



LIBRARY of PARLIAMENT
BIBLIOTHÈQUE du PARLEMENT

BACKGROUND PAPER



Influenza Pandemic

Publication No. 2004-57-E
Revised 24 July 2012

Sonya Norris
Norah Kielland

Social Affairs Division
Parliamentary Information and Research Service

Influenza Pandemic **(Background Paper)**

HTML and PDF versions of this publication are available on IntraParl (the parliamentary intranet) and on the Parliament of Canada website.

In the electronic versions, a number of the endnote entries contain hyperlinks to referenced resources.

Ce document est également publié en français.

Library of Parliament ***Background Papers*** provide in-depth studies of policy issues. They feature historical background, current information and references, and many anticipate the emergence of the issues they examine. They are prepared by the Parliamentary Information and Research Service, which carries out research for and provides information and analysis to parliamentarians and Senate and House of Commons committees and parliamentary associations in an objective, impartial manner.

CONTENTS

1	INTRODUCTION.....	1
2	THE FLU AND THE VIRUSES THAT CAUSE IT.....	1
3	HOW THE INFLUENZA VIRUS ELUDES OUR IMMUNE SYSTEM.....	2
4	INFLUENZA A VIRUS.....	3
5	PANDEMICS OF THE 20 TH CENTURY.....	3
5.1	The 1918 “Spanish Flu”.....	3
5.2	The 1957 Asian Flu.....	4
5.3	The 1968 Hong Kong Flu.....	4
6	THE “AVIAN” FLU.....	4
7	THE “SWINE” FLU.....	6
8	INTERVENTIONS.....	6
9	THE CANADIAN PANDEMIC INFLUENZA PLAN.....	7
10	WORLD HEALTH ORGANIZATION’S INFLUENZA PANDEMIC PREPAREDNESS AND RESPONSE.....	10
11	CONCLUSION.....	12
SELECTED BIBLIOGRAPHY		

INFLUENZA PANDEMIC

1 INTRODUCTION

On 11 June 2009 the World Health Organization declared the first global influenza pandemic since 1968. The virus responsible for the pandemic is of swine origin but also contains genes from 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 past few years, and its limited spread to humans, initiated widespread speculation that it could spark the next influenza (flu) pandemic among humans.

A pandemic is an outbreak of a specific illness in multiple areas covering a vast geographic area. This paper will examine the origins of the flu and describe some flu pandemics that have afflicted humankind in the past. It will describe the “avian” flu that has persisted for years, and also the “swine” flu that has spread to over one hundred countries worldwide. Finally, it will explore interventions for combating the flu as well as the plans, both Canadian and international, for pandemic preparedness.

2 THE FLU AND THE VIRUSES THAT CAUSE IT

Influenza, or 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. Although nausea, vomiting, and diarrhea sometimes accompany influenza infection, especially in children, gastrointestinal symptoms are rarely prominent. The term “stomach flu” is a misnomer that is sometimes used to describe gastrointestinal illnesses caused by other micro-organisms.

Viruses are unique organisms that cannot be clearly categorized as either living or non-living. They infect another organism by attaching to it 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 influenza 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 three main types (A, B, and C) based on differences within two of its major internal proteins. Type A influenza virus is found in a variety of birds and mammals and can mutate easily, while type B is confined to humans. Influenza virus types A and B are both associated with significant illness and death in humans. Type C does not appear to affect humans.

Influenza virus type A is further divided into subtypes based on membrane proteins (proteins on the virus's external surface). Surface proteins are significant, since they are the principal targets of the immune response. In type A, subtypes are distinguished by differences in the surface proteins hemagglutinin (HA) and neuraminidase (NA). HA is associated with the virus's affinity to bind to a host cell via a receptor in order to infect it, while NA is involved in the virus's escape back out of the host cell after infection. The notation HxNy is used to refer to the various subtypes. Subtypes are further divided into strains. Although there are 15 known HA subtypes and 9 NA subtypes of influenza virus type A, only two subtypes are currently circulating in humans: H1N1 and H3N2. Type B influenza virus has not been found to include different subtypes.

