EDITORIAL

# Current H1N1 Influenza Epidemic- Recent Update

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Influenza is an acute, typically febrile, respiratory illness that occurs in outbreaks of varying severity, usually during winter months and mostly affecting the patients with extremes of ages (children and old people). Influenza viruses cause epidemic disease (influenza virus types A and B) and sporadic disease (type C) in humans [1]. During large-scale influenza A outbreaks, rates of hospitalization for lower respiratory tract disease increase for infants and children. This is also one cause of outbreaks of unexplained fever in infants less than 2 to 3 months of age [2].

**Influenza Virus:**

The influenza viruses are members of the Orthomyxoviridae family in the genus Influenza virus. The type A influenza viruses are widely distributed in the animal kingdom (equine and swine viruses) and are particularly prevalent among birds. The influenza virion consists of an outer lipoprotein envelope surrounding central nucleocapsid material. The diameter of the virion is about 100 to 120 nm. The envelope is uniformly studded with spike-like projections that protrude from the viral membrane on its outer surface. The spikes are of two varieties: viral hemagglutinin (HA) and neuraminidase (NA). The inner surface of the envelope consists of the nonglycosylated viral membrane protein (M). The core ribonucleoprotein (RNP) encompasses a single-stranded RNA genome that is segmented. Each of the eight RNA fragments codes for one of eight viral polypeptides. The segmented nature of the influenza genome allows for exchange of RNA segments when two different influenza virions infect the same cell (genetic recombination). This property has great significance for the epidemiology of and control of pandemic influenza.

Classification of the influenza viruses as types A, B, and C is based on the antigenic properties of the internal RNP and M proteins. In addition to type-specific antigens, influenza viruses also possess strain-specific antigens that reside in the HA and NA moieties. A standard nomenclature has been devised to classify strains of influenza A viruses according to the antigenic characteristics of their HA and NA molecules (eg, H1N1 or H3N2). Humoral immunity is conferred by strain-specific antibodies directed at the HA and NA antigens, whereas type-specific antibodies do not neutralize viral infectivity. The degree of antigenic variation among influenza B viruses is less than among type A viruses. Influenza C is biochemically distinct from both type A and B. [3]

**Swine Flu:**

Swine influenza is a highly contagious respiratory disease in pigs caused by one of several swine influenza A viruses. Transmission of swine influenza viruses to humans is uncommon. However, the swine influenza virus can be transmitted to humans via contact with infected pigs or environments contaminated with swine influenza viruses. Once a human becomes infected, he or she can then spread the virus to other humans, presumably in the same way as seasonal influenza is spread (i.e., via coughing or sneezing). The current epidemic is caused by the H1N1 serovar of Influenza A.

Human cases of swine influenza A (H1N1) have been reported worldwide in 2009. Cases of influenza-like illness were first reported in Mexico on March 18; the outbreak was subsequently confirmed as swine influenza A [4]. As of 1600 GMT, 3 May 2009, 18 countries have officially reported 898 cases of influenza A (H1N1) infection. Mexico has reported 506 confirmed human cases of infection, including 19 deaths [5]. The United States Government has reported 226 laboratory confirmed human cases from 30 states, including one death [6]. The following countries have reported laboratory confirmed cases with no deaths - Austria (1), Canada (85), China, Hong Kong Special Administrative Region (1), Costa Rica (1), Denmark (1), France (2), Germany (8), Ireland (1), Israel (3), Italy (1), Netherlands (1), New Zealand (4), Republic of Korea (1), Spain (40), Switzerland (1) and the United Kingdom (15). So far no cases have been reported from India.

**Swine Influenza - A Pandemic:**

By April 29, 2009, Swine flu had pushed the World Health Organization to raise its pandemic alert level to phase 5, which means that a pandemic is imminent. The WHO's pandemic alert phases are as follows [7] (Fig. 1):

**Phase 1:** A virus in animals has caused no known infections in humans.

**Phase 2:** An animal flu virus has caused infection in humans.

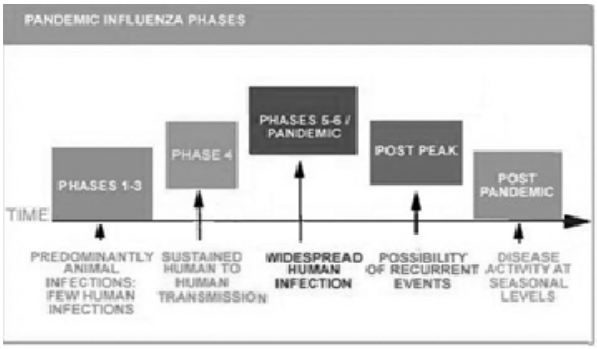
**Phase 3:** Sporadic cases or small clusters of disease occur in humans. Human-to-human transmission, if any, is insufficient to cause community-level outbreaks.

**Phase 4:** The risk for a pandemic is greatly increased but not certain. The disease-causing virus is able to cause community-level outbreaks.

**Phase 5:** Still not a pandemic, but spread of disease between humans is occurring in more than one country of one WHO region.

**Phase 6:** This is the pandemic level. Community-level outbreaks are in at least one additional country in a different WHO region from phase 5. A global pandemic is under way.

**Figure 1. Pandemic Influenza Phases [7]**



An influenza pandemic occurs when a new influenza virus appears against which the human population has no immunity, resulting in epidemics worldwide with enormous numbers of deaths and illness. With the increase in global transport, as well as urbanization and overcrowded conditions, epidemics due the new influenza virus are likely to quickly take hold around the world. Outbreaks of influenza in animals, especially when happening simultaneously with annual outbreaks of seasonal influenza in humans, increase the chances of a pandemic, through the merging of animal and human influenza viruses. During the last few years, the world has faced several threats with pandemic potential, making the occurrence of the next pandemic a matter of time. Current epidemiological models project that a pandemic could result in 2 to 7.4 million deaths globally [8].

The most recent pandemics included the 1889 pandemic, the 1918-1919 Spanish pandemic (influenza virus subtype H1), the 1957 pandemic (subtype H2N2), the 1968-1969 pandemic (Hong Kong subtype H3N2), and, to a lesser extent, the Russian pandemic in 1977 (subtype H1N1) [9]. The 1918 Spanish influenza pandemic infected one third of the world's population (an estimated 500 million people) and caused approximately 50 million deaths [10].

**Pathogenesis:**

Influenza infection is initiated by virus inoculation in the upper or lower airways. This infection can be transmitted by the hand-to-nose route, by droplets of infectious respiratory secretions, or by small droplet aerosol. It attaches to the respiratory epithelium by interaction of the HA molecule with cell-membrane receptors. In successful infection, virus begins to replicate in the respiratory epithelium; it is then shed into the respiratory secretions, and local spread ensues. The eventual result is death of respiratory epithelial cells with desquamation, loss of ciliary function and decreased mucus production [2]. The entire airway from pharynx to alveoli may be involved. Viral infection of the alveolar epithelium can result in a diffuse pneumonia that can be life-threatening. These changes permit secondary bacterial invasion either directly through the epithelium or, in the case of the middle ear space, through obstruction of the normal drainage through the eustachian tube. In humans, the influenza replicative cycle is confined to the respiratory epithelium. With primary infection, virus replication continues for 10-14 days [1].

This course is determined, in part, by the presence or absence of virus-specific serum IgG and secretory IgA antibody. Antibody to the HA of the virus is apparently most important in resistance to infection, but antibody to the NA also has a contributory role. Cellular immune responses are important in terminating established infection. Respiratory mucus contains certain glycopeptides that inhibit virus attachment to the cells of the respiratory mucosa. However, these glycopeptides can be inactivated by viral NA if this enzyme is not neutralized by specific antibody of the host. Cytokines like Tumor necrosis factor and Interferon may also be responsible for inhibiting viral replication. Heterotypic immunity is generally not seen in humans.

**Clinical Manifestations:**

Manifestations of swine influenza are similar to those of seasonal influenza except that most cases of swine influenza have occurred in previously healthy young adults [4]. Patients present with symptoms of acute respiratory illness, including the following: Fever, cough, sore throat, body aches, headache, chills and fatigue, diarrhea and vomiting are also possible. Persons with these symptoms should call their health care provider promptly. If an antiviral agent is warranted, it should ideally be initiated with 48 hours from the onset of symptoms. The duration of illness is typically 4-6 days. The infectious period for a confirmed case is defined as 1 day prior to the onset of symptoms to 7 days after onset. Signs of severe disease include apnea, tachypnea, dyspnea, cyanosis, dehydration, altered mental status, and extreme irritability [11].

**Diagnosis:**

As per CDC guidelines [12] ***a confirmed case*** of Swine origin influenza virus (S-OIV) infection is defined as a person with an acute febrile respiratory illness with laboratory confirmed S-OIV infection at CDC by one or more of the following tests:

1. real-time RT-PCR
2. viral culture

A ***probable case*** of S-OIV infection is defined as a person with an acute febrile respiratory illness who is positive for influenza A, but negative for H1 and H3 by influenza RT-PCR.

A ***suspected case*** of S-OIV infection is defined as a person with acute febrile respiratory illness with onset.

• Within 7 days of close contact with a person who is a confirmed case of S-OIV infection, or

• Within 7 days of travel to community either within the United States or internationally where there are one or more confirmed cases of S-OIV infection, or • Resides in a community where there are one or more confirmed cases of S-OIV infection.

**Treatment:**

CDC recommendations for the treatment of swine flu are [13]:

**a. Home isolation:**

1. Patients who develop flulike illness (i.e. fever with either cough or sore throat) should be strongly encouraged to self-isolate in their home for 7 days after the onset of illness or at least 24 hours after symptoms have resolved, whichever is longer.
2. To seek medical care, patient should contact their health care providers to report illness (by telephone or other remote means) before seeking care at a clinic, physician's office, or hospital.
3. Patients who have difficulty breathing or shortness of breath or who are believed to be severely ill should seek immediate medical attention.
4. If the patient must go into the community (e.g. to seek medical care), he or she should wear a face mask to reduce the risk of spreading the virus in the community when coughing, sneezing, talking, or breathing. If a face mask is unavailable, ill persons who need

to go into the community should use tissues to cover their mouth and nose while coughing.
5. While in home isolation, patients and other household members should be given infection control instructions, including frequent hand washing with soap and water. Use alcohol-based hand gels (containing at least 60% alcohol) when soap and water are not available and hands are not visibly dirty. Patients with swine influenza should wear a face mask when within 6 feet of others at home.

**b. Household contacts who are not ill**
1. Remain home at the earliest sign of illness.
2. Minimize contact in the community to the extent possible.
3. Designate a single household family member as caregiver for the patient to minimize interactions with asymptomatic persons.

**c. School dismissal and childcare facility closure**
1. Strong consideration should be given to close schools upon a confirmed case of swine flu or a suspected case epidemiologically linked to a confirmed case.
2. Decisions regarding broader school dismissal within these communities should be left to local authorities, taking into account the extent of influenza like illness within the community.
3. Cancellation of all school or childcare related gatherings should also be announced.
4. Encourage parents and students to avoid congregating outside of the school if school is canceled.
5. Duration of schools and childcare facilities closings should be evaluated on an ongoing basis depending on epidemiological findings.
6. Consultation with local or state health departments is essential for guidance concerning when to reopen schools. If no additional confirmed or suspected cases are identified among students (or school-based personnel) for a period of 7 days, schools may consider reopening.
7. Schools and childcare facilities in unaffected areas should begin preparation for possible school closure.

**d. Social distancing**
1. Large gatherings linked to settings or institutions with laboratory-confirmed cases should be canceled (e.g., sporting events or concerts linked to a school with cases); other large gatherings in the community may not need to be canceled at this time.
2. Additional social distancing measures are currently not recommended.
3. Persons with underlying medical conditions who are at high risk for complications of influenza should consider avoiding large gatherings.

**e. Supportive care:** Treatment is largely supportive and consists of bed rest, increased fluid consumption, cough suppressants, and antipyretics and analgesics (e.g., acetaminophen, nonsteroidal anti-inflammatory drugs) for fever and myalgia. Aspirin or aspirin-containing products should not be administered to any confirmed or suspected ill case of swine influenza A (H1N1) virus infection aged 18 years old and younger due to the risk of Reye syndrome. For relief of fever, other anti-pyretic medications are recommended such as acetaminophen or non steroidal anti-inflammatory drugs.

Severe cases may require intravenous hydration and other supportive measures. Treatment of hospitalized patients and patients at higher risk for influenza complications should be prioritized.

**f. Medications:** CDC has approved the use of antiviral agents like Oseltamavir and Zanamivir whereas drugs like amantadine and rimantadine are to be used since the virus is resistant to them. Antiviral treatment with zanamivir or oseltamivir should be initiated as soon as possible after the onset of symptoms. Evidence for benefits from treatment in studies of seasonal influenza is strongest when treatment is started within 48 hours of illness onset. However, some studies of treatment of seasonal influenza have indicated benefit, including reductions in mortality or duration of hospitalization even for patients whose treatment was started more than 48 hours after illness onset. Recommended duration of treatment and prophylaxis is shown in Table 1, 2 & 3.

