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Swine Influenza A (H1N1)

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GENERAL INFORMATION

Influenza Viruses

Influenza viruses are enveloped RNA viruses, their strains are classified by their

Simultaneous infection of a cell by two influenza viruses may allow recombination

Pigs may play an important role in the evolution of human pandemic strains because pig's trachea contains receptors for both avian and human influenza viruses as well as swine viruses; therefore, the domestic pig supports the growth of viruses of human, avian and swine origin. Thus, it has been proposed that genetic re-assortment of influenza virus may occur in pigs, leading to a novel strain.

Swine flu viruses are similar to other influenza viruses, which change constantly. Over the years, different variations of swine flu viruses have emerged. At present, there are four main subtypes for influenza A virus, which have been isolated in pigs: H1N1, H1N2, H3N2, and H3N1. However, most of the recently isolated influenza viruses from pigs have been A (H1N1) viruses[2-3].

Swine Flu in Pigs

Swine flu is a respiratory disease of pigs caused by type A swine influenza virus that regularly causes outbreaks of influenza in pigs. Swine flu viruses cause high levels of illness and low death rates in pigs. It usually circulates among swine throughout the year, but most outbreaks occur during the late fall and winter months similar to outbreaks in humans. The classical swine flu virus (an

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influenza type A (H1N1) virus) was first isolated from a pig in 1930. The signs of swine flu in pigs can include sudden onset of fever, depression, coughing (barking), discharge from the nose or eyes, sneezing, breathing difficulties, eye redness or inflammation and going off feed[4], see figure 1, 2 and 3.

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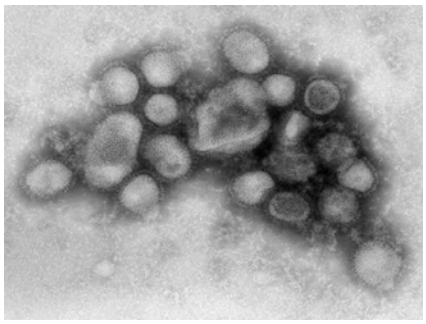


Figure 1

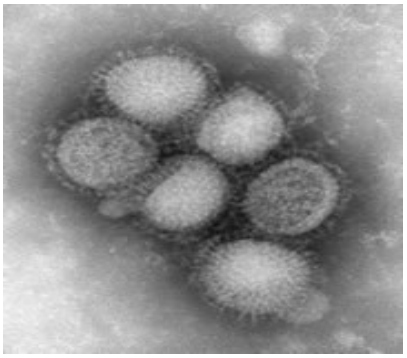


Figure 2

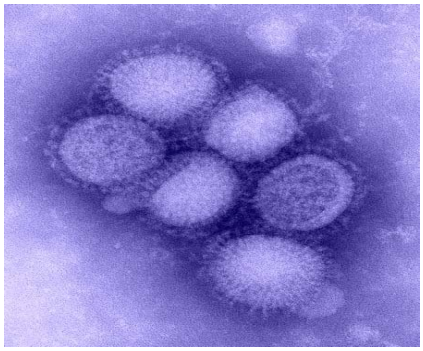


Figure 3

Figure (1, 2 and 3): Are Images of The Newly Identified H1N1 Influenza Virus; These Images Were Taken in The CDC Influenza Laboratory

Swine Flu Infection in Humans

Swine flu viruses do not normally infect humans. However, sporadic human infections with swine flu have occurred in the past. Most commonly, these cases had occurred in persons with direct exposure to pigs[3]. Influenza virus are not transmitted to human by eating pork or pork products provided proper handling and cooking (Cooking pork to

an internal temperature of 160°F kills the swine flu virus), rather it is transmitted through direct close contact with infected pigs.

The first isolation of a swine influenza virus from a human occurred in 1974, which confirmed the speculation that it was of swine origin and it could infect humans. Since then CDC has used to receive reports of approximately one human infected with swine influenza virus every 1-2 years in the United States. However, during December 2005 to January 2009, twelve cases of human infection with swine influenza were reported; five of the twelve cases occurred in patients who had direct exposure to pigs, six patients reported being near pigs and the exposure in one case was unknown[5].

Symptoms of Swine Flu in Humans

The disease caused by swine flu in humans vary from mild to severe, with a symptoms that is similar to the symptoms of human seasonal influenza and include fever, lethargy, lack of appetite and coughing, runny nose, sore throat, occasionally nausea, vomiting and diarrhea[4].

High-Risk Group

A person who is a high-risk for complications of swine influenza A (H1N1) virus infection is defined as the same as for seasonal influenza, which include the following groups of patients:

- Children aged six months to five years (59 months)
- Persons aged 50 years or older
- Children and adolescents (aged six months to eighteen years) who are receiving long-term aspirin therapy and who might be at risk for developing Reye's syndrome after influenza virus infection
- Pregnant women
- Adults and children who have chronic pulmonary conditions (including asthma), cardiovascular (except hypertension), renal, hepatic, hematological, or metabolic disorders (including diabetes mellitus)
- Adults and children who have immunosuppression
- Adults and children who have cognitive dysfunction, spinal cord injuries, seizure disorders, or other neuromuscular disorders, which could compromise respiratory function or management of respiratory secretions
- Adults and children with conditions, which could increase the risk of aspiration
- Residents of nursing homes and other chronic-care facilities

Complications of swine flu are expected to be similar to seasonal influenza:

- Exacerbation of underlying chronic medical conditions
- Upper respiratory tract disease (sinusitis, otitis media, croup)
- Lower respiratory tract disease (pneumonia, bronchiolitis, status asthmaticus),
- Cardiac (myocarditis, pericarditis)
- Musculoskeletal (myositis, rhabdomyolysis)
- Neurologic (acute and post-infectious encephalopathy
- Encephalitis
- Febrile seizures (status epilepticus)
- Toxic shock syndrome and secondary bacterial pneumonia associated with or without sepsis

Current Situation of Swine Flu Pandemic

On April 17, 2009, CDC diagnosed two children with febrile respiratory illness caused by infection of swine influenza A (H1N1) virus; both were resident of southern California. The viruses from the two cases are closely related genetically, and contained a unique combination of gene segments that previously has not been reported among swine or human influenza viruses in the United States or elsewhere. Neither child had contact with pigs; the source of the infection was unknown[6].

On April 24, six additional cases were reported in San Diego County, California (three cases), Imperial County, California (one case), and Guadalupe County, Texas (two cases).

Mexican public health authorities have reported increased level of respiratory disease, including reports of severe pneumonia cases and deaths; the specimens collected from patients with respiratory disease in Mexico were tested by the CDC laboratory and has identified the same strain of swine influenza A (H1N1) as identified in the US cases[7].

From 29 April 2009, the situation continued to progress rapidly. Total of nine countries have officially reported 148 cases of swine influenza A (H1N1) infection. The United States Government has reported 91 laboratory confirmed human cases and one death. Mexico has reported 26 confirmed human cases of infection and seven deaths.

The following countries have reported laboratory confirmed cases and no deaths:

- Austria one case
- Canada 13 cases
- Germany 3 cases
- Israel 2 cases
- New Zealand 3 cases
- Spain 4 cases
- United Kingdom 5 cases

Based on assessment of all available information, WHO Director-General raised the current level of influenza pandemic alert from phase 4 to 5 (Phase 5 is characterized by human-to-human spread of the virus into at least two countries in one WHO region.) While most countries would not be affected at this stage, the declaration of Phase 5 is a strong signal that a pandemic is imminent and that the time to finalize the organization, communication, and implementation of the planned alleviation measures is short[8], see figure 4.

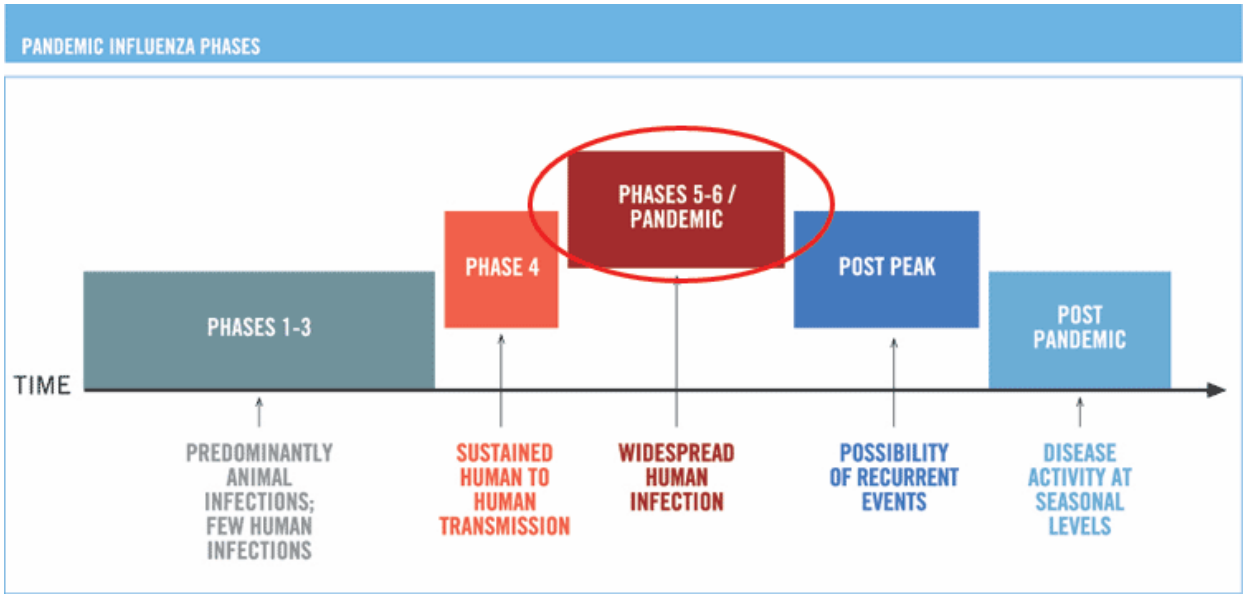


Figure 4: Phases of Pandemic

CASE DEFINITIONS OF SWINE-ORIGIN INFLUENZA A (H1N1) VIRUS[9]

Confirmed Case

A confirmed case of swine-origin influenza A (H1N1) virus infection is defined as an acute febrile respiratory illness in a person followed by laboratory confirmation of swine-origin influenza A (H1N1) virus at CDC reference laboratory. Either one of the following tests could do the confirmation:
1) Real-time reverse transcription-polymerase chain reaction (rRT-PCR), or
2) Viral culture

Probable Case

A probable case of swine-origin influenza A (H1N1) virus infection is defined as acute febrile respiratory illness in a person who is positive for influenza A, but negative for H1 and H3 by influenza rRT-PCR.

Suspected Case

A suspected case of swine-origin influenza A (H1N1) virus infection is defined as acute febrile respiratory illness in a person:

- The onset is within 7 days of close contact with a person who has a confirmed case of swine-origin influenza A (H1N1) virus infection, or
- The onset is within 7 days of travel to a community, either within the United States or internationally, which has one or more confirmed swine-origin influenza A (H1N1) cases, or
- Who resides in a community in which one or more confirmed swine-origin influenza cases have occurred.

Acute respiratory illness is defined as recent onset of at least two of the following: Rhinorrhea or nasal congestion, sore throat, cough, associated with or without fever or feverishness.

Human to Human Transmission of Swine Flu

Human-to-human transmission thought to occur in the same way as seasonal flu occurs in people, through large particle respiratory droplet transmission, when an infected person coughs or sneezes near a susceptible person. Transmission via large particle droplets requires close contact between the source and the recipient persons because droplets do not remain suspended in the air and generally travel only a short distance, which is less than a meter through the air. Contact with respiratory droplet contaminated surface is another possible source of transmission, for example, touching contaminated surface with flu viruses and then touching the mouth or nose.

Because data from swine-origin influenza viruses are limited, the potential for ocular, conjunctival, or gastrointestinal infection is unknown. Since this is a novel influenza A virus in humans, transmission from infected persons to close contacts might be common. All respiratory secretions and bodily fluids (diarrheal stool) of swine-origin influenza A (H1N1) cases should be considered potentially infectious.

Infectious Period of Swine Flu among Humans

Infected people may be able to infect others one day before symptoms develop and up to 7 or more days after becoming sick. Young children and immuno-compromised hosts might be potentially contagious for longer periods than others might.

Close Contact

Is defined as within six feet of an ill person and who is a confirmed or suspected case of swine-origin influenza A (H1N1) virus infection during the case's infectious period.

Incubation Period

The estimated incubation period is unknown and could range from 1-7 days, and it is more likely to be 1-4 days.

Testing for Swine-Origin Influenza A (H1N1) Virus[10]

Clinicians should consider the possibility of swine influenza virus infections in patient presenting with febrile respiratory illness if he/she fulfills the criteria of case definition.

If swine flu is suspected, clinicians should obtain nasopharyngeal swab/aspirate or nasal wash/aspirate for swine influenza testing. For patients who are intubated, an endotracheal aspirate should also be collected. *The specimens should be placed into sterile viral transport media (VTM) and immediately placed on ice or cold packs or at 4° C (refrigerator) for transport to the laboratory.*

Recommended test is Real-time RT-PCR for influenza A, B, H1, H3. Currently, swine-origin influenza A (H1N1) virus will test positive for influenza A and negative for H1

and H3 by real-time RT-PCR. If reactivity of real-time RT-PCR for influenza A is strong, it is more suggestive of a novel influenza A virus. Confirmation of swine-origin influenza A (H1N1) virus is performed at a reference laboratories[10].

GUIDELINES FOR ANTIVIRAL TREATMENT AND PROPHYLAXIS

Antiviral Susceptibility

The swine influenza A (H1N1) virus is susceptible to the Neuraminidase Inhibitor (Zanamivir and Oseltamivir). It is resistant to the Adamantine (Amantadine and Rimantadine)[9].

Antiviral Treatment

Antiviral treatment should be considered for confirmed or suspected cases of swine-origin influenza A (H1N1) virus infection. Treatment of hospitalized patients and patients at higher risk for influenza complications should be prioritized.

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 starts within 48 hours of the onset of illness. However, some studies of seasonal influenza have indicated some benefits, which include reductions in mortality or duration of hospitalization for patients whose treatment was started more than 48 hours after the onset of illness. The recommended duration of treatment is five days, see Table 1[9].

Table 1: Swine Influenza Antiviral Medication Dosing Recommendations

Agent, group Oseltamivir		Treatment	Chemoprophylaxis
Adults		75 mg capsule twice per day for 5 days	75 mg capsule once per day
Children (age, 12 months or older), weight:	15 kg or less	60 mg per day divided into 2 doses	30 mg once per day
	15–23 kg	90 mg per day divided into 2 doses	45 mg once per day
	24–40 kg	120 mg per day divided into 2 doses	60 mg once per day
	>40 kg	150 mg per day divided into 2 doses	75 mg once per day
Agent, group Zanamivir			
Adults		Two 5 mg inhalations (10 mg total) twice per day	Two 5 mg inhalations (10 mg total) once per day

Children	Two 5 mg inhalations (10 mg total) twice per day (age, 7 years or older)	Two 5 mg inhalations (10 mg total) once per day (age 5 years or older)

Additional Therapy

Additional therapy such as antibacterial agents should be used at the discretion of the clinicians according to the patient's clinical presentation.

For antibacterial treatment of pneumonia, clinical guidance for community-acquired pneumonia should be followed.

In hospitalized patients with severe community-acquired pneumonia (CAP) requiring intensive care unit admission, methicillin-resistant *Staphylococcus aureus* (MRSA) infection should be suspected and treated empirically in addition to other causes of CAP if they have either cavitary necrotizing infiltrates or empyema.

Antiviral Chemoprophylaxis

Oseltamivir or Zanamivir are recommended for antiviral chemoprophylaxis of swine-origin influenza A (H1N1) virus infection, see Table 1.

The duration of antiviral chemoprophylaxis is 10 days after the last known exposure to an ill confirmed case of swine-origin influenza A (H1N1) virus infection. Post exposure prophylaxis should be considered for contact during the *infectious period*. If the contact occurred more than 7 days earlier, prophylaxis is not necessary. For pre-exposure protection, chemoprophylaxis should be given during the potential exposure period and continued for 10 days after the last known exposure to an ill confirmed case of swine-origin influenza A (H1N1) virus infection[9].

Antiviral Chemoprophylaxis Is Recommended for the Following Groups:

1. Household close contacts of a confirmed or probable case and who are at high-risk for complications of influenza, for example, persons with certain chronic medical conditions, persons 65 year or older, children younger than five years old and pregnant women
2. Health care workers or public health workers who were not using appropriate personal protective equipment during close contact with an ill confirmed, probable, or suspect case of swine-origin influenza A (H1N1) virus infection

Antiviral Chemoprophylaxis Could Be Considered for the Following Groups:

1. Household close contacts of a suspected case and who are at high-risk for complications of influenza, for example, persons with certain chronic medical conditions, persons 65 years or older, children younger than 5 years old, and pregnant women
2. Children attending school or daycare who are at high-risk for complications of influenza (children with certain chronic medical conditions) and who had close contact (face-to-face) with a confirmed, probable or suspected case

3. Health care workers who are at high-risk for complications of influenza, for example, persons with certain chronic medical conditions, persons 65 years or older, and pregnant women who are working in an area of the healthcare facility that have patients with confirmed swine-origin influenza A (H1N1) cases or who is caring for patients with any acute febrile respiratory illness
4. Travelers to Mexico who are at high-risk for complications of influenza, for example, persons with certain chronic medical conditions, persons 65 years or older, children younger than five years old, and pregnant women
5. First responders (police, EMS and others) who are at high-risk for complications of influenza, for example, persons with certain chronic medical conditions, persons 65 years or older, children younger than five years old, and pregnant women and who are working in areas with confirmed cases of swine-origin influenza A (H1N1) virus infection

Special Consideration for Children under One Year of Age

Children under one year of age are at high risk for complications from seasonal human influenza virus infections. The characteristics of human infections with swine-origin A (H1N1) viruses are still being studied; it is not known whether infants are at higher risk for complications associated with swine-origin A (H1N1) infection compared to older children and adults.

Limited safety data on the use of Oseltamivir or Zanamivir are available from studies on children less than one year of age. Oseltamivir is not licensed for use in children less than one year of age, available data come from the use of Oseltamivir for treatment of seasonal influenza. These data suggest that severe adverse events are rarely associated with the use of Oseltamivir in children younger than one year old with seasonal influenza. Limited retrospective data on the safety and efficacy of Oseltamivir in this young age group have not demonstrated age-specific drug-attributable toxicities to date, the Infectious Diseases Society of America recently noted. Because infants typically have high rates of morbidity and mortality from influenza, infants with swine-origin influenza A (H1N1) infections may benefit from treatment using Oseltamivir, see Table 2 and 3.

Table 2: Oseltamivir Dosing Recommendations of Antiviral Treatment for Children Younger than One Year of Age

Age	Recommended Treatment Dose for 5 Days
<3 months	12 mg twice daily
3-5 months	20 mg twice daily
6-11 months	25 mg twice daily

Table 3: Oseltamivir Dosing Recommendations of Antiviral Chemoprophylaxis for Children Younger than One Year of age

Age	Recommended Prophylaxis Dose for 10 Days
<3 months	Not recommended unless the situation necessitates critical due to limited data on use in this age group

3-5 months	20 mg once daily
6-11 months	25 mg once daily

Healthcare providers should be aware of the lack of data on safety and dosing when considering Oseltamivir use in a seriously ill young infant with confirmed swine-origin A (H1N1) influenza or who has been exposed to a confirmed case of swine A (H1N1). The infant should be carefully monitored for adverse events when Oseltamivir is used[9].

Aspirin or aspirin-containing products (bismuth subsalicylate, Pepto-Bismol) 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's syndrome. For relief of fever, other anti-pyretic medications are recommended such as Acetaminophen or non Steroidal Anti-inflammatory drugs.

Special Consideration for 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 for 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. However, no adverse effects have been reported among women who received Oseltamivir or Zanamivir during pregnancy or among infants born to women who have received Oseltamivir or Zanamivir. Pregnancy should not be considered as an absolute contraindication to Oseltamivir or Zanamivir use. Because of its systemic activity, Oseltamivir is preferred for treatment of pregnant women. The drug of choice for prophylaxis is less clear. Zanamivir may be preferable because of its limited systemic absorption; however, respiratory complications, which might be associated with Zanamivir because of its inhaled route of administration, need to be considered, especially in women at risk for respiratory problems[9].

Infection Control Guidelines for Swine Flu

Patients with suspected or confirmed case-status should be placed in a single-patient room with the door kept closed. If available, an airborne infection isolation room (AIIR) with negative pressure air handling and 6 to 12 air changes per hour can be used. Air can be exhausted directly outside or be re-circulated after filtration by a high efficiency particulate air (HEPA) filter. For suctioning, bronchoscopy, or intubation, use a procedure room fitted with negative pressure air equipment.

The ill person should wear a surgical mask whenever he/she is outside the room and should be encouraged to wash his/their hands frequently and follow respiratory hygiene practices. Cups and other utensils used by the ill person should be washed with soap and water before their use by other persons.

Standard, droplet and contact precautions should be used for all patient care activities and maintained for seven days after the onset of the illness or until symptoms have

resolved. Maintain adherence to hand hygiene by washing with soap and water or using hand sanitizer immediately after removing gloves and other equipment and after any contact with respiratory secretions.