3 HOW THE INFLUENZA VIRUS ELUDES OUR IMMUNE SYSTEM

Based on descriptions of past epidemics and pandemics suggestive of influenza, humans have probably coexisted with flu viruses for at least 400 years. Viruses have been successful and continue to thrive because they can exist within some animals without causing illness and because they are often able to escape destruction by an animal's immune system. When exposed to a virus, our immune response includes the production of antibodies that help to remove, or clear, the virus from our bodies. In order for a virus to avoid being destroyed by antibodies, it must be able to keep a step ahead of the host's immune response. This is done through antigenic variation, meaning that spontaneous genetic mutations in the virus bring about variations in the cell surface proteins mentioned above that provoke the immune response. This variation is brought about in two ways: antigenic drift and antigenic shift.

Antigenic drift (the means by which variations in the seasonal flu virus are brought about) refers to small mutations in the genes for NA and HA that may or may not bring about a structural change in the protein. This is a slow and inefficient means to elude host immunity, and therefore the seasonal flu vaccine is believed to afford some degree of protection even if the specific strain of virus is different.

Antigenic shift, on the other hand, describes major antigenic change whereby a virus with a new protein is introduced into the human population. This can happen in two different ways. First, it may occur when a new virus results from reassortment, or mixing, of animal and human influenza viruses. For example, this could occur when a person who is already infected with a human flu virus is also infected with an avian virus. Within the human host, the viruses mix (reassort) and a new virus containing a combination of human and avian flu virus genes is produced. Second, antigenic shift may occur when an animal flu virus evolves over time and at some point is introduced into a human population. For example, a non-pathogenic (not producing sickness) avian virus could evolve slowly – over years or decades – in the bird population, totally isolated from any human exposure. At some point it could cross the species barrier to humans and cause illness. This second form of antigenic shift appears to be much rarer than the first. Both types of antigenic shift may also occur through an intermediate host, most often pigs. Antigenic shift occurs only among influenza A viruses, and poses a greater risk for human epidemics and pandemics

than does antigenic drift. This is because drift does not necessarily bring about a significant change in the viral protein structure, and therefore the host's existing antibodies may still be effective.

4 INFLUENZA A VIRUS

As indicated earlier, type A flu virus is found in birds and mammals, including humans. Birds, however, specifically shorebirds and waterfowl, appear to be the natural reservoir for influenza A virus. Birds infected with the viruses generally suffer no illness, although infrequently there may be flu-like symptoms. Infected birds excrete high levels of virus, and if excreted into bodies of water the virus may survive for several weeks. Other susceptible avian species, such as chickens or turkeys, may then become infected through contact with or by drinking the water. A seemingly harmless virus in waterfowl such as ducks and geese may cause significant illness, or death, in another avian species such as chickens. The avian flu type A H5N1, which caused concern in recent years, is harmless for ducks but is very pathogenic, or deadly, for chickens.

Reports of humans becoming infected with avian flu virus are rare, and such cross-species infections have proven very difficult to achieve under experimental conditions. This suggests that avian flu viruses are very limited in their ability to thrive in a human host. It has been the general consensus that an avian virus would have to acquire one or more genes from a human influenza A virus before it could effectively cross the species barrier. Because pigs can be infected with both avian and human influenza A viruses, it has been proposed that pigs may be the intermediate host required for the genetic reassortment needed before the virus can cross the species barrier and infect humans. The type A H1N1 virus which originated in pigs and became infectious to humans in early 2009 has been responsible for the first global influenza pandemic of the 21st century.

5 PANDEMICS OF THE 20TH CENTURY

As discussed above, the influenza virus outpaces the human immune response through antigenic shift. Three antigenic shifts in the 20th century produced pandemics, all of which have been described as being caused by type A viruses of avian origin. It has been estimated that there have been as many as 20 flu pandemics in the past 250 years.

5.1 THE 1918 “SPANISH FLU”

By the fall of 1918, Europeans had begun to refer to this outbreak as the “Spanish flu” probably because Spain, as a neutral country in World War I, had not imposed censorship of news about the disease that was sweeping many combatant countries. The most deadly of the recent pandemics, this flu killed between 20 and 40 million people worldwide, 30,000–50,000 in Canada alone.

