



Influenza A(H1N1)09: New Zealand's response to the pandemic threat

Lance C Jennings

In April 2009 a novel influenza A(H1N1) virus came to the world's attention when it caused outbreaks in humans in Mexico and USA. Within 2 weeks, New Zealand's public health authorities were being challenged. The return of a group of schoolchildren with symptoms of influenza to Auckland on April 25 from Mexico triggered the activation of New Zealand's Influenza Pandemic Action Plan (NZIPAP).¹

On April 29, the World Health Organization (WHO) raised the pandemic threat to Phase 5 followed by New Zealand declaring it a notifiable and quarantinable disease on April 30. The WHO was initially reluctant to declare a pandemic, largely based on the perceived mildness of the disease. However, with the obvious widespread community spread in Southern Hemisphere countries entering their traditional influenza seasons, the WHO declared a Pandemic (Phase 6) on June 11.² New Zealand has responded to this threat with perhaps one of the country's largest public health responses ever attempted.

The perception that the pandemic being caused by the novel (H1N1)09 virus is trivial is of concern. Influenza can be a serious disease, and annually we are affected by seasonal influenza outbreaks and epidemics of varying severity, population burden in terms of absenteeism from school or work, and individual burden in terms of severe illness, hospitalisation, and death. On average, 300 New Zealanders die each year directly or indirectly as a result of influenza. The virus associated with the current pandemic is causing illnesses with classic influenza signs and symptoms of mild to moderate severity (including high fever, headache, malaise, and cough—often with nausea, vomiting, and diarrhoea).

Estimates of up to 50% of the population being infected by this virus over the coming months will undoubtedly be associated with increasing numbers of people (especially those with underlying medical conditions) with severe illness requiring hospitalisation and possibly dying from this virus. We should not become complacent about this novel A(H1N1)09 virus, because influenza A viruses have a track record of unpredictability, however at the same time we should not panic as the threat can be managed with strong Ministry of Health and Government leadership.

The virus

This novel virus was dubbed "swine influenza" by the media because of the virus' origins from known swine influenza A virus lineages. Several influenza A virus subtypes circulate in pigs (e.g. H1N1, H1N2, H3N1, H3N2) causing a highly contagious acute respiratory disease, but they rarely infect humans. However since 1998 a North American triple reassortant H1N1 swine virus has been circulating and associated with human infections.

Analysis of the newly emerged A(H1N1)09 virus has shown that 6 of the viruses 8 genomic segments were derived from the North American swine virus, with the 2 remaining segments being derived from Eurasian swine viruses.^{3,4} Through these reassortments, this virus has gained the ability to spread efficiently between humans.

Characteristically influenza A viruses become genetically unstable when they move out of their natural host and continue to evolve. Ten clades of A(H5N1) 'avian' virus have evolved and are now circulating in domestic poultry since this viruses movement away from it's natural aquatic avian host in 1996. Historical data from the 1918 pandemic suggest that the A(H1N1) 'Spanish' virus caused a mild wave, followed several months later by a second pandemic wave associated with increased pathogenicity.

The question remains as to whether this A(H1N1)09 virus will return as successive waves of seasonal influenza as with the 1957 H2N2 and 1968 H3N2 pandemic viruses, or will it return with increased pathogenicity? (the sting in the "scorpion's" tail so to speak).

New Zealand's pandemic response

Containment strategies—New Zealand's pandemic planning has evolved since 1997 (when it was initially a response framework) to the operational Action Plan (NZIPAP) of today.^{1,5,6} The phases of this plan are straightforward, with initial efforts focused on containment: "keeping it out" and "stamping it out".

Following the entry into New Zealand of the first confirmed cases on April 25, the response focus was on border management with the identification and follow-up of symptomatic international travellers and their immediate contacts. Controls at international airports—along with the use of isolation, quarantine, and oseltamivir (Tamiflu™) for treatment of laboratory confirmed cases and prophylaxis of their contacts—appeared to delay community transmission of this novel virus through May into June.

