MCEIRS
GENERAL INFLUENZA TRAINING

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Influenza in Companion Animals

Minnesota Center of Excellence for Influenza Research and Surveillance
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INTRODUCTION

Influenza in Companion Animals

This module will familiarize you with influenza viruses in companion animals, such as horses, dogs and other animals. Transmission, prevention, and control will also be discussed.
LESSON 1: OVERVIEW OF INFLUENZA VIRUSES

In this lesson we will cover

- Influenza A Virus
- Wild Birds as a Reservoir for Influenza Viruses
- Transmission of Influenza Viruses
- Influenza in Domestic Species

INFLUENZA A VIRUS

Influenza viruses belong to the Orthomyxoviridae family of segmented negative-sense RNA viruses. The genus influenza A consists of a single species: influenza A virus, which is the cause of type A influenza. Influenza A viruses cause illness in a variety of mammals and are the most common cause of influenza in humans. Influenza B is also an important cause of influenza in humans, whereas influenza C is a relatively uncommon cause of human disease. Influenza D has recently been found in swine and cattle, but is not known at this time to cause disease in humans.

Influenza A virus subtypes (shown in Figure 1) are defined by two of the surface proteins that are part of the structure of the virus:

- HA - Hemagglutinin
- NA – Neuraminidase

There are 18 different HA antigens (H1 to H18) and 11 different NA antigens (N1 to N11) for influenza A. These antigens give rise to the subtype designation. Subtypes H1 to H16 and N1 to N9 are found in birds (mostly wild birds) and some of these subtypes have been found in mammals. H17N10 and H18N11 were discovered in bats in Guatemala in 2009 and in Peru in 2013, respectively. The NA genes in these influenza subtypes are highly divergent from other known influenza NAs and researchers propose that the attachment and activation of these viruses occur by a different mechanism than other influenza viruses. As of January 2017, these two subtypes appear to be unique to the bat population, but have been shown to infect and replicate in other mammalian cells (such as canine cell lines).
WILD BIRDS AS A RESERVOIR FOR INFLUENZA VIRUSES

Wild birds are considered to be the reservoir for influenza A viruses. All HA and NA subtypes of influenza A viruses All HA and NA subtypes of the influenza A virus (except for H17N10 and H18N11, which as of January 2017 had only been identified in bats) have been found in avian species (especially waterfowl and shore birds). Aquatic birds generally do not show any clinical signs of infection, but the viruses replicate in the intestinal tract of the birds and are shed into the environment.

TRANSMISSION OF INFLUENZA VIRUSES

Current information suggests that the influenza A virus can remain infective on environmental surfaces for 6 days or less. However, influenza viruses can survive in cool, moist environments or in water for days to months. Influenza viruses are generally species specific, but evolutionary changes in the viral genome can affect the virulence and species specificity of the virus. These changes occur through small mutations in the genome (genetic drift) or through major changes in the HA or NA (genetic shift). This can occur through reassortment of viruses from the same species or, in the case of interspecies transmission, through reassortment of viruses from different species.

In mammals, influenza viruses are transmitted primarily by large-droplet spread. Sneezing or coughing can disperse respiratory secretions (large droplets) contaminated with viral particles into the air, which are then inhaled by nearby people or animals. Large droplets can contaminate surfaces, leading to fomite transmission.

Influenza viruses also can be transmitted by airborne spread (inhalation of small viral particles suspended in the air).

INFLUENZA IN DOMESTIC SPECIES

Influenza A viruses cause clinical illness in a variety of species, including birds, humans, pigs, horses, dogs, ferrets, sea mammals, and other wild mammals. Influenza viruses cause economically important disease in agricultural species, including poultry (such as chickens and turkeys) and swine.

In poultry, avian influenza viruses are classified according to the disease severity in domestic chickens, with two recognized forms: Highly pathogenic avian influenza (HPAI) and low-pathogenic avian influenza (LPAI).

HPAI: Highly pathogenic avian influenza (previously known as fowl plague) is rare. It causes severe disease in domestic poultry and can cause mortality rates of up to 100% in affected flocks. Only certain subtypes of H5 (such as H5N1) and H7 (such as H7N7) have been associated with HPAI. (These subtypes also have been associated with LPAI.)
**LPAI:** Low-pathogenic avian influenza occurs more frequently than HPAI. It generally causes mild upper respiratory symptoms in domestic poultry and does not typically cause death.

**INFLUENZA IN DOMESTIC SPECIES**

In swine, influenza causes outbreaks of respiratory disease in herds. Disease caused by swine influenza virus (SIV) is characterized by rapid onset and spread through the herd with relatively low mortality (approximately 1% to 3%).

Swine also have receptors for and can become infected with avian and human influenza viruses. Swine have been theorized to be “mixing vessels” for reassortment of influenza viruses. Reassortment can result in more virulent influenza viruses or viruses that can infect different species. Reassortment is of concern because of its potential to develop pandemic influenza strains.

SIV has been associated with H1N1, H3N2, and H1N2 reassortant viruses.
LESSON 2: EQUINE INFLUENZA

In this lesson we will cover:

- History of Equine Influenza
- Clinical Signs
- Diagnosis
- Treatment
- Transmission

HISTORY OF EQUINE INFLUENZA

Equine influenza virus (EIV) is an important respiratory disease of horses and other equines, including mules and donkeys.

Although mortality is relatively low, EIV spreads rapidly, can result in extended recovery time, and can have significant negative impacts on equine populations, especially in the racing industry. There are two subtypes of EIV known as equine-1 (H7N7) and equine-2 (H3N8).

- EIV had been suspected as the cause of outbreaks of respiratory disease in horses for centuries, but the virus was first isolated from a horse in Czechoslovakia in 1956 during a widespread outbreak of respiratory disease.
- Equine-2 was first isolated in Miami and has caused several outbreaks in North America, Europe, Africa, and Asia.
- The equine-1 virus continued to cause outbreaks of disease in Europe.
- Equine-1 was last isolated in Egypt in 1989.
- A more severe H3N8 strain caused an outbreak of disease in China, but this strain does not appear to have become established in the equine population.
- An outbreak of H3N8 EIV occurred in race horses in Australia, a country that had previously been free of the virus.
- More recently, detection of antibody to the virus in horses suggests that the equine-1 virus may be continuing to circulate at low levels in Europe and Asia.
- Equine-2 continues to be the main circulating subtype.

