

# Public health, preparedness and the World Health Organization response to swine flu in 2009

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From March 1918 to June 1920, an influenza pandemic swept the world, spreading among the Inuit tribes in the Arctic and to remote Pacific Islanders, killing over 10 million people in the Indian subcontinent. It is estimated that about one in three people was infected and that between 50 and 100 million people died worldwide. At the start of the epidemic, the medical profession believed that influenza was caused by Pfeiffer's bacillus, but by the end, they were convinced that this was no bacterial disease, but a form of respiratory infection spread by secretions, spitting, coughs and sneezes. There was no cure and supportive therapies were limited, though quacks abounded and recommended strange potions to prevent disease. Unlike the seasonal flu, this new version, or "Spanish flu," killed mainly young people, with between 2% and 20% of those infected dying. Bodies were buried without coffins in mass graves because there were not enough coffin makers or grave diggers to cope with the number of deaths. By some estimates, 3-6% of the world's population died in two years. In today's world, that would mean wiping out the entire population of North America.

With no specific therapy, how did the epidemic stop? It is believed, but not proven, that the virus may have mutated to a less virulent form, or that the number of susceptible individuals declined to a point where transmission of the virus could no longer continue at high rates. Studies using tissue from bodies buried in permafrost in Alaska showed over 80 years later that the 1918 flu pandemic was caused by an H1N1 virus that probably resulted in a cytokine storm, causing severe disease and death in susceptible individuals (1).

In 2009, another H1N1 virus emerged in Mexico, again causing disease in younger individuals, and spreading rapidly to neighbouring countries. The virus was first officially recognised in April 2009 in Veracruz, Mexico and spread within a few weeks to the United States of America. Initially, each case was reported and counts maintained of persons affected. Persons rapidly became states and then countries, and in June 2009, most countries stopped counting as the World Health Organization (WHO) issued a statement declaring the influenza epidemic, now known as "swine flu," a pandemic (2). By this stage, intensive efforts by scientists applying genome sequencing and analysis showed that the virus was a new variant of H1N1, a triple reassortant virus which had further combined with a Eurasian pig flu virus to result in a virus with a shuffled set of swine, human and avian sequences.

From seasonal influenza, we know well that influenza viruses change their genetic code rapidly enough for new vaccines

to be made each year in most developed countries, so what was so special about this virus to induce a state of near panic? With all infectious diseases, the two key factors that determine how much damage is done are transmissibility, or the ability to spread, and virulence, or the ability to cause severe disease. A disease that is highly transmissible, like the common cold, spreads rapidly but is not considered an epidemic or pandemic because it is not a serious illness. It is annoying at most, and recovery is usually spontaneous. A disease that causes severe damage is much more of a concern. For example, gram negative septicaemia frequently results in death even when appropriate antibiotic treatment is attempted. But this is not considered an epidemic or a pandemic because of the low transmissibility of this infectious condition.

So how does the WHO decide that influenza has become a pandemic? The WHO uses a six stage classification going from Phase 1 when no viruses circulating in animals have caused disease in humans, to Phase 2 where an animal virus causes disease in humans, to Phase 3 when animal or animal-human viruses cause small clusters of disease, but without human to human transmission, to Phase 4 where human to human transmission takes place in community-level outbreaks, to phase 5 where at least two countries in a WHO region are affected, and phase 6 where at least three countries in at least two WHO regions are affected (3). The purpose of this classification is for countries to be able to use a structure for communication with their own and world bodies, for organisation of response and for implementation of control and mitigation measures. Following this classification, the WHO responded appropriately in declaring the H1N1 outbreak a pandemic by June.

This resulted in measures similar to and beyond those taken for the Severe Acute Respiratory Syndrome (SARS) in 2003. SARS had appeared in southern China by February 2003, and was an atypical pneumonia that was highly transmissible and had about 10% overall mortality, with highest rates in the elderly. The ease with which SARS spread and the reported high mortality resulted in measures such as airport screening of passengers, contact tracing and quarantine. Very strict infection control and barrier nursing methods were adhered to in hospitals, particularly because of the early publicity surrounding transmission to healthcare personnel (4). With these measures in place, the incidence of SARS decreased rapidly and the epidemic ended by June 2003. As with SARS, airport screening, contact tracing and quarantine were introduced for passengers arriving from affected countries in

almost all parts of the world, but it rapidly became clear that although the initial cases of H1N1 in each country may have been from travellers, the increasing count of cases and the lack of travel history showed that H1N1 very rapidly established domestic transmission in many parts of the world.