This situation may have reflected the virus's inherent epidemiological characteristics which we do not fully understand. Regardless, it bought valuable time to strengthen the public health services' frontline capacity, the diagnostic capacity in the countries' five virology laboratories, and other aspects of the primary, secondary health care, and other government department's responses.

Pivotal to the public health response was the laboratory identification of the novel (H1N1)09 virus. Molecular tests (RT-PCR) were (and remain) the most sensitive assay for the detection of this virus. Initial identification involved the exclusion of seasonal influenza A(H3N2) and (H1N1) subtypes, and confirmation by genetic sequencing, however by the second week of May New Zealand virus laboratories were able to specifically identify the (H1N1)09 virus and shorten the time for result availability to within 24 hours. Rapid influenza antigen detection methods, including the rapid antigen tests (RAT)⁷ and direct fluorescent antibody (DFA) tests have been shown to be less sensitive and of restricted value.

Both border management and containment strategies are not widely supported by the WHO, except containment at the source of the emergence of a novel virus.⁸ New Zealand is well placed as it is an island nation and has a well developed pandemic

action plan and public health infrastructure. For these reasons, the early distribution of public health information with clear instructions on what travellers should do if they developed influenza symptoms within 7 days of travel on all flights into New Zealand, and the placing of clearly identifiable public health staff at all international airports, were achievable and actively carried out.

The cases identified were largely individuals developing symptoms who contacted the public health service or their general practitioner, triggering the vigorous public health follow-up, respiratory sample collection, laboratory confirmatory testing, and subsequent contact tracing of confirmed cases. This approach was apparently successful for 6 weeks. Could we have done better?

It is interesting to review the maritime quarantine strategies carried out in the Pacific region during the 1918/19 pandemic. The Western Samoa maritime quarantine was broken in 1918 by the *SS Tahune*, from Auckland resulting in the introduction of virus and a 22% mortality, while neighbouring American Samoa maintained full quarantine which kept the virus out until 1921. No deaths were recorded in American Samoa.⁹ This is clearly supportive of our border management approach.

In 2008 an Otago University Pandemic Influenza Research Group undertook a very extensive research project funded by the US CDC to assess screening methods for influenza in arriving airline passengers. A pilot study by Duncan and colleagues,¹⁰ and subsequent main study outcomes which included an initial screening of more than 18,000 passengers arriving at Christchurch International Airport from June–September 2008 (not yet published), clearly are in support of New Zealand’s border management. Results indicate that it is at least feasible to also detect people with influenza symptoms at our international borders.

Management strategies—The rapid spread of A(H1N1)09 in Victoria, Australia during the last week of May and continuing global spread placed increasing pressure on the countries ‘keep it out’ strategy. By the week of June 16 it became clear that community spread was occurring in Auckland, Wellington and Christchurch, and containment efforts were stressing both the public health service and virology services. Movement to the “management” phase of New Zealand’s response was not announced until June 19, however.

Although swine flu clinics were already in action in more severely affected communities of Christchurch and Wellington, this allowed the establishment of community-based assessment centres (CBACs) and the response to focus on individuals more severely affected by influenza and needing antiviral treatment or hospitalisation.

Wellington, closely followed by Christchurch, were the first communities in New Zealand to experience an escalation in community transmission. A possible reason for this may relate to the specific communities initially affected. In Christchurch, the (H1N1)09 virus was introduced into the Samoan community on about June 3 by a member of that community returning from Melbourne with the virus. The subsequent amplification of infection amongst this closely linked community probably then resulted in the seeding of schools, work, and other communities in Christchurch, followed by exponential spread through the community.

In Wellington, communities in Porirua and Wainuiomata have been severely affected, clearly indicating that this virus is amplified in socioeconomic communities where crowding may exist. In Canada, outbreaks of (H1N1)09 amongst indigenous Inuit Indians were associated with severe disease and hospitalisation, providing a clear warning that certain New Zealand Pacific Island and Māori populations may also be at greater risk from this virus.

Pharmaceutical preparedness

Pharmaceutical interventions, which include antivirals and vaccines, clearly separate our ability to respond to the current pandemic as compared to influenza pandemics in the past, particularly the 1918–19 pandemic.