CLINICAL SIGNS

The incubation period of EIV is 1 to 3 days.

Morbidity is generally high (up to 100%), while mortality is generally low (1% to 2%). Mortality rates are higher in donkeys, foals, and horses in poor health.
Horses ages 1 to 5 years, unvaccinated horses, and horses that are in frequent contact with other horses are at highest risk for infection.

Some horses will not show signs but will be subclinically infected and capable of shedding virus.

The disease can last 2 to 10 days, and shedding of the virus can last for 7 to 10 days after clinical signs have resolved. A carrier state for EIV has not been demonstrated in horses.

**DIAGNOSIS**

Diagnosis of equine influenza is based on history and clinical signs.

Differential diagnosis can include:

- Equine viral arteritis
- Equine herpes virus 1, 2, or 4
- Streptococcus equi
- Bacterial pneumonia
- Non-infectious lung disease
- Hendra virus

**Equine viral arteritis**
Can cause respiratory disease, vasculitis, and spontaneous abortions. Clinical signs include fever, anorexia, depression, copious nasal discharge, inflamed nasal passages, conjunctivitis, and swelling in limbs and ventral abdomen. Can be spread in semen.

**Equine herpes virus 1, 2, or 4**
Can cause respiratory disease, neurologic disease, and spontaneous abortions. Respiratory signs include coughing, nasal discharge, fever, enlarged lymph nodes, and anorexia. Highly contagious.

**Streptococcus equi**
Known as strangles. Clinical signs include fever, thick white/yellow mucopurulent nasal discharge, moist cough, difficulty swallowing, depression, anorexia, and swollen mandibular lymph nodes that abscess and drain. Prolonged shedding of the bacteria.

**Bacterial pneumonia**
May be secondary to viral infection. Clinical signs include fever, coughing, mucopurulent nasal discharge, and abnormal lung sounds.

**Non-infectious lung disease**
Can be inflammatory, allergic, or obstructive; usually not associated with fever. Clinical signs include coughing, exercise intolerance, and dyspnea.
**Hendra virus**

Seen in Australia; carried by fruit bats; spread by close contact; clinical signs include fever, depression, anorexia, difficulty breathing, and high mortality rate; is a zoonotic disease that can be fatal in humans.

Diagnosis of equine influenza can be accomplished by performing the following tests:

- Virus isolation (VI) - Detection of the virus in nasal or nasopharyngeal swabs
- Polymerase chain reaction (PCR) - Uses nasopharyngeal swabs; more specific and faster than VI
- Immunoassay - Stall-side kit tests for influenza A antigen
- Serology - Paired acute and convalescent sera showing a fourfold increase in antibody titer

**TREATMENT**

Treatment for EIV is supportive. Rest, fluids, and non-steroidal anti-inflammatory drugs are used. Antibiotics may be needed if secondary infections develop.

Horses should be rested 1 week for every day of fever. Coughing may persist, and recovery from EIV can be prolonged (up to 3 to 4 months or longer in some horses). Loss of training, racing, or showing time can economically harm the equine industry.

The use of antiviral drugs is not common, often due to cost. Effectiveness of these drugs in horses is unknown. Antiviral drugs are not approved for use in horses, so any use would be considered extralabel.

**TRANSMISSION**

EIV is primarily spread by the aerosol route. Coughing horses can disperse virus as far as 50 yards. The virus also can be spread in the environment through contaminated equipment, feed, clothing, vehicles, or other fomites.

Newly introduced horses are the most common source of influenza viruses in a herd. Outbreaks also are seen at race tracks, sale barns, or horse shows, where mixing of horses occurs.
LESSON 3: PREVENTION AND CONTROL OF EQUINE INFLUENZA

In this lesson we will cover:

- Biosecurity
- Outbreak Response
- Biosecurity Practices in Equine Facilities

BIOSECURITY

Biosecurity measures can be taken in equine facilities to prevent or reduce the spread of pathogens, including equine influenza viruses. The effectiveness of biosecurity practices will vary, depending on the facility. Disease outbreaks may be more difficult to control in high-traffic facilities such as race tracks and show arenas.

FACILITY

Designers of equine facilities should consider incorporating an isolation or quarantine area to prevent contact between sick and healthy horses. Equine facilities should be constructed of materials that are easy to clean and disinfect. Concrete, metal, and other solid surfaces are easier to clean than unsealed wood walls and dirt floors.

Adequate ventilation in the barn is important to reduce aerosol transmission of virus. Isolation facilities ideally should be in a separate building, but at a minimum, separate ventilation should be provided.

QUARANTINE PRACTICES

New horses should be of known health and vaccination status and quarantined for a minimum of 2 weeks before being added to the herd. This also applies to horses that have left the farm and been in contact with other horses at races, shows, breeding, etc.

Ideally, quarantined horses should be cared for by separate handlers, and separate equipment should be used. If this is not possible, quarantined animals should be cared for last on the daily schedule. Separate clothing and/or boots should be worn by caretakers.

Footbaths can be used outside of quarantine facilities. Any equipment or supplies that leave the isolation area should be cleaned and disinfected before being used in the main herd.
Horses that develop respiratory disease should remain in isolation for 3 weeks after recovery.

PERSONNEL

Persons working with horses should practice basic hygiene, such as washing hands well with soap and water between horses. The use of alcohol-based hand gels also is acceptable.

Personnel should use dedicated clothing and footwear in the barn, especially if they have horses of their own.

VEHICLES

On-farm vehicles should be cleaned and disinfected after use. Vehicles coming onto the farm should be free from contamination with manure if they have been at other equine facilities.

MANURE MANAGEMENT

Manure should be properly disposed of to prevent contamination of the facility or food and water supplies.

PEST MANAGEMENT

Rodents, birds, insects, and other pests can function as fomites. Control programs should be in place. Domestic animals (e.g., barn cats) should not move between quarantine and housing areas.

EQUIPMENT AND SUPPLIES

Equipment and supplies should be labeled specific to each horse and not shared if possible. Equipment that must be shared should be cleaned with detergent and disinfected between uses. Medications (multiple-dose, topical) should be labeled and used for a specific horse only.

