



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.

Elsevier hereby grants permission to make all its COVID-19-related research that is available on the COVID-19 resource centre - including this research content - immediately available in PubMed Central and other publicly funded repositories, such as the WHO COVID database with rights for unrestricted research re-use and analyses in any form or by any means with acknowledgement of the original source. These permissions are granted for free by Elsevier for as long as the COVID-19 resource centre remains active.

Respiratory Diseases of Ferrets

David Perpiñán, DVM, MSc, PhD, Diplomate ECZM (Herpetology)

OUTLINE

Canine Distemper, 71

- History and Physical Examination, 71
- Diagnosis, 71
- Treatment, 72
- Prevention, 72

Influenza, 72

- History and Physical Examination, 72
- Diagnosis, 72
- Treatment, 73
- Prevention, 73

Pneumonia, 73

- History and Physical Examination, 74
- Diagnosis, 74
- Treatment, 74
- Prevention, 74

Pulmonary Mycoses, 74

- History and Physical Examination, 74
- Cryptococcosis, 74
- Blastomycosis, 75
- Coccidioidomycosis, 75
- Infection by *Pneumocystis carinii*, 75

Other Causes of Respiratory Signs, 75

Primary respiratory disease is uncommon in ferrets. The most common causes are canine distemper virus (CDV) and influenza virus, although several other diseases may manifest with respiratory signs.

CANINE DISTEMPER

Canine distemper virus (CDV) is an RNA virus of the genus Morbillivirus in the family Paramyxoviridae. Different viral strains vary in virulence, but CDV is typically fatal in ferrets. Because it is ubiquitous among dogs, ferrets risk being exposed through canine contacts. Reservoirs of CDV are members of the families Canidae, Mustelidae, and Procyonidae, although bears, marine mammals, pangolins, hyenas, and certain other mammals are susceptible to CDV.²³

Canine distemper virus is most commonly transmitted by aerosol exposure but can also be spread by direct contact with conjunctival and nasal exudates, urine, feces, and skin.^{1,23} Ferrets shed virus within approximately 7 days after exposure.¹ Fomites are also implicated in transmission; CDV is viable for up to 20 minutes on gloves.²³ Once in a ferret's body, CDV appears to spread hematogenously.²³ The incubation period is typically 7 to 10 days, although incubation periods of up to 56 days have been reported.^{23,35}

History and Physical Examination

Characteristics of infection vary greatly depending on the strain of CDV, route of infection, infective dose, and immune status of the ferret. Infection with CDV should be suspected in any unvaccinated and exposed ferret showing compatible clinical signs, particularly in animals with exposure to wildlife or feral dogs or those subjected to stressful conditions.²³

Initial clinical signs are lethargy, photophobia, and loss of appetite, which are quickly followed by systemic disease affecting the dermatologic, respiratory, and neurologic systems. Erythematous and pruritic rashes can appear on the footpads and chin, around the mouth and eyes, and in the interscapular and perineal areas. Rashes develop into hyperkeratosis and crusts (Fig. 6.1). Respiratory signs include dyspnea, tachypnea, oculonasal discharge, and, more rarely, coughing and sneezing. Fever is sporadic. Neurologic signs (e.g., paresis, muscle tremors, incoordination, convulsions, and coma) can be seen during advanced stages of the disease. Immunosuppression can result in secondary bacterial infections, particularly in the lungs.^{1,23,35}

Diagnosis

History of exposure and consistent clinical signs are highly suggestive of infection. Although clinical signs initially can resemble those of influenza, clinical signs of CDV are much more severe and manifest as a combination of respiratory, neurologic, and dermatologic signs not seen with influenza.

Antemortem diagnostic testing consists primarily of antigen detection by fluorescent antibody labeling or polymerase chain reaction (PCR) on conjunctival, tonsillar, or respiratory samples. A mild nonregenerative anemia and an increase in alpha and beta globulins may be evident on blood tests, and radiographic changes may be suggestive of pneumonia.^{23,35}

On postmortem examination, CDV inclusion bodies may be seen in the respiratory system, skin, brain, and urinary bladder. Inclusion bodies are usually intracytoplasmic but can be intranuclear.^{23,35} Antigen detection can be performed with fresh, frozen, or formalin-fixed tissue samples.^{1,23}



Fig. 6.1 Severe crusting dermatitis on the face in a ferret with advanced canine distemper.

