

Preparing for the influenza pandemic: the government response

In February 2003, a small group of scientists and clinicians met in Sydney to map out how Australia could best respond if a case of smallpox occurred in Australia. The day was interrupted by a teleconference on the two deaths in Hong Kong of family members who had been in South China. One was confirmed to have avian influenza, H5N1, the same virus which had caused 18 cases and six deaths in Hong Kong in 1997.

After the teleconference, the group mused as to what was going to be the most threat to the world – small pox, avian flu or was it perhaps the strange pneumonia that was killing people in Southern China. In 2003 it turned out to be the latter, which became known as SARS, Severe Acute Respiratory Syndrome.

The world went into battle mode against the SARS corona virus, and it seemed as if avian influenza had dropped out of sight. In January 2004, almost 6 months since the spread of SARS had been halted and disease controllers around the world were beginning to relax, laboratory tests confirmed the presence of H5N1 in human cases of severe respiratory disease in Vietnam. Vietnam, Korea, Japan and Thailand reported outbreaks of H5N1 in poultry. In late January, Thailand began to report human cases. In the ensuing months, Cambodia, Laos, Indonesia and China also reported detection of H5N1 in poultry.

The incident room in the Australian Department of Health and Ageing (DoHA) was still in operation following the SARS outbreak. The team searched the web for reports or rumours of respiratory illness anywhere in the world, examining the

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epidemiological detail and analysing the threat – this time the threat of pandemic influenza.

The Australian government was quick to react to the warnings and provided in the 2004 budget funds to purchase sufficient influenza antivirals for treatment courses for 4 million Australians or sufficient for prophylaxis of 1 million workers for 6 weeks in the event of a pandemic. Funds were designated to upgrade the incident room and increased resources were assigned for public laboratories. Over \$10 million was provided to enhance surveillance technology, enabling online reporting and outbreak control. Highly Pathogenic Avian Influenza Affecting Humans (HPAIAH) was proclaimed a quarantinable disease on 23 March 2004.

The Australian Action Plan for Pandemic Influenza had been endorsed in 2003. This plan laid out basic actions for each level of alert and stages of the pandemic and was aligned to the World Health Organization plan. The plan was a guide for States and Territories to make more detailed plans. However, the plan did not take into account the unprecedented situation of widescale avian outbreaks; clarity on antiviral and quarantine strategy was also required.

The experience of the anthrax hoaxes in the USA and the global impact of SARS

made it clear that a detailed national approach was needed. The National Influenza Pandemic Action Committee (NIPAC) – comprised of epidemiology, clinical and laboratory experts and chaired by the Chief Medical Officer, Professor John Horvath – was requested to rewrite the plan.

The strategies put forward by NIPAC had to be considered by the Communicable Disease Network of Australia (CDNA), by the Public Health Laboratory Network (PHLN) – the national operative networks of communicable disease control – and by the Australian Health Disaster Management and Policy Committee (AHDMPAC) – an overarching national policy committee comprised of disaster experts and the chief health officers from each jurisdiction and chaired by Ms Mary Murnane, the Deputy Secretary of the DoHA.

After a lull in the early northern summer of 2004, poultry outbreaks and human cases began to recur in August in Vietnam and Thailand. A human fatality reported in Thailand was thought likely to be a result of human to human transmission. An outbreak of H5N1 in a Thailand zoo killed 147 tigers. In April, China reported widespread deaths in different species of wild birds at Qinghai Lake in central China. Cambodia, in February 2005, reported its first human case. International concern increased.

The Australian government moved to secure a pandemic vaccine supply. Two companies, CSL Ltd in Australia and Sanofi Pasteur based in France, were awarded 3 year contracts to supply seasonal influenza vaccine – the contracts are tied to capacity

to provide pandemic vaccine.

NIPAC recommended that the key strategies in pandemic response should be containment and maintenance of essential services. The pandemic phases were written to determine activities dependent on the extent of the spread overseas and, separately, the spread within Australia.

The decision that border control would be used is inherent in the plan. The debate on border control was not whether it would be effective, but rather could it slow the introduction and spread to Australia. The modelling available indicated that it could, but only if controls were rigorously applied*.

The evidence in regard to the antivirals was scrutinised. The Vietnamese and Thai strains of H5N1 were demonstrated to be resistant to the amantadines¹. It was clear that the neuraminidase inhibitors, oseltamivir and zanamivir, were 80-90% effective in preventing influenza and viral shedding but their efficacy in treatment in preventing severe complications or mortality is currently insufficient^{2,3}.

Trials with seasonal influenza have shown a reduction in the duration of illness in treatment of about 1 day, reduction in minor complications and a reduction in viral shedding²⁻⁴. Recent clinical information from Vietnam indicates that an increased dose may be needed both for prophylaxis and for treatment for H5N1⁵.

