

INFLUENZA VIRUS TYPE A

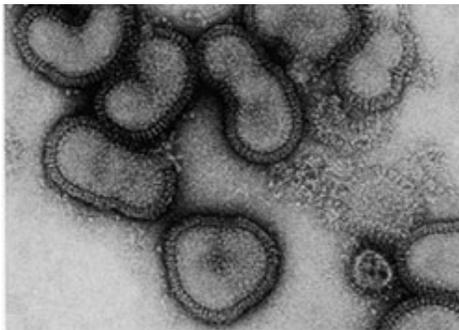
PATHOGEN SAFETY DATA SHEET - INFECTIOUS SUBSTANCES

INFECTIOUS AGENT

NAME: Influenza virus type A (excluding 1918 influenza A (H1N1) strain and subtypes H5, H7 and H9).

SYNONYM OR CROSS REFERENCE: *Orthomyxovirus*, grippe, and flu.

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, of which subtypes H1N1 and H3N2 are currently circulating among humans in seasonal influenza outbreaks. Antigenic alterations occur frequently in influenza HA and NA antigenic sites and these are the mechanism for virus adaptation to the host and survival. Small alterations are referred to as antigenic drift, whereas larger alterations caused by reassortment are referred to as antigenic shift. Influenza pandemics may occur as a result of antigenic shifts if the mutation of the virus leads to efficient human-to-human transmission. Only three hemagglutinin subtypes (H1, H2, H3) and two neuraminidase subtypes (N1 and N2) have established stable lineages in the human population since 1918.



Influenza virus¹⁾



Influenza virus type A²⁾

HAZARD IDENTIFICATION

PATHOGENICITY/TOXICITY: An acute viral disease of the upper respiratory tract characterized by fever (temperature 37.8°C or above), headache, myalgia, malaise, sore throat, non-productive cough, sneezing and nasal discharge. Among children, otitis media, nausea and vomiting are commonly reported. Pulmonary complications of influenza include pneumonia (viral and bacterial), croup, asthma and bronchitis. Myocarditis and pericarditis are occasional cardiac complications. Fatality due to influenza is generally low, except in those with chronic lung or heart conditions. Secondary bacterial pneumonia after influenza is a leading cause of mortality worldwide.

EPIDEMIOLOGY: Influenza caused approximately 36,000 deaths per year in the United States between 1990 and 1999, and approximately 226,000 hospitalizations between 1979 and 2001.

Influenza can occur in pandemics and epidemics, localized outbreaks, and as sporadic cases. In temperate climates, epidemics of influenza typically occur during the late fall and winter seasons, whereas in tropical and subtropical regions influenza epidemics occur throughout the year. Historical evidence suggests that more severe, worldwide pandemics have occurred at 10 to 40 year intervals since the 16th century.

A pandemic that occurred in 1957-1958 (Asian flu) was caused by influenza virus A subtype H2N2, that resulted from the reassortment of circulating human H1N1 and avian H2N2 viruses, and is estimated to have caused 70,000 deaths in the United States.

Another influenza pandemic that occurred in 1968-1969 (Hong Kong flu), was caused by an H3N2 strain of influenza that was the result of a reassortment between circulating human H2N2 and avian H3 viruses and is estimated to have caused 34,000 deaths in the United States. Together, the Asian and Hong Kong flu pandemics resulted in 1 to 2 million deaths worldwide.

Since the Hong Kong flu (H3N2) pandemic, the number of influenza-associated hospitalizations has typically been greater during seasonal influenza epidemics caused by influenza A/H3N2 viruses than during seasons in which other influenza A virus subtypes have predominated.

During the summer of 2002, an epidemic of respiratory illness with 22,646 cases and a 3% case-mortality affected Madagascar and was attributed to a strain of H3N2.

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 (CDC) estimates 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.

Influenza A subtypes H1N1 and H3N2 are still currently circulating in the human population and are included in current vaccines.

HOST RANGE: Humans, swine, horses, domestic and wild avian species (predominantly ducks), geese, and shorebirds.

INFECTIOUS DOSE: Unknown for specific influenza A subtypes. The infectious dose for the influenza A variant, Influenza A2, is greater than 790 organisms via the nasopharyngeal route. Influenza A (subtype not specified) is more infectious by aerosol inhalation (50% human infectious dose (HID₅₀) = 0.6 – 3.0 median tissue culture infectious doses (TCID₅₀)) than by intranasal drop inoculation (HID₅₀ = 127 – 320 TCID₅₀).

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 amounts of virus can be infective for 2 to 8 hours via stainless steel surfaces and for a few minutes via paper tissues.

INCUBATION PERIOD: Short, usually 1 to 3 days.

COMMUNICABILITY: Highly communicable. Infected persons can shed detectable amounts of influenza virus the day before symptoms begin. Adults usually shed the virus for 3 to 5 days, and up to 7 days in young children.

DISSEMINATION

RESERVOIR: Humans are the principle reservoir of human influenza A viruses. The avian reservoir of influenza A viruses is wild birds, predominantly ducks, geese, and shorebirds. Animal reservoirs are suspected as sources of new human subtypes. Influenza A viruses are also frequently isolated in pigs and horses. Swine have been demonstrated to have receptors for both human and avian influenza viruses and as such are considered potential mixing vessel for human and avian viruses. This could result in a reassortment which may be infectious to man with antigenic characteristics for which the human population is immunologically naïve.

ZOONOSIS: Transmission from pigs to man has been demonstrated. There are documented cases of human infections with swine influenza viruses, and zoonotic infection may occur frequently in those involved directly or indirectly in swine farming; however, the illness is mild and

person-to-person transmission is very limited. In the case of pandemic H1N1 influenza, the person-to-person transmission measured by basic reproduction number (R_0) was almost the same ($R_0 = 1.4$ to 1.6) as seasonal influenza ($R_0 = 0.9$ to 2.1), and the disease may range from mild to acute.

