High Pathogenic Avian Influenza A - HPAI

Basic agent information

Section I - Infectious Agent

Risk Group:
- RG3

Synonym or Cross reference:
- Avian influenza, bird flu, Orthomyxovirus, H5N1, H1N1

Characteristics:
- Members of the Orthomyxoviridae family of segmented, negative sense, single-stranded RNA viruses
- Type A influenza viruses are subdivided on the basis of the antigenic nature of their membrane-bound surface glycoproteins: hemagglutinin (HA) and neuraminidase (NA). To date 16 HA and 9 NA subtypes have been detected in wild birds and poultry. Antigenic alterations occur frequently in influenza HA and NA antigenic sites and are the mechanisms for the virus adaptation to the host and survival
- Small alterations are referred to as antigenic drifts, whereas larger alterations are referred to as antigenic shifts. Influenza pandemics may occur as a result of antigenic shifts if the mutation of the virus leads to efficient human-to-human transmission

Section II - Dissemination

Reservoir:
- Wild aquatic birds are the main reservoir of Influenza A viruses. Virus transmission has been reported from wild waterfowl to poultry, sea mammals, pigs, horses and humans.
- Viruses are also transmitted between pigs and humans, and from poultry to humans
- Equine Influenza viruses have recently been transmitted to dogs
- Mice do not shed Influenza viruses in nasal secretion, and thus Influenza viruses are not transmitted between mice

Zoonosis:
- Yes, direct or indirect contact with infected animals

Vectors:
- None

Research use considerations

Section III - Laboratory Hazards

Laboratory-Acquired Infections:
- None reported to date
Sources/Specimens:
- Respiratory tissues, human secretions and infected animals. In addition, the virus may be present in the intestines and cloacae of infected avian species. Influenza A may be disseminated in multiple organs in infected species.

Primary hazards:
- Inhalation of virus from aerosol generated when aspirating, dispensing or mixing virus-infected samples (tissues, feces, secretions) from infected animals. Laboratory infection can also occur from direct inoculation of mucous membranes via virus-contaminated gloves following the handling of tissues feces and/or secretions from infected animals

Special Hazards:
- Genetic manipulation of virus has an unknown potential for altering host range, pathogenicity and/or for introducing transmittable viruses with novel antigenic composition into humans

Section IV- Stability and Viability
Susceptibility to Disinfectants:
- Susceptible to disinfectants, including sodium hypochlorite (freshly made 1:10 dilution of bleach), Clidox, 60 to 95% ethanol, 2% alkaline glutaraldehyde, 5 to 8% formalin and 5% phenol

Physical Inactivation:
- Susceptible to moist heat at 121°C for 20 minutes or dry heat at 170°C for 1 hour, 160°C for 2 hours or 121°C for at least 16 hours

Survival Outside Host:
- Infectious Influenza virus has been maintained on fomites for up to 2 weeks and in water from 3 months to 1 year

Section V- Recommended Precautions
Containment Requirements:
- Biosafety Level 3 containment equipment, facility and practices, for all activities involving the handling of potentially infectious clinical materials and cultures

Protective Clothing:
- Impervious gloves when direct contact with infectious materials is unavoidable, gown (with tight wrists and tie in back), PAPR use in BSL3/ABSL3

Other Precautions:
- Animal Biosafety Level 3 facilities and practices

Health and Medical

Section VI- Health Hazard
Pathogenicity:
- The World Organization for Animal Health (OIE) established criteria for designating avian influenza viruses as being highly pathogenic. These criteria include that the isolate:
  - 1) is lethal in 75% of 4 to 8 week old susceptible chickens infected intravenously
  - 2) exhibits trypsin-independent growth in cell culture
- 3) encodes an HA harboring a multibasic cleavage site
- H5N1 infection results in systemic viral replication, a substantial induction of cytokine production (cytokine storm) in the respiratory system, and severe pneumonia
- Ferrets and mouse models of H5N1 infections revealed a fatal disease outcome marked by pulmonary pathology and virus dissemination to other organs.
- Although avian Influenza A viruses usually do not infect humans, rare cases of human infections with avian influenza viruses have been reported. Most human infections with avian influenza A viruses have occurred following contact with infected poultry. Symptoms of avian influenza in humans have ranged from typical human flu-like symptoms (fever, cough, sore throat and muscle aches) to eye infections, pneumonia, severe respiratory diseases (such as acute respiratory distress) and other severe and life-threatening complications.

