

Review

Swine flu: A threat to human health

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Influenza virus has caused major global epidemics since 1918. Although this commonly circulating viral strain is not virulent enough to cause mortality, but the re-assortment of viral genome to mutate at a very high rate can lead to the emergence of a highly virulent strain that may lead to next pandemics. Swine flu is an example of re-assortment of two viruses in pig causing thousands of deaths in the whole world especially in the United States of America by zoonotic jumps. This review addresses the biological and epidemiological aspects of swine flu virus and efforts to have a control on the virus globally.

Key words: Swine influenza, serotypes, pandemic, vaccine.

INTRODUCTION

Flu is an ancestrally old illness which started in birds initially and then slowly diversified to all warm blooded animals on earth in an era of thousands of years. Global population affected by annual flu is estimated to be 5 - 15%. Although most flu cases are mild but may cause severe illness in 3 - 5 million people and about 250,000 - 500,000 deaths worldwide. Mostly chronically unhealthy people, the old and high risk populations of infants face severe illness and deaths in industrial countries (EPI Fact Sheet, 2007). Though the forms of animals are different organisms but flu viruses can travel from one organism to another organism of different species. Humans are also included in this exchange of viruses. Re-assortment is the process through which a virus organizes its genetic material and thus a hybrid variety of super-virus comes into existence. Because this is a newly originated form so there is no innate or adaptive immunity present and flu spreads effectively and easily. Swine flu is a respiratory disease caused by a reassortant virus and has elements

of virus found in pigs. Swine flu virus acts similar to the Spanish flu, 1918, which caused the death of 20 million people; swine flu is showing the same age related mortality. Swine flu caused a pandemic flu outbreak by spreading from human to human worldwide. Because it is caused by a re-assortant virus so no one has immunity against this virus and is at risk of being caught by flu. So not only children, older people and diseased persons but also healthy people are at risk. Swine flu virus is made up of tiny droplets and can spread through so many ways.

Epidemiology

The key thing is going to be the epidemiology. Swine flu virus is a "reassortant virus" containing genes from a number of sources. Though the swine flu virus is specie specific but it can easily cross the specie barrier and zoonotic jumps were seen in swine flu virus from pigs to humans. Once in humans, it can spread in whole population with ease. Normally when virus jumps from one species to another, it gets ill- adapted due to its inability to multiply and spread in the foreign territory. But swine flu virus got well adapted to humans, enabling it to transmit efficiently from one person to the next. Swine flu infection transmits to humans through pigs and then human-to-human transmission is possible but spread is

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Abbreviations: SARS, Severe acute respiratory syndrome; CDC, Centre of Disease Control; WHO, World Health Organization; DHS, Department of Homeland Security; FDA, Federal Drug Administration.

Table 1. Pandemics of 20th century due to influenza virus.

Pandemic due to flu virus and causative strain	Prototype strain	Subtype	Infected people	Death rate	Case fatality rate
Spanish flu	A/FM1/47	H1N1 (Yu-Chia et al., 2006; Li 2008)	0.5-1 billion infected	20-100 million (WHO, 2005; Knobler et al., 2005; Patterson et al., 1991)	>2.5% (Taubenberger et al., 2006)
Asian flu	A/Singapore/57	H2N2 (Yu-Chia et al., 2006)		2 million (WHO, 2005)	<0.1% (Taubenberger et al., 2006)
Hong Kong flu	A/Hong Kong/68	H3N2 (Yu-Chia et al., 2006)		1 million (WHO, 2005)	<0.1% (Taubenberger et al., 2006)
Seasonal flu		Mainly A/ H3N2, A/H1N1 and B	(5-15%) 340 million - 1 billion (WHO, 2009)	250,000-500,000/year (WHO, 2003)	<0.05% (Taubenberger et al., 2006)
Russian flu	A/USSR/77	H1N1			

limited to close contacts or closed groups of people. According to the working party report of UK Government in 2000, "There's something like 500,000 people airborne around planet Earth at any instant in time". This shows the potential of swine flu virus to spread far and wide very quickly and can lead to a pandemic. Swine flu outbreak occurs in pigs in autumn and in winter in temperate zones. Disease is considered as endemic. Sporadic human infections and outbreaks are occasionally reported.

GLOBAL PANDEMICS OF 20TH CENTURY DUE TO INFLUENZA VIRUS

Three major global epidemics of the 20th century have been caused by Influenza A virus, the Spanish flu in 1918 - 1919, the Asian Flu in 1956 - 1958 and the Hong Kong flu in 1968 - 1969 by undergoing major genetic changes for which population did not poses significant immunity [WHO Fact Sheet; Kilbourne, 2006]. Over the past century several pandemic threats have been caused by H1N1 subtype, which include the 1947 pseudo-pandemic, swine flu outbreak 1976 and Russian flu 1977 [Kilbourne ED, 2006]. The SARS epidemic by SARS coronavirus in South East Asia further increased the level of alerts. Then the advent of H5N1 bird flu outbreaks further increased the level of preparedness though the strains have limited human-to-human transmission ability [Yu-Chia et al., 2006; Beigel et al., 2005]. Table 1 shows the effect of Influenza virus on people in 20th century.

SWINE FLU

Swine flu, a global outbreak took its origin from a large pig farm in Mexican town of La Gloria in Veracruz State with evidence that Mexico was already in midst of an epidemic for months before the outbreak was recognized. It was first detected in Mexico City on March 18, 2009 (Kilbourne, 2006). This new strain was first diagnosed in two children, having no contact with pigs, by the CDC, first on April 14, 2009 in San Diego County, California and a few days later in near by Imperial County, California (New York Times, 2009), which was not identified as a new strain in Mexico until April 24, 2009 (Morb Mortal Wkly Rep, 2009). WHO has been notified of swine flu cases from the United States and Spain. The government closed down most of the private and public offices and facilities of Mexico City to stop the spread of disease. WHO declared it as pandemic in early June and noticed the moderate severity of disease. From Mexico the virus spread with un-plecedented speed to Southern hemisphere and less developed countries. Outbreaks in North America, South America, Europe (including the United Kingdom, Italy and Sweden), Africa (Kenya), and in parts of the Eastern Asia including China and Japan has also been reported.

Swine flu is a highly contagious acute respiratory disease of pigs, caused by Swine Influenza A Virus, referred to as the novel H1N1. The most common subtype is H1N1 in case of swine flu but other serotypes e.g. H1N2, H3N1, H3N2 are also found circulating in pigs. It is thought that H3N2 strain was originally introduced into the

Table 2. Various techniques used for the laboratory diagnosis of swine influenza.

Procedure	Influenza type detected	Acceptable specimen	Time for results (h)
Real time PCR	A	Naso pharyngeal (NP) swab, throat swab, nasal wash, bronchial wash, nasal aspirate, sputum	2
Antigen detection ELISA	A	Naso pharyngeal (NP) swab, throat swab, nasal wash, bronchial wash, nasal aspirate, sputum	2 - 3

pigs by humans [News Report, 2009]. Swine flu virus spreads by direct or indirect contact among pigs by aerosols and remains asymptomatic there. High morbidity and low fertility rate is observed in case of swine flu.

SYMPTOMS

Swine flu shows clinical symptoms similar to seasonal flu and acute upper respiratory tract infection. The extent of this disease in humans is still unknown due to the escape of mild or asymptomatic case from recognition. An algorithm has been drawn up by the Health Protection Agency in the UK as to how they intend to assess the people suffering with swine flu. Geography is the first point on the algorithm according to which disease activity is seen in people coming from the same area. This obviously includes parts of the US but chiefly Mexico.