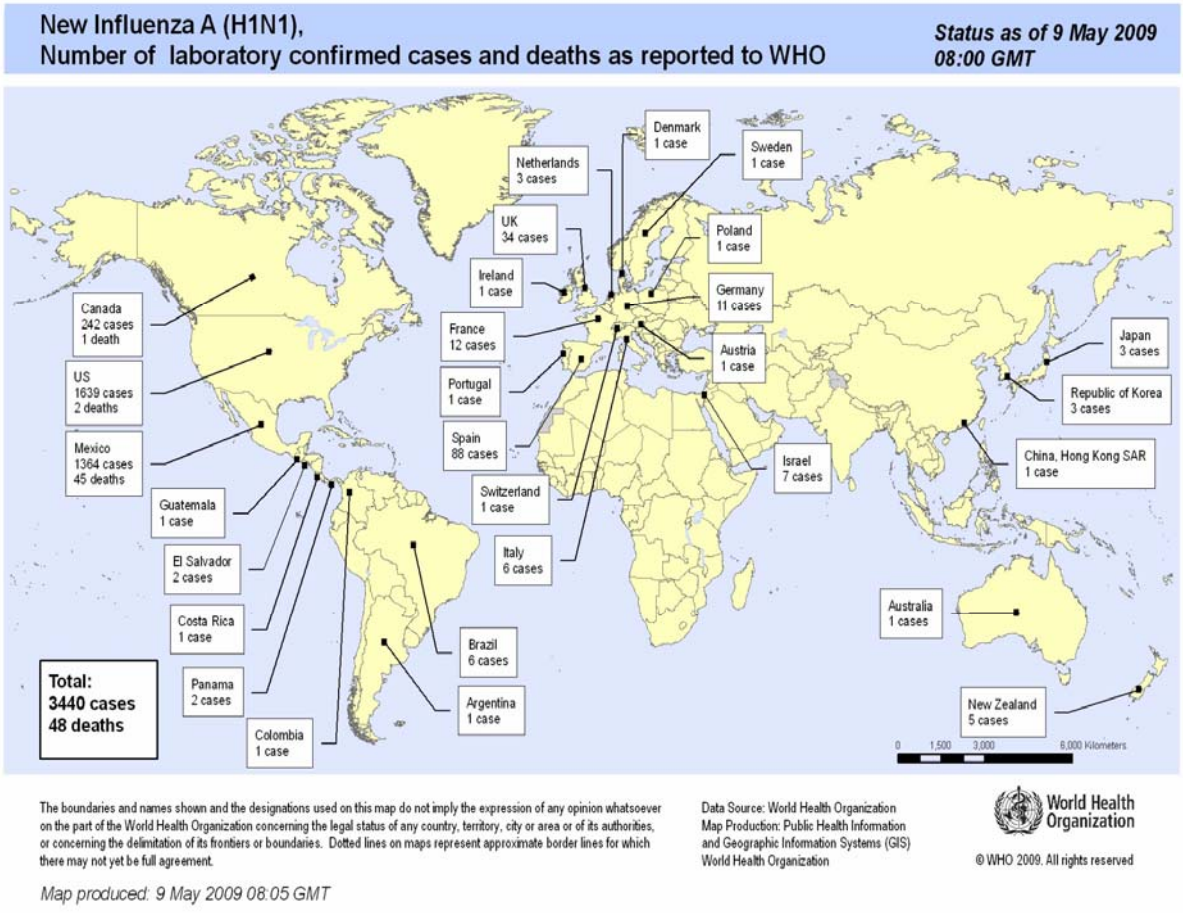
Personnel providing care to or collecting clinical specimens from suspected or confirmed cases should wear disposable N95 respirator, disposable non-sterile gloves, gowns, and eye protection (goggles) to prevent conjunctival exposure[11].

As of 06:00 GMT, 9 May 2009, 29 countries have officially reported 3440 cases of influenza A (H1N1) infection[12].

Mexico has reported 1364 laboratory confirmed human cases of infection, including 45 deaths. The United States has reported 1639 laboratory confirmed human cases, including two deaths. Canada has reported 242 laboratory confirmed human cases, including one death.

The following countries have reported laboratory confirmed cases with no deaths

- Argentina one case
- Australia one case
- Austria one case
- Brazil 6 cases
- China one case
- Colombia one case
- Costa Rica one case
- Denmark one case
- El Salvador 2 cases
- France 12 cases
- Germany 11 cases
- Guatemala one case
- Ireland one case
- Israel 7 cases
- Italy 6 cases
- Japan 3 cases
- Netherlands 3 cases
- New Zealand 5 cases
- Panama 2 cases
- Poland one case
- Portugal one case
- Republic of Korea 3 cases
- Spain 88 cases
- Sweden one case
- Switzerland one case
- United Kingdom 34 cases



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