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Pandemic Influenza

Publication No. 2004-57-E
Revised 7 July 2015

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Ce document est également publié en français.

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PANDEMIC INFLUENZA

1 INTRODUCTION

On 11 June 2009 the World Health Organization declared the first global influenza (flu) pandemic since 1968. The virus responsible for the pandemic was of swine origin, but was found to contain genes from both avian and human influenza viruses. Until the appearance of this new virus in early 2009, the persistence of “avian” flu in Asian countries over the previous few years, and its limited spread to humans, had initiated widespread speculation that it could spark the next flu pandemic among humans.

A pandemic is an outbreak of a specific illness in multiple areas covering a vast geographic area. This paper will describe flu viruses and the flu pandemics that have afflicted humankind, and discuss the plans, both Canadian and international, for pandemic preparedness.

2 INFLUENZA VIRUSES AND THE HUMAN IMMUNE RESPONSE¹

Influenza (flu) is caused by viruses that infect the respiratory and/or gastrointestinal tract of mammals and birds. Compared with most other viral respiratory infections, such as the common cold, influenza infection often causes a more severe illness. Typical symptoms of the flu include fever, cough, sore throat, runny or stuffy nose, headache, muscle aches, and often extreme fatigue.²

Viruses are unique organisms that cannot be clearly categorized as either living or non-living but are generally considered to be non-living. They can reproduce only by infecting another organism, attaching to and injecting their own genetic material into the host's cell. The host's genetic replication machinery is then “hijacked” to produce multiple copies of the different viral components, which are repackaged as intact viruses that then leave the cell and go on to infect more host cells.

The flu virus contains RNA (ribonucleic acid) as its genetic material (rather than deoxyribonucleic acid, or DNA, found in all other forms of life) and can be divided into types A, B and C, based on protein differences. Only types A and B affect humans. While Type A influenza virus affects both birds and mammals, including humans, and can mutate easily, type B affects only humans. Both Type A and B flu viruses are associated with significant illness and death in humans.

Type A flu viruses are known to include several subtypes. These subtypes relate to differences in surface proteins (proteins on the virus's external surface). Surface proteins are the principal target of the immune response. The subtype names relate to the two surface proteins that vary from one subtype to the next: “H” refers to the protein hemagglutinin and “N” refers to the protein neuraminidase. No subtypes of Type B influenza virus are known.

When exposed to a virus, our immune system responds by producing antibodies to the two surface proteins. An effective response would result in the removal of the virus from our bodies. In order to survive, viruses must be able to avoid being destroyed by antibodies, and this is accomplished by two mutation mechanisms that bring about changes to the surface proteins. One type of mutation, called antigenic drift, introduces very small changes into the surface proteins; many of these changes do not affect the immune response. This type of mutation is sufficiently slow that seasonal flu vaccines can provide some degree of protection. However, the second type of mutation, called antigenic shift, introduces large changes in the viral proteins and may also occur when a virus infects a different species, usually pigs. These large mutations happen only in type A flu viruses and pose the greatest risk for human flu pandemics.

3 AN OVERVIEW OF HUMAN FLU PANDEMICS

As many as 20 flu pandemics may have occurred in the past 250 years; three of them occurred in the 20th century. The most notorious of the three, as it was the most deadly, was the 1918 “Spanish Flu.” The virus that caused it was an H1N1 subtype, and estimates place the death toll between 20 and 40 million people worldwide, with 30,000–50,000 in Canada alone. In 1957, an outbreak of an H2N2 subtype in southern China, dubbed “the Asian flu,” quickly spread around the globe. It was the first pandemic for which a vaccine was prepared. The third pandemic of the 20th century, the 1968 “Hong Kong flu,” was caused by an H3N2 subtype. Both the Asian and Hong Kong pandemics were substantially less deadly than the Spanish; each caused an estimated 1 million deaths worldwide.³

Some experts expected the next human flu pandemic to evolve from an avian virus of the H5N1 subtype that had caused a persistent outbreak among poultry in Asia toward the end of the 20th century and into the 21st century.⁴ The strain has infected humans from time to time over the last 20 years, but these infections largely resulted from contact with infected poultry. The countries most affected have been Egypt and Indonesia where most of the total 440 human deaths occurred. No sustained human-to-human transmission has yet been detected.⁵

In 2009, a new strain of subtype H1N1 of swine origin was detected in two children in California. The unique genetic sequence of the new strain permitted easy transmission of the virus among people and also significant illness. H1N1 spread quickly around the world. By the end of June 2009, over 77,000 cases had been confirmed in 116 countries – within two weeks of the World Health Organization’s announcing a global influenza pandemic, the first pandemic in the 21st century. Canada confirmed 7,983 cases of H1N1 influenza, 538 of which required hospitalization. Twenty-five deaths⁶ occurred, despite urgent and successful efforts to develop a vaccine and provide vaccination to all Canadians who requested it.