There has been considerable controversy as to the geographic as well as viral origins of this pandemic. The virus that caused it was an H1N1 subtype. Biological samples kept from soldiers who died in the pandemic, as well as samples taken from bodies buried in the permafrost in Alaska of victims who were known to have died from the pandemic strain, have been recently analyzed and sequenced. All the genes within the responsible virus appear to be of avian origin. That is, there was no reassortment with human, or other animal, flu genes. This finding indicates that the H1N1 virus that produced the 1918 pandemic arose from the second, less common, type of antigenic shift described above: an animal virus that is transmitted to the human species, or another animal species, without any mixing with other viruses. Investigators believe that the virus was an avian strain that had evolved in isolation from the typical wild waterfowl influenza gene pool for some time. It then emerged into circulation among humans, probably via an animal host (as yet unknown, but most likely swine). Recent analysis of the 1918 influenza virus suggests that efficient person-to-person transmission depends on yet another gene that codes for a polymerase enzyme which, like the HA and NA genes, has been found to have several variations.

5.2 THE 1957 ASIAN FLU

As mentioned earlier, only two subtypes of influenza type A are currently circulating in the human population, H1N1 and H3N2. While the 1957 pandemic was caused by H2N2, it has not been isolated from any outbreaks since and is not believed to be in circulation any longer.

The outbreak first erupted in southern China in February 1957 and had spread worldwide by November of that year. The virus was first isolated in Japan in May 1957 and was found to possess distinctly different HA and NA antigens than the previously recognized H1N1 viruses. Almost 70,000 people died, and the mortality rate was especially high among children, at greater than 50%.

5.3 THE 1968 HONG KONG FLU

The virus responsible for this flu pandemic was isolated in Hong Kong in July 1968. Again, children were especially affected, with mortality rates as high as 40%. Genetic studies have established that the viruses responsible for the pandemics of 1957 and 1968 were both the products of antigenic shift through reassortment. H2N2, of the 1957 pandemic, is believed to have arisen through reassortment between an avian influenza A virus and a circulating human influenza A (H1N1) virus. The virus responsible for the 1968 pandemic was found to have the same NA as the previously circulating H2N2, but a new HA. The 1968 influenza type A H3N2 virus was a reassortment of a new avian influenza A and the circulating H2N2.

6 THE “AVIAN” FLU

The “avian” flu that is being monitored in Asia and the Middle East is type A subtype H5N1, which, as stated earlier, is not one of the subtypes known to be circulating in the human population.

In May 1997, H5N1 was first isolated from a three-year-old child in Hong Kong. Genetically similar influenza A H5N1 had been isolated from sick chickens on nearby farms in the same year. The child, therefore, was suspected to have become infected with a purely avian strain through infected chickens. Although there was no direct link between the sick child and these farms, the child's school kept chicks and ducklings that may have been obtained from neighbouring farms. Within six months, 17 more cases were identified; of the total of 18 people infected, 6 died. Studies revealed that, up to this time, all infections were poultry-to-human and not human-to-human. Closure of live bird markets and mass extermination of poultry and fowl in Hong Kong in December 1997 seemed to be successful in stopping the outbreak.

The strain did not re-emerge until 2003, when two family members in Hong Kong became infected and one died. It has not been determined how or where these infections originated. In 2004, 44 people became infected with H5N1, of whom 32 died. Most of these people had close contact with poultry, and there was little evidence of efficient person-to-person transmission. The virus continued to persist, and the number of countries affected grew over the next few years. According to the World Health Organization, human infections had been reported in 15 countries as of 6 July 2012, with a total of 607 human cases of H5N1 infection and 358 deaths.

The H5N1 virus subtype represents a concern for public health. In 2003, this subtype underwent certain changes that produced a new strain that may have increased pathogenicity. The so-called "Z strain" has spread to several countries in various animal species. The strain is characterized by pathogenicity in a broader range of animals than normally seen and by resistance to older antiviral drugs. Although transmission of this virus from birds to humans has been documented for most of the cases, human-to-human transmission has been demonstrated as probable in two cases. Therefore, because of the documented increase in the virus's pathogenicity in animals and humans, as well as its ability to be transmitted human-to-human, there is concern that H5N1 could be responsible for a future flu pandemic.

For the current avian H5N1 to spark another pandemic, several factors must converge. They include:

- the emergence of a new influenza A virus, i.e., a variant of the H5N1 subtype, arising from a major genetic change, such as an antigenic shift;
- efficient transmission of the virus from person to person; and
- a susceptible population with little or no immunity.

The first of these conditions could include a reassortment of the current avian virus with a human virus, which appears not to have happened yet. The persistence of this virus in Asia, however, leads many experts to speculate that this reassortment is likely to happen.

