Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

CHAPTER 6

Respiratory Diseases

Heather W. Barron, DVM, Diplomate ABVP (Avian), and Karen L. Rosenthal, DVM, MS

Although there are few causes of primary respiratory disease in captive ferrets, several diseases may present with respiratory symptoms. Canine distemper virus (CDV) and influenza virus are the most common causes of primary respiratory disease. While distemper is invariably fatal in ferrets, influenza often resolves over the course of a couple of weeks unless it is complicated by bacterial pneumonia. Dyspnea, tachypnea, coughing, and other respiratory signs may manifest with a variety of conditions, including Aleutian disease, heartworm disease, congestive heart failure, lymphoma, trauma, anemia, heatstroke, anaphylactic reactions, and metabolic disturbances. Normal respiratory rate in ferrets is 33 to 36 breaths per minute; documenting this rate should be part of every physical examination along with careful auscultation.

CANINE DISTEMPER VIRUS

Canine distemper virus belongs to the *Morbillivirus* genus, which also includes the measles virus (MV). Although different strains of the virus vary in virulence, canine distemper is typically a fatal disease in ferrets. It is one of the most prevalent viral diseases of dogs, and because it is ubiquitous, ferrets risk being exposed to this virus through canine companions. Reservoirs of CDV include members of the families Canidae, Mustelidae, and Procyonidae.

The virus is most commonly transmitted by aerosol exposure.[2] Direct contact with conjunctival and nasal exudates, urine, feces, and skin can also cause infection.[21] Ferrets shed virus in all body excretions, and shedding begins about 7 days after exposure.[2] Fomites are also implicated in transmission; on gloves, the virus is viable for up to 20 minutes.[21] Once in a ferret's body, the virus appears to spread by viremia.[43] The incubation period in ferrets is typically 7 to 10 days, although incubation periods of up to 56 days have been reported in natural infections.[21,44]

HISTORY AND PHYSICAL EXAMINATION

Infection with CDV should be suspected in any unvaccinated, exposed ferret showing compatible clinical signs. Unvaccinated ferrets of any age are equally susceptible to this disease. In dogs, pyrexia develops 3 to 6 days after infection with CDV and is soon followed by anorexia and a serous nasal discharge.[2] A serous ocular discharge then appears; this discharge quickly becomes mucopurulent.

In ferrets, the first sign of disease is usually a papular dermatitis on the chin, followed by a cheilitis characterized by swelling and crusting. These changes may be accompanied by dermatitis on the anus and inguinal area,[21] which is orange-tinged in some ferrets. Other clinical signs are anorexia, depression, dyspnea, pyrexia, photophobia, pruritus, blepharospasm, and abundant mucopurulent oculonasal discharge. Hyperkeratosis of the planum nasale and footpads (Fig. 6-1) often occurs. Vomiting and diarrhea, which are seen in dogs with CDV, are uncommon in ferrets.

The respiratory system is the preferred site for the virus to replicate.[43] Secondary bacterial infections, which are responsible

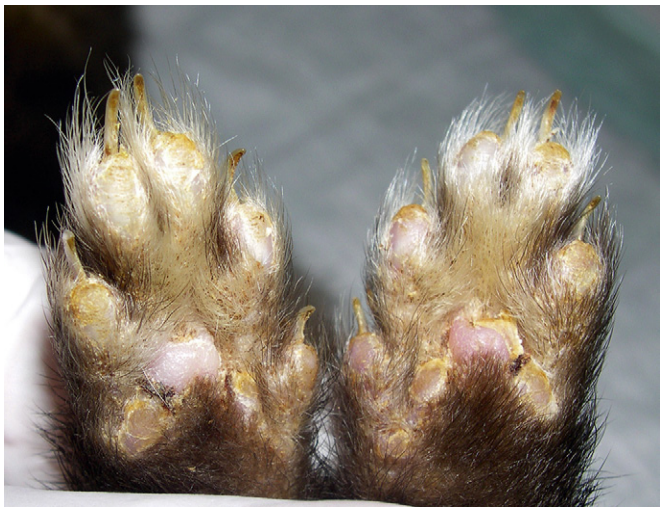

Fig. 6-1 Hyperkeratotic footpads in a ferret diagnosed with canine distemper virus (CDV). *Photograph courtesy of Dr. David Perpinan.*

for many of the severe respiratory symptoms and death, are caused by the immunosuppressive effects of the virus.[57]

Seizures and blindness are common in dogs with CDV infection,[57] and neurologic signs may manifest without previous systemic signs.[2] In ferrets with advanced CDV infection, incoordination, torticollis, and nystagmus can be present.[2]

DIAGNOSIS

In the past, most laboratory tests available for the diagnosis of distemper were hampered by low sensitivity, low specificity, or both. A plasma sample can be submitted to measure an antibody titer against CDV. However, because both infected and vaccinated ferrets can have a positive titer, a positive result is not diagnostic of disease. In practical terms, if a ferret that has not been vaccinated has a positive titer, this test can confirm CDV infection. A fluorescent antibody test can be done on conjunctival smears, mucous membrane scrapings, or blood smears to identify CDV antigen in cells.[21] However, this test is useful only in the first few days of disease, and false-negative results are possible. Modified live viral strains used for vaccination do not interfere with this test.[57]

Polymerase chain reaction (PCR) assays have been developed and may be used for ante- or postmortem diagnosis. Recent research suggests that nested PCR assays are more sensitive for antemortem diagnosis than reverse transcriptase PCR (RT-PCR).[30,51] Samples of blood, urine, feces, or tissues or deep pharyngeal swabs should be submitted to commercial laboratories for CDV PCR testing. False-positive results may be seen in the first few weeks after vaccination with modified live vaccines. Killed and vector-recombinant vaccines do not interfere with PCR testing.