VACCINATION

Although vaccination of at-risk horses is recommended, efficacy of vaccines for EIV is a debated topic. Despite vaccination programs, outbreaks still occur in both vaccinated and unvaccinated horse populations.

Vaccination for EIV may prevent or reduce clinical signs of disease, but it may not prevent shedding of virus. Thus, partially immune and apparently healthy horses can play a part in maintaining and spreading the virus. Vaccination also may interfere with
diagnostic tests for influenza. It may be difficult to differentiate between vaccination and infection, further complicating control efforts.

The presence of maternal antibody may interfere with the vaccination of foals but is essential for protection from disease. Adequate collostral levels can be ensured by vaccinating the mare prior to foaling.

The process of genetic drift also has caused changes in the virus and must be considered when selecting vaccine strains. In addition, at least two major lineages of the H3N8 virus (an American strain and a European strain) recently have been in circulation, and immunity is not cross-protective.

Inactivated or killed-virus vaccines are commonly used in vaccination programs and induce humoral immunity. In some instances, the potency of killed vaccines to stimulate antibody has been variable and immunity is short lived. Frequent boosters are needed.

Natural infection with EIV has been shown to induce longer immunity (up to 1 year), and induces both humoral and cellular immunity. Modified live vaccines (MLV) may mimic natural infection and provide longer protection. Clinical signs may be reduced, but shedding of virus, while reduced, will still occur. Concerns with using the modified live virus vaccine include potential reassortment events with circulating influenza viruses and the emergence of more highly pathogenic strains.

Recombinant vaccines also have been developed. Vectored vaccines incorporate genes from EIV into the genome of a nonpathogenic virus such as the canary pox virus. These vaccines also can induce both cellular and humoral immunity. Other recombinant methods of vaccine development are being explored.

VACCINATION SCHEDULES

Appropriate vaccination schedules are important for the prevention of EIV. In the United States, the American Association of Equine Practitioners recommends the following schedule:

**Adult Horses**

*Previously Vaccinated*

- At high risk (high risk includes performance, show or other horses in frequent contact with other horses): every 6 months
- Lower risk: once per year

*Non-Vaccinated or Unknown Vaccination History*

- Single dose of MLV or
- Series of 3 doses of inactivated vaccine with 4-6 weeks between the first and second vaccine and the third dose 3-6 months later or
- 2 doses of vectored vaccine 4-6 weeks apart then every 6 months

**Pregnant Mares**

*Previously Vaccinated*

- 4-6 weeks before foaling with inactivated or vectored vaccine

*Non-Vaccinated or Unknown Vaccination History*

- Series of 3 doses of inactivated vaccine with 4-6 weeks between the first and second dose, and the third dose 4-6 weeks before foaling or
- 2 doses of vectored vaccine 4-6 weeks apart, with the second dose no later than 4 weeks before foaling

**Foals**

*Previously Vaccinated* (In the case of foals, vaccination status refers to the mare.)

At 6 months:
- Single dose of MLV or
- Series of 3 doses of inactivated vaccine with 4-6 weeks between the first and second dose, and the third dose at 10-12 months of age

*Non-vaccinated or Unknown Vaccination History*

Use the same schedule as with a pregnant mare unless there is a high risk (such as an outbreak). If a foal is vaccinated before 6 months of age, the vaccine series should be repeated, according to the schedule at 6 months of age.

**OUTBREAK RESPONSE**

Since influenza is transmitted primarily by the aerosol route, sick horses should be isolated and housed in a separate air space from healthy horses. Access to the isolation areas should be restricted. If possible, separate caretakers should care for sick horses. Caretakers should wear dedicated or disposable clothing and footwear and wash hands well. The use of gloves may also reduce pathogen transmission. Equipment, medications, etc should not be shared between sick and healthy horses.

Administration of booster vaccines to healthy horses during an outbreak of influenza is recommended. The use of an MLV in unvaccinated horses would be appropriate since it can produce immunity within 5 days.
The barn should be quarantined for at least 3 weeks once all horses have recovered.

The facility should be cleaned and disinfected after an outbreak. Organic matter should be removed from stalls and common areas and cleaned well with detergent. Disinfectants should be sprayed on all solid surfaces and left to air dry. The cleaning and disinfection process may need to be repeated.

In facilities with wood surfaces and dirt floors, cleaning and disinfection is more difficult. As much organic matter as possible should be removed, stall walls scrubbed, and any equipment (such as water buckets) removed, cleaned, and disinfected.

Disinfectants effective against EIV include quaternary ammonium, phenol, and 10% bleach solutions. Disinfectants are not effective in the presence of organic debris; therefore, cleaning surfaces, materials, or equipment before disinfection is important. Label instructions should be followed for dilution and contact-time information.

Healthy horses should be watched for signs of illness through observation and rectal-temperature monitoring. Sick horses should be isolated as soon as possible.
LESSON 4: INTERSPECIES TRANSMISSION OF INFLUENZA VIRUSES INVOLVING HORSES

In this lesson we will cover:

- Avian Origin of Equine Influenza
- Avian-Like Influenza Virus in Horses
- Equine Influenza in Dogs

AVIAN ORIGIN OF EQUINE INFLUENZA

Avian influenza viruses have been shown to be transmitted to other species, including mammals. Both the equine-1 (H7N7) and equine-2 (H3N8) influenza viruses are thought to have been originally transmitted from birds to horses.

The discovery of equine influenza-like genes in a virus isolated from a wild duck also suggests interspecies transmission of influenza between horses and birds.

AVIAN-LIKE INFLUENZA VIRUS IN HORSES

The outbreak of equine influenza in China in 1989 was caused by an H3N8 virus that was genetically distinct from any other circulating equine influenza virus. Clinical signs were similar to those caused by the equine-2 virus and included fever, dry cough, and conjunctivitis. The mortality rate was higher than with other strains of equine influenza (up to 20%). Genetic analysis revealed that the virus was of recent avian origin.

Another outbreak of the same virus occurred in 1990, but the morbidity and mortality rates were lower. The virus continued to circulate for several more years in China but has not been detected outside of China.