Treatment

There is no specific treatment for canine distemper in ferrets, and the mortality rate may be as high as 100%. Depending on the strain, death can occur within 5 to 35 days after clinical signs first appear and may or may not be preceded by neurologic disease.²³ With advanced disease, euthanasia is usually the most humane option. However, treatment may be successful in some cases, particularly in infections with strains of low pathogenicity and when affected ferrets are treated very early in the course of disease. Treat with broad-spectrum antibiotics (e.g., amoxicillin/clavulanate 12.5 mg/kg orally [PO] every 12 hours), vitamin A (50,000 IU [15 mg] of retinol palmitate intramuscularly [IM] every 24 hours for 2 days), vitamin C (250 mg intravenously [IV] every 24 hours for 3 days), and hyperimmune serum against CDV (1 mL IV; if not commercially available, use serum from a healthy, vaccinated ferret). Vaccination may be effective when performed very soon after infection, especially in the face of an outbreak. Supportive and symptomatic therapies include meloxicam, famotidine, diphenhydramine (to help reduce pruritus), buprenorphine, bronchodilators, fluid therapy, and nutritional support. Even with treatment, inform owners that recovery is uncommon.^{23,35}

Prevention

Vaccination has greatly reduced the incidence of canine distemper in ferrets. Immunity against CDV is long-lasting after recovery from natural infection or booster vaccination. However, immunity may become compromised on exposure to a highly virulent strain or to a large quantity of virus, or if the ferret becomes immunocompromised or stressed. In the face of an outbreak of canine distemper, remove/isolate all affected animals, and vaccinate healthy ferrets immediately. See [Chapter 2](#) for an in-depth discussion of CDV vaccines, vaccination protocols, and vaccine-associated adverse reactions.

Canine distemper virus is relatively labile and is destroyed by heat, ultraviolet light, drying, detergents, and disinfectants.²³ Routine cleaning and disinfection procedures effectively destroy CDV on hard surfaces.

INFLUENZA

Ferrets are susceptible to influenza virus types A and B of the class Orthomyxoviridae. Natural outbreaks or clinical cases of influenza have occurred in ferrets with common human influenza type A viruses, the human strain of pandemic H1N1 virus, and swine-origin H1N1 influenza virus.^{8,33,41,44} 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.⁴⁴ Ferrets have long been important animal models for the transmission, pathogenicity, and treatment of influenza A virus in humans.⁴⁹

Ferrets contract influenza from infected people or other infected ferrets. Although all ferrets are susceptible to influenza, the disease is typically more severe in neonates than in older ferrets. Although the virus can be transmitted from ferrets to humans,³⁰ there is only one report of this, from the 1930s. 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.⁴⁰ Influenza virus is transmitted primarily by aerosol droplets, and the risk of transmission is greatest from the height of pyrexia through the next 3 to 4 days.⁴² In ferrets, as in people, influenza primarily causes upper respiratory disease. Influenza A subtypes vary in virulence and their association with secondary bacterial infections, both of which account for the difference in severity of clinical signs.^{3,36} Infection with highly pathogenic human influenza viruses also produces severe disease in ferrets.⁴⁶

History and Physical Examination

Clinical signs appear within 48 hours of exposure to influenza virus and include sporadic pyrexia, mild respiratory signs (e.g., sneezing, serous oculonasal discharge), lethargy, anorexia, photophobia, and conjunctivitis.^{4,23,30,42} Hearing loss, limited enteritis, and hepatic and renal dysfunction have also been reported.^{21,23,37} Influenza in neonates and severe cases in older ferrets may evolve to bronchitis, pneumonia, otitis, periorbital and perinasal dermatitis, and neurologic signs such as ataxia, torticollis, and hind limb paresis.^{6,39} Death can occur from lower airway obstruction, secondary pulmonary infections, or from neurologic disease.³⁰