**Table 1. Recommended doses of zanamivir and oseltamivir antiviral medications for the treatment of influenza A and B in children 1-18 years-old**

| | **1-6 years** | **7-18 years** | | |
|---|---|---|---|---|
| **Zanami-** | - | 10 mg (2 inhalations) twice daily for 5 days | | |
| | Upto 15 kg | 15-23kg | 23-40 kg | >40kg |
| **Oseltamivir** | 30 mg twice a day for 5 days | 45 mg twice a day for 5 days | 60 mg twice a day for 5 days | 75 mg twice a day for 5 days |

**Table 2: Recommended doses of zanamivir and oseltamivir antiviral medications for the prophylaxis of influenza A and B in children 1-18 years-old**

| | **1-4 years** | **5-18 years** | | |
|---|---|---|---|---|
| **Zana mivir** | | 10 mg (2 inhalations) once daily for 10 days after the last known exposure | | |
| | Upto 15 kg | 15-23kg | 23-40 kg | >40kg |
| **Osel-ta** | 30 mg once a day for 10 days after the last known | 45 mg once a day for 10 days after the last known exposure | 60 mg once a day for 10 days after the last known | 75 mg once a day for 10 days after the last known |

Antiviral chemoprophylaxis with either oseltamivir or zanamivir is ***recommended*** for the following:
1. Household close contacts who are at high-risk for complications of influenza (children younger than 5 years old, pregnant women, persons >65 years old and those with certain chronic medical conditions) of a confirmed or suspected case.

2. School children or daycare attendees who are at high-risk for complications of influenza (children younger than 5 years old, pregnant women, persons >65 years old and those with certain chronic medical conditions) who had close contact (face-to-face) with a confirmed, probable, or suspected case. 3. Children who traveled to Mexico who are at high-risk for complications of influenza (children younger than 5 years old pregnant women, persons >65 years old and those with certain chronic medical conditions).

**Table 3. Recommended doses of oseltamivir antiviral medication for the treatment and prevention of S-OIV influenza for children less than 1 year of age.**

| Age | Recommended treatment dose | Recommended prophylaxis |
|---|---|---|
| **<3 months** | 12 mg twice daily for 5 days | |
| **3-5 months** | 20mg twice daily | 20 mg once a day for 10 days |
| **6-11 months** | 25 mg twice daily for 5 days | 25 mg once a day for 10 days |

**g. Pregnant women:**Oseltamivir and zanamivir are "Pregnancy Category C" medications, indicating that no clinical studies have been conducted to assess the safety of these medications in pregnant women. Because of the unknown effects of influenza antiviral drugs on pregnant women and their fetuses, oseltamivir or zanamivir should be used during pregnancy only if the potential benefit justifies the potential risk to the embryo or fetus.

**h. Preventive measures for health care personnel:** The CDC has issued interim recommendations for controlling the spread of swine influenza in health care settings [14]. Recommended measures for care of patients with suspected or confirmed swine influenza include the following:

• Suctioning, bronchoscopy, or intubation should be performed in a procedure room with negative-pressure air handling.

• Patients should wear a surgical mask when outside their room.

• Encourage patients to wash their hands frequently and to follow respiratory hygiene practices. Cups and other utensils used by the ill person should be washed with soap and water before use by other persons. • Routine cleaning and disinfection strategies used during influenza seasons can be applied. • Standard, droplet, and contact precautions should be used for all patient care activities and maintained for 7 days after illness onset or until symptoms have resolved.

• Health care personnel should wash their hands with soap and water or use hand sanitizer immediately after removing gloves and other equipment and after any contact with respiratory secretions. • Personnel providing care to or collecting clinical specimens from patients should wear disposable nonsterile gloves, gowns, and eye protection (e.g., goggles) to prevent conjunctival exposure.

• As per previous recommendations regarding mask and respirator use during influenza pandemics, personnel engaged in aerosol-generating activities (e.g., collection of clinical specimens, endotracheal intubation, nebulizer treatment, bronchoscopy) and/or resuscitation involving emergency intubation or cardiacpulmonary resuscitation should wear a fit-tested disposable N95 respirator.

• Pending clarification of transmission patterns for the 2009 swine influenza A (H1N1) virus, personnel providing direct patient care for suspected or confirmed cases should wear a fit-tested disposable N95 respirator when entering the patient's room.

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