EQUINE INFLUENZA IN DOGS

Transmission of an influenza virus from one species to another occurs but rarely results in sustained transmission within the new species. In 2004, an outbreak of respiratory disease occurred in racing greyhounds in Florida. The virus was very closely related to an H3N8 equine influenza virus.

Evidence suggests that the virus was transferred from horses to dogs in a single event and then gradually adapted to dogs, becoming endemic in racing greyhounds and pet dogs in some areas of the United States.
In 2002 and 2003, a different equine H3N8 virus was found in a kennel in the United Kingdom; however, sustained dog-to-dog transmission of the virus did not occur.

During the 2007 equine influenza outbreak in Australia, several dogs became infected with the equine virus, but it did not become established in dogs.
LESSON 5: CANINE INFLUENZA

In this lesson we will cover:

- Canine Influenza: an Emerging Disease
- Clinical Signs of CIV
- Diagnosis and Treatment of CIV
- Prevention and Control of CIV

CANINE INFLUENZA: AN EMERGING DISEASE

Canine influenza is a recently recognized and emerging disease in dogs. The H3N8 canine influenza virus (CIV) is thought to have originated from an equine influenza virus. Although first discovered in 2004, serologic evidence suggests that the virus may have been circulating in racing greyhounds as early as 1999.

The virus has been found in 42 states in the United States and as of 2016, is endemic in Colorado, Florida, New York, and Pennsylvania.

An H3N2 influenza virus was isolated from dogs in Korea in 2007. This virus seems to have originated from an entirely avian influenza virus. The virus was also found in China and caused an outbreak in dogs in Thailand in 2012. In March 2015, this virus was found in dogs in the Chicago area in the US. During 2015, the H3N2 canine influenza virus spread to 23 states in 5 months and, as of November 2016, has been found in a total of 30 states. Georgia and Illinois have seen the highest number of cases.

Dogs also can become infected with the HPAI H5N1 virus as well as the pH1N1 2009 virus, but neither of these viruses has become established in the canine species.

Because the viruses are novel in dogs, most dogs are susceptible to infection, and up to 100% of exposed dogs may become infected. Transmission occurs via:

- Direct contact
- The aerosol route through a dog’s coughing or sneezing
- Contact with nasal secretions spread by contaminated objects or human hands, clothing, etc

CIV has not been found in feces.

The viruses spread quickly, and up to 80% of exposed dogs may become ill. The mortality rate has generally been low for both the H3N8 and the H3N2 virus, ranging from 1% to 8%.

Virus shedding is heaviest during the incubation period before dogs are showing any signs of illness and can continue for 7 to 10 days after onset of clinical signs. Up to 20%
to 25% of dogs that become infected can shed and spread the virus without ever showing clinical signs.

There is no evidence that humans can become infected with canine-adapted strains of influenza.

**CLINICAL SIGNS OF CANINE INFLUENZA**

There are two forms of canine influenza: a mild form and a severe form. The incubation period for canine influenza is 2 to 4 days.

**Mild form:**
- Persistent moist or dry cough (duration 10 to 30 days)
- Low-grade fever
- Purulent nasal discharge
- Lethargy
- Anorexia

**Severe form:**
- High fever (104F to 106F)
- Increased respiratory rate
- Pneumonia
- Secondary bacterial infections
- Death from hemorrhagic pneumonia (seen in racing greyhounds)

Dogs infected with the H3N8 virus can shed virus for up to 10 days, while dogs infected with the H3N2 virus can shed virus for up to 24 days.

**DIAGNOSIS AND TREATMENT OF CIV**

The major differential diagnosis for canine influenza is infectious tracheobronchitis (kennel cough).

Kennel cough is a highly infectious respiratory disease in dogs characterized by a persistent dry cough and caused by a complex of respiratory pathogens including:

- *Bordetella bronchiseptica*
- Parainfluenza virus
- Canine adenovirus 2
- Canine distemper virus
- Other secondary bacterial pathogens

Risk factors for canine influenza are similar to those for kennel cough (i.e., contact with dogs at racetracks, shows, boarding facilities, kennels, etc).
Diagnosis is typically made by serology owing to the short period of virus shedding, which makes direct detection of CIV difficult. Acute (within the first 7 days) and convalescent (10 to 14 days later) serum samples are taken and a fourfold rise in antibody is diagnostic. Nasal or oropharyngeal swabs can be tested by real-time RT-PCR but are only reliable during the first 4 days of infection, when viral shedding is highest.

Treatment for canine influenza is supportive. Fluids and cough suppressants may be used. Antibiotics may be used in the case of secondary bacterial infections. Hospitalization for routine cases is not recommended because of the highly infectious nature of the disease. Dogs that require hospitalization should be isolated.

Antiviral drugs such as oseltamivir (Tamiflu) have been used off-label in dogs, but their use is controversial. Safety and efficacy of these drugs in dogs are not known, and most often dogs present too late in the course of the disease for the drugs to be effective. There also are concerns about development of viral resistance to the drugs and the public health implications that would follow.

**PREVENTION AND CONTROL OF CIV**

A vaccination for CIV H3N8 is available. It is a killed-virus vaccine and may reduce the signs and the severity of the disease but will not prevent infection or shedding of the virus. Two vaccines for CIV H3N2 have been conditionally approved. These vaccines are also killed-virus vaccines.

The vaccines are given in two initial doses, 2 to 4 weeks apart and boosted annually. The vaccines are strain-specific and do not appear to be cross-protective against the two CIV subtypes.

Vaccination is recommended for dogs in endemic areas or in high-risk situations, such as spending time in boarding or kennel facilities, dog daycare, or exposed to other dogs in dog parks, dog shows, etc.

Dogs recovering at home should be kept away from other dogs. Owners should wash hands and change clothes before handling other dogs. Kennels, food, water bowls, and other materials in contact with sick dogs should be cleaned and disinfected.

Dogs in a veterinary hospital or clinic should be isolated in an area with separate ventilation.

Canine influenza is not known to be transmissible from dogs to humans. However, veterinary staff can inadvertently transmit the virus from infected dogs to other susceptible dogs. Therefore, good infection control practices to prevent the spread of CIV should be followed.
LESSON 6: INFLUENZA IN OTHER COMPANION ANIMALS

In this lesson we will cover:

Influenza in:
- Ferrets
- Cats
- Pocket Pets
- Pet Pigs
- Pet Birds

INFLUENZA IN FERRETS

Ferrets are susceptible to influenza viruses of human, avian, and swine origin. Ferrets can become infected with both type A and type B human influenza viruses.