7 THE “SWINE” FLU

The conditions listed above were met in early 2009 – not by the H5N1 strain, but by a previously unknown H1N1 strain of swine origin. On 28 and 30 March 2009, two children in different areas of California became ill and sought medical attention. As a fortuitous result of their both being part of different trials, swabs were taken to test for the virus that had made them ill and were sent for typing to the Centers for Disease Control and Prevention (CDCP) in Atlanta. By mid-April 2009 CDCP confirmed both samples to be a novel swine-origin influenza A (H1N1) virus with a unique genetic sequence that had not previously been identified.

As required by the International Health Regulations, these cases were reported to the World Health Organization (WHO). In addition, CDCP notified state and local public health officials and enhanced surveillance was implemented. The Public Health Agency of Canada (PHAC) was also alerted, and on 24 April it issued a news release confirming its collaboration with officials in the United States as well as Mexico, where the disease had originated. On 26 April, PHAC announced the first confirmed cases of H1N1 in Canada: 2 in British Columbia and 4 in Nova Scotia. By the end of May the number of cases had risen to 1,336 with 2 confirmed deaths. As of 29 June there were 7,983 confirmed cases, 538 requiring hospitalization, and 25 deaths. H1N1 also spread quickly around the world, and by the end of June over 77,000 cases had been confirmed in 116 countries, more than doubling the confirmed cases from two weeks earlier when the WHO had raised the pandemic alert to level 6, a global influenza pandemic.

As of 2 July, efforts to define the most vulnerable population had proven difficult. It had been apparent from the outset that individuals over 60 years of age were not the most vulnerable – due, it is believed, to a latent immunity to other H1N1 strains which circulated decades ago. Early updates from public health officials suggested that those with underlying health conditions were most at risk; however, it has subsequently been reported that about half of those hospitalized were previously healthy. Although the virus normally causes only mild to moderate disease, officials urged caution and vigilance given the persistence of the virus well beyond the normal “flu season” and the chance that it could mutate and become more severe as the next influenza season begins.

PHAC has since developed a seasonal flu shot that protects against H1N1 and other flu virus strains, as H1N1 continues to circulate in low levels.

8 INTERVENTIONS

There is a certain level of optimism that future pandemics, while inevitable, may be controllable. The WHO and most developed countries have surveillance programs that will allow early detection of outbreaks. In the event of a pandemic, moreover, certain interventions can help reduce the spread or severity of the outbreak.

The first of these interventions is isolation. This measure was used very successfully during the outbreak of severe acute respiratory syndrome (SARS) in 2003. An

efficient surveillance and reporting system permits effective identification of infected individuals, who can be quarantined to prevent further spread. This is a critical step in limiting the spread of any communicable disease.

Medical interventions that are now available include vaccines and antiviral drugs. A vaccine for the flu was first tested in 1935 and has been recommended for general use since the 1960s. Because the virus evolves so rapidly, a new vaccine must be designed each year. The current vaccine used in most countries worldwide contains three inactivated virus types: a type B influenza and a recently circulating strain of each influenza type A H1N1 and H3N2. Although the vaccine designed (in advance) for a given flu season is unlikely to be an exact match for the type A strains that actually circulate, there is evidence that vaccination still offers some protection. However, because vaccines take at least three months to produce, they are of limited use at the outset of an outbreak. In the event that a new and virulent strain appeared in humans, the infection could spread significantly before a vaccine is made available. This has been observed in the H1N1 pandemic.

The other intervention that can be employed in the face of a flu outbreak is antiviral medication. Antivirals will likely be used as the first medical intervention in the event of a pandemic, given the time required to prepare a new vaccine. Currently, four antivirals are approved for use in fighting the flu. Two drugs are categorized as M2 inhibitors; these are amantadine and rimantadine. These drugs interfere with a viral protein called M2 and prevent activation of the viral genetic material. M2 inhibitors, however, are associated with significant side effects on the gastrointestinal and central nervous systems. The flu virus also seems to become quickly resistant to these drugs.

The second class of antivirals are NA inhibitors; these are zanamivir and oseltamivir. These drugs inhibit the action of NA and prevent the new virus from leaving an infected cell. In the Netherlands in 2003, an outbreak of an avian influenza type A H7N7 was effectively controlled with the use of oseltamivir. This antiviral drug has also been shown to be effective against H5N1. NA inhibitors have less severe side effects than the M2 inhibitors. Development of new anti-influenza drugs is an active area of research.