**Epidemiology:**
- High pathogenicity avian Influenza A (H5N1) virus infection occurs mainly in birds and is highly contagious among birds, causing high mortality among domestic poultry. Worldwide outbreaks are reported among poultry and wild birds.
- H5N1 infections to humans are rare and most cases have been associated with direct poultry contact during poultry outbreaks. While the H5N1 virus does not now infect people easily, infections in humans is very serious when it occurs (up to 50% fatality).
- Rare cases of limited human-to-human spread of H5N1 virus may have occurred but there is no evidence of sustained human-to-human transmission.

**Host Range:**
- Avian species, humans, ferrets, guinea pigs, mouse, swine, wild animals.

**Infectious Dose:**
- Mouse Infectious Dose 50 (mID50) for A/Viet Nam/1203/2004 (isolate from lethal human infection) = 1.8 50% egg infectious dose (eID50).
- The mID50 for some H5N1 isolates is remarkably low (0.6 to 11 plaque forming units).
- The Human Infectious Dose 50 (hID50) via aerosol is 0.6 to 3 Tissue Culture Infectious Dose 50 (tcID50) and by intranasal droplet infection is 127-320 tcID50.

**Natural Mode of Transmission:**
- Transmission of Influenza in humans can occur via respiratory infection by aerosols and droplets (from coughing and sneezing) or from contact transmission from contaminated surfaces. Closed environment and crowds favor transmission. Transmission of Influenza virus from donors who are shedding large amount of virus can be infective for 2 to 8 hours via stainless steel surfaces and for a few minutes via paper tissues.

**Incubation Period:**
- Usually 1-3 days.

**Communicability:**
- H5N1 does not transmit readily between humans. Rare cases of limited human-to-human spread of H5N1 virus may have occurred but there is no evidence of sustained human-to-human transmission.

Section VII- Medical
Surveillance:
- Any personnel currently working or worked in the past 5 days with avian Influenza viruses experiencing any symptoms of influenza-like illness will report to the Principal Investigator. Signs/symptoms include fever, runny nose, headache, muscle ache, viral isolation from nasal specimen.
- If necessary, nasopharyngeal samples would be collected and tested for Influenza A virus by standard RT-PCR screening as outlined by CDC guidelines

Immunization:
- Prior to staring work, all individuals working with influenza viruses or working with animals infected with influenza viruses are very strongly encouraged to receive immunization with the seasonal influenza virus vaccine
- The seasonal influenza vaccine affords protection against H1N1, H3N2 and Influenza B viruses. It is not known how much cross-protection against H5N1 virus will be afforded by seasonal vaccines. There are no currently licensed vaccines for H5N1 influenza viruses

Drug Susceptibility:
- Susceptible to neuraminidase inhibitors: Oseltamivir and Zanamavir

Prophylaxis:
- 5 days regimen of Oseltamivir (Tamiflu) – doses of 75 mg, twice a day, orally.
- Oseltamivir-resistant H5N1 isolates have been recovered from human patients; effective prophylaxis may require the combined use of antivirals

Clinical Monitoring, including fever watch:
- All laboratory personnel working directly with Influenza viruses and the facility staff working in the areas where the H5N1 virus research is being conducted are required to report any flu-like symptoms to the Principal Investigator, the Office of Biological Safety and UCOM to seek treatment. If visiting the Emergency room, the patient should wear a face-mask and declare to the nursing staff/physicians that they conduct research with High Pathogenic H5N1 Avian Influenza and ask to be directly placed in a “severe respiratory illness isolation room”.
- Respiratory virus panel test on Nasopharyngeal samples
- If test is positive for H5N1 virus, patient will remain in quarantine at home until recovery

Treatment:
- Antiviral drugs: Oseltamivir, Amantadine, Rimantadine or Zanamavir
- 5 days regimen of Oseltamivir (Tamiflu) – doses of 75 mg, twice a day, orally.
- Antibiotic treatment (in combination with antiviral treatment) may also be used to prevent or treat secondary bacterial pneumonia
- Quarantine and isolation at home until recovery

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