In a few months, swine flu had overtaken seasonal influenza strains, and public health practitioners were engaged in both decision making regarding the use or futility of control measures and the evaluation of excess morbidity of H1N1 disease. All through this period, media reports recorded each case, trumpeted each death and conducted their own investigations into the adequacy of diagnostic testing, monitoring of new cases and medical management of the disease and its complications, as well as the limited supplies of anti-viral drugs. As children were reported positive, schools were closed, neighbourhoods shunned families of quarantined residents and hospitals worried about their ability to cope with increasing patient loads. All through this period, there were epidemiologists and others saying that the instituted control measures were of limited use and that the epidemic should be allowed to take its course, so that it would settle rapidly into a similar pattern as seasonal flu.

Within a few months, this appeared to be happening, and by January 2010, Dr Margaret Chan of the WHO announced that the peak appeared to be over in the northern hemisphere but vigilance needed to be maintained in the southern hemisphere where winter was yet to come. Shortly after the announcement, health professionals and the public began to ask whether the labelling of the H1N1 outbreak had been appropriate, whether the management by the WHO had led to unnecessary panic and how such situations should be handled in the future. There was also a perception that the threat of disease had been exaggerated by pharmaceutical companies hoping to make a profit on anti-viral drugs and vaccines. This has now led to a wider discussion on the issues of conflict of interest, and the relationships of experts advising the WHO with pharmaceutical companies (5).

From the categorisation of phases by the WHO, the H1N1 outbreak was called a pandemic when it fit the definition. However, the response of screening, contact tracing, the use of oseltamivir or zanamivir, social distancing, hand hygiene and quarantining may have delayed, but did not succeed in limiting, spread of disease, resulting in a use of resources that is now being deemed wasteful.

Certainly, during the early phase, governments and individuals were engaged in a desperate scramble for drugs and vaccines, and predictions were being made that people were going to get sick and die because of unavailability and stock-piling by hoarders. As drug and vaccine companies ramped up production, their products sold quickly, with the result that most major vaccine manufacturers began reporting substantially increased profits in late 2009 and 2010 (6).

It can be argued that the WHO was basing its actions on a plan that had been laid down based on the experience with SARS

and avian influenza caused by H5N1, both of which result in high mortality, and in the case of H1N1, it was not clear initially what the clinical spectrum of disease was going to be. To take an example from another recent natural phenomenon, when a volcano erupted and governments closed air space resulting in 750,000 stranded passengers, the pressure built up rapidly. Airlines lost millions of dollars a day and began to ask, "Isn't this an over-reaction?" Opposition parties in affected countries called the incumbent government over-cautious and accused them of actions leading to significant economic losses.

The reactions would be expected to be similar in any potential disaster that does not happen, or with any response that changes routine practices or uses significant resources. The WHO applied its experience to a situation that did not turn out as severe as expected because the virus spread more rapidly and caused less excess morbidity than anticipated. A recent study in *PLoS Currents: Influenza* based on an estimation of years of life lost (YLL) states that the 2009 epidemic resulted in a much lower mean age of mortality with the lower end of their YLL estimate comparable to the estimate for an H3N2-dominated, or more severe flu season, while the upper end is greater than that for the 1968 pandemic (7). Given that "swine flu" has been seen before in the 20th Century, resulting in the pandemic of 1918 and outbreaks in 1976, and given that the entire genome of the 2009 H1N1 virus was sequenced by June 2009, was it really possible to have handled the outbreak differently? The revised International Health Regulations (IHR) came into force in 2007, and the pandemic H1N1 is the first public health emergency of international concern since then. The IHR played a central role in the global response to the pandemic and in April 2010, an external review process was initiated to investigate the global handling of the H1N1 pandemic and to make recommendations for the future (8).

Today we have sophisticated methods of diagnosis, the ability to rapidly characterise new infectious agents using genomic sequencing, and the potential to use these tools to make vaccines, but we have limited availability of effective anti-viral drugs. In hindsight it is always possible to have 20:20 vision, but in the throes of an evolving situation, it is difficult to make a call that is the perfect response. All we can hope for is to be aware of the circumstances that influence decision making, particularly those driven by media and commerce, to learn from history and not repeat it.

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