1918 Influenza: Influenza A, H1N1

Basic agent information

Section I- Infectious Agent

Risk Group:
- RG3

Synonym or Cross reference:
- Spanish Flu
- 1918 Flu
- El Grippe

Characteristics:
- SELECT AGENT
- Much of what is known about the 1918 Influenza is from anecdotal or concurrent medical observations made during the epidemic. Animal studies show that the pathogenicity and virulence of 1918 H1N1 virus is similar to highly pathogenic influenza virus viruses.
- 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 f the virus leads to efficient human-to-human transmission
- 1918 HA is antigenically similar to 2009 H1N1, and the 2009 H1N1 vaccine or antigenically similar seasonal vaccines afford cross-protection against the 1918 H1N1 virus.

Section II- Dissemination

Reservoir:
- There are currently no known reservoirs for 1918 influenza, but H1N1 influenza strains are known to circulate in pigs and bird species.

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. 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:
- This strain of influenza was responsible for the “Spanish flu” pandemic from 1918-1919, which killed up to 50 million people worldwide, many more than the subsequent pandemics of the 20th century.
- Most influenza epidemics/pandemics have a higher fatality rate for older adults, very young children, or those who are otherwise immunocompromised. This pandemic was different in that it was highly virulent for young, otherwise health adults between the ages of 20 – 40 years.
- The biological properties that confer virulence to this strain remain poorly understood.

Epidemiology:
- Regarding the 1918 strain: Anectodal and epidemiological evidence during the pandemic, such as the example above.
- For other H1N1 strains: The 2009 H1N1 pandemic resulted in rates of infection ranging from 11% (New Zealand) to 21% (Pittsburgh, USA) of the population, depending on location. As of March 13, 2010, the U.S. Centers for Disease Control and Prevention estimate that in the United States 60 million people were infected with 2009 H1N1, resulting in 270,000 hospitalizations and 12,270 deaths. Overall mortality rate was less than 0.5%, and morbidity and mortality were predominant in young adults and less common for adults over 60 years old.

Host Range:
- Humans
- Other mammalian species pigs, ferrets and mice have been shown to be susceptible.

Infectious Dose:
- Mouse LD50= 2.7 x10^{10} PFU; Ferret LD50 < 10^{6} PFU
- Unknown for humans

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 steal surfaces and for a few minutes via paper tissues

Incubation Period:
- For other, well-understood strains of influenza, usually 1-3 days

Communicability:
- During the pandemic of 1918-1919, the virus was shown to be extraordinarily communicable from person-to-person.
Section VII- Medical

Surveillance:
- The 2009 H1N1 vaccine elicits cross-reactive antibodies against 1918 H1N1 virus. As the laboratory workers are vaccinated with 2009 H1N1-like seasonal vaccine, we anticipate that they will be sero-positive for antibodies against 1918. Hence, baseline serum will not be archived.

- Any personnel currently working with or have previously worked with the virus in the past 10 days 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:
- Several studies show that HA of 1918 strain is antigenically similar to HA of 2009 H1N1 virus. 2009 H1N1 or similar vaccine provides cross-protection against the 1918 strain.
- Prior to starting 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. The 2009 H1N1-like component in the vaccine can afford protection against 1918 virus.
- All unexpected events and illnesses will be reported. The extent of reporting is dependent on the assessed risk to the individual and the environment.
- Personnel who have worked in the ABSL-3 laboratory will report any fever, respiratory symptoms, or other symptoms compatible with illness due to pathogens studied in the ABSL-3 laboratory to the principal investigator and the Biosafety Officer. If necessary the personnel will report to employee health services and will undergo antiviral treatments. If the personnel develops any clinical signs consistent with influenza virus infection, the Principal Investigator and Biosafety Officer will notify appropriate authorities will be notified. The personnel will remain in quarantine at predetermined facility until recovery and will seek medical consultation.

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

Prophylaxis:
- **Prophylaxis shall be provided only after medical evaluation**
- 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 1918 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 1918 Influenza and ask to be directly placed in a “predetermined severe respiratory illness isolation facility, rather than home isolation”.
- Respiratory virus panel test on Nasopharyngeal samples
- If test is positive for the 1918 virus, patient will remain in quarantine at predetermined facility

**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 predetermined facility, until infection can be ruled out by testing.

All SRA approved workers will be provided a medical (wallet) card which includes agent(s) that individual works with and emergency contact numbers. Additionally, all SRA cleared person will be trained on Health watch and this agent profile.

Date approved: