General Practitioner's Section
SWINE FLU - Are We on The Verge of a Pandemic?

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Abstract
Swine flu is a respiratory disease, caused by influenza type A which infects pigs. There are many types, and the infection is constantly changing. Until now it has normally not infected humans, but the latest form clearly does, and can be spread from person to person - probably through coughing and sneezing. The World Health Organization has confirmed that at least some of the human cases are a never-before-seen version of the H1N1 strain of influenza type A. H1N1 is the same strain which causes seasonal outbreaks of flu in humans on a regular basis.

But this latest version of H1N1 is different: it contains genetic material that is typically found in strains of the virus that affect humans, birds and swine. Flu viruses have the ability to swap genetic components with each other, and it seems likely that the new version of H1N1 resulted from a mixing of different versions of the virus, which may usually affect different species, in the same animal host. All cases outside of Mexico reported to date have consisted of mild influenza like illness. The disease can be diagnosed by a blood test RT-PCR.. Viral culture can also be used to isolate the virus. The virus is susceptible to treatment with the neuraminidase inhibitors (Anti Virals), Oseltamivir and Zanamivir.

SWINE FLU - THE BASICS
• Symptoms usually similar to seasonal flu - but deaths recorded in Mexico
• It is a new version of the H1N1 strain which caused the 1918 flu pandemic
• Too early to say whether it will lead to a pandemic
• Current treatments do work, but there is no vaccine
• Good personal hygiene, such as washing hands, covering nose when sneezing advised

Introduction
Has globalization made us more catastrophe-prone? At this stage, no one knows. The virus that has caused the outbreak of swine flu is a strain of the H1N1 type that contains bird, pig and human genes in a combination never seen before. Immunity to it will thus be limited. Scientists are working to establish the precise nature of the virus, the symptoms it causes and its capacity to cause disease and death. Concern that the world could be on the brink of the first influenza pandemic in more than 40 years has escalated as France, Hong Kong, New Zealand and Spain reported potential new cases in which people had been infected with swine flu and Canada confirmed several new cases and cases from a total of nine countries have been reported so far as at the time of writing this article. In the U.S., where 20 such infections have been confirmed, federal health officials declared a public-health

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emergency. Meanwhile, in hard-hit Mexico, where more than 80 people have died from what is believed to be swine flu, the government closed all public schools and cancelled hundreds of public events in Mexico City. Though the World Health Organization (WHO) is referring to the situation as a “public-health emergency of international concern,” the apparent emergence in several countries of an entirely new strain of H1N1 flu virus has led some scientists to believe that it is only a matter of time before the WHO declares pandemic status, a move that could prompt travel bans to infected countries.

The influenza virus is constantly mutating. That's why we can't get full immunity to the flu, the way we can to diseases like chicken pox, because there are multiple strains of the flu virus and they change from year to year. On April 21, 2009, the Centers for Disease Control and Prevention (CDC) issued an MMWR Dispatch describing 2 cases of swine influenza A (H1N1) infection that occurred in Southern California in April. While both patients recovered uneventfully, the isolated viruses harbour novel genetic characteristics not seen in swine flu isolates in the U.S. prior to this event. The other striking feature of these cases is that there was no known contact with swine, raising the question of efficient human-to-human transmission of this virus. Subsequent investigation has uncovered 40 additional cases in the United States—all of whom have recovered uneventfully—and reports of severe morbidity and mortality in Mexico. Several other countries including Canada, Scotland, and Spain are reporting confirmed cases.

Influenza viruses circulate among waterfowl, swine, and humans, but other mammals may also be infected. Until 1997, avian viruses were thought to be unable to infect humans directly, as they were thought to require a “mixing-vessel” (e.g., swine) as an intermediary to allow the virus to adapt to humans. The first isolation of a swine flu virus from a human occurred in 1974, confirming a long held suspicion that swine flu viruses could infect humans. The most widely known incident of swine flu in humans centres on an outbreak of a lethal influenza virus at Fort Dix in New Jersey in 1976. During that outbreak, 13 soldiers had severe respiratory illness, and 1 soldier died. A novel H1N1 swine influenza virus (Hsw1N1) was isolated.

**Symptoms**

Symptoms of swine flu in humans appear to be similar to those produced by standard, seasonal flu. These include fever, cough, sore throat, body aches, chills and fatigue. It is worth remembering that seasonal flu often poses a serious threat to public health: each year it kills 250,000 - 500,000 around the world. So far, most cases of swine flu around the world appear to be mild, albeit with diarrhoea more common than is found with seasonal flu. Even though the virus makes us sick, our immune systems can usually muster enough of a response so that the flu is rarely fatal for healthy people. Unlike past infections with swine flu, the current outbreak strain efficiently spreads from person to person. The incubation period of the disease is approximately one to seven days. The infectiousness period begins 1 day prior to symptoms and continues for seven days after symptoms commence. The diagnosed cases in the US represent only the tip of the iceberg. All cases outside of Mexico reported to date have consisted of mild influenza-like illness with the exception of the prominence of nausea, vomiting, and diarrhoea although now reports of deaths due to this disease are trickling in from other countries like UK, France and other...
countries. Other neighbouring Countries should be prepared to see severe cases with fulminant pneumonia given the experience in Mexico.