Diagnosis

A presumptive diagnosis is based on compatible clinical signs and history, antigen detection in oculonasal secretions, and recovery within 4 to 5 days.²³ Antigen detection tests can be performed using fresh or frozen tissues, nasal swabs, or bronchoalveolar washes.²³ Antigen detection tests commonly available in diagnostic laboratories include immunofluorescence, rapid immunoassay, and real-time reverse transcription PCR. In-clinic antigen detection tests (e.g., Directigen Flu; Becton Dickinson, Franklin Lakes, NJ) are also available in many countries. Hematologic and biochemical values in affected ferrets are generally within reference intervals, although a transient leukopenia can be seen in some cases.²¹

TABLE 6.1 Clinical Distinctions Between Canine Distemper Virus and Influenza Virus Infection in Ferrets

Clinical Findings	Canine Distemper Virus	Influenza Virus
Nasal and ocular discharge	+++ (Mucopurulent)	++ (Mucoserous)
Sneezing	+	+++
Coughing	+	+++
Pyrexia	+++ (> 104°F [40°C])	++ ^b
Dermatitis (chin, lips, inguinal)	+++	—
Footpad hyperkeratosis	++	—
Central nervous system signs	+ ^a	—
Outcome	Approaches 100% fatality	Self-limiting ^c

^aMay be seen in advanced stages of disease (rarely the only signs).

^bOccurs early in the disease course and may be resolved by the time of presentation.

^cCan be fatal in neonates.

An important differential diagnosis is canine distemper, but influenza is generally less severe. Table 6.1 highlights important distinctions between influenza and canine distemper.

Treatment

Influenza has an approximately 5 to 7 day course in adult ferrets and is associated with low mortality rates. The disease is generally mild, and treatment, when necessary, consists of supportive care. Instruct owners to offer favorite foods, chicken or beef broth, or specialized carnivore diets (e.g., Carnivore Care; Oxbow Animal Health, Murdock, NE). Force-feed and offer water by syringe as needed. If clinical signs progress, consider using palliative agents such as cough suppressants, bronchodilators, or decongestants. Antibiotics and parenteral fluids are rarely required but may be indicated in severe cases and in neonates.¹⁹ Use of antipyretics to control fever is debatable, because fever is an important host defense mechanism. In a recent meta-analysis of the use of antipyretics in animal models of influenza virus, risk of death increased with the use of certain antipyretics (aspirin, paracetamol, and diclofenac).¹³

Experimental studies have shown that antiviral treatment in ferrets can prevent disease, reduce clinical signs, and reduce virus-induced lesions. Human antiviral drugs used in experimental studies to treat ferrets with influenza include oseltamivir (2.5 to 5 mg/kg PO every 12 hours for 10 days; increase to 12.5 mg/kg PO every 12 hours in severe cases) (Tamiflu; Genentech, San Francisco, CA) and zanamivir (0.3 to 1 mg/kg every 12 hours, or up to 12.5 mg/kg one-time intranasal dose) (Relenza; GlaxoSmith Kline, Research Triangle Park, NC) alone or in combination with amantidine.^{3,11,15,20} Other agents used experimentally to treat or prevent influenza in ferrets include cyanovirin-N, human monoclonal antibodies, and interferon α .^{17,24,38} However, because of antiviral resistance, potential adverse effects, and minimal efficacy, these drugs have limited to no practical use in clinical situations. Because many antiviral drugs developed for use in people are tested in ferrets, new drugs that

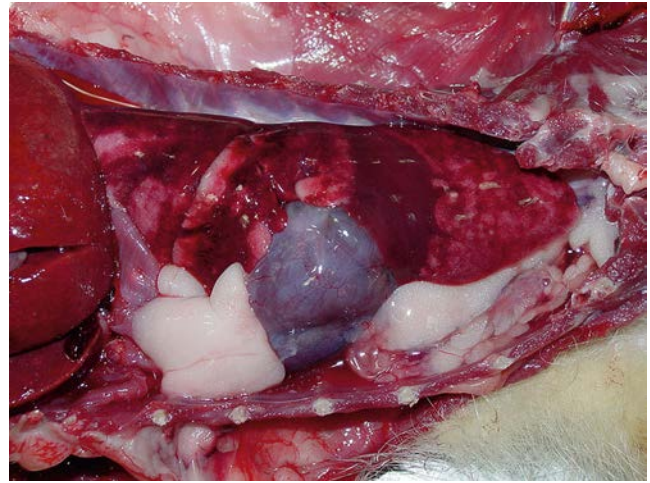


Fig. 6.2 Bacterial pneumonia in a ferret. The lungs are diffusely congested with dark areas of consolidation.