A positive postmortem diagnosis can be made by fluorescent antibody staining of imprints from lymph nodes, bladder epithelium, and cerebellum.[2] Histopathologic examination of affected cells can also confirm the disease. Inclusion bodies of CDV are usually intracytoplasmic but can be intranuclear. Inclusions are generally found in the epithelial cells of the trachea, urinary bladder, skin, gastrointestinal tract, lymph nodes, spleen, and salivary glands.[21] Diffuse interstitial pneumonia may be present. In the central nervous system, inflammatory cell invasion with demyelination is observed.[2]

History of exposure and clinical signs can be highly suggestive of infection. Nonspecific test results can include leukopenia, alpha- and beta-hyperglobulinemia, and radiographic evidence of lung congestion or consolidation.[21,44,57] Nonregenerative anemia and increased serum levels of alpha and beta globulins are the most common routine laboratory changes.[44]

Clinical signs of infection with CDV can initially resemble those of influenza. However, within 1 to 2 days, the nasal and ocular discharge turns from serous to mucopurulent, and dermatitis develops around the chin and lips. When it is present with other clinical signs typical of CDV, this dermatitis is pathognomonic for CDV infection. Also, ferrets infected with CDV tend to be much sicker than those with influenza.

TREATMENT

No specific treatment exists for CDV infection in ferrets, and the mortality rate may be up to 100%. Death generally occurs 12 to 16 days after exposure to ferret-adapted CDV strains and 21 to 35 days after exposure to canine wild virus strains. Euthanasia of affected ferrets is usually the most humane option. Palliative treatment consists of supportive care and antibiotics for secondary bacterial infections. Administration of anti-canine distemper hyperimmune serum may be useful if given early in the course of the disease.[44]

PREVENTION

Vaccination is the best way to prevent CDV infection in ferrets. However, CDV vaccines are insufficient to induce protection in very young ferrets because of interference from maternal antibodies acquired via colostrum in the first few days of life. Because CDV is closely related to MV, vaccination with MV vaccine may offer cross protection at 5 to 6 weeks of age without interference from maternal antibodies.[64] Otherwise, CDV vaccinations may be started at 6 or 8 weeks of age for kits from nonimmune or immune dams, respectively, and then continued every 3 to 4 weeks until the kits are at least 12 to 14 weeks old. At present, the recommendation is to revaccinate yearly. However, results of currently ongoing research demonstrate that antibody titers may remain high for several years, suggesting that boosters could be given less frequently. In other species, titers of 1:32 are considered protective, and in a clinical trial involving 66 CDV-vaccinated ferrets, average antibody titers were found to be over 1:1000 a year postvaccination (HL Heller, 2009, personal communication).

Currently, only one CDV vaccine approved by the U.S. government is available for ferrets: PureVax Ferret Distemper Vaccine (Merial, Athens, GA). Production of Fervac-D (United Vaccines, Madison, WI), the only other approved ferret distemper vaccine, was permanently discontinued by the manufacturer. Avoid use of multivalent canine vaccines, which can be associated with adverse effects. Vaccine strains of CDV that have been propagated in cell lines of canine origin may induce distemper disease in ferrets. Signs of vaccine-induced distemper may include mild purulent upper respiratory tract infection with pyrexia that resolves in a week or progresses to fulminating distemper during the same time frame (see Chapter 2).

Anaphylactic reactions in ferrets have been reported after vaccination.[24,40] Most of these reactions occur after vaccination

with canine distemper vaccines. Most reactions usually happen within 30 minutes after vaccination, with clinical signs of vomiting, diarrhea, pale mucous membranes, weak pulses, tachycardia, and lethargy. If a reaction occurs, treat the ferret for anaphylactic shock with epinephrine, parenteral fluids, steroids, antihistamines, and oxygen therapy as needed. It is prudent to suggest that a ferret owner remain in the hospital for up to 30 minutes after CDV vaccination in case a reaction should occur. PureVax ferret distemper vaccine is a recombinant canarypox vector vaccine that appears to be less likely to cause anaphylaxis. A possible link between myofasciitis and distemper vaccination has been suggested.[22]

If an outbreak of CDV occurs in a group of susceptible ferrets, all affected animals should be removed and the healthy ferrets vaccinated immediately. However, vaccinating nonimmunized ferrets may not stop infection and subsequent death in the face of an outbreak.[21]

CDV is relatively labile and its infectivity is destroyed by heat, drying, detergents, and disinfectants.[57] Routine cleaning and disinfection procedures effectively destroy CDV on hard surfaces.

INFLUENZA

Ferrets are susceptible to infection from both influenza type A and B viruses of the class Orthomyxoviridae. Natural outbreaks or clinical cases of influenza in ferrets have occurred with common human influenza type A viruses, the human strain of pandemic H1N1 virus, and swine-origin H1N1 influenza virus.[10,42,55,58] The pathogenicity of type B influenza virus in ferrets appears to be low. In a recent report documenting natural cases of pandemic H1N1 influenza in ferrets, transmission was most likely from infected humans in the household.[58] The influenza virus H3N8 that emerged in dogs in 2004 is most closely related to the equine influenza virus, whereas influenza A viruses affecting ferrets appear to have a pattern of viral attachment more similar to avian and human influenza subtypes.[15,62] Although there is a theoretical potential of the virus being transmitted from ferrets to humans,[36] there is only one report, from the 1930s, that documents a probable transmission of virus to humans. In that report, an animal-passage influenza strain was inoculated into a laboratory ferret, and a laboratory investigator was infected after close contact with the animal.[54] Ferrets have long been important animal models of transmission, pathogenicity, and treatment studies of influenza virus in humans.

