

## Presiding Officers' Science Series

### Note No. 4 – December 2009

## Influenza

This Note has been prepared under the auspices of the Presiding Officers to provide Parliamentarians and their staff with policy-relevant background material on Influenza, which has received a significant amount of national and international attention in 2009 as offering the potential for a disastrous global pandemic. The Q&A format of the Note is designed to explain the nature of influenza and the possible dangers widespread infection presents to the community.

This Note considers the following questions:

- What is influenza?
- How dangerous is seasonal influenza?
- How can we prevent or treat seasonal influenza?
- What is the difference between seasonal and pandemic influenza?
- What are the options for controlling pandemic influenza?

### *What is influenza?*

In humans, influenza is caused by a virus that infects the nose, throat and lungs. Influenza viruses penetrate the cells that line the surface of the respiratory tract. There they hijack the cell machinery to produce many thousands of new viruses; these then burst out of the cells and go on to infect more cells. They are then spread in droplets produced by coughing and sneezing. The viruses cannot multiply outside the body but they can survive for many hours on hands and surfaces.

In temperate climates, influenza is highly **seasonal** – the great majority of cases occur in the winter when a variety of factors, such as low temperature and humidity, favour survival of the virus. A spike in influenza cases is observed every winter in Victoria, although the timing and extent of influenza illness varies considerably from year to year.

Two types of influenza virus, A and B, cause significant disease in humans. Whereas type B viruses only infect humans, all type A viruses originated in aquatic birds, their natural host. From time to time, one of these avian influenza viruses infects and becomes adapted to another host species, such as swine, horses or humans.

The type A influenza viruses are further classified into subtypes based on their surface proteins, the haemagglutinin (H) and neuraminidase (N) molecules. Of the 16 H subtypes and the 9 N

subtypes found in birds, only a small number are known to have adapted to humans. Since the late 1970s, seasonal influenza in humans has been due to the influenza A subtypes H1N1 and H3N2, as well as type B viruses, all of which are circulating somewhere in the world at any time. The relative contribution of each of these three groups of viruses varies from year to year and region to region – even between the states and territories of Australia.

Influenza virus infection of birds does not usually cause serious disease. An exception is the H5N1 “**bird flu**” virus which devastates domestic poultry flocks and occasionally infects humans who come into close contact with infected birds. Of about 450 human cases of H5N1 infection reported to the World Health Organisation (WHO) by December 2009, nearly 60% have died. Fortunately this virus has not yet acquired the ability to transmit easily between humans.

A different influenza subtype, H3N8, is found in horses in most countries of the world and was responsible for the **equine influenza** outbreak in Australia in 2007. H3N8 influenza has also jumped from horses into dogs in the USA. Australian horses and dogs are currently free of H3N8.

#### *How dangerous is seasonal influenza?*

When influenza viruses infect the nose, throat and lungs, they destroy the surface cells that protect tissues from the outside world. This causes inflammation and accumulation of fluid, and allows other microbes such as the pneumococcal bacteria that cause pneumonia to gain a foothold.

The severity of disease caused by seasonal influenza infection is quite variable. Most people with healthy immune systems produce antibodies that bind influenza viruses and help to destroy them, so that they recover within a week or two without lasting damage. In addition, over time most people build up a level of immunity to seasonal influenza, either through vaccination or because they are exposed to the viruses in the winter, so that even if they are infected, the disease is relatively mild. Some people may even be infected without displaying any symptoms.

In people who can't fight the infection, such as the very young and the elderly, or those who are immunocompromised (such as transplant patients who must take immunosuppressive drugs to prevent rejection), the lungs may be so damaged that they are unable to breathe and the disease can be fatal. Seasonal influenza is estimated to kill an average of about 2000 people in Australia, and 250,000 – 500,000 people worldwide, each year. In Australia, the median age of death from seasonal influenza is 83 years.

#### *How can we prevent or treat seasonal influenza?*

The transmission of influenza viruses from one person to another can be limited by social isolation and by personal **hygiene** to prevent virus spread through coughing, sneezing and touch. However, the effectiveness of these approaches is reduced by the fact that an infected person can infect others for about a day before he or she experiences symptoms.

**Antiviral drugs** are useful in some circumstances. Two anti-influenza drugs in particular, marketed as Tamiflu and Relenza (the latter was designed and developed in Australia), can be used to prevent the development of influenza following exposure to the virus or to reduce the

duration of illness once a person is infected. These drugs have some limitations: for example, they need to be taken within 48 hours of onset of symptoms for best effect, they are not suitable for long-term use and influenza viruses can develop resistance to them. The drugs can nevertheless be especially useful for treating disease in vulnerable patients or for controlling outbreaks, for example in aged care facilities.

Specific immunity is the most effective barrier to influenza infection. Most people become immune during influenza infection itself by producing antibodies that neutralise the virus. The problem is that influenza viruses have an extraordinary capacity to mutate: their genetic code undergoes small changes (mutations) that can lead to alterations in the shape of proteins on the surface of the virus, allowing it to escape neutralisation by antibodies. Earlier strains of influenza virus are rapidly replaced by new strains that can avoid the population's "herd immunity". As a result, the immunity developed during infection with an H3N2 influenza virus last winter will offer diminishing protection against H3N2 infections in winters to come.