potentially can be used for treating ferrets with influenza are likely to become available in the future.²³

Prevention

Preventing influenza relies primarily on avoiding exposure to infected individuals. Newborn ferrets are protected by maternal antibodies in the jill's milk. Experimentally, ferrets remain resistant to infection from the same influenza viral strain by 5 weeks after primary infection.²³

Vaccinating ferrets against influenza virus is not generally recommended. Influenza is a relatively benign disease in ferrets, and the wide antigenic variation of the virus results in low vaccination efficacy. However, if vaccination is deemed advisable, use a live or recombinant rather than an inactivated vaccine to induce a more robust immune response.^{14,27} Currently, no influenza vaccines are licensed for ferrets; however, most vaccines licensed for people have been tested in ferrets.

PNEUMONIA

Pneumonia is not commonly diagnosed in ferrets. Viral causes of pneumonia include CDV and influenza virus, and these conditions often involve secondary bacterial infections. Pneumonia may appear rarely as part of systemic infections, such as with Aleutian disease virus and ferret systemic coronavirus.^{18,23,32,47}

Bacterial pneumonia without an underlying pathology is rare in ferrets (Fig. 6.2). Primary or secondary bacterial pathogens reported to cause pneumonia in ferrets include *Streptococcus zooepidemicus*, other streptococcal species, *Escherichia coli*, *Klebsiella pneumoniae*, *Pseudomonas aeruginosa*, *Pseudomonas luteola*, *Bordetella bronchiseptica*, *Listeria monocytogenes*, and numerous mycobacterial species.^{10,23,26,31,43,48} Infection with *P. luteola* is associated with pyothorax, mediastinal lymphadenopathy, and multiple white nodules in the lung.³¹ A novel *Mycoplasma* species was identified as a cause of respiratory disease in young ferrets aged 6 to 8 weeks in a large breeding facility. Ferrets exhibited nonproductive coughing; less common clinical signs included hemoptysis, labored breathing, sneezing, and conjunctivitis. The disease was characterized by high morbidity (95%) and very low mortality rates.²²

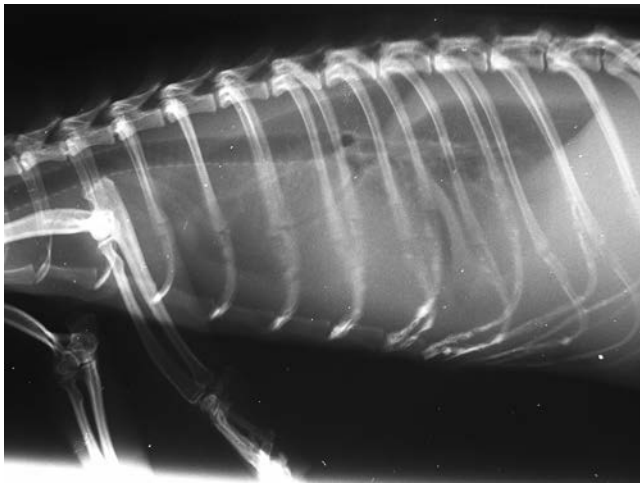


Fig. 6.3 Lateral radiograph of a ferret showing pleural effusion, as can be seen with endogenous lipid pneumonia or *Pseudomonas luteola* infection.

Endogenous lipid pneumonia is a disease characterized by the accumulation of foamy macrophages in the pulmonary parenchyma. It is an idiopathic condition that is identified incidentally at necropsy and is believed to be secondary to other conditions such as systemic coronavirus in ferrets.³⁴ In rare cases, endogenous lipid pneumonia alone has been associated with severe respiratory signs and death.³⁴

History and Physical Examination

Ferrets with pneumonia can exhibit 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.⁴³

Diagnosis

The diagnosis of pneumonia is based on clinical signs, radiographic findings, and results of supportive diagnostic tests. Pneumonias caused by viruses have been described previously in this chapter. Results of a complete blood cell count may reveal leukocytosis caused by a neutrophilia with a left shift in cases of bacterial infection. Very rarely, pneumonia in young ferrets may be caused by Aleutian disease virus, with hypergammaglobulinemia and positive serologic results.