Influenza virus is transmitted primarily by aerosol droplets from ferret to ferret or from human to ferret. The virus can be transmitted beginning at the height of pyrexia and continuing for the next 3 to 4 days.[56] In ferrets as in people, influenza primarily causes upper respiratory disease. The different subtypes of influenza A viruses vary in virulence and likelihood of developing secondary bacterial infections, which accounts for the difference in severity of clinical signs.[4,30,46]

HISTORY AND PHYSICAL EXAMINATION

Ferrets contract influenza after being exposed to infected people or other infected ferrets. All ferrets are susceptible to influenza, although the disease is typically more severe in neonates than in older ferrets. After a short incubation period, the body temperature increases and then decreases approximately 48 hours later.[14,21,36,49] The fever may be biphasic throughout the course of the disease. Bouts of sneezing, epiphora, and a mucoid or mucopurulent nasal discharge are common. Clinical signs can appear within 48 hours of exposure.[14,36] Affected ferrets may become lethargic and anorexic,[56] and photophobia and conjunctivitis may be present.[5] Neonates develop a much more severe upper respiratory tract infection than adults, and death may ensue from lower airway obstruction.[9,53]

Clinical signs involving the lower respiratory tract are less common than those of the upper respiratory tract. Infection of the lower respiratory tract is usually confined to the bronchial epithelium[51] and results from secondary bacterial infection. Death can ensue from secondary pulmonary infection with Lancefield group C hemolytic streptococci.[36] Neonates are more likely than older ferrets to develop bronchiolitis and pneumonia[14] and to die from lower respiratory tract infection.[51]

Influenza virus can infect the cells of the intestinal mucosa and cause a limited enteritis.[23] The potential for hepatic dysfunction has been described in ferrets infected experimentally with influenza.[31] Hearing loss has also been associated with influenza infection in ferrets.[48]

DIAGNOSIS

The availability of anti-influenza drugs, which must be given early in infection in order to be effective, has emphasized the need for early diagnosis. Traditionally, a diagnosis of influenza was based on the presence of clinical signs typical of infection, a history of exposure to infected individuals, isolation of the virus from nasal secretions, and a high antibody titer.[36] However, serologic testing and virus isolation are primarily retrospective tools. Experimentally, an enzyme-liked immunosorbent assay can detect antibodies against influenza A and can be used to rapidly establish a serologic diagnosis.[10] Antibodies against influenza virus have been detected within 3 days after infection.[38,41] More recently, polymerase chain reaction (PCR) assays and in-clinic antigen detection assays like Directigen Flu (Becton Dickinson, Franklin Lakes, NJ), have become available and are able to differentiate between human influenza types A and B with a simple nasopharyngeal swab taken within the first 48 to 72 hours after clinical signs develop. An important differential is CDV; Table 6-1 highlights important distinctions between influenza and distemper.

Diagnostic tests available for influenza include rapid immunoassay, immunofluorescence assay, PCR assay, serology, and viral culture. A transient leukopenia can be seen with this disease. Increases in concentrations of blood urea nitrogen, creatinine, alanine aminotransferase, potassium, and albumin have been reported in infected ferrets, but plasma biochemical values are usually within reference intervals.[31]

TREATMENT

Influenza has a 7- to 14-day course in adult ferrets and is associated with a low mortality rate. Most ferrets can be treated at home. Instruct owners to offer favorite foods, chicken or beef broth, or specialized diets (e.g., Carnivore Care, Oxbow Animal Health, Murdock, NE; Eukanuba Maximum-Calorie, The Iams Company, Dayton, OH). Force-feed and offer water by syringe as needed. If pneumonia is not a complicating factor, use a pediatric cough suppressant without alcohol (at the pediatric dosage on a per weight basis). Also a bronchodilator, such as aminophylline (4 mg/kg PO, IM q12h), may be used for symptomatic

Table 6-1 Clinical Distinctions between Canine Distemper Virus and Influenza Virus Infections

Clinical Findings	Canine Distemper Virus	Influenza
Nasal and ocular discharge	+++ (Mucopurulent)	++ (Mucoserous)
Sneezing	+	+++
Coughing	+	+++
Pyrexia	+++ (> 40°C)	++[b]
Dermatitis (chin, lips, inguinal)	+++	—
Footpad hyperkeratosis	++	—
Central signs	+[a]	—
Outcome	Almost 100% fatal	Self-limiting[c]

Frequency of clinical signs: +, may be present; ++, common; +++, usual presentation; —, absent.
[a]Central nervous system signs seen in advanced stages of disease (rarely the only signs).
[b]Pyrexia occurs early in the course of disease and may be resolved by the time of presentation.
[c]Influenza virus infection can be fatal in neonates.

therapy. As with any flu patient, parenteral fluids to maintain hydration and antibiotics to treat secondary bacterial infections may be indicated. To relieve nasal congestion, intranasal delivery of phenylephrine can be effective.[7]

The antiviral medication amantadine (6 mg/kg PO q12h) (Symmetrel; ENDO Pharmaceuticals, Chadds Ford, PA) has been experimentally effective in treating ferrets with influenza, although resistance in humans is widely reported.[15] Other antiviral medications include neuraminidase inhibitors like zanamivir (12.5 mg/kg as a one-time intranasal dose) (Relenza; GlaxoSmith Kline, Research Triangle Park, NC), and oseltamivir (5 mg/kg PO q12h × 10 days) (Tamiflu; Roche, Nutley, NJ). These have been shown to prevent and treat influenza infection and either agent may be used to greater effect in combination with amantadine.[4,19,28] However, resistance to oseltamivir appears to be emerging among some influenza strains.[52] Because ferrets are a good model with which to study influenza infection in people, they are frequently used in experimental studies to develop new anti-influenza drugs.[63] Anti-influenza drugs used in humans may therefore be used to treat pet ferrets. Antibiotics can be used to control secondary bacterial infections of the respiratory tract. In neonates, death typically results from secondary bacterial infections; antibiotic therapy may thus reduce neonate mortality.[25]