The US Centres for Disease Control and Prevention (CDC) noted that although the virus was very serious but the world wide cases were usually mild. CDC noted that the hospitalizations and deaths had been of persons that had underlying weekend immune system conditions, heart diseases, asthma, diabetes or obesity (Pakspectator, 2009). According to symptom algorithm it is a temperature of 38 degrees or a history of a temperature of 38 degree not only respiratory symptoms e.g. runny nose or a headache, fever, cough, sore throat, body aches, chills, fatigue, but also diarrhea and vomiting have been observed in some cases. Emergency warning signs in children and adults are thus highlighted.

In children

Fever with rash, fast breathing or breathing trouble, bluish skin color, not drinking enough fluids, unbearable irritability in children, not waking up or interacting, flu-like symptoms improve but return with fever and cough.

In adults

Shortness or difficulty in breathing, Pressure or pain in abdomen or chest, sudden dizziness, confusion, persistent or severe breathing, flu-like symptoms improve but

return with fever and cough (CDC, 2009).

VULNERABLE GROUP OF PEOPLE

Vulnerable group of people includes pregnant women, care takers of less than 6 months old infants, health care workers, adults with Asthma and diabetes and people with immune-compromised systems. In a worst case scenario, 40% of the workforce are estimated by CDC might be unable to work at the peak of pandemic (Los Angeles Times, 2009).

SPREAD OF SWINE FLU VIRUS

The actual transmission is from pig to pig but swine flu virus can also jump from pig to human and once in human, it can spread from human to human very easily through coughing, sneezing, touching nose, mouth or contaminated surfaces. Currently H1N1 flu has been mild for most people; however it should not disregard the epidemic mild as is expected to come back and spread. Everyone should be vaccinated against swine flu; however the vaccine will become available in batches and the entire population cannot be vaccinated at once. Table 2 shows the various techniques used in the laboratory for the diagnosis of swine influenza.

Global spread of swine flu

Until 16th April, 2010, worldwide more than 209 countries and overseas territories or communities have reported laboratory confirmed cases of pandemic influenza H1N1 2009, including at least 17,798 deaths. Table 3 describes the deaths caused by swine flu in the world.

Swine flu in Pakistan

In Pakistan, National Centre of Excellence in Molecular Biology has detected 3 cases out of 77 suspects while Khan Laboratory Multan has detected 3 cases out of 7 suspects. Total confirmed cases detected, using real-time PCR on WHO recommended kit, are 6 out of 84 suspects and out of these only 2 deaths have been reported until 16th April, 2010 (Idrees, 2010).

Table 3. Deaths caused by swine flu in the world.

Region	Deaths*
WHO regional office for Africa (AFRO)	168
WHO regional office for the Americas (AMRO)	At least 8274
WHO regional office for the Eastern Mediterranean (EMRO) **	1019
WHO regional office for Europe (EURO)	At least 4776
WHO regional office for South-East Asia (SEARO)	1757
WHO regional office for the Western Pacific (WPRO)	1804
Total*	At least 17798

*The reported number of fatal cases is an under representation of the actual numbers as many deaths are never tested or recognized as influenza related. **No update since 7 March 2010 [Pandemic (H1N1) 2009, 2010].

PREVENTION AND CURE

Vaccination

There are generally two kinds of vaccines, 1) Inactivated virus vaccine and; 2) Live attenuated vaccine (LAIV). In August 2009, no vaccine was thought to be available before the end of 2009 by WHO. Influenza virus changes quickly and it was thought that if virus mutated further then it could be more virulent and less susceptible to any new vaccine. When WHO declared the new H1N1 swine flu as the first pandemic of the 21st century on June 12th, a day after this declaration, Novartis AG (Swiss Pharmaceutical Company) announced the successful production of first batch of swine flu vaccine that was ready for sale in October, 2009.

Vaccination planning

More than 30 countries have asked Novartis to supply them with a swine flu vaccine. According to WHO several other drug makers have vaccine approved and ready for sale since September 2009 and CDC has already developed a vaccination plan.