VECTORS: None

STABILITY AND VIABILITY

DRUG SUSCEPTIBILITY: Seasonal influenza viruses are sensitive to the neuraminidase inhibitors oseltamivir (Tamiflu), and zanamivir (Relenza), and to amantadine, and rimantadine, which inhibit the M2 ion channel protein activity and block viral uncoating. The 2009 H1N1 virus is susceptible to neuraminidase inhibitors, including oseltamivir (Tamiflu) and zanamivir (Relenza), but usually resistant to amantadine and rimantadine. Sporadic instances of oseltamivir-resistant 2009 H1N1 viruses have been documented.

DRUG RESISTANCE: A significant increase in resistance to oseltamivir, adamantanes (amantadine, and rimantadine) has been observed recently.

SUSCEPTIBILITY TO DISINFECTANTS: Influenza A is susceptible to disinfectants, including sodium hypochlorite (freshly made 1:10 dilution of bleach), 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: Influenza A virus can survive for 24 to 48 hours on hard, nonporous surfaces such as stainless steel and plastic and for approximately 8 to 12 hours on cloth, paper and tissues.

FIRST AID / MEDICAL

SURVEILLANCE: Monitor for symptoms of influenza. Confirm diagnosis with RT-PCR (favored) or point-of-care testing and give appropriate antiviral treatment. Laboratory confirmation of the virus is not routinely performed, occurring only during an epidemic and consists of inoculating cell cultures with swabs or washings taken from the nose during the first days of illness.

FIRST AID/TREATMENT: Fluids and rest. Antiviral agents (mainly oseltamivir) can be employed to treat influenza A. Antibiotic treatment (in combination with antiviral treatment) may also be used to prevent or treat secondary bacterial pneumonia.

IMMUNIZATION: The most effective strategy for reducing the effect of influenza is through annual vaccination using a live, attenuated influenza vaccine (LAIV) or an inactivated influenza vaccine (TIV). Both LAIV and TIV contain strains of influenza viruses that are antigenically equivalent to the annually recommended strains: 1 influenza A (H3N2) virus, 1 influenza A (H1N1) virus and 1 influenza B virus. Each year, one or more virus strain might be changed on the basis of global surveillance for influenza viruses and the spread of new strains. LAIV is administered intranasally by sprayer, whereas TIV is administered intramuscularly by injection. LAIV is currently approved only for use among healthy persons aged 5 to 49 years. During the 2009 H1N1 pandemic, an adjuvanted inactivated vaccine was developed by Glaxo Smith Kline (Pandemrix), which was authorized for use by the European Commission, with priority given to at risk populations, pregnant women, health care workers, and those in close contact with immunocompromised individuals. The FDA approved 4 vaccines against the novel 2009 H1N1 for use in the United States on September 15, 2009: inactivated vaccines manufactured by Sanofi Pasteur, Novartis Vaccines and Diagnostics Limited, and CSL Limited; and a live attenuated intranasal vaccine manufactured by Medimmune LLC.

PROPHYLAXIS: Vaccines are available for influenza A subtypes H1N1 and H3N2; however, chemoprophylactic drugs must not be overlooked in the control or prevention of influenza. Antiviral prophylaxis must be initiated within 3 days of the detected illness of the index cases to be effective in slowing transmission. Available drugs for prophylaxis are the neuraminidase inhibitors, zanamivir (10mg twice daily for 5 days) and

oseltamivir (75mg once daily for 7 to 10 days). The M2 inhibitor, amantadine can also be used for chemoprophylaxis during outbreaks of seasonal influenza.

LABORATORY HAZARDS

LABORATORY-ACQUIRED INFECTIONS: Fifteen reported cases up to 1974. Animal-associated infections are not reported; however, risk is high from infected ferrets.

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 animal species.

PRIMARY HAZARDS: Inhalation of virus from aerosols 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 transmissible viruses with novel antigenic composition into humans.

EXPOSURE CONTROLS / PERSONAL PROTECTION

RISK GROUP CLASSIFICATION: Risk Group 2. This risk group applies to the species as a whole, and may not apply to every strain.

CONTAINMENT REQUIREMENTS: Containment Level 2 facilities, equipment, and operational practices for work involving infectious or potentially infectious materials and cultures. These containment requirements apply to the species as a whole, and may not apply to each strain within the species. A detailed risk assessment should be conducted for activities involving animal work to determine whether additional operational practices should be considered.

PROTECTIVE CLOTHING: For diagnostic work: Lab coat. Gloves when direct skin contact with infected materials or animals is unavoidable. Eyes protection must be used where there is a known or potential risk of exposure to splashes.

OTHER PRECAUTIONS: All procedures that may produce aerosols, or involve high concentrations or large volumes should be conducted in a biological safety cabinet (BSC). The use of needles, syringes, and other sharp objects should be strictly limited. Additional precautions should be considered with work involving animals or large scale activities.

HANDLING AND STORAGE

SPIILLS: Allow aerosols to settle and, wearing protective clothing, gently cover spill with paper towels and apply suitable disinfectant, starting at perimeter and working towards the centre. Allow sufficient contact time (30 minutes) and then clean the area.

DISPOSAL: Decontaminate before disposal by steam sterilization, chemical disinfection, or incineration.

STORAGE: In sealed containers that are appropriately labeled.

REFERENCE

Pathogen Safety Data Sheet (PSDS) for influenza virus type A has been modified from the ones produced by the Public Health Agency of Canada as educational and informational resources for laboratory personnel working with infectious substances.

- 1) Picture from www.euro.who.int
- 2) Picture from www.vetmed.auburn.edu