The use of antipyretic drugs to control fever is of questionable merit because fever is an important host defense mechanism. In one study, ferrets given aspirin had lowered body temperature, but they shed more virus and their viral levels decreased less rapidly than those of ferrets not treated with an antipyretic.[26] In a recent meta-analysis of the use of antipyretics in animal models of influenza virus, risk of mortality increased with the use of antipyretics (aspirin, paracetamol, and diclofenac).[17] This suggests that fever is instrumental in restricting the severity of infection.[26,53]

PREVENTION

Controlling influenza rests mainly on preventing exposure of susceptible ferrets to infected individuals. Newborn ferrets are protected from disease by milk-derived antibodies in immunized dams.[27] Experimentally, ferrets remain resistant to infection from the same influenza strain 5 weeks after primary infection.[21]

Vaccinating ferrets against influenza virus is not generally recommended for several reasons. Influenza is a relatively benign disease in ferrets, and the wide antigenic variation of the virus makes vaccination difficult. Also, vaccination seems to confer only short-term immunity.[21] However, if a vaccine is being given, the use of a live or recombinant rather than an inactivated vaccine should be considered, because they may induce a greater protective effect.[18,33]

PNEUMONIA

Pneumonia is not a common diagnosis in ferrets. Viral causes of pneumonia include CDV and influenza virus. Aleutian disease virus, a parvovirus, is associated with interstitial pneumonia in mink kits[1] and should be considered as a possible cause of pneumonia and dyspnea in ferrets, especially the young.[60] Respiratory syncytial virus has been shown to cause rhinitis and infection in the lungs of ferrets, but clinical signs of pneumonia have not been seen.[47]

Pyogranulomatous pneumonia has recently been reported in association with a systemic coronavirus infection in ferrets; it appears to produce a disease syndrome similar to the dry form of feline infectious peritonitis (see Chapter 3).[23,37,45]

Bacterial pneumonia (Fig. 6-2) is characterized by a suppurative inflammatory process that affects the bronchial tree, the lung lobes, or both. Reported primary bacterial pathogens that cause pneumonia in ferrets are *Streptococcus zooepidemicus*, other streptococcal species, and numerous mycobacterial species.[12,32,50,61] Gram-negative bacteria such as *Escherichia coli*, *Klebsiella pneumoniae*, and *Pseudomonas aeruginosa* have been isolated from ferrets.[20] Other bacteria that have been isolated from the lungs of ferrets include *Bordetella bronchiseptica* and *Listeria monocytogenes*.

An acute hemorrhagic syndrome has recently been described in young ferrets (8-24 weeks of age) and may result in interstitial pneumonia. Affected ferrets have a prolonged prothrombin time (PT) and activated partial thromboplastin time (APTT) when compared with unaffected ferrets.[29]

Pneumocystis carinii is known to infect the lungs of ferrets. Latent infections can become active with immune suppression.[3,11] Diagnosis is based on identifying the organism in a tracheal or lung wash. Treatment recommendations for *P. carinii*

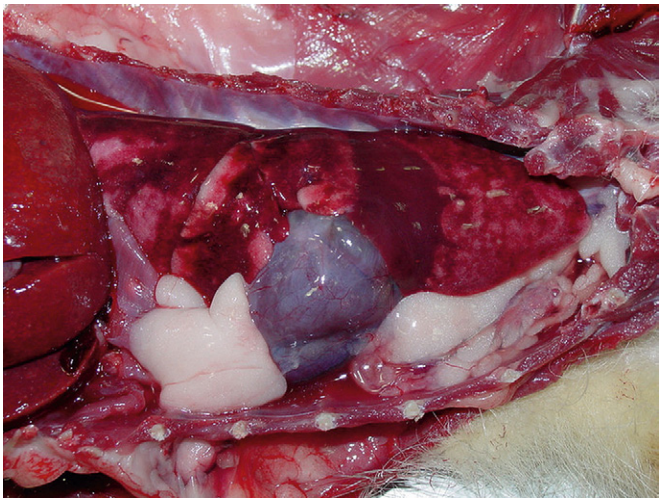

Fig. 6-2 Bacterial pneumonia in a ferret. The lungs are diffusely congested with dark areas of consolidation.

pneumonia, based on those for dogs, include pentamidine isethionate or trimethoprim-sulfamethoxazole.

Two cases of mild endogenous lipid pneumonia have been documented on histologic examination of ferrets at necropsy at the Animal Medical Center (New York, NY) (K. Quesenberry, personal communication, 2003), and one case of mortality due to endogenous lipid pneumonia was confirmed at necropsy (D. Perpinan, personal communication, 2009). In suspected cases, lung aspiration or bronchiolar lavage may help to provide antemortem diagnosis, although biopsy is needed for definitive diagnosis. Documented cases in rodents and other mustelids appear to be idiopathic or secondary to other disease processes.[6] Successful treatment of lipid pneumonia has been achieved in people with prednisolone and thus may be a therapeutic option in ferrets.[8]

Although exogenous lipid pneumonia has not been documented in ferrets, caution should be exercised in treating animals with a mineral oil-based preparation for gastrointestinal disease (e.g., trichobezoar). Chronic aspiration of mineral oil products has been associated with lipid pneumonia in cats and people.[13,39]

HISTORY AND PHYSICAL EXAMINATION

Ferrets with pneumonia exhibit typical clinical signs such as labored breathing, dyspnea, cyanotic mucous membranes, increased lung sounds, nasal discharge, fever, lethargy, and anorexia. Fulminant pneumonia leading to sepsis and death has been reported.[20]

DIAGNOSIS

The diagnosis of pneumonia should be based on the clinical signs, radiographic findings, and results of supportive diagnostic tests. Results of the CBC may reveal leukocytosis caused by a neutrophilia with a left shift. In young ferrets with evidence of interstitial pneumonia, positive results of serologic tests and high concentrations of gamma globulins may support a diagnosis of Aleutian mink disease.