Global Threat?

On April 27, 2009 the WHO has raised the pandemic level to stage 4 indicating small clusters of localized human to human spread of the swine influenza. At the same time, the very nature of globalization puts us at greater risk. International air travel means that infections can spread very quickly. And while the WHO can prepare a new swine flu vaccine strain in fairly short order, we still use a laborious, decades-old process to manufacture vaccines, meaning it would take months before the pharmaceutical industry could produce its full capacity of doses - and even then, there wouldn't be enough for everyone on the planet.

Indeed, the greatest risk from a pandemic might not turn out to be from the swine flu virus itself - especially if it ends up being relatively mild - but the "collateral damage" if governments respond to the emergency by instituting border controls and disrupting world trade. Not only would the global recession worsen - a 2008 World Bank report estimated that a severe pandemic could reduce the world's GDP by 4.8%. In the 20th century we had two mild flu pandemics, in 1968 and 1957, and the severe "Spanish flu" pandemic of 1918, which killed an estimated 40 to 50 million people worldwide.

Of course, declaring a pandemic isn't a decision that should be taken lightly. For the WHO, phase 4 might trigger an attempt to keep the virus from spreading by instituting strict quarantines and blanketing infected areas with antivirals. But we appear to have missed the opportunity to contain the disease at its source since the virus is already crossing borders with ease. That would leave the WHO and individual countries to fall back on damage control, using antivirals and old-fashioned infection control - like closing schools, limiting public gatherings and even restricting travel - to slow the spread of the virus. But such efforts would likely inflict serious damage on an already faltering global economy - and the truth is, we don't know how well those methods will work.

So How Scared Should We Be?

That depends on whom you ask. Officials at the WHO have emphasized that while the swine flu situation is serious, they're responding with an abundance of precautions. And there are simple things that people can do to protect themselves, like practicing better hygiene (wash hands frequently and cover mouth and nose when sneezing) and staying away from public places or travelling if they feel sick. But the truth is that every outbreak is unpredictable, and there's a lot we don't know yet about the new swine flu. There hasn't been flu pandemic for more than a generation, and there hasn't been a truly virulent pandemic since long before the arrival of mass air transit. We're in terra incognito here. Panic would be counterproductive - especially if it results in knee-jerk reactions like closing international borders, which would only complicate the issue.

Diagnosis

The disease can be diagnosed by a blood test RT-PCR. This is required to confirm the diagnosis of swine flu. Viral culture can also be used to isolate the virus. The virus is susceptible to treatment with the neuraminidase inhibitors (Anti Virals), Oseltamivir and Zanamivir. It is resistant to amantadine and rimantidine. Standard treatment for seasonal flu should be employed (i.e. either zanamivir alone or oseltamivir in

combination with an adamantane to cover the possibility of resistant seasonal flu). The Centre of Disease Control, USA position is that “Empiric antiviral treatment should be considered for confirmed, probable or suspected cases of swine influenza A (H1N1) virus infection.” Antivirals are most effective when given within 48 hrs. of the symptom onset, but there is evidence of decreasing mortality and hospital stays with antiviral treatment started later than 48 hrs. It would be justified to not treat uncomplicated cases. In fact, the vast majority of the early US cases did not receive antiviral treatment and recovered uneventfully.

1. A confirmed case of swine influenza A (H1N1) virus infection is defined as a person with an acute febrile respiratory illness with laboratory confirmed swine influenza A (H1N1) virus infection at CDC by one or more of the following tests:
   - Real-time RT-PCR
   - Viral culture

2. A probable case of swine influenza A (H1N1) virus 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, or positive for influenza A by an influenza rapid test or an influenza immunofluorescence assay (IFA) plus meets criteria for a suspected case

3. A suspected case of swine influenza A (H1N1) virus 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 swine influenza A (H1N1) virus infection, or within 7 days of travel to communities either within the United States or internationally where there are one or more confirmed swine influenza A(H1N1) cases, or resides in a community where there are one or more confirmed swine influenza cases

**Antiviral Treatment**

**Confirmed, Probable and Suspected Cases of Swine-origin Influenza A (H1N1) Virus Infection**

Recommendations for use of antivirals may change as data on antiviral effectiveness, clinical spectrum of illness, adverse events from antiviral use, and antiviral susceptibility data become available.

Antiviral treatment should be considered for confirmed, probable 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.

