

All health professionals should receive the 2009 H1N1 influenza vaccine

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The 2009 H1N1 influenza pandemic reached Australia and New Zealand in winter 2009. For the great majority of people infected, the disease was mild, causing no more than an unpleasant dose of the “flu”. For a small proportion, it caused critical illness or death, and for a 12-week period in 2009 placed a major strain on intensive care resources.^{1,2} From an intensive care perspective, infection with the novel 2009 H1N1 virus led to a high incidence of acute respiratory distress syndrome associated with viral pneumonitis, which required specific ventilation and oxygenation strategies, including prolonged high positive end-expiratory pressure, high-frequency oscillation ventilation, and extracorporeal membrane oxygenation.³ This affected previously healthy young and middle-aged people as well as risk groups, including those with chronic lung disease, obesity and pregnancy.¹

After some initial media hysteria, public health authorities put considerable effort into reassuring the public that, despite the declaration of a pandemic, most people would have mild disease or none at all. Perhaps these public health reassurances were too good, because there has been relatively poor uptake (<25%) of the free 2009 H1N1 vaccine by the community, including health professionals, since it became available. This is potentially a major problem, as the 2010 influenza season will arrive shortly (or a second wave of H1N1 even earlier), and a large part of the population is likely to remain vulnerable to infection.

It is not known how any second wave of the 2009 H1N1 virus will behave in 2010. Virulence may change during the northern hemisphere winter. Oseltamivir was used frequently for severely ill patients in 2009, but resistance to this agent is now emerging,⁴ which may decrease therapeutic options.

Overall, an estimated 20% of the Australian population were exposed to the novel H1N1 virus in 2009 (Professor Lyn Gilbert, Westmead Hospital, Sydney, NSW, personal communication), with about 200 confirmed deaths. National records over the past decade indicate 50–100 proven influenza deaths per year⁵ (Dr Clayton Chiu, National Centre for Immunisation Research and Surveillance of Vaccine Preventable Diseases, Sydney, NSW, personal communication). In contrast, seasonal influenza is estimated to cause up to 2500 deaths per year, mainly in elderly people. Paradoxically, the 2009 H1N1 pandemic may have caused fewer deaths because of the low incidence of

infection in elderly people, possibly because they have protective antibody from H1N1 exposure in childhood.

A vaccine against the novel H1N1 virus was developed rapidly by CSL in Australia and has been freely available since 30 September 2009.^{6,7} To date, fewer than 30% of the Australian population are thought to have been vaccinated, leaving potentially more than half the young population (age, <65 years) susceptible when the virus returns from the northern hemisphere for the 2010 flu season, which could start as early as Easter. Although in 2009 the disease was not preventable by vaccination, in 2010 it is a totally preventable infectious disease, and it is a major concern that failure to vaccinate may lead to significant avoidable morbidity and mortality. For health professionals on the “front line”, there is no excuse!

A number of reasons have been advanced by people who have chosen not to be vaccinated, which we address here.

“The vaccine has been rushed to market and is under-tested and potentially unsafe.” The vaccine was developed and manufactured using exactly the same techniques used every year for influenza vaccine, by one of the world’s most experienced vaccine-makers. It came to market after 5 months’ development, which is exactly the time taken each year for seasonal vaccine development. From CSL’s extended surveillance of seasonal influenza vaccine (Fluvax), the reported incidence of major morbidity caused by the vaccine is extremely rare,⁸ and substantially less than the incidence of major morbidity caused by the virus.

“The multidose vials are dangerous.” The CSL influenza A (H1N1) 2009 monovalent vaccine became available in September 2009 in multidose vials, which caused community and professional concern about safety. Multidose vials have been widely used for influenza and other vaccinations,^{9,10} and the use of simple protocols dramatically reduces any risk of vial contamination and disease transmission. Multidose vials are restricted to use on a single day. Over 5 million doses had been distributed by early December 2009, although the actual number administered is certainly less because of inevitable wastage.

“The 1976 H1N1 vaccine caused a huge amount of Guillain-Barré syndrome in the United States — isn’t this a similar virus?” After an outbreak of 1976/H1N1 influenza at a US military base in 1976, 45 million doses of H1N1/New Jersey/1976 vaccine were administered. Vac-

ination was suspended after 10 weeks because of reports of 532 new cases of Guillain–Barré syndrome, or just under one case per 100 000 vaccinations.¹¹ Subsequent investigation showed that the high incidence of Guillain–Barré syndrome in 1976 in the US was a one-off event, which has not been repeated with seasonal influenza vaccines. The 2009 H1N1 virus is genetically distinct (> 10%) from 1976/H1N1 and so is structurally very different and unlikely to induce Guillain–Barré syndrome. Subsequent epidemiological studies were not able to find any increased risk of the syndrome after vaccination for seasonal influenza.¹² Influenza itself is more likely to cause the syndrome, with up to an 18-fold increase in risk after flu-like illness (odds ratio, 18.6 [95% CI, 7.5–46.4] in one study; and relative incidence, 7.4 [95% CI, 4.4–12.4] in another), and a relative incidence within 90 days of vaccination of 0.76 (95% CI, 0.41–1.4).^