Avian influenza and planning for pandemics

There is currently no need to panic

At a recent forum of the Australian Health Policy Institute in Sydney, the Editor of the Journal expressed concerns about Australia's ability to cope with avian flu, and asked whether he could sleep soundly in his bed. We attempt to answer his concerns.

Influenza is justifiably feared. In 1918–1919, 40 to 50 million people (2%–3% of the world's population) died in the "Spanish" influenza pandemic.[1] Subsequent influenza pandemics occurred in 1957 and 1968. Although the mortality of the later pandemics was far less, the potential for another major pandemic is ever present. Annual influenza outbreaks have caused more deaths overall than pandemics, but gentle antigenic "drift", caused by minor mutations in the viral genome, allows the annual development of a new influenza vaccine, matched as closely as possible with predicted circulating strains. Pandemic strains caused by antigenic "shift" are, by definition, unpredictable, and unlikely to be prevented in the short term by vaccines.

In 1999, stimulated by human infections caused by avian influenza in Hong Kong, the World Health Organization (WHO) published a pandemic preparedness plan, and urged countries to make their own plans.[2] How well prepared is Australia?

The origin of pandemics: The segmented genome of the influenza A virus favours genetic reassortment, which can lead to antigenic shift to a new, potentially pandemic, strain. Pandemic strains arise when a new type of haemagglutinin is introduced into humans. Pigs may act as a mixing vessel for reassortment by supporting growth of both avian and human viruses, or a human might be co-infected with both avian and human strains. Pandemic influenza spreads rapidly and affects children and young adults, causing enormous social disruption.[1]

Avian influenza: Birds, particularly aquatic and migratory species, are natural hosts of all 15 haemagglutinin subtypes of influenza A virus, whereas only a few of these viruses have established transmissible infections in humans, pigs and other mammals.[1]

Avian influenza strains readily infect domestic poultry and are highly pathogenic to birds.[3] Since mid-December 2003, there has been a catastrophic outbreak of avian influenza in Asia, caused by a highly pathogenic H5N1 strain. Eight countries have confirmed outbreaks, mostly in commercial poultry, although wild birds have been infected. In 2 months, over 100 million birds in Asia died or were culled.[3]

There was great alarm when human infections with this avian strain were reported, with high mortality in both adults and children. However, despite the extent of the outbreak in birds, very few human cases have been reported. By 24 March 2004, 57 cases had been notified from Vietnam (37) and Thailand (20), of which 23 (40%) were fatal. All cases followed exposure to infected poultry. The number of unreported human cases is uncertain, but the absence of documented human-to-human spread is reassuring.[3]

The greatest concern is that there will be reassortment between the current avian H5N1 strain and circulating human or porcine influenza viruses, producing a novel, virulent human strain.

Pandemic planning: Australia has been actively planning action to cope with an influenza pandemic since 1997. The framework for a pandemic plan was published in 1999,[4] and an action plan was

published in 2003.[5] A National Influenza Pandemic Action Committee (NIPAC), formed in 2003, continues to plan for future pandemics and has closely monitored the avian influenza situation. Although NIPAC is an anagram of "panic", the message so far is that there is no need to panic.

A major concern of the audience at the health policy forum was the large number of different agencies involved in planning for a pandemic — a veritable "spaghetti junction". Who should coordinate these agencies? Given the complexity of pandemic planning, we believe it is entirely appropriate that there are many different players, coordinated, as is now the case, by the Australian Department of Health and Ageing.[6]

Planning for pandemic influenza overlaps to an extent with planning for outbreaks of other viral infections. Australian pandemic planning has benefited from the need to develop plans to cope with a potential epidemic of SARS (severe acute respiratory syndrome)[7] and possible bioterrorist attack with smallpox virus.[8]

NIPAC is addressing many facets of planning, including:

- *Border protection.* Although Australia is an island, modern air travel and the high infectivity of influenza preclude total exclusion of a pandemic. Because influenza can be transmitted before symptoms appear, screening incoming passengers for reported symptoms, as was done for SARS, would be less effective, but might delay widespread introduction of influenza. Even weeks of delay could be invaluable for vaccine development and distribution.
- *Immunisation.* It would probably take at least 6 months after the onset of a pandemic for significant quantities of vaccines specific to the pandemic strain to become available.[9] WHO is currently developing H5N1 viruses suitable for vaccine production as rapidly as possible.
- *Antivirals.* The H5N1 virus is resistant to amantadine, but sensitive to the neuraminidase inhibitors oseltamivir and zanamavir, which can be used for both treatment and prophylaxis. It has been suggested that countries should stockpile antivirals.[10] There was some evidence of their benefit in humans during the 2003 outbreak of highly pathogenic avian H7N7 influenza A in Dutch poultry farms.[1] However, antivirals are very expensive and in short supply, and realistically could only be used as a stop-gap measure to "buy time" by treating early cases and protecting essential staff.
- *Laboratory diagnosis.* Influenza is difficult to differentiate clinically from "influenza-like illnesses", necessitating laboratory testing of appropriate respiratory samples for confirmation. However, testing is not often done routinely (at least in adults). SARS and the threat of avian influenza suggest testing should be more widely available to facilitate decisions about infection control, but few laboratories provide rapid viral diagnosis. The network of WHO influenza and other public-health laboratories in Australia is actively developing rapid tests to detect H5N1 influenza.
- *Infection control measures to limit spread.* Children are at high risk of contracting and dying of influenza,[1] and are an important source of infection for the elderly.[11] In a pandemic, it would almost certainly be necessary to close schools, childcare centres and public gatherings to reduce spread.
- *Respiratory hygiene.* Simple respiratory hygiene, such as covering the nose and mouth when sneezing, and disposing of used tissues promptly in "no-touch" receptacles, is as important as the use of masks.[12]
- *Communication.* The level of public concern and, in many countries, panic during the SARS outbreak vividly illustrates the importance of effective public communication. It is vital that authorities do not leave the dissemination of information about outbreaks to the popular press.

There is currently no need to panic about avian influenza, as human cases are extremely rare and have followed close exposure to birds. Human-to-human spread of avian influenza has not been described.

While Australia is well prepared to cope if an influenza pandemic started tomorrow, the unpredictability of these pandemics, their rapid spread and high attack rates mean it is impossible to be totally reassuring. Like the rest of us, the Editor of the Journal, if he wants to sleep soundly, will just have to cope with uncertainty.

David Isaacs
Senior Staff Specialist, Allergy, Immunology and Infectious Diseases
Children's Hospital at Westmead, Sydney, NSW

Dominic E Dwyer
Senior Staff Specialist, Virology, Westmead Hospital, Sydney, NSW

Alan W Hampson
WHO Collaborating Centre for Reference and Research on Influenza
Melbourne, VIC
davidi@chw.edu.au

1 Nicholson KG, Wood JM, Zambon M. Influenza. *Lancet* 2003; 362: 1733-1745.
2 World Health Organization. Department of Communicable Disease Surveillance and Response. Influenza pandemic preparedness plan. The role of WHO and guidelines for national and regional planning. Geneva: WHO, 1999. WHO/CDS/CSR/EDC/99/1.
3 World Health Organization. Communicable diseases surveillance and response. Avian influenza. Available at: www.who.int/csr/disease/avian_influenza/en/ (accessed Jun 2004).
4 Influenza Pandemic Planning Committee. A framework for an Australian Influenza Pandemic Plan. *Commun Dis Intell* Tech Rep Series 4, 1999.
5 Commonwealth of Australia. Australian action plan for pandemic influenza. Canberra: Australian Department of Health and Ageing, 2003.
6 Australian Department of Health and Ageing. A special report from the Commonwealth Chief Medical Officer: protecting Australia from communicable diseases: everybody's business. January 2004. Available at: www.health.gov.au/pubhlth/publicat/document/metadata/cmo.htm (accessed Mar 2004).
7 Australian Department of Health and Ageing. Severe acute respiratory syndrome. Available at: www.health.gov.au/sars/index.htm (accessed Mar 2004).
8 Commonwealth of Australia. Guidelines for smallpox outbreak, preparedness, response and management. Canberra: Australian Department of Health and Ageing, 2004.
9 Nguyen-Van-Tham JS, Hampson AW. The epidemiology and clinical impact of pandemic influenza. *Vaccine* 2003; 21: 1762-1768.
10 Webby RJ, Webster RG. Are we ready for pandemic influenza? *Science* 2003; 302: 1519-1522.
11 Reichert TA, Sugaya N, Fedson DS, et al. The Japanese experience with vaccinating schoolchildren against influenza. *N Engl J Med* 2001; 344: 889-896.
12 Centers for Disease Control and Prevention. Respiratory hygiene/cough etiquette in healthcare settings. Available at: www.cdc.gov/flu/professionals/infectioncontrol/resphygiene.htm (accessed Mar 2004). ❑