Early in the disease, radiographs may show an interstitial pattern that changes to an alveolar pattern (Fig. 6-3) as the pneumonia progresses. If aspiration pneumonia is present, dependent lung lobes are primarily involved. Marked bronchial patterns suggest primary airway disease.

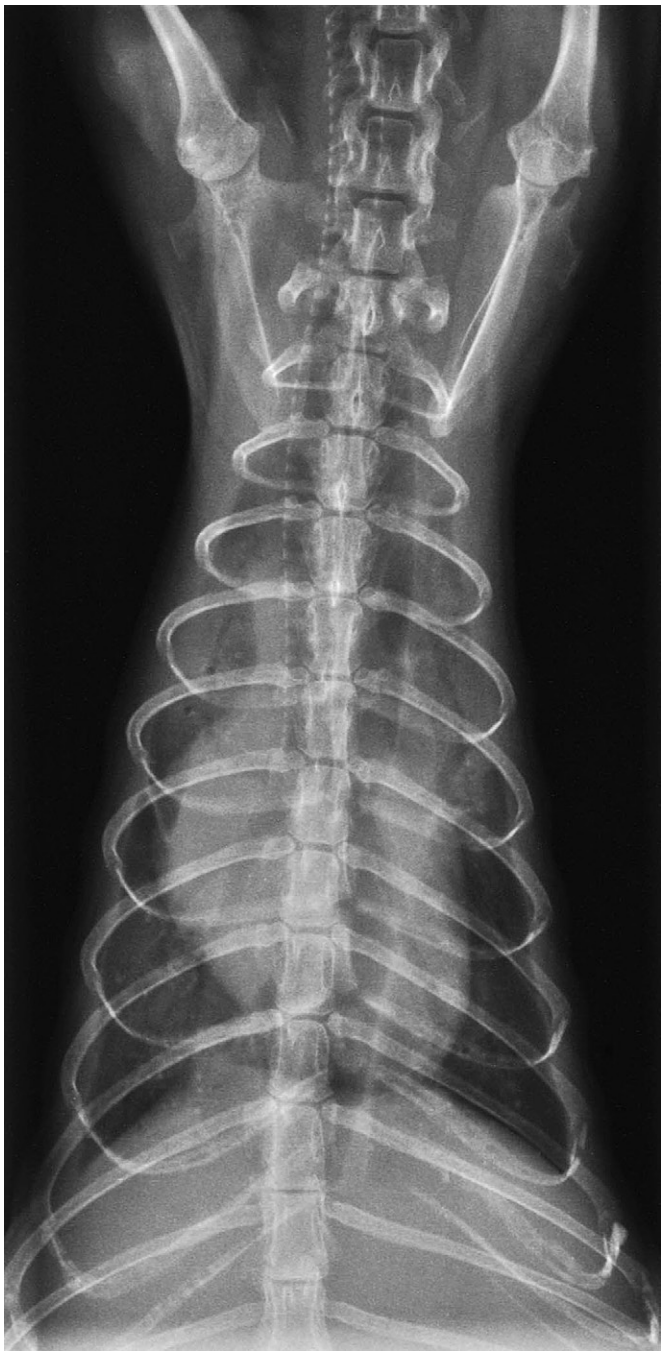

Fig. 6-3 Ventrodorsal radiograph demonstrating an alveolar pattern and air bronchograms in a ferret with pneumonia. *Photograph courtesy of Dr. Nico Schoemaker.*

Microbial cultures of tracheal or lung wash samples are invaluable in establishing a diagnosis and in treating ferrets with pneumonia. Submit samples for culture (aerobic or anaerobic bacterial, fungal, mycobacterial, or other) based on cytologic analysis of the collected fluid and debris. Cytologic assessment of tracheal wash samples from a ferret with pneumonia typically reveals septic inflammation and degenerating neutrophils. Results may also suggest the severity, cause, and chronicity of disease.

TREATMENT

Treat ferrets with pneumonia with good supportive care, including fluid therapy, force-feeding, and oxygen therapy as needed as well as with antimicrobials tailored according to test results. First-line antibiotics to consider before the results of culture and sensitivity testing are known are the quinolones, trimethoprim-sulfamethoxazole, chloramphenicol, or the cephalosporins. Anecdotally, azithromycin at a dose of 5 mg/kg PO q24h also appears to be effective. In a report of two ferrets with mycobacterial pneumonia, both responded successfully to clarithromycin.[32] Combination antibiotic therapy may be indicated.

The prognosis depends on the cause of pneumonia and response to treatment. Most ferrets with bacterial pneumonia respond to antibiotic therapy and supportive care.

PREVENTION

Bordetellosis is rare in ferrets. Nonetheless there is pervasive information in the lay literature about disease prevention. The best way to prevent *B. bronchiseptica* infection is to avoid hospitalizing ferrets where dogs, rabbits, or other common carriers are present. Anectdotally, a killed, injectable *Bordetella* bacterin may be effective in preventing bordetellosis in ferrets when used in accordance with manufacturer recommendations for dogs; however, no published reports supports this claim. The canine modified live intranasal *Bordetella* bacterin may cause disease in ferrets and is not recommended.

PULMONARY MYCOSES

Pulmonary mycoses are uncommon in pet ferrets. Because ferrets in the United States are usually indoor pets, exposure to mycotic spores, which are mainly found in the soil, is unlikely.