Ferrets have been used as experimental models for human influenza viruses. Receptors for the virus in the respiratory tract, clinical signs, and the course of the disease in ferrets are similar to those in humans.

Although it is more common for humans to transmit the virus to ferrets, the influenza virus can be transmitted in either direction between the two species.

Ferrets also have been experimentally infected with avian influenza viruses, including the HPAI H5N1 virus, and with swine, seal, and equine influenza viruses.

An influenza virus of swine origin caused an outbreak in a colony of ferrets in 2009. The outbreak was caused by a triple reassortant H1N1 virus and led to severe disease and death in some animals.

In addition to direct contact, influenza virus has been transmitted between ferrets via infectious droplets. Transmission also has occurred in utero in ferrets during experimental infection. Viral shedding occurs for 3 to 4 days following the onset of clinical signs.

Clinical signs of influenza in ferrets include:

- Fever
- Lethargy
- Anorexia
- Sneezing
- Coughing
- Nasal discharge
- Ocular discharge
- Occasionally photophobia, conjunctivitis, unilateral otitis
- Secondary bacterial infections, including pneumonia, can occur

Disease caused by human influenza B virus is usually mild in ferrets and mortality is generally low, except for neonatal and geriatric ferrets that are more susceptible to secondary infections.

Diagnosis is based on history of exposure and clinical signs. The main differential diagnosis is canine distemper virus. Influenza generally has a shorter and milder course than distemper in ferrets. Serology, virus isolation, or enzyme-linked immunosorbent assay (ELISA) tests for influenza A viruses can be used in diagnosis.

Treatment for influenza in ferrets is supportive. Fluids, parenteral nutrition, cough suppressants, and antihistamines have been used. The antiviral drug amantadine hydrochloride has been used in ferrets, but resistance develops quickly.

Antibiotics are used for secondary infections. The use of antipyretic medication such as NSAIDs is not recommended, as the fever seems to aid in more rapid clearance of the virus. Vaccinations are not available, and vaccines intended for other species are not recommended.

Prevention of influenza in ferrets involves reducing exposure to the virus. Ferrets with influenza should be isolated, and infection control measures (such as cleaning and disinfection of cages, food and water dishes, and other materials) should be implemented.

The term "reverse zoonosis" is sometimes used when referring to the transmission of influenza viruses from people to ferrets. Owners with respiratory infections should avoid contact with their ferrets.

The use of gloves and masks can reduce droplet transmission of the virus to ferrets. Veterinarians should be vaccinated for influenza and should take precautions, such as good hand hygiene, to reduce influenza transmission when working with ferrets.

**INFLUENZA IN CATS**

In December 2016, an outbreak of avian influenza H7N2 occurred in a cats in a New York City animal shelter. The outbreak spread to other shelters in the city, causing hundreds of potentially infected cats to be quarantined. Clinical signs of the disease include sneezing, coughing, and runny eyes and noses.

A veterinarian who had extensive contact with the shelter cats became infected, suffering mild disease. Over 350 at-risk individuals were tested, but as of the end of January 2017, no further human cases were detected.
Cats have been shown to be susceptible to infection with the HPAI H5N1 avian influenza virus and the human pH1N1 2009 influenza virus. Prior to the emergence of these subtypes, clinical manifestations of influenza virus infection had not been reported in cats.

A serosurvey of both domestic and feral cats in Italy in 2007 showed no circulating antibodies to influenza A viruses. In one report, experimental infection with human and avian influenza viruses did not result in disease.

**INFLUENZA IN POCKET PETS**

Mice have been used as experimental models for avian H5N1 influenza virus infections, although they have not been an efficient model for human influenza studies. Rats appear to be resistant to infection with influenza viruses.

Antibodies to several influenza subtypes have been reported in snakes, toads, and frogs.

Guinea pigs, rats, mice, and rabbits are not known to become naturally infected with influenza viruses. Guinea pigs have been experimentally infected with human (H3N2) viruses. The guinea pigs were highly susceptible to the virus and transmitted the virus to uninfected guinea pigs.

**INFLUENZA IN PET PIGS**

Pet pigs, including pot-bellied pigs, are swine and therefore are susceptible to swine influenza viruses, human influenza viruses, and avian influenza viruses.

Clinical signs of influenza in pigs include coughing, fever, anorexia, weight loss, lethargy, sneezing, ocular or nasal discharge, labored breathing, conjunctivitis, and sometimes spontaneous abortion. The disease is usually mild and of fairly short duration, but secondary infections and pneumonia can occur. Diagnosis can be made using virus isolation, PCR, or serology. Treatment is supportive with use of antibiotics for secondary infections if necessary.

Efforts should be made to reduce contact between pet pigs and avian reservoirs, especially ducks and other water birds. People with respiratory disease should not be in contact with pigs. Vaccination for swine influenza is available and can be used in pet pigs, but these vaccines will not prevent infection with avian or human strains.

**INFLUENZA IN PET BIRDS**

Pet birds are susceptible to avian influenza viruses. Although not seen in pet birds, commercial turkeys have been shown to be infected with swine and human influenza viruses.
Avian influenza is an important pathogen in chickens, and the disease presents in pet chickens as LPAI or HPAI.

Signs of HPAI in chickens include cyanotic combs and wattles, edema of the face and limbs, subcutaneous hemorrhages, and difficulty breathing. Sudden death with no preceding signs also occurs.

Signs of LPAI include decreased egg production or mild respiratory signs, including coughing, sneezing, and ocular discharge. Birds infected with LPAI viruses may not show any clinical signs.

Ducks do not typically display any signs of infection with most influenza strains but can become infected and shed virus. Since 2002, ducks infected with the HPAI H5N1 virus have demonstrated clinical signs, including death.

Psittacine (parrots and related species) and passeriform (perching) birds also can become infected with avian influenza viruses. H3 or H4 subtypes have been isolated from pet birds without clinical signs imported to the United States. An H5N2 virus was isolated from a clinically ill parrot that subsequently recovered.