4 THE CANADIAN PANDEMIC INFLUENZA PLAN

In December 2006, the Public Health Agency of Canada (PHAC) issued the “Canadian Pandemic Influenza Plan for the Health Sector” (the Plan).⁷ Several annexes to the Plan have been revised since that time. The Plan serves as an outline for planning, preparedness and response to pandemic influenza by different levels of government.

Canada’s first pandemic influenza plan was issued in 1988. It is periodically updated in light of research, experiences in Canada and experiences in other countries with disease outbreaks. The Plan is based on basic principles of public health and emergency response. Its goals are to minimize illness and death while also minimizing social disruption, efforts that require collaboration and coordination of activities by all levels of government.

The Plan employs the “pandemic phases” defined in the World Health Organization’s (WHO) pandemic plan, and specifies the response component, the actions required and the levels of government involved for each phase. The Plan involves three periods of response, as defined below⁸:

1. Interpandemic period – phases 1 and 2 (no human infection, possible animal outbreaks);
2. Pandemic alert period – phases 3, 4 and 5 (limited human infections and clusters of outbreaks, transmission of animal infection to humans); and
3. Pandemic period – phase 6 (sustained transmission in the general population).

Following phase 6, a post-pandemic period, or recovery phase, overlaps with the return to the interpandemic period. The WHO plan refers to this phase as a transition phase.

For each phase, the plan describes the extent to which surveillance, vaccine programs, antiviral medications, health services, public health measures and communications must be implemented as well as the extent to which each level of government has a role in the listed activities.

National surveillance is carried out by PHAC under its FluWatch program, which collects information through a network of labs, hospitals, doctor’s offices and provincial and territorial ministries of health. FluWatch reports are produced weekly or bi-weekly throughout the year. Surveillance also includes PHAC’s ongoing contact with the WHO, which informs the agency of any possible global outbreaks.⁹

In addition, PHAC maintains the Global Public Health Intelligence Network (GPHIN), which is a secure, Internet-based early warning system that gathers preliminary reports of public health significance by monitoring global media sources on a real-time, 24/7 basis. Notifications about events that may have serious public health consequences are immediately forwarded to users. This system is not limited to influenza and can include other infectious diseases, incidents of contaminated food and water, bioterrorism and exposure to chemical and radio-nuclear agents, and natural disasters.¹⁰

PHAC's Centre for Emergency Preparedness and Response funds and maintains a national emergency strategic stockpile (NESS), which includes a central depot in Ottawa and eight other warehouses located across Canada. The NESS provides emergency supplies quickly to provinces and territories when requested, and a 24-hour response capability is maintained. The Agency manages the NESS by assessing and refurbishing stockpile units and distributing medical and pharmaceutical supplies at the request of provinces. The NESS contains hospital supplies ranging from beds and blankets to pharmaceuticals and antibiotics and includes several field (or mobile) medical units. The units can be deployed within 24 hours and set up in existing buildings such as schools and community centres.¹¹

Antiviral stocks are maintained in the NESS, as well as in the National Antiviral Stockpile that was established in 2004.¹² Generally speaking, vaccines cannot be stockpiled because they can be prepared only once a virus strain has emerged. Instead, Canada maintains a 10-year contract with a domestic manufacturing company to produce sufficient vaccine for all Canadians in the event of a pandemic.¹³

Canada's Pandemic Preparedness Plan was put into action during the 2009 H1N1 influenza pandemic. In fall 2010, the Standing Senate Committee on Social Affairs, Science and Technology undertook a study on the effectiveness of Canada's reaction to the pandemic. The report, entitled *Canada's Response to the 2009 H1N1 Influenza Pandemic*, was tabled in December 2010. Overall, Canada's response was found to be successful and the planning effectively reduced the impact of the virus. The report warned, however, that Canada's infrastructure could have been overwhelmed if the H1N1 virus had been more infectious or if it had produced illness in a broader population base.¹⁴