HISTORY AND PHYSICAL EXAMINATION

Not all animals with mycoses exhibit signs consistent with pulmonary disease. If lesions develop in the lungs, animals usually cough. Other signs consistent with a mycotic infection are wasting, lethargy, anorexia, lymph node enlargement, lameness, ocular and nasal discharge, and draining tracts unresponsive to antibiotic therapy.[16,59] The prognosis for ferrets with pulmonary mycoses is poor.

CRYPTOCOCCOSIS

Cryptococcosis, caused by *Cryptococcus bacillisporus* (formerly *C. neoformans var gattii*) and *C. neoformans var grubii*, has been diagnosed in a small number of ferrets.[34,35] Infection can cause rhinitis, pneumonia, and pleuritis. Additionally, regional lymph node involvement is common and may also be expected to cause dyspnea when the retropharyngeal or mediastinal lymph nodes are involved.[34] Invasive cryptococcal rhinitis has been successfully treated with itraconazole and surgical debulking.[35]

BLASTOMYCOSIS

Blastomycosis, caused by *Blastomyces dermatitidis*, is endemic in the southeastern United States, the Mississippi River Valley, and the Ohio River Valley.[59] Experimentally, the incubation period is 5 to 12 weeks. The mycelial phase is found in the soil, and the yeast form is found in the tissues. Diagnosis is made on the basis of a history of travel to an endemic region, clinical signs consistent with disease, results of cytologic assessment, positive periodic acid-Schiff reaction, or culture of *B. dermatitidis*. Amphotericin B and ketoconazole or itraconazole are recommended for treatment.[59] Dosages should be based on those used for cats.

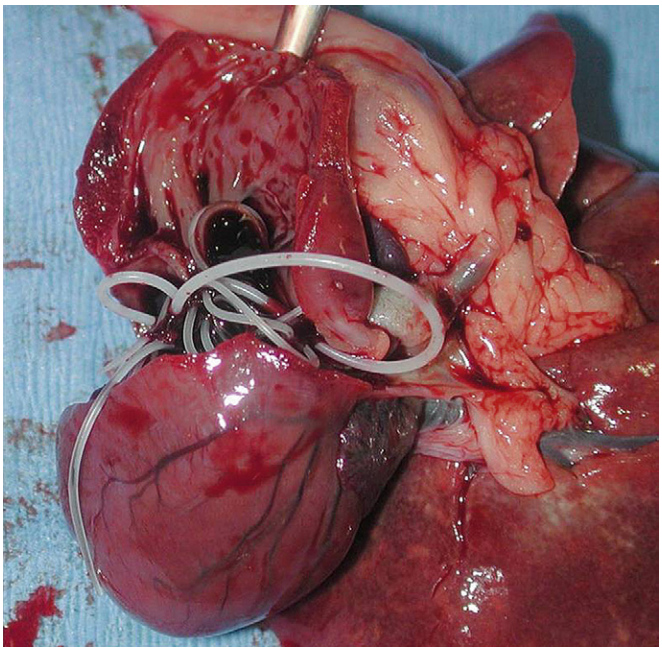

Fig. 6-4 The heart of a ferret that presented for moderate dyspnea and coughing. Necropsy demonstrated 3 female and 7 male *Dirofilaria immitis* worms in the heart.

COCCIDIOIDOMYCOSIS

Coccidioides immitis, the causative agent of coccidioidomycosis, is endemic in the southwestern United States and parts of Latin America. Primary infection develops after a susceptible host inhales the mycelia. Once in the host, spherules form and then produce endospores.[16,59] Pulmonary signs develop 1 to 3 weeks after infection. Diagnosis of this disease is based on identifying the spherules on cytologic examination; they appear as refractile double-walled bodies.[54] Recommended treatment, which is based on that for cats with coccidioidomycosis, includes the use of amphotericin B and ketoconazole or itraconazole.[16,59]

OTHER CAUSES OF RESPIRATORY SIGNS

Differential diagnoses for tachypnea, dyspnea, and respiratory distress are similar to those for other small animals. After the history and physical examination, chest and abdominal radiography is the most important tool to differentiate the causes of lower respiratory tract symptoms. Ferrets that have severe traumatic injuries, such as from a fall from a great height, can develop pneumothorax or diaphragmatic hernia. These animals should be managed as one would a dog or cat with the same injuries. Ferrets with heartworm disease often present with coughing and tachypnea as the only clinical signs, even with moderate worm burdens (see Chapter 5) (Fig. 6-4).