Biosecurity measures are important for preventing influenza in pet birds. The source of the birds should be known. Legally imported birds are usually quarantined and tested for diseases such as influenza. However, imported birds often are smuggled into the United States and other countries; such birds may not undergo appropriate screening.

Newly acquired birds should be kept separate from other birds for at least 30 days. Separate materials and supplies should be used for quarantined birds, and owners should wash hands after handling new birds.

Since avian influenza viruses can be spread through fecal contamination, cleaning and disinfection protocols are important to decrease the spread of disease.

Owners should change shoes and clothing after being around other birds at poultry markets, fairs, or other farms before coming into contact with their own birds.

In the United States, the US Department of Agriculture has a campaign titled, “Biosecurity for Birds.” Informational brochures, posters, and other educational materials are available and are targeted to owners of backyard poultry and pet birds. Information can be found at: http://www.aphis.usda.gov/animal_health/birdbiosecurity/
LESSON 7: INFLUENZA IN OTHER COMPANION ANIMALS

In this lesson we will cover:

The HPAI H5N1 Virus in:

- Cats
- Pet Birds
- Ferrets
- Other Animals

THE HPAI H5N1 VIRUS IN CATS
While all influenza A viruses are thought to have originated from avian reservoirs, the transmission of avian influenza viruses to other species has been sporadic. The HPAI H5N1 virus has demonstrated the ability to infect an unusually broad range of species.

While sustained transmission within these species generally has not occurred, the virus can cause severe clinical signs and high mortality in many species. Neurologic and other systemic lesions are seen, along with respiratory involvement. Some animals can become subclinically infected as well. Naturally occurring and experimentally induced infections may differ in clinical presentation.

HPAI H5N1 avian influenza has caused disease and death in large captive felines as well as in domestic cats.

In naturally occurring cases, clinical signs include fever, depression, anorexia, difficulty breathing, and protrusion of the third eyelid. Neurologic manifestations can include ataxia and convulsions. Infections can also be subclinical in cats.

Antibodies with or without clinical disease have been demonstrated in domestic cats in many areas where outbreaks of HPAI H5N1 have occurred in domestic or wild birds, although the risk of infection appears to be low.

H5N1 influenza virus in cats likely results primarily from the consumption of infected bird carcasses. Respiratory transmission can also occur.

The virus can be shed from the respiratory tract, or in feces and urine. Cat-to-cat transmission has been demonstrated experimentally.

Diagnosis of HPAI H5N1 can be made via PCR using pharyngeal swabs, and treatment is supportive.

Cats should be isolated, and contact with people should be severely limited. The use of personal protective equipment when handling the cat, and sedation for sample
collection, is highly recommended. Strict infection-control and disinfection protocols should be followed.

The use of antiviral medications such as oseltamivir (Tamiflu) was not effective in tigers during an outbreak in Thailand, but its efficacy in domestic cats is unknown.

The potential role of domestic cats in the transmission and spread of HPAI H5N1 is unknown, but preventive measures are recommended in high-risk areas.

Cats should be kept indoors and away from domestic or wild birds.

Cats should not be fed uncooked poultry meat.

There is currently no vaccination available, although research is ongoing.

**H5N1 IN DOGS**

In Thailand, HPAI H5N1 was the reported cause of death in a domestic dog that had consumed an infected duck. Antibodies to the virus have also been demonstrated in dogs.

**H5N1 IN PET BIRDS**

HPAI H5N1 virus in chickens can cause up to 100% mortality. Domestic duck and geese infected with HPAI H5N1 can show neurologic signs and high mortality. Pigeons have appeared to be resistant to natural infection. HPAI H5N1 was reported in a parrot that subsequently died.

**H5N1 IN FERRETS**

Experimental infection of ferrets with HPAI H5N1 resulted in mild or severe disease. Ferrets can shed virus from the intestinal tract as well as the respiratory tract.

**H5N1 IN OTHER ANIMALS**

Naturally occurring cases have not been reported in rabbits, and experimental infection was not successful. HPAI H5N1 has not been reported in horses. Antibodies to H5N1 virus have been found in pigs, but natural infections have not resulted in severe clinical disease. Antibodies also have been found in rats and mice living around affected poultry markets, but no virus was isolated.
LESSON 8: pH1N1 2009 INFLUENZA IN COMPANION ANIMALS

In this lesson we will cover:

- pH1N1 2009 in cats, ferrets and dogs

THE PH1N1 2009 VIRUS IN CATS, FERRETS AND DOGS

Pandemic H1N1 2009 (pH1N1 2009) influenza virus was first diagnosed in humans in Mexico in April 2009 and was declared a pandemic by the World Health Organization in June 2009.

The pH1N1 2009 influenza virus also has infected animals, with infections generally occurring following exposure to infected humans. Companion animals, including ferrets, dogs, and cats, have been diagnosed after family members had experienced influenza symptoms.

Besides companion animals, pH1N1 2009 influenza has been diagnosed in pigs, turkeys, and cheetahs.

Signs of pH1N1 2009 influenza in companion animals involve the respiratory system. Sneezing, nasal discharge, and cough, as well as fever and lethargy, were reported. Some animals with more severe illness died. A specific pH1N1 2009 diagnostic test has been developed for dogs and cats.

CATS: 10 cats were diagnosed with pH1N1 2009 influenza from November 2009 to January 2010; 3 of the cats died.

FERRETS: Like other human influenza A viruses, the pH1N1 2009 influenza virus can infect ferrets. In October and November 2009, there were 8 reported cases in three households; 1 ferret died.

DOGS: The pH1N1 2009 virus was diagnosed in 2 dogs in China and a dog in the United States. None of the dogs died.

Although not reported, pet birds or pet pigs are likely susceptible to infection, since pH1N1 2009 influenza has been diagnosed in commercial turkeys and pigs.
LESSON 9: INFECTION CONTROL FOR INFLUENZA VIRUSES IN VETERINARY CLINICS AND HOSPITALS

In this lesson we will cover:

- Infection Control Practices
- Facilities
- Personnel Hygiene and Personal Protective Equipment (PPE)
- Cleaning and Disinfection

VETERINARY CLINICS AND HOSPITALS

INFECTION CONTROL PRACTICES

Infection control practices in veterinary clinics and hospitals are important to prevent the spread of infectious agents, including influenza viruses. Veterinary clinics and hospitals should develop individualized infection control programs based on the types of animals seen and the risks present in the geographic area.