Early in the disease, radiographs may show an interstitial pattern that progresses to an alveolar pattern with worsening pneumonia. In cases of aspiration pneumonia, dependent lung lobes are primarily involved. Marked bronchial patterns suggest primary airway disease. Pleural effusion may be evident radiographically in some conditions, such as endogenous lipid pneumonia and *P. luteola* infection (Fig. 6.3).

Microbial cultures of samples from bronchoalveolar lavages (BAL) are invaluable for definitive diagnosis and treatment. Submit samples for culture (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 degenerative neutrophils. Results may also suggest the severity, cause, and chronicity of disease. The bronchointerstitial

pneumonia caused by *Mycoplasma* species may produce few inflammatory cells on cytologic examination of BAL samples; however, those samples can be submitted for PCR. Foamy macrophages can be seen on BAL cytology in cases of endogenous lipid pneumonia.⁵

Treatment

Treat affected ferrets with supportive care, including fluid therapy, force-feeding, and oxygen therapy, as well as antimicrobials tailored to test results. First-line empirical antibiotic choices include amoxicillin/clavulanate, a fluoroquinolone, trimethoprim-sulfamethoxazole, or a cephalosporin. Treatment for mycoplasmosis should include doxycycline, enrofloxacin, or azythromycin.²² In a report of two ferrets with mycobacterial pneumonia, both responded successfully to clarithromycin,²⁶ but combination antibiotic therapy may be preferable. Corticosteroid therapy is used to treat endogenous lipid pneumonia in people.^{5,34}

The prognosis depends on the cause of pneumonia and response to treatment. Most ferrets with bacterial pneumonia respond to antibiotic therapy and supportive care. In some cases that recover from *Mycoplasma* infection, ferrets become chronic carriers and may have recurring episodes of coughing.

Prevention

Help prevent pneumonia by avoiding stress and overcrowding.

PULMONARY MYCOSES

Pulmonary mycoses are uncommon in pet ferrets because most pet ferrets live indoors and are rarely exposed to mycotic spores. However, cases have been described involving fungal organisms such as *Pneumocystis carinii*, *Blastomyces dermatitidis*, *Coccidioides immitis*, and *Cryptococcus bacillisporus* (formerly *Cryptococcus neoformans* var. *gattii*). Ferrets treated with steroids (e.g., for insulinoma, endogenous lipid pneumonia, lymphoma, Aleutian disease, and some cases of enteritis) may be at increased risk of mycoses. Although particular mycotic infections are endemic in certain areas of the United States, they are rare in Europe.

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 mycotic infections include anorexia, wasting, lethargy, lymphadenopathy, lameness, ocular and nasal discharge, and draining tracts unresponsive to antibiotic therapy.^{12,45} The prognosis for ferrets with pulmonary mycoses is poor.

Cryptococcosis

Cryptococcosis, caused by *C. bacillisporus* (which is part of the *C. gatti* complex) and *C. neoformans* var. *grubii*, has been diagnosed in a small number of ferrets.^{28,29} *Cryptococcus* species grow in soil and bird droppings.¹⁶ Infection can cause rhinitis, pneumonia, and pleuritis. Regional lymph node involvement is also common and may cause dyspnea if the retropharyngeal or

mediastinal lymph nodes are involved.²⁸ Additionally, infection of any other organ of the body is possible. Invasive cryptococcal rhinitis has been successfully treated with itraconazole and surgical debulking.²⁹ Other cases of systemic cryptococcosis have been treated with itraconazole, with better results in early stages of the disease.^{16,28}

Blastomycosis

Blastomycosis, caused by *B. dermatitidis*, is endemic in the southeastern United States, the Mississippi River Valley, and the Ohio River Valley.⁴⁵ Two cases of chronic granulomatous mycosis, primarily affecting the lungs, were reported in ferrets from the United States, one of which occurred in a ferret housed indoors.^{7,25} Both presented with respiratory signs, and neither survived.