NIPAC put forward that, in the first instance, the antivirals should be used to stop the disease spreading. Therefore they should be used to protect those in contact with cases or at high risk of exposure to cases. It was deemed that 10% of the antiviral stockpile be used for treatment in the first phases of the pandemic and their efficacy in treatment assessed 'on the run'. Once

containment is no longer possible, the strategy will change to 'maintenance of essential services'.

The strategy of antiviral use will depend on its effectiveness in treatment and prevention and also the time to availability of a vaccine. The use of antivirals for those with ongoing exposure, such as hospital workers and primary care teams, is likely to be continuous, that is 'pre-exposure'; for others, it maybe pre or post exposure, dependent on risk.

The publication in June 2005 of the revised pandemic plan for Australia, entitled *Australia's Management Plan for Pandemic Influenza (AMPPI)* delineates the phases and actions in each phase and the criteria for movement from disease containment to maintenance of social functioning strategy⁶. The major strategies require further refinement and more detail is needed in such areas of clinical management, standardisation of data collection and management of vulnerable groups. A revised AMPPI will be available early in 2006.

Determining the likely effectiveness of quarantine is also problematic. Mass quarantine is logistically difficult, yet NIPAC has recommended that it be considered in phases "Overseas 5 and Overseas 6" when transmission is beginning to occur rapidly overseas and there are no cases in Australia. Mass quarantine of incoming aircraft would likely only be possible if there was a marked reduction in international travel.

Home quarantine should be used otherwise. Preliminary results of modelling work carried out by Australian experts in the field indicate that home quarantine, even at less than 70% compliance, is likely to be effective in slowing the spread⁷. Models of home quarantine are being discussed with primary care providers, who would have a major role in caring and

monitoring families in quarantine.

Early in 2005, NIPAC, with the DoHA and the National Health and Medical Research Council (NHMRC), convened a symposium to determine urgent research priorities in pandemic influenza. The symposium reflected Australia's extraordinary achievements already in the field and the capacity to define and go forward with a coherent approach. NHMRC put forward \$7.5 million toward determined priorities which ranged from vaccine development and diagnostic tests to assessment of community concerns and perceptions.

CSL Ltd, in August 2005, commenced clinical trials for H5N1 vaccine. DoHA provided CSL Ltd \$5 million to accelerate the trials so that results will be available by the end of 2006. The trials aim to test antigen levels, plus or minus adjuvant.

Also in August, the first human cases in Indonesia were reported. These cases, which have primarily occurred around Jakarta, as notified by WHO, now stand at 17 cases with 12 deaths (15 January 2006). Avian culling is not being attempted in many areas and consideration is being given to vaccination.

Regional and global powers have stepped up preparations to develop a regional approach. Australia has committed expertise and resources to the area, concentrating on improving capacity for surveillance both in animals and humans. The government has announced a \$100 million package to assist Asian and Pacific countries to respond to the pandemic threat, bringing the total resource commitment to the region to date to \$141 million.

The far reaching effects of a pandemic on a community demand a whole of sector approach. In the latter half of 2005, key industries have moved to contingency

planning for the event of a pandemic and the likely 30-50% absenteeism. The major decisions in the event of a pandemic would be made across the whole of government. A governance process to allow this to occur quickly has been set up.

In December 2005 the government decided to further increase domestic resources toward pandemic influenza preparation. Funding was granted for a range of initiatives – purchasing another 4 million courses of antivirals (sufficient to treat 8 million of Australia's population), stockpiling of a suitable vaccine or vaccine antigen of 2 million doses, providing additional equipment such as masks, needles, syringes and ventilators for the National Medicines Stockpile, implementing an extensive professional and community education programme, improving surveillance in primary care and in hospitals, and improving central resources by setting up an Office of Health Protection for Australia.

January 2006 has seen the spread of H5N1 across the base of Russia to Turkey. Two deaths in a family in Turkey of H5N1 resulted in the wide scale testing of humans and culling of poultry. The number of cases in Turkey has risen more rapidly than in any other country and stands at 20 (not yet notified by WHO but laboratory confirmed). It is not clear why so many and why all at once. Testing has also shown H5N1 in two asymptomatic children in Turkey. Recent research in Vietnam links mild-moderate influenza illness with contact with infected poultry⁸.

The current count (15 January 2006) of WHO notifications is 147 cases with 78 fatalities. Experts and researchers around the world are working hard to make sense of this virus, to try and understand not only the prevalence of infection in humans but also why it hasn't jumped and if it will ever jump to become transmissible in humans. Maybe it won't, but history leads us to believe otherwise.

* A modified Susceptible Exposed Infectious Removed (SEIR) model, provided by modellers at the Australian National University, and the

Centers for Disease Control Meltzer models (available on the CDC website) were used by the incident room team to model pandemic spread and value of intervention at the border.

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