9 THE CANADIAN PANDEMIC INFLUENZA PLAN

In December 2006, Canada's federal-provincial/territorial Pandemic Influenza Committee issued its most recent plan entitled "Canadian Pandemic Influenza Plan for the Health Sector." The mandate of the Committee, which first convened in March 2002, is to provide advice, expertise and recommendations, liaison and other activities associated with all phases of a flu pandemic. The plan is meant as an outline for planning, preparedness and response to pandemic influenza by the different levels of government.

Canada has had a pandemic influenza plan since 1988. It is periodically updated in light of research, experience within 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. These aims can be realized only if the different levels of government are able to coordinate their activities.

The plan's December 2006 update employs the "pandemic phases" defined in the WHO's revised April 2005 pandemic plan, specifying the response component, the actions required and the levels of government involved for each phase. This revision involved renaming the phases to more accurately reflect changes in public health action and an increased emphasis on animal outbreaks, and to focus greater attention on the early phases when rapid intervention might contain or delay the spread of the virus to humans. The pandemic response is now separated into three periods of response, followed by a fourth recovery period, as defined below:

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

During the interpandemic period (phases 1 to 2), new emphasis is placed on addressing human health risks posed by animal outbreaks. The pandemic alert period (phases 3 to 5) now addresses the situation of the evolution or adaptation of a novel animal influenza virus with pandemic potential. It places greater emphasis on rapid intervention in an attempt to contain or delay the spread of a new influenza virus subtype in humans. Although it is uncertain if such "containment" measures would be effective or feasible, it is still useful to consider potential early interventions for planning purposes. A post-pandemic period, or recovery phase, is also discussed; this would be expected to occur following phase 6 (i.e., the pandemic period), after which there would be a return to the interpandemic period.

For each phase the plan describes surveillance, vaccine programs, antiviral medications, health services, emergency services, public health measures and communications. The plan describes in detail the actions required for each component and specifies, for each of those actions, which levels of government have a role.

The pandemic alert phases defined by the WHO reflect ease and level of transmission, rather than severity of disease. Considerable discussion arose following the appearance and 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 less than a 1% fatality rate. The WHO has entered into discussions regarding whether there should be a parallel alert system that reflects the disease severity. The WHO emphasized that the full picture of disease severity continued to evolve throughout the H1N1 outbreak. In addition, the influenza virus is constantly undergoing antigenic drift which can produce a change in disease severity in an easily propagating strain.

National surveillance is carried out by PHAC under “FluWatch.” The Viral Respiratory Diseases Section, within the Immunization and Respiratory Infections Division of PHAC’s Centre for Infectious Disease Prevention and Control (CIDPC), produces regular FluWatch reports, summarizing influenza surveillance activities in Canada. Reports are produced weekly during the influenza season (October to May) and biweekly during the off season (June to September). Influenza surveillance is a collaborative effort between provincial and territorial ministries of health, participating laboratories, The College of Family Physicians of Canada, sentinel physicians, and the CIDPC.

PHAC maintains contact with the WHO and is kept informed of any possible global outbreaks. Additionally, 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 but can include other infectious diseases, contaminated food and water, bioterrorism and exposure to chemical and radio-nuclear agents, and natural disasters.

PHAC’s Centre for Emergency Preparedness and Response funds and maintains a \$300-million national emergency stockpile system (NESS), which includes a central depot in Ottawa and eight other warehouses located across Canada, to provide emergency supplies quickly to provinces and territories when requested. 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. It includes 165 field (or mobile) hospitals, each with a 200-bed capacity. The units can be deployed within 24 hours to be set up in existing buildings such as schools and community centres.

Antiviral stocks have received much attention in discussions of pandemic preparedness. On 4 February 2005, the federal minister of health announced that the government would be establishing a National Antiviral Stockpile and securing sufficient oseltamivir, known by the trade name Tamiflu, to treat nearly 1 million Canadians. Since that time, the stockpile has been increased to 55 million doses, sufficient to treat about 5.5 million Canadians.