5 WORLD HEALTH ORGANIZATION'S INFLUENZA PANDEMIC PREPAREDNESS AND RESPONSE

The WHO Global Influenza Surveillance and Response System (GISRS) is used to help WHO recommend the content of the influenza vaccine for the upcoming influenza season. It also serves as a global alert mechanism for the emergence of influenza viruses with pandemic potential. The network, in its original form, was created in 1952 to establish a system of laboratories that would enable the WHO to advise member states as to what influenza control measures are useful, useless or harmful.¹⁵

The components of the WHO GISRS are:

- National Influenza Centres (NICs) – about 150 in 112 countries, including Canada – which collect clinical samples from patients with influenza-like illness;
- WHO Collaborating Centres and Essential Regulatory Laboratories, which perform genetic analyses of the samples submitted by NICs;
- FluNet, which is a virological surveillance database used to track the movement of influenza viruses and interpret epidemiological data;

- WHO H5 Reference Laboratories, which are an ad hoc component of the GISRS that collect, monitor and analyze H5N1 and other subtypes with the potential to infect humans;
- WHO External Quality Assessment Project, which monitors the performance of NICs and improves their capacity, and promotes good standards of practice; and
- the WHO itself, which coordinates all information.

The WHO has issued influenza pandemic preparedness guidance since 1999. The most recent WHO pandemic plan, issued in 2013, is entitled *Pandemic Influenza Risk Management*.¹⁶ This version differs from earlier versions in that the severity of disease, and not simply the ease and level of viral transmission, is taken into account when designing appropriate responses. This change resulted from the discussion that arose following the spread of H1N1 in 2009 about the prudence and effectiveness of declaring a global influenza pandemic in which a relatively low proportion of infected individuals required hospitalization and which had a low mortality rate.

Other roles carried out by the WHO in the event of an influenza pandemic include maintaining worldwide surveillance and disseminating information regarding flu outbreaks, and emphasizing the need for a coordinated response with respect to vaccine production and the importance of stockpiling antivirals and vaccines.

The WHO plan uses a “whole of society” approach that clarifies the roles of various stakeholders – namely, national governments, health sectors, non-health sectors and individuals – in mitigating the effects of a possible pandemic. The plan is intended to be used in conjunction with an array of other relevant WHO materials, including the *WHO Checklist for Influenza Pandemic Preparedness Planning*¹⁷ and *Pandemic Influenza Preparedness Framework*.¹⁸

6 CONCLUSION

The first influenza pandemic of the 21st century was declared in June 2009 by the World Health Organization, and gave countries – including Canada – a valuable opportunity to put their pandemic influenza plans to the test. As the threat of an influenza pandemic persists, because of the flu viruses’ ability to mutate and become highly infectious and deadly, work on pandemic preparedness will remain a priority for Canada and the rest of the world.

NOTES

1. N. J. Cox and K. Subbarao, “Global Epidemiology of Influenza: Past and Present,” *Annual Review of Medicine*, Vol. 51, 2000, pp. 407–421; and David Earn et al., “Ecology and evolution of the flu,” *Trends in Ecology and Evolution*, Vol. 17, No. 7, 2002, pp. 334–340.

2. Although nausea, vomiting, and diarrhea sometimes accompany influenza infection, especially in children, gastrointestinal symptoms such as those are rare (U.S. Centers for Disease Control and Prevention [CDC], "[Flu Symptoms & Severity](#)," *Influenza (Flu)*). The term "stomach flu" is sometimes used to describe gastrointestinal illnesses caused by other micro-organisms (U.S. CDC, "[Misconceptions about Seasonal Flu and Flu Vaccines](#)").
3. Cox and Subbarao (2000), pp. 412–413.
4. Arnold S. Monto, "The Threat of an Avian Influenza Pandemic," *New England Journal of Medicine*, Vol. 352, 2005, pp. 323–325.
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6. WHO, "[Pandemic \(H1N1\) 2009 – update 56](#)," 1 July 2009.
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9. PHAC, "[Influenza surveillance](#)."
10. PHAC, personal communication.
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13. PHAC, "Government of Canada Awards Contracts for the Supply of Influenza Vaccines," News release, 25 March 2011.
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16. WHO, "[Pandemic Influenza Risk Management – WHO Interim Guidance](#)," 2013.
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