New Zealand's pandemic preparedness planning has ensured that an antiviral (oseltamivir) stockpile, sufficient treatment doses for 31% of the population has been put in place. Oseltamivir from the stockpile has been used extensively during the containment phase, and now for the treatment of more severe illnesses during the management phase. Individuals travelling to affected countries have also been able to access oseltamivir by prescription, placing pressure on the private market supplies.

Pharmacy distribution of oseltamivir to individuals with influenza symptoms through pharmacist prescribing (a novel strategy pioneered with seasonal influenza over the past two winters) has been reviewed.¹¹ It has been proposed that Pharmacists should be able to make a clinical evaluation by telephone, rather than the currently required face-to-face clinical evaluation. This strategy would complement the commonsense advice to stay at home if you are sick.

Because of international concerns about the development of resistance in the (H1N1)09 virus to oseltamivir, and the co-circulation of seasonal (H1N1) virus known to be resistant to oseltamivir, the national stockpile has been reviewed and now contains zanamivir (Relenza™). The development of widespread resistance of the seasonal influenza A(H1N1) virus to oseltamivir (through the H275Y mutation) is not believed to be directly linked to drug usage, although drug induced resistance can occur. To date, drug induced resistance has resulted in viruses which are unable to spread and are of no clinical relevance. It is prudent though to maintain virological surveillance and flexibility in our pharmaceutical response strategies, especially as oseltamivir resistance in an A(H1N1)09 viral isolate has now been reported.¹²

Our best protection against influenza is receiving an influenza vaccine; however, pandemic vaccines with current technologies cannot be produced until the novel pandemic virus has emerged, and are unlikely to be commercially available for 4 to 6 months and after the first wave of a pandemic.¹³ As part of the NZIPAP, a 100,000-dose stockpile of influenza A(H5N1) whole virus cell-culture derived pre-pandemic vaccine, and a forward purchasing agreement with CSL for the supply of an egg-derived split virus pandemic vaccine, are in place.

Vaccine manufacturers are expected to have influenza A(H1N1)09 vaccines available from August 2009. Their availability following the likely peak of our New Zealand pandemic should not delay any decision to acquire such a vaccine however it will inevitably delay any decision to utilise such a vaccine. Indeed, this may be to our

advantage, it will allow more time for human trial data to become available, and a more complete safety and efficacy assessment to be made by Medsafe.

Looking to the future

Of major concern is our inability to predict the evolution of influenza A viruses, especially now that there is an additional novel influenza A virus capable of causing disease in humans which is spreading globally.

The simple concept of influenza A virus evolution through point mutations (as with antigenic drift) or through gene reassortment (antigenic shift) may be more complex and also involve other genetic recombination events.¹⁴

The circulation among humans globally of this novel A(H1N1)09 virus along with seasonal H1N1 and H3N2 viruses—and in parallel the highly pathogenic A(H5N1) and A(H9N1) avian viruses in domestic poultry (both of which are capable of causing human infections associated with high mortality) and the swine influenza A lineages—is possibly unprecedented

We must not become complacent about influenza and continue pandemic preparedness activities at all levels in our community. The education initiatives on basic respiratory hygiene among school children, such as the ‘Sneeze Safe’ programme (www.sneezesafe.co.nz) and handwashing and social distancing (staying at home when you have symptoms of influenza) will have longer term benefits to the health of New Zealanders.

Similarly, initiatives by the National Influenza Strategy Group (NISG) have seen an unprecedented increased uptake of seasonal influenza vaccine, which in the face of the co-circulation of seasonal H1N1 and H3N2 viruses, will lessen the likelihood of individuals suffering from multiple influenza A virus infections.

New Zealand is also well placed to contribute to the global research efforts on influenza to understand these viruses, their evolution and the disease that they cause. The call for a research agenda has been made and pandemic research priorities identified,¹⁵ however little progress has been made toward achieving this.

Early on in this pandemic, New Zealand had the third largest number of cases globally, however our focus (and rightly so) was on mounting a public health response. Had a research capacity been identified in advance, optimal use of the collected case history, epidemiological, surveillance and virological data could have been made more widely available and especially to the international community.