Who should be vaccinated first?

The Public Health Agencies should work on priority list, deciding where the first batches should go. Several articles have been published showing that, unlike seasonal flu, the new H1N1 flu strains attack younger people and new pandemic strain tend to be more deadly in younger patients as S-OIV infection can cause severe acute respiratory distress syndrome and death in young to middle aged (Rogelio et al, 2009; Chowell et al., 2009; MMWR, 2009). The descendants of the 1918 flu have genetically modified themselves to be better able to survive and spread (CDC, 2009; MMWR, 2009). Therefore young people should be vaccinated first when a vaccine

becomes available. It would protect not only them, but them, but also unvaccinated adults.

Second group on priority should be health workers as they need to be protected from infection by the virus. According to the morbidity and mortality weekly report a sample of 26 health-care workers found that half became infected while at work (CDC, 2010). Next priority should be given to countries where the infection is more severe such as Mexico. Patients with chronic obstructive pulmonary disease, disease of the heart, and other parts of the body should be put on vaccination list before get vaccinate the whole population.

Antiviral medications

CDC has issued recommendations for clinicians on the use of antiviral medications for the prevention and treatment of swine flu. There are two classes of medicines available which are effectively used in some countries for the prevention and treatment of the disease, 1) Adamantanaes (amantadine and remantadine), and inhibitors of influenza neuraminidase (oseltamivir and zanamivir). Swine flu virus developed resistance against amantadine and remantadine but are sensitive to oseltamivir and zanamivir. There are insufficient recommendations on the use of antivirals in the treatment and prevention of swine flu virus infection. Based on virus' susceptibility profile national and local authorities are recommending to use oseltamivir and zanamivir for the treatment and prevention of disease (CDC, 2010). FDA has authorized emergency use of Oseltamivir (Tamiflu ®) and Zanamivir (Ralenza®) under certain circumstances not included in FDA-approved uses or outside the FDA-approved uses in response to the declaration of public health emergency involving 2009 H1N1 influenza A virus made by Secretary of Health and Human Services on April 26, 2009 (Pan American Health Organization, 2009). In addition, FDA has recently issued intravenous drug (Paramivir) for the treatment of swine flu in certain hospitalized adults and pediatric patients.

Other preventive measures

First prevention is to keep the infected children at home. Children showing flu symptoms should be monitored; they may not have swine flu but can develop it. Home treatment remedies including adequate liquid intake and rest, soup to ease congestion, aspirin intake for instance and antiviral drugs may help in the treatment of infection.

An updated guidance for employers of all sizes was developed by the US Department of Health and Human Services (HHS) and the Centres for Disease Control and Prevention (CDC) with input from the US Department of Homeland Security (DHS) to use in response to 2009 H1N1 flu. To slow down the spread of infection, air line passengers in Asia and other countries were quarantined with flu symptoms while some countries pre-screened passengers.

Disease can also be prevented by having no contact with pigs. Initial screening and then activating various molecular tests, using tests that can detect the genetic material of the virus are seen to be useful for the early diagnosis of swine flu. Swine flu virus can be killed by cooking the pig meat at 70°C and not transmitted through properly cooked pig meat (Press release, 2009). So properly cooked pig meat is safe to eat (WHO, 2009). People getting flu are recommended to stay at home from work or school and to avoid crowds to avoid spread of virus further. Facial masks are of little use and may benefit in case of close contact with infected people but can't replace other precautions because they are not designed to filter viruses and other biological agents (Mayo Clinic, 2009). Swine flu can be prevented by proper hand washing, balanced diet with fresh fruits and vegetables, whole grains and lean protein, sufficient sleep, regular exercise and avoiding crowds.

IS THE SWINE FLU A LARGE MEDICAL SCANDAL OF 21ST CENTURY?

It is said that swine flu is a large medical scandal of 21st century. Whether it is true or not, this is a contradictory matter. The purpose of this article is just to provide information to the readers.

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