external quality control for laboratories providing PCR testing is not currently performed.

An intranasal coronavirus vaccine that may protect some cats from developing feline infectious peritonitis virus infection is currently available. The vaccine appears to be relatively safe. In pet cats, the seroprevalence of coronavirus infection is approximately 20% to 70%, but the incidence of disease due to feline infectious peritonitis virus infection is only 1 in 5000 single cat households. Since the incidence of disease is low, cats are commonly exposed to coronaviruses prior to vaccination, the duration of immunity is short, and the efficacy is less than 100%, coronavirus vaccination is currently considered optional for pet cats. The vaccine may be indicated for seronegative cats entering a known coronavirus-infected household or cattery. The efficacy of this vaccine has not been proven in cats with positive coronavirus serology. Many

cats that are to be exposed to coronaviruses have done so by 16 weeks of age and so if used, the vaccine may be more effective at 8 and 12 weeks of age.

A Giardia spp. vaccine has been introduced for use in cats. When given twice, the vaccine lessens numbers of cysts shed and lessens clinical disease on challenge with one heterologous strain. While the no significant side-effects were reported in preliminary studies, the vaccine is adjuvanted and given SQ and so may ultimately be proven to be associated with fibrosarcomas. Since the disease is usually not life-threatening and has response to therapy of at least 90%, routine use in client-owned cats seems unnecessary. Additionally, it is now known that there are multiple Giardia spp., including a feline specific strain. It is unknown whether the vaccine is protective against strains other than the one used in challenge studies. Based on a study in dogs, it has been proposed that the vaccine may have utility as a immunotherapeutic agent in cats with recurrent or persistent infection. However, in one experimental study, the vaccine was ineffective for the treatment of giardiasis.

A killed ringworm vaccine is available for use in cats. This vaccine is indicated for treatment of disease in some situations but not as a preventative. Since the product is adjuvanted, granuloma formation occurs in some cats.

ABSTRACT ONE

Parenteral administration of feline viral rhinotracheitis, calicivirus, and panleukopenia vaccines induces antibodies that react with Crandall Reese feline kidney cell lysates and feline renal cell lysates.

Michael R. Lappin, DVM, PhD, Wayne A. Jensen, DVM, PhD, Tracey D. Jensen, DVM, MS, et al. In review, Am J Vet Res 2004.

The viruses used in many commercially available feline herpesvirus 1, calicivirus, and panleukopenia (FVRCP) vaccines are grown on the Crandall Reese Feline Kidney (CRFK) cell line. We vaccinated two kittens with each of four commercially available FVRCP vaccines grown on the CRFK cell line. The kittens were vaccinated three times as kittens and boosted once on week 50 of the study. Two additional kittens per group each were inoculated with 10 µg, 50 µg, or 50 µg CRFK lysate plus alum 11 times over the 50 week study period. Renal biopsies for histopathological evaluation were collected prior to the study and on week 56. CBC, serum biochemical analysis, urinalysis, microalbuminuria assay, ELISA for detection of antibodies against CRFK lysate, and ELISA for detection of antibodies against lysed feline renal cells (FRC) were performed on samples collected throughout the study. Antibodies against CRFK antigens were detected by ELISA in each cat inoculated with CRFK lysate and five of six cats administered a parenteral FVRCP vaccine. Antibodies against FRC were detected by ELISA in all the cats administered CRFK lysate alone or a parenteral FVRCP vaccine. Clinical pathological and histopathological abnormalities were minimal. Parenteral administration of vaccines containing CRFK proteins induces CRFK antibodies and FRC antibodies in some cats. However, the clinical pathological and histopathological results suggest that hypersensitization with CRFK proteins is not associated with detectable renal disease in the time period studied.

ABSTRACT 2

Use of serologic tests to predict resistance to feline herpesvirus 1, feline calicivirus, and feline parvovirus infection in cats.

Lappin MR, Andrews J, Simpson D, Jensen WA. J Am Vet Med Assoc 2002;220:38-42.

Serum antibody responses to feline panleukopenia virus (FPV), feline herpesvirus 1 (FHV-1), and feline calicivirus (FCV) were compared to resistance to challenge with the respective virulent viruses in experimental cats. In total, 72 laboratory-reared cats were used and then adopted to private homes. In 4 separate experiments, cats were either vaccinated against FPV, FHV-1, and FCV using an intranasal vaccine or one of two subcutaneous vaccines or maintained as unvaccinated controls. Between 9 and 36 months after vaccination, the cats were challenged with virulent viruses using USDA protocols for vaccine approval. ELISAs for detection of FPV, FHV-1, and FCV antibodies were developed. Serum antibody levels as determined by ELISAs as well as hemagglutination inhibition (HI) for FPV and serum neutralization (SN) for FHV-1 and FCV were correlated to resistance to viral challenge.

When used with vaccinated cats, the positive predictive value of FPV, FHV-1, and FCV antibodies as detected by ELISAs were 100%, 90.5%, and 100%, respectively. When used with vaccinated cats, the positive predictive value of FPV, FHV-1, and FCV antibodies as detected by HI or SN were 100%, 91.3%, and 100%, respectively. The ELISAs were also applied to sera from 276 client-owned cats. The seroprevalences for FPV, FHV-1, and FCV were 68.5%, 70.7%, and 92.4%, respectively. When used with vaccinated cats, positive antibody tests for FPV, FHV-1, FCV correlate to resistance to challenge in most cats regardless of vaccine type or interval. Since the majority of client-owned cats are seropositive for these agents, use of arbitrary vaccination intervals is likely to lead to unnecessary vaccination of some cats.