A review of our national efforts to keep out, contain and manage this novel (H1N1)09 pandemic will be essential as our experience will not only benefit the further evolution of our pandemic action plan, but also the global community, especially the Northern hemisphere countries as they enter their winter influenza seasons.

Competing interests: None known.

Author information: Lance C Jennings, Clinical Associate Professor, University of Otago, Christchurch (and Canterbury Health Laboratories, Christchurch)

Correspondence: A/Prof Lance Jennings, Canterbury Health Laboratories,
PO Box 151, Christchurch 8011, New Zealand. Fax: +64 (0)3 3640075; email:
lance.jennings@cdhb.govt.nz

References:

1. Ministry of Health. New Zealand Pandemic Action Plan, September. Wellington: MoH; 2006.
<http://www.moh.govt.nz/moh.nsf/indexmh/nz-influenza-pandemic-action-plan-2006>.
2. World Health Organization. World now at start of 2009 influenza pandemic. Geneva: WHO; 2009.
http://www.who.int/mediacentre/news/statements/2009/h1n1_pandemic_phase6_20090611/en/index.html
3. Novel, Swine Origin A(H1N1) Virus Investigation Team. Emergence of a Novel Swine-Origin Influenza A(H1N1) in Humans. *New Engl J Med* 2009;361:1–11
4. Fraser C, Donnelly CA, Cauchemez S et al. Pandemic potential of a strain of influenza A(H1N1): early findings. *Science* 2009.
<http://www.sciencemag.org/cgi/rapidpdf/117062v2.pdf>
5. Jennings L. Avian influenza: a public health risk for New Zealand. *NZMJ* 2004;117(1192).
<http://www.nzma.org.nz/journal/117-1192/843>.
6. Jennings L. New Zealand's preparedness for the next influenza pandemic *NZMJ* 2005;118(1211). <http://www.nzma.org.nz/journal/118-1211/1343/>.
7. Hurt AC, Baas C, Deng Y-M, et al. Performance of influenza rapid point-of-care tests in the detection of swine lineage A(H1N1) influenza viruses. *Influenza Other Respir Viruses* 2009;3:171–6.
8. World Health Organization. WHO Interim Protocol: Rapid operations to contain the initial emergence of pandemic influenza. Geneva: WHO; 2007.
http://www.who.int/csr/disease/avian_influenza/guidelines/draftprotocol/en/index.html.
9. McLeod M, Kelly H, Wilson N, Baker M. Border control measures in the influenza pandemic plans of six South Pacific nations: a critical review. *N Z Med J* 2008;121:62–72.
<http://www.nzmj.com/journal/121-1278/3163/>
10. Duncan AR, Priest PC, Jennings LC, et al. Screening for Influenza Infection in International Airline Travelers. *American Journal of Public Health* 2009 [In Press].
11. Jennings L. How Can Influenza Vaccines and Antivirals be Best Delivered in the Industrialized World? New Zealand. Presentation at: Infectious Diseases Society of America: US Seasonal and Pandemic Influenza 2008. Arlington, Virginia, USA (18–20 May) 2008.
<http://www.hivma.org/WorkArea/showcontent.aspx?id=11358>
12. ECDC. First isolation of a secondary oseltamivir-resistant A(H1N1)v strain in Denmark. 1 July 2009.
http://www.ecdc.europa.eu/en/files/pdf/Health_topics/0907_Influenza_AH1N1v_Resistance_TA_Oseltamivir.pdf
13. Jennings LC, Monto AS, Chan PKS, et al. Stockpiling pre-pandemic influenza vaccines: a new cornerstone of pandemic preparedness plans. *The Lancet Infect Dis* 2008;8:650–8.
14. Ghedin E, Fitch A, Boyne A, et al. Mixed Infection and the Genesis of Influenza Diversity. *PNAS* 2009[In Press].
15. Wilson N, Baker MG, Jennings LC. The clioepidemiology of pandemic influenza and next steps for pandemic influenza research in New Zealand. *N Z Med J*. 2008;121:(1284).
<http://www.nzma.org.nz/journal/121-1284/3307/>