Although vaccine cannot be stockpiled for an influenza pandemic – it can be prepared only once the virus strain has emerged – Canada has taken two steps to improve our capacity to secure a vaccine supply in response to a pandemic. First, the federal government has secured a 10-year contract with a manufacturing company to produce sufficient vaccine for all Canadians in the event of a pandemic. Second, in the 2005 federal budget it dedicated \$34 million over five years for the development of a prototype vaccine that would help accelerate the production of such a vaccine, should it become necessary.

In 2010, the Evaluation Services Directorate, an internal but independent division of PHAC, conducted a joint evaluation of the response of PHAC and Health Canada to the H1N1 pandemic. The report, *Lessons Learned Review: Public Health Agency of Canada and Health Canada Response to the 2009 H1N1 Pandemic*, provided a general assessment of Canada's H1N1 pandemic response. While the response was found to be generally effective, the assessment identified areas that required further attention. Recommendations included improving federal/provincial/territorial collaboration and capacity regarding pandemic preparedness and response, continuing work regarding federal emergency management, and improving influenza risk communication strategies aimed at various types of audiences. Soon after *Lessons Learned* was published, PHAC responded to these recommendations and released an action plan articulating how each recommendation would be addressed.

10 WORLD HEALTH ORGANIZATION'S INFLUENZA PANDEMIC PREPAREDNESS AND RESPONSE

The WHO Global Influenza Surveillance and Response System (GISRS), formally known as the Global Influenza Surveillance Network, is used to enable the WHO to recommend twice annually the content of the influenza vaccine for the subsequent influenza season. It also serves as a global alert mechanism for the emergence of influenza viruses with pandemic potential, and has contributed to the understanding of influenza epidemiology. The network was established in 1952, in response to a WHO Expert Committee's recommendation that an international network of laboratories be created that would enable the WHO to advise member states as to what influenza control measures are useful, useless or harmful.

The components of the WHO GISRS are:

- National Influenza Centres (NICs), which collect clinical samples from patients with influenza-like illness in order to isolate representative strains;
- WHO Collaborating Centres, which perform antigenic and genetic analyses of the isolates 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, as well as promotes good standards of practice; and
- the WHO itself, which coordinates all information.

Currently, 138 institutions from 110 countries, including Canada, are recognized by the WHO as National Influenza Centres.

The World Health Organization has recognized that a successful vaccination program is the best way to limit the impact of flu pandemics. In November 2004, the WHO held an informal meeting with influenza vaccine manufacturers, national licensing agencies and government representatives on influenza pandemic vaccines. The summary report that followed, *Vaccines for Pandemic Influenza*, outlines measures that should be taken in order to ensure an adequate supply of effective vaccine. Some of the aspects that participants agreed on were that: clinical trials to establish vaccine formulation should be coordinated internationally to facilitate the exchange of information; strategies for stretching limited supplies of vaccine (termed antigen-sparing strategies) must be explored; domestic licensing and international marketing of vaccines must be facilitated; and the establishment of national and international stockpiles of bulk antigen (to expedite formulation of pandemic vaccine) must be a priority.

On 20 January 2005, the WHO issued a report entitled *Influenza Pandemic Preparedness and Response*. This was subsequently updated in April 2005. The report emphasized the importance of the WHO's role in maintaining worldwide surveillance and disseminating information regarding flu outbreaks. It also reiterated the need for a coordinated response with respect to vaccine production and the importance of stockpiling antivirals and vaccines. Further, the WHO produced a document in 2006 called "WHO strategic action plan for pandemic influenza," which set out two main objectives, namely:

- to exploit all feasible opportunities to prevent the H5N1 virus from developing the ability to spark a pandemic; and, should this fail,
- to ensure that measures are in place to minimize mortality, morbidity and social and economic disruption during the next pandemic.

To achieve these goals, the plan identifies five priority areas for strategic action:

1. reduce human exposure to the H5N1 virus;
2. strengthen the early warning system;
3. intensify rapid containment operations;
4. build capacity to cope with a pandemic; and
5. coordinate global scientific research and development.

In response to the third of these five priorities, the WHO issued in May 2007 an interim protocol called "Rapid operations to contain the initial emergence of pandemic influenza." Briefly, the protocol adopts a geographic approach in which antiviral medications and non-pharmaceutical measures are rapidly deployed to the "containment zone," a defined area surrounding the initial cases, while intensive surveillance is conducted in a "buffer zone" outside of the containment zone.