Influenza-like illness in pet pigs, ferrets, cats, or birds could be caused by an influenza strain to which humans are susceptible (such as pH1N1 2009 or certain avian strains).

In addition, influenza viruses in these animals could potentially be transmitted to other susceptible animals in the clinic.

In the United States, the National Association of State Public Health Veterinarians has published a “Compendium of Veterinary Standard Precautions for Zoonotic Disease Prevention in Veterinary Personnel,” which describes infection control practices for veterinary clinics and hospitals. The Canadian Committee on Antibiotic Resistance has published “Infection Prevention and Control Best Practices for Small Animal Veterinary Clinics.”

FACILITIES

Veterinary clinics and hospitals should have an isolation area to house and treat animals that have infectious diseases such as influenza. This area should be separate from the main housing, treatment, and surgical areas and should have separate ventilation. Ideally, isolation facilities for birds should be separated from those of mammals. Access to the isolation area should be limited.

Equipment needed for the care and treatment of the animal in the isolation room should be kept in the room, including dedicated cleaning supplies. Any equipment taken out of the room should be disassembled and thoroughly cleaned and disinfected.
One of the most important infection control methods is proper hand washing. If soap and water are unavailable, an alcohol-based hand cleaner can be used.

Staff should wash their hands

- Before and after handling each animal
- After coming into contact with animal saliva, urine, feces, blood, or other body secretions
- After cleaning cages
- Before eating meals, taking breaks, smoking, or leaving the facility
- Before and after using the restroom
- After removing gloves

PERSONNEL HYGIENE AND PERSONAL PROTECTIVE EQUIPMENT (PPE)

Staff should wear a barrier gown over clothes and wear gloves when handling sick animals, cleaning cages, or coming into contact with body secretions. The gown and gloves should be discarded before working with other animals. Footwear worn in isolation areas should be easy to clean and disinfect, or disposable booties should be used.

Ideally, dedicated clothing should be worn in the clinic or hospital. Staff should bring a change of clothes to wear home at the end of the day.

Staff should not allow animals to "kiss" them or lick their faces and should not eat, drink, smoke, apply makeup, etc in animal care areas.

To prevent spread of influenza from humans to companion animals, veterinary workers should be vaccinated annually against seasonal influenza (and against any pandemic strains if a pandemic occurs) and should stay home from work if they have confirmed or suspected influenza illness.

Use of additional PPE such as goggles, face shields, head coverings, and respiratory protection should be considered in the case of potential exposure to HPAI, especially HPAI H5N1. Additional PPE, including respiratory protection, should also be considered when working with animals potentially infected with other zoonotic influenza strains, such as pH1N1 2009.

N-95 or other types of respirators should be used to prevent aerosol or droplet exposure. N-95 respirators are commercially available but need to be fitted by a specialist in order for the respirator to be effective.

CLEANING AND DISINFECTION
Cages, kennels, and equipment should be cleaned of organic matter before disinfecting all surfaces. Food and water bowls and toys should be thoroughly cleaned and disinfected before reuse.

Disinfectants commonly used in veterinary clinics, such as dilute bleach, quaternary ammonium compounds, and phenols, are effective against influenza viruses. Disinfectants should be used according to the label directions.
GLOSSARY

**Anorexia** - Lack or loss of appetite for food.

**Antibody** - A type of glycoprotein molecule produced during a humoral (adaptive) immune response that binds antigens, often with a high degree of specificity and strength.

**Antigenic Drift** - One of two ways that influenza viruses can change (the other is antigenic shift, see above). Antigenic drift refers to small, gradual changes that occur through point mutations in the two genes that contain the genetic material to produce the main surface proteins, hemagglutinin and neuraminidase. These point mutations occur unpredictably and result in minor changes to these surface proteins. Antigenic drift produces new virus strains that may not be recognized by antibodies to earlier influenza strains. This process works as follows: a person infected with a particular influenza virus strain develops antibodies against that strain. As newer virus strains appear, the antibodies against the older strains might not recognize the "newer" virus, and infection with a new strain can occur. This is one of the main reasons why people can become infected with influenza viruses more than one time and why global surveillance is critical in order to monitor the evolution of human influenza virus strains for selection of which strains should be included in the annual production of influenza vaccine. In most years, one or two of the three virus strains in the influenza vaccine are updated to keep up with the changes in the circulating influenza viruses. For this reason, people who want to be immunized against influenza need to be vaccinated every year.

**Antigenic Shift** - Antigenic shift is one of two ways that influenza viruses can change (the other is antigenic drift, see above). Antigenic shift refers to an abrupt, major change to produce a novel influenza A virus subtype in humans (i.e., one that has not circulated previously among people). Antigenic shift can occur either through direct animal (poultry)-to-human transmission or through mixing of human influenza A and animal influenza A virus genes to create a new human influenza A subtype virus through a process called genetic reassortment. Antigenic shift results in a new human influenza A subtype.

**Antigens** - A substance that elicits a specific (as opposed to nonspecific) immunological response. Foreign antigens typically stimulate a response from the body's adaptive immune system resulting in the production of antibodies and effector T-cells; antigens that produce an immune response can also be called “immunogens”

**Ataxia** - Failure of muscular coordination; irregularity of muscular action.

**Biosecurity** - Security from transmission of infectious diseases, parasites and pests. Also refers to the prevention of exposure to disease agents through management practices.

**Cellular (cell-mediated) immunity** - A type of adaptive immune response
mediated by T cells of the immune system.

**Colostral (colostrum)** - The thick yellow secretion present in the mammary glands, very rich in maternal antibodies and essential in providing passive immunity to the newborn.

**Conjunctivitis** - Inflammation of the conjunctiva, which is the transparent lubricating membrane that covers the eyeballs and under surface of the eyelids.

**Endemic** - A condition or disease that is present in a predictable, continuous pattern in a population at all times; applies to a condition or disease that is clustered in space but not in time.

**Epidemic** - A disease occurring suddenly in humans in a community, region or country in numbers clearly in excess of normal.

**Epizootic** - A disease occurring suddenly in animals in a community, region or country in numbers clearly in excess of normal.