Specific immunity can be induced deliberately with **vaccines**. In recent decades in Australia, as in most developed countries, influenza vaccines have contained representative seasonal H1N1, H3N2 and type B viruses. Each virus is grown up in bulk in eggs, then chemically inactivated and purified before being combined into a single vaccine. Because the viruses are inactivated, the vaccine itself cannot cause infection, although some mild symptoms may be experienced as the vaccine activates the immune system.

Seasonal influenza vaccines are updated regularly so that they contain virus strains circulating at the time production must commence, about 5 months before release of the vaccine in autumn. Annual vaccination is recommended so that individuals have some immunity against current strains whether or not they have recently experienced an influenza infection. The WHO Collaborating Centre for Reference and Research on Influenza in Melbourne participates in the development of the WHO's twice-yearly recommendations on virus strains for inclusion in vaccines for the southern and northern hemispheres; many of the viruses used in vaccines around the world in recent years were isolated at the Melbourne Centre.

*What is the difference between seasonal and pandemic influenza?*

Seasonal influenza occurs every year throughout the world, infecting an estimated 10 – 15% of the human population. By contrast, pandemics occur only occasionally, at unpredictable intervals.

An influenza pandemic (global epidemic) occurs when a new influenza A virus emerges to which the general population has no immunity. The new virus spreads rapidly around the world, regardless of the season, and may infect more than 50% of the human population in the first year or two of circulation.

There were three pandemics, of dramatically different severity, in the 20<sup>th</sup> century: in 1918-19 "Spanish influenza" killed at least 50 million people worldwide, or about 2.5% of the whole human population, whereas "Asian influenza" in 1957 and "Hong Kong influenza" in 1968 killed about two million and one million people, respectively.

Where do these new influenza viruses come from? We now know that the three pandemics of the 20<sup>th</sup> century, as well as the 2009 pandemic, emerged through a process of "reassortment". This occurs when different influenza A viruses infect an animal at the same time. The genetic material

of the influenza virus is in 8 pieces so that, when two different influenza viruses (for example, from a pig and a human) infect one person or animal together, the viruses can mix to create new combinations of the 8 pieces of genetic code. Occasionally, a new combination has the ability to spread easily between humans, initiating a pandemic.

The **pandemic “swine flu” virus** which was first detected in Mexico and the US in April 2009 was the product of a series of reassortments that started at least 10 years ago. Although all 8 gene segments originally came from birds, they had more recently been carried by viruses that infected pigs and humans. For example, the “H” component came from a virus that was circulating in swine in North America and the “N” component came from a virus that was circulating in swine in Asia. It is not known when, where or in which animal species the virus mixing occurred that finally gave rise to the new pandemic virus.

The subtype of the 2009 pandemic virus is H1N1. This is the cause of some confusion because, as noted above, a seasonal H1N1 virus was already circulating in humans before the pandemic began and has been included in the seasonal influenza vaccine for many years. Genetic analysis shows that the seasonal and pandemic H1N1 viruses are distant relatives but their evolutionary paths separated so long ago that antibodies induced by infection or vaccination with one of them offer little protection against the other.

As for seasonal influenza, pandemic influenza viruses cause a wide spectrum of disease. Even the 1918 pandemic virus, which killed so many people, caused only a mild infection in 95% of those who contracted it. In Australia and other developed countries, the 2009 pandemic influenza has been mild in the great majority of cases. Nevertheless, a significant number of people have experienced severe or fatal disease. In Australia, the median age of death from the new virus is 48 years, 35 years younger than for seasonal influenza. More than one-third of those deaths were in previously healthy people.

#### *What are the options for controlling pandemic influenza?*

Once a pandemic is spreading in the community, the options for controlling it are broadly the same as for seasonal influenza: social isolation, respiratory and hand hygiene, antiviral drugs and vaccines. However, the choice of control strategy, in particular the extent to which social and economic activity is interrupted and medical stockpiles are deployed, should depend on the circumstances – severity of the disease, the age and characteristics of affected people, the sensitivity of the virus to particular drugs, the available public resources and other factors. Assessing these issues can be challenging early in a pandemic when information about the new virus is limited.

In a pandemic, as for seasonal influenza, vaccination is the most effective way to control the disease. Many pandemic plans therefore focus on slowing the spread of the new virus to minimise its impact on the community while a specific vaccine is produced. It has been recognised for many years that, even using established methods of seasonal influenza vaccine production, the first wave of pandemic infections would probably be over before the new vaccine was ready. This occurred in Australia and other southern hemisphere countries in 2009.

Despite this constraint, vaccination remains an appropriate public health strategy for the management of this latest pandemic virus. The history of past pandemics suggests that the 2009

H1N1 virus will cause influenza outbreaks in Australia in 2010. Whether those outbreaks will be more or less severe than those experienced in 2009 cannot be predicted with certainty.

An important goal of research and development in many institutes, universities and vaccine manufacturers, in Australia and elsewhere, is the invention of novel influenza vaccine technologies that will speed up vaccine production or, even better, overcome the need to make a new vaccine for each new virus.

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