Only RT-PCR or viral culture can confirm infection with swine-origin influenza A (H1N1) virus. The test performance of rapid antigen tests and immunofluorescence tests for detection of swine-origin influenza A (H1N1) virus is unknown. Persons who might have swine-origin influenza A (H1N1) virus and who test positive for influenza A using one of these tests should have confirmatory RT-PCR or viral culture testing to confirm the presence of swine-origin influenza A (H1N1) virus. A negative rapid antigen or immunofluorescence test cannot be used to rule out swine-origin influenza A (H1N1) virus infection.

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 is five...
days. Recommendations for use of antivirals may change as data on antiviral susceptibilities and effectiveness become available. Antiviral doses recommended for treatment of swine-origin influenza A (H1N1) virus infection in adults or children 1 year of age or older are the same as those recommended for seasonal influenza (Table 1). Oseltamivir use for children < 1 year old was recently approved by the U.S. Food and Drug Administration (FDA) under an Emergency Use Authorization (EUA), and dosing for these children is age-based.

Note: Areas that continue to have seasonal influenza activity, especially those with circulation of oseltamivir-resistant human A (H1N1) viruses, might prefer to use either zanamivir or a combination of oseltamivir and rimantadine or amantadine to provide adequate empiric treatment or chemoprophylaxis for patients who might have human influenza A (H1N1) infection.

**Antiviral Chemoprophylaxis**

For antiviral chemoprophylaxis of swine-origin influenza A (H1N1) virus infection, either oseltamivir or zanamivir are recommended. Duration of antiviral chemoprophylaxis post-exposure 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 (e.g., one day before until 7 days after the case’s onset of illness). If the contact occurred more than 7 days earlier, then 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.

Antiviral chemoprophylaxis with either oseltamivir or zanamivir is **recommended** for the following individuals:

1. Household close contacts who are at high-risk for complications of influenza (e.g., persons with certain chronic medical conditions, persons 65 or older, children younger than 5 years old, and pregnant women) of a confirmed or probable case.

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 during the case’s infectious period.

Antiviral chemoprophylaxis with either oseltamivir or zanamivir can be **considered** for the following:

1. Household close contacts who are at high-risk for complications of influenza (e.g., persons with certain chronic medical

**Table 1 : Swine-origin influenza antiviral medication dosing recommendations**

<table>
<thead>
<tr>
<th>Agent, group</th>
<th>Treatment</th>
<th>Chemoprophylaxis</th>
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<tbody>
<tr>
<td>Oseltamivir</td>
<td></td>
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<tr>
<td>Adults</td>
<td>75mg capsule twice per day for 5 days</td>
<td>75mg capsule once per day</td>
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<tr>
<td>Children (age, 12 months or older), weight:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>15 kg or less</td>
<td>60 mg per day divided into 2 doses</td>
<td>30 mg once per day</td>
</tr>
<tr>
<td>15–23 kg</td>
<td>90 mg per day divided into 2 doses</td>
<td>45 mg once per day</td>
</tr>
<tr>
<td>24–40 kg</td>
<td>120 mg per day divided into 2 doses</td>
<td>60 mg once per day</td>
</tr>
<tr>
<td>&gt;40 kg</td>
<td>150 mg per day divided into 2 doses</td>
<td>75 mg once per day</td>
</tr>
</tbody>
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(*Table extracted from Infectious Disease Society of America (IDSA) guidelines for seasonal influenza.*)
conditions, persons 65 years or older, children younger than 5 years old, and pregnant women) of a suspected case.

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 (e.g., persons with certain chronic medical conditions, persons 65 or older, and pregnant women) who are working in an area of the healthcare facility that contains patients with confirmed swine-origin influenza A (H1N1) cases, or who is caring for patients with any acute febrile respiratory illness.

4. Travellers to Mexico who are at high-risk for complications of influenza (e.g., persons with certain chronic medical conditions, persons 65 or older, children younger than 5 years old, and pregnant women). (Note: A travel warning is currently in effect indicating that nonessential travel to Mexico should be avoided).

5. First responders who are at high-risk for complications of influenza (e.g., persons with certain chronic medical conditions, persons 65 or older, children younger than 5 years old, and pregnant women) and who are working in areas with confirmed cases of swine-origin influenza A (H1N1) virus infection.

6. Oseltamivir (Tamiflu) is available in India and the Govt is procuring large stocks from Cipla, Roche and other companies to prepare for any emergency situation.

Bibliography


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**Chemotherapy, Bevacizumab, and Cetuximab in Metastatic Colorectal Cancer**

Capecitabine, oxaliplatin, and bevacizumab are standard treatment for metastatic colorectal cancer. This trial tested whether adding cetuximab to this combination is beneficial. The addition of cetuximab resulted not only in shorter progression-free survival than standard treatment but also in a reduced quality of life.