**Fomite** - Inanimate objects or materials on which disease producing agents may be conveyed.

**Genetic Drift** - See Antigenic Drift

**Genetic Reassortment** - The exchange of gene segments between viruses that have a segmented genome.

**Genome** - The complete genetic information (either DNA or, in some viruses, RNA) of an

**Hemagglutinin (HA)** - An important surface structure protein of the influenza virus that is an essential gene for the spread of the virus throughout the respiratory tract. This protein enables the virus to attach itself to a cell in the respiratory system and penetrate it. It is used to name influenza A subtypes and is referred to as the "H" in the influenza virus subtype (e.g., H5N1).

**Host** - An organism on or in which a parasite lives.

**HPAI (Highly Pathogenic form of Avian Influenza)** - Often fatal in chickens and turkeys. HPAI spreads more rapidly than LPAI and has a high mortality rate in domestic birds.

**Humoral immunity** - A type of adaptive immune response mediated by the production of antibodies.

**Incubation period** - The period between time of infection and the appearance of symptoms of the disease; during this time the infectious agent is multiplying within the host.

**Isolation** - The segregation of patients with a communicable disease.

**Killed vaccine** - Inactivated vaccine; one with organisms that have been killed.
LPAI (Low Pathogenic form of Avian Influenza) - Naturally occurs in wild birds and can spread to domestic birds. In wild birds, LPAI strains generally do not cause signs of infection. In domestic birds, the illness is not severe and mortality rates are low. LPAI H5 and H7 strains have the potential to mutate into HPAI and are therefore closely monitored.

**Modified live vaccine** - A vaccine prepared from live microorganisms that have lost their virulence (i.e., have been attenuated) but have retained their ability to induce protective immunity.

**Morbidity** - Disease; morbidity rate is the incidence or prevalence of disease in a specific population during a specified interval of time or a specific point in time.

**Mortality** - Death; mortality rate is a measure of the number of deaths in a population during a specified interval of time.

**Mutation** - Any alteration in a gene from its natural state. Specific mutations and evolution in influenza viruses cannot be predicted, making it difficult if not impossible to know if or when a virus such as H5N1 might acquire the properties needed to spread easily among humans.

**Necropsy** - Examination of a body after death.

**Neuraminidase (NA)** - An important surface structure protein of the influenza virus that is an essential enzyme for the spread of the virus throughout the respiratory tract. This protein enables the virus to escape the host cell and infect new cells. It is used to name influenza A subtypes and is referred to as the "N" in the influenza virus subtype (e.g., H5N1).

**Outbreak** - Presence of disease in numbers in excess of normal in a specific geographic area or population.

**Pandemic** - A worldwide outbreak of a disease in humans in numbers clearly in excess of normal. A global influenza pandemic may occur if three conditions are met:
- A new subtype of influenza A virus emerges for which there is little or no immunity in the human population.
- The virus can spread easily from person to person in a sustained manner.

**Panzootic** - A worldwide outbreak of a disease in animals in numbers clearly in excess of normal.

**Pathogenic** - Causing disease or capable of doing so.

**Personal Protective Equipment** - Any devices or clothing worn by the worker to protect against hazards in the environment. Examples are respirators, gloves, and goggles.

**Polymerase chain reaction (PCR)** - The amplification of a specific DNA sequence.

**Prevalence** - The proportion of individuals (humans or animals) in a population having a disease or specific characteristic (such as a positive antibody test to a particular pathogen).

**Quarantine** - A period of time during which an animal that might have a
disease is kept away from other animals so that the disease cannot spread.

**Recombinant vaccine** - A vaccine created by recombinant DNA technology.

**Reservoir** - A person or animal that serves as a host to a pathogenic agent, generally without visible symptoms of the disease or injury.

**Seasonal Flu** ("Common Flu", "Winter Flu") - Influenza caused by one of the common influenza subtypes known to be circulating in the human population; seasonal influenza peaks in the winter months in the Northern and Southern Hemispheres and tends to be year-round in tropical regions.

**Serology** - The study of blood serum for evidence of infection (such as testing serum for antibodies to a specific pathogen or antigen).

**Serosurvey** - A survey of the serology status of serum from a group of animals or people to provide an estimate of the prevalence of a specific disease in a defined population.

**Strain** - Influenza virus subtypes are further characterized into strains. New strains of influenza viruses replace older strains through the process of antigenic drift (i.e., small mutations in the genetic material of the virus).

**Subclinical** - Without clinical manifestations; said of the early stages or very mild form of a disease.

**Swine Flu** - A respiratory disease in pigs caused by influenza A virus. Outbreaks in swine herds are common; the illness is relatively mild, and most animals recover. Domestic birds can be a source of influenza A in swine, and transmission from humans to swine and from swine to humans has occurred.

**Vectored vaccine** - The use of viruses as vectors to carry select genes from a pathogen for immunization.

**Virulence** - A pathogen's ability to invade host tissues and the severity of disease produced.

**Virulent** - Highly lethal; causing severe illness or death.

**Virus** - Any of various simple submicroscopic parasites of plants, animals, and bacteria that often cause disease and that consist essentially of a core of RNA or DNA surrounded by a protein coat. Unable to replicate without a host cell, viruses are typically not considered living organisms.

**Viral shedding** - Excretion of live viruses from the body of an infected host.
**Virus Isolation** - The gold standard test used to diagnose AI virus infections. The virus is isolated in embryos inside chicken eggs. A series of tests follow to specifically identify H and N subtypes of the AI virus.

**Zoonoses** - Diseases that transfer from animals to humans.
RESOURCES


[Web page: https://www.avma.org/KB/Resources/Reference/Pages/Canine-Influenza-Backgrounder.aspx]

[Web page: https://www.avma.org/KB/Resources/FAQs/Pages/Control-of-Canine-Influenza-in-Dogs.aspx]

[Web page: https://www.avma.org/News/JAVMANews/Pages/091215k.aspx]


CDC H7N2 Questions and Answers. https://www.cdc.gov/flu/fluincats/h7n2-cat-questions-answers.htm


Cornell University, College of Veterinary Medicine. Canine Influenza H3N2 Updates. https://ahdc.vet.cornell.edu/news/civchicago.cfm


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All glossary definitions are found at one or more of the following sources (or are adapted from those sources):

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