References

1. Alexandersen S, Larsen S, Aasted B, et al. Acute interstitial pneumonia in mink kits inoculated with defined isolates of Aleutian mink disease parvovirus. *Vet Pathol*. 1994;21:216-228.
2. Appel M. Canine distemper virus. In: Appel M, ed. *Virus infections of carnivores*. New York: Elsevier Science; 1987:133-139.
3. Bauer NL, Paulsrud JR, Bartlett MS, et al. *Pneumocystis carinii* organisms obtained from rats, ferrets, and mice are antigenically different. *Infect Immun*. 1993;61:1315-1319.
4. Boltz DA, Rehq DE, McClaren J, et al. Oseltamivir prophylactic regimens prevent H5N1 influenza morbidity and mortality in a ferret model. *J Infect Dis*. 2008;197(9):1315-1323.
5. Buchman CA, Swarts JD, Seroky JT, et al. Otologic and systemic manifestations of experimental influenza A virus infection in the ferret. *Otolaryngol Head Neck Surg*. 1995;112:572-578.
6. Caswell JL, Williams KJ. Respiratory system. In: Grant Maxie M, ed. *Jubb, Kennedy, and Palmer's pathology of domestic animals*. 2nd ed. Edinburgh, UK: Saunders Elsevier; 2007:523-653.
7. Chen KS, Bharaj SS, King EC. Induction and relief of nasal congestion in ferrets infected with influenza virus. *Int J Exp Pathol*. 1995;76:55-64.
8. Chin NK, Hui KP, Sinniah R, et al. Idiopathic lipoid pneumonia in an adult treated with prednisolone. *Chest*. 1994;105:956-957.
9. Collie MH, Rushton DI, Sweet C, et al. Studies of influenza virus infection in newborn ferrets. *J Med Microbiol*. 1980;13:561-571.
10. de Boer GF, Back W, Osterhaus AD. An ELISA for detection of antibodies against influenza A nucleoprotein in humans and various animal species. *Arch Virol*. 1990;115:47-61.
11. Dei-Cas E, Brun-Pascaud M, Bille-Hansen H, et al. Animal models of pneumocystosis. *FEMS Immunol Med Microbiol*. 1998;22:163-168.
12. de Lisle GW, Kawakami RP, Yates GF, et al. Isolation of Mycobacterium bovis and other mycobacterial species from ferrets and stoats. *Vet Microbiol*. 2008;132(3-4):402-407.
13. De Souza HJM, dos Santos AE, Ferreira AMR, et al. Chronic lipidic pneumonia in a cat. *Feline Pract*. 1998;26:16-19.
14. Doggart L. Viral disease of pet ferrets. Part II. Aleutian disease, influenza, and rabies. *Vet Tech*. 1988;9:384-389.
15. Dubovi EJ, Bradley LN. Canine influenza. *Vet Clin North Am Small Anim Pract*. 2008;38(4):827-835.
16. DuVal-Hudelson KA. Coccidioidomycosis in three European ferrets. *J Zoo Wildl Med*. 1990;21:353-357.
17. Eyers S, Weatherall M, Shirtcliffe P, et al. The effect on mortality of antipyretics in the treatment of influenza infection: systematic review and meta-analysis. *J R Soc Med*. 2010;103(10):403-411.
18. Fenton RJ, Clark A, Potter CW. Immunity to influenza in ferrets. XIV: comparative immunity following infection or immunization with live or inactivated vaccine. *Br J Exp Pathol*. 1981;62:297-307.
19. Fenton RJ, Morley PJ, Owens IJ, et al. Chemoprophylaxis of influenza A virus infections, with single doses of zanamivir, demonstrates that zanamivir is cleared slowly from the respiratory tract. *Antimicrob Agents Chemother*. 1999;43:2642-2647.
20. Fox JG. Bacterial and mycoplasmal diseases. In: Fox JG, ed. *Biology and diseases of the ferret*. 2nd ed. Philadelphia: Lippincott Williams & Wilkins; 1998:321-354.
21. Fox JG, Pearson RC, Gorham JR. Viral diseases. In: Fox JG, ed. *Biology and diseases of ferrets*. 2nd ed. Philadelphia: Lippincott Williams & Wilkins; 1998:355-374.
22. Garner MM, Ramsell K, Shoemaker NJ, et al. Myofasciitis in the domestic ferret. *Vet Pathol*. 2007;44:25-38.
23. Garner MM, Ramsell K, Morera N, et al. Clinicopathologic features of a systemic coronavirus-associated disease resembling feline infectious peritonitis in the domestic ferret. *Vet Pathol*. 2008;45(2):236-246.
24. Greenacre CB. Incidence of adverse events in ferrets vaccinated with distemper or rabies vaccine: 143 cases (1995-2001). *J Am Vet Med Assoc*. 2003;223(5):663-665.
25. Husseini RH, Collie MH, Rushton DI, et al. The role of naturally-acquired bacterial infection in influenza-related death in neonatal ferrets. *Br J Exp Pathol*. 1983;64:559-569.
26. Husseini RH, Sweet C, Collie MH, et al. Elevation of nasal viral levels by suppression of fever in ferrets infected with influenza viruses of differing virulence. *J Infect Dis*. 1982;145:520-524.
27. Husseini RH, Sweet C, Overton H, et al. Role of maternal immunity in the protection of newborn ferrets against infection with a virulent influenza virus. *Immunology*. 1984;52:389-394.
28. Ilyushina NA, Hoffman E, Saloman R, et al. Amantadine-oseltamivir combination therapy for H5N1 influenza virus infection in mice. *Antivir Ther*. 2007;12(3):363-370.
29. Johnson-Delaney CA, Reavill DR. Ferret acute hemorrhagic syndrome, In *Proceedings*. Assoc Avian Vets and Assoc of Exot Mam Vets, 2008; 49–50.
30. Jóżwik A, Frymus T. Comparison of the immunofluorescence assay with RT-PCR and nested PCR in the diagnosis of canine distemper. *Vet Res Commun*. 2005;29(4):347-359.
31. Kang ES, Lee HJ, Boulet J, et al. Potential for hepatic and renal dysfunction during influenza B infection, convalescence, and after induction of secondary viremia. *J Exp Pathol*. 1992;6:133-144.
32. Lunn JA, Martin P, Zaki S, Malik R. Pneumonia due to Mycobacterium abscesses in two domestic ferrets *(Mustela putorius furo)*. *Aust Vet J*. 2005;83(9):542-546.
33. Mahmood K, Bright RA, Mytle N, et al. H5N1 VLP vaccine induced protection in ferrets against lethal challenge with highly pathogenic H5N1 influenza viruses. *Vaccine*. 2008;26(42):5393-5399.
34. Malik R, Alderton B, Finlaison D, et al. Cryptococcosis in ferrets: a diverse spectrum of clinical disease. *Aust Vet J*. 2002;80(12):749-755.
35. Malik R, Martin P, McGill J, et al. Successful treatment of invasive nasal cryptococcosis in a ferret. *Aust Vet J*. 2000;78(3):158-159.
36. Marini RP, Adkins JA, Fox JG. Proven or potential zoonotic diseases of ferrets. *J Am Vet Med Assoc*. 1989;195:990-994.
37. Martinez J, Ramis AJ, Reinacher M, et al. Detection of feline infectious peritonitis virus-like antigen in ferrets. *Vet Rec*. 2006;158:523.
38. McLaren C, Butchko GM. Regional T- and B-cell responses in influenza-infected ferrets. *Infect Immunol*. 1978;22:189-194.
39. Midulla F, Strappini PM, Ascoli V, et al. Bronchoalveolar lavage cell analysis in a child with chronic lipid pneumonia. *Eur Respir J*. 1998;11:239-242.
40. Moore GE, Glickman NW, Ward MP, et al. Incidence of and risk factors for adverse events associated with distemper and rabies vaccine administration in ferrets. *J Am Vet Med Assoc*. 2005;226(6):909-912.
41. Ochi A, Danesh A, Seneviratne C, et al. Cloning, expression and immunoassay detection of ferret IFN-gamma. *Dev Comp Immunol*. 2008;32(8):890-897.
42. Patterson AR, Cooper VL, Yoon KJ, et al. Naturally occurring influenza infection in a ferret *(Mustela putorius furo)* colony. *J Vet Diag Invest*. 2009;21(4):527-530.
43. Pearson RC, Gorham JR. Viral disease models. In: Fox JG, ed. *Biology and diseases of the ferret*. 2nd ed. Philadelphia: Lippincott Williams & Wilkins; 1998:487-498.
44. Perpinan D, Ramis A, Tomas A, et al. Outbreak of canine distemper in domestic ferrets *(Mustela putorius furo)*. *Vet Rec*. 2008;163(8):246-250.
45. Perpinan D, Lopez C. Clinical aspects of systemic granulomatous inflammatory syndrome in ferrets *(Mustela putorius furo)*. *Vet Rec*. 2008;162:180-184.

46. Peltola VT, Boyd KL, McAuley JL, et al. Bacterial sinusitis and otitis media following influenza virus infection in ferrets. *Infect Immunology*. 2006;74(5):2562-2567.
47. Prince GA, Porter DD. The pathogenesis of respiratory syncytial virus infection in infant ferrets. *Am J Pathol*. 1976;82:339-352.
48. Rarey KE, DeLacure MA, Sandridge SA, et al. Effect of upper respiratory infection on hearing in the ferret model. *Am J Otolaryngol*. 1987;8:161-170.
49. Ryland LM, Gorham JR. The ferret and its diseases. *J Am Vet Med Assoc*. 1978;173:1154-1158.
50. Saunders GK, Thomsen BV. Lymphoma and Mycobacterium avium infection in a ferret *(Mustela putoris furo)*. *J Vet Diagn Invest*. 2006;18(5):513-515.
51. Shin YJ, Cho KO, Cho HS, et al. Comparison of one-step RT-PCR and a nested PCR for the detection of canine distemper virus in clinical samples. *Aust Vet J*. 2004;82(1-2):83-86.
52. Sy CL, Lee SS-J, Liu M-T, et al. Rapid emergence of oseltamivir resistance [letter]. *Emerg Infect Dis*. Apr 2010;16(4). http://www.cdc.gov/EID/content/16/4/723.htm. Accessed 1/12/2011.
53. Smith H, Sweet C. Lessons for human influenza from pathogenicity studies with ferrets. *Rev Infect Dis*. 1988;10:56-75.
54. Smith W, Stuart-Harris CH. Influenza infection of man from the ferret. *Lancet*. 1936;228:121-123.
55. Spickler AR. Influenza. Technical Fact Sheet. The Center for Food Security and Public Health, Iowa State University. Available at http://www.cfsph.iastate.edu/DiseaseInfo/disease.php?name=influenza&lang=en. Accessed 1/12/2011.
56. Squires S, Belyavin G. Free contact infection in ferret groups. *J Antimicrob Chemother*. 1975;1:35-42.
57. Swango LJ. Canine viral diseases. In: Ettinger SJ, ed. *Textbook of veterinary internal medicine*. Philadelphia: WB Saunders; 1989:298-311.
58. Swenson SL, Koster LG, Jenkins-Moore M, et al. Natural cases of 2009 pandemic H1N1 influenza A virus in pet ferrets. *J Vet Diagn Invest*. 2010;22(5):784-788.
59. Taboada J. Systemic mycoses. In: Ettinger SJ, Feldman EC, eds. *Textbook of veterinary internal medicine*. 5th ed. Philadelphia: WB Saunders; 2000:453-476.
60. Une Y, Wakimoto Y, Nakano Y, et al. Spontaneous Aleutian disease in a ferret. *J Vet Med Sci*. 2000;62(5):553-555.
61. Valheim M, Djonne B, Heiene R, Caugant DA. Disseminated *Mycobacterium celatum* (Type 3) infection in a domestic ferret *(Mustela putorius furo)*. *Vet Pathol*. 2001;38:460-463.
62. Van Riel D, Munster VJ, McAuley AL, et al. Human and avian influenza viruses target different cells in the lower respiratory tract of humans and other mammals. *Am J Pathol*. 2007;171(4):1215-1223.
63. Yoshimoto J, Yagi S, Ono J, et al. Development of anti-influenza drugs: II. Improvement of oral and intranasal absorption and the anti-influenza activity of Stachyflin derivatives. *J Pharm Pharmacol*. 2000;52:1247-1255.
64. Welter J, Taylor J, Tartaglia J, et al. Vaccination against Canine Distemper Virus Infection in Infant Ferrets with and without Maternal Antibody Protection, Using Recombinant Attenuated Poxvirus Vaccines. *J Virol*. 2000;74(14):6358-6367.