In 2009, the WHO pandemic influenza plan was updated again to incorporate recent advances in emergency planning, response preparation and antiviral drug supply. These advancements related to the practical experience gained from previous outbreaks, such as the H5N1 and SARS, and the implementation of the *International*

Health Regulations in 2007, which provided a regulatory framework to address international health concerns. The revised 2009 pandemic influenza plan clarified and simplified the six-phase structure introduced in the previous 2005 plan in order to more accurately define pandemic risks. In addition, it utilized a “whole of society” approach that clarified the roles of various stakeholders – namely, national governments, health sectors, non-health sectors and individuals – in mitigating the effects of a possible pandemic. The 2009 influenza pandemic plan serves as a guidance document with recommended actions in the event of a pandemic influenza outbreak. The plan is intended to be used in conjunction with an array of other relevant WHO materials, such as the *WHO Checklist for Influenza Pandemic Preparedness Planning*.

The threat of a future H5N1 pandemic rejuvenated interest in GISRS and caused member states to not only scrutinize pandemic responses and procedures, but also to recognize the difficulties faced by developing countries in combatting viral outbreaks. In response, in 2011, the WHO adopted the *Pandemic Influenza Preparedness Framework for the Sharing of Influenza Viruses and Access to Vaccines and Other Benefits*. This framework aimed to strengthen the GISRS by encouraging a collaborative approach to the distribution of key information and resources (i.e., influenza vaccines, diagnostic materials and antiviral drugs) among member states, the pharmaceutical industry and interest groups in order to ensure transparent, equitable, efficient and fair access. It acknowledged concerns surrounding the capacity to produce sufficient influenza vaccines in the event of a global pandemic, a concern which is particularly pronounced among developing countries that face additional challenges developing, producing and accessing vaccines and resources. It also emphasized the need to share key resources as a means of mitigating pandemic risks. To address these concerns, the framework created legally binding regimes to both promote efficient dissemination of key information and resources, and clearly define the roles and responsibilities of the WHO, national laboratories and pharmaceutical industries. An advisory group of 18 members representing both developed and developing countries was also created to monitor and assess the implementation of the framework.

11 CONCLUSION

The first influenza pandemic of the 21st century was declared in June 2009 by the World Health Organization, providing countries – including Canada – the first opportunity to put the new pandemic plan into action. While some criticized the declaration, citing the relative mild-to-moderate disease pattern, others noted that severity is not a criterion in the determination of a pandemic. Nonetheless, this experience provided valuable insight into Canada’s pandemic preparedness, and demonstrated that while there were areas of our influenza pandemic plan that required more attention, it was generally effective. As illustrated in the recent revisions to the WHO’s pandemic plan and framework, continued work on pandemic preparedness remains a priority as the threat of pandemic influenza is still a concern among experts.

SELECTED BIBLIOGRAPHY

Belshe, Robert. "The Origins of Pandemic Influenza – Lessons from the 1918 Virus." *New England Journal of Medicine*, Vol. 353, 2005, pp. 2209–2211.

Cox, N. J., and K. Subbarao. "Global Epidemiology of Influenza: Past and Present." *Annual Review of Medicine*, Vol. 51, 2000, pp. 407–421.

Dawood, Fatimah S., et al., "Emergence of a Novel Swine-Origin Influenza A (H1N1) Virus in Humans." *New England Journal of Medicine*, Vol. 360, 2009, pp. 2605–2615.

Earn, David J. D., Jonathan Dushoff, and Simon A. Levin. "Ecology and evolution of the flu." *Trends in Ecology and Evolution*, Vol. 17, 2002, pp. 334–340.

Laver, Graeme, and Elspeth Garman. "The Origin and Control of Pandemic Influenza." *Science*, Vol. 293, 2001, pp. 1776–1777.

Monto, Arnold S. "The Threat of an Avian Influenza Pandemic." *New England Journal of Medicine*, Vol. 352, 2005, pp. 323–325.

[Public Health Agency of Canada.](#)

Taubenberger, Jeffery K., et al. "Capturing a Killer Flu Virus." *Scientific American*, Vol. 292, 2005, pp. 62–71.

Ungchusak, Kumnuan, et al. "Probable Person-to-Person Transmission of Avian Influenza A (H5N1)." *New England Journal of Medicine*, Vol. 352, 2005, pp. 333–340.

[World Health Organization.](#)