Coccidioidomycosis

Coccidioides immitis is endemic in the southwestern United States and parts of Latin America. Among the few cases of coccidioidomycosis reported in ferrets, clinical signs included cough, nasal discharge, anorexia, lethargy, and wasting. A diffuse interstitial pattern is generally observed on thoracic radiographs, and complement fixation or detection of spores in cytologic samples may yield positive results. The reported animals did not survive, in part due to the chronicity of the condition. Recommended treatment is based on that for cats with coccidioidomycosis and includes the use of amphotericin B and ketoconazole or itraconazole.^{12,16,45}

Infection by *Pneumocystis carinii*

Originally considered a protozoan, *P. carinii* is known to involve the lungs and cause infection in immunocompromised ferrets. Latent infections can become active with immunosuppression, and organisms can also be transmitted via aerosol exposure.^{2,9,16} Diagnosis is based on identifying the organism in a tracheal or lung wash, using culture or PCR testing. Treatment recommendations for *P. carinii* pneumonia, based on those for dogs, include pentamidine isethionate or trimethoprim-sulfamethoxazole.¹⁶

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, diagnostic imaging (i.e., radiography or computed tomography) is the most important tool to differentiate the causes of lower respiratory tract symptoms. Ferrets that have severe traumatic injuries, such as from a high fall, 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). Congestive heart failure, heatstroke, anemia, anaphylactic reactions, and other systemic conditions such as lymphoma, Aleutian disease, and systemic coronavirus can also produce respiratory clinical signs.

REFERENCES

1. Appel M. Canine distemper virus. In: Appel M, ed. *Virus Infections of Carnivores*. New York, NY: Elsevier Science; 1987: 133–139.
2. Bauer NL, Paulsrud JR, Bartlett MS, et al. *Pneumocystis carinii* organisms obtained from rats, ferrets, and mice are antigenically different. *Infect Immun*. 1993;61(40):1315–1319.
3. Boltz DA, Rehg 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.
4. 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(4):572–578.
5. Caswell JL, Williams KJ. Respiratory system. In: Grant Maxie M, ed. *Jubb, Kennedy, and Palmer's Pathology of Domestic Animals*. Edinburgh, UK: Saunders Elsevier; 2007:523–653.
6. Collie MH, Rushton DI, Sweet C, Smith H. Studies of influenza virus infection in newborn ferrets. *J Med Microbiol*. 1980;13(4):561–571.
7. Darrow BG, Mans C, Drees R, et al. Pulmonary blastomycosis in a domestic ferret (*Mustela putorius furo*). *J Exot Pet Med*. 2014;23(2):158–164.
8. 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(1):47–61.
9. Dei-Cas E, Brun-Pascaud M, Bille-Hansen H, et al. Animal models of pneumocystosis. *FEMS Immunol Med Microbiol*. 1998;22(1):163–168.
10. de Lisle GW, Kawakami RP, Yates GF, Collins DM. Isolation of *Mycobacterium bovis* and other mycobacterial species from ferrets and stoats. *Vet Microbiol*. 2008;132(3–4):402–407.
11. Duan S, Boltz DA, Seiler P, et al. Oseltamivir-resistant pandemic H1N1/2009 Influenza virus possesses lower transmissibility and fitness in ferrets. *PLoS Pathogens* *PLoS Pathogens*. 2010;6(7):e1001022. <https://doi.org/10.1371/journal.ppat.1001022>.
12. DuVal-Hudelson KA. Coccidioidomycosis in three European ferrets. *J Zoo Wildl Med*. 1990;21(3):353–357.
13. Evers 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.
14. 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.
15. 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(11):2642–2647.
16. Fox JG. Mycotic diseases. In: Fox JG, Marini RP, editors. *Biology and Diseases of the Ferret*. 3rd ed. Ames, IA: John Wiley & Sons; 2014:573–585.
17. Friesen RHE, Koudstaal W, Koldijk MH, et al. New class of monoclonal antibodies against severe influenza: prophylactic and therapeutic efficacy in ferrets. *Plos One*. 2010;5(2):e9106. <https://doi.org/10.1371/journal.pone.0009106>.
18. 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.
19. 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(5):559–569.

20. 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.
21. 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(1–2):133–144.
22. Kiupel M, Desjardins DR, Lim A, et al. Mycoplasmosis in ferrets. *Emerg Infect Dis.* 2012;18(11):1763–1770.
23. Kiupel M, Perpiñán D. Viral diseases of ferrets. In: Fox JG, Marini RP, eds. *Biology and Diseases of the Ferrets*. 3rd ed. Iowa City, IA: Wiley Blackwell; 2014. 439–517.
24. Kugel D, Kochs G, Obojes K, et al. Intranasal administration of alpha interferon reduces seasonal influenza A virus morbidity in ferrets. *J Virol.* 2009;83(8):3843–3851.
25. Lenhard A. Blastomycosis in a ferret. *J Am Vet Med Assoc.* 1985;186(1):70–72.
26. 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.
27. 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.
28. 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.
29. 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.
30. Marini RP, Adkins JA, Fox JG. Proven or potential zoonotic diseases of ferrets. *J Am Vet Med Assoc.* 1989;195(7):990–994.
31. Martínez J, Martorell J, Abarca ML, et al. Pyogranulomatous pleuropneumonia and mediastinitis in ferrets (*Mustela putorius furo*) associated with *Pseudomonas luteola* infection. *J Comp Pathol.* 2012;146:4–10.
32. Martinez J, Ramis AJ, Reinacher M, et al. Detection of feline infectious peritonitis virus–like antigen in ferrets. *Vet Rec.* 2006;158(15):523.
33. 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.
34. Perpiñán D, Ramis A. Endogenous lipid pneumonia in a ferret (*Mustela putorius furo*). *J Exot Pet Med.* 2011;20(1):51–55.
35. Perpiñán D, Ramis A, Tomás A, et al. Outbreak of canine distemper in domestic ferrets (*Mustela putorius furo*). *Vet Rec.* 2008;163(8):246–250.
36. Peltola VT, Boyd KL, McAuley JL, et al. Bacterial sinusitis and otitis media following influenza virus infection in ferrets. *Infect Immun.* 2006;74(5):2562–2567.
37. Rarey KE, DeLacure MA, Sandridge SA, Small Jr PA. Effect of upper respiratory infection on hearing in the ferret model. *Am J Otolaryngol.* 1987;8(3):161–170.
38. Smee DF, Bailey KQ, Wong MH, et al. Treatment of influenza A (H1N1) virus infections in mice and ferrets with cyanovirin-N. *Antiviral Res.* 2008;80(3):266–271.
39. Smith H, Sweet C. Lessons for human influenza from pathogenicity studies with ferrets. *Rev Infect Dis.* 1988;10(1):56–75.
40. Smith W, Stuart-Harris CH. Influenza infection of man from the ferret. *Lancet.* 1936;228(5890):121–123.
41. 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 4/8/2018.
42. Squires S, Belyavin G. Free contact infection in ferret groups. *J Antimicrob Chemother.* 1975;1(suppl 4):35–42.
43. Swennes AG, Fox JG. Bacterial and mycoplasmal diseases. In: Fox JG, Marini RP, eds. *Biology and Diseases of the Ferret*. Ames, IA: John Wiley & Sons; 2014:519–552.
44. 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.
45. Taboada J. Systemic mycoses. In: Ettinger SJ, Feldman EC, eds. *Textbook of Veterinary Internal Medicine*. Philadelphia: WB Saunders; 2000:453–476.
46. Tumpey TM, Maines TR, Van Hoven N, et al. A two–amino acid change in the hemagglutinin of the 1918 influenza virus abolishes transmission. *Science.* 2007;315(5812):655–659.
47. Une Y, Wakimoto Y, Nakano Y, et al. Spontaneous Aleutian disease in a ferret. *J Vet Med Sci.* 2000;62(5):553–555.
48. 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(4):460–463.
49. van Riel D, Munster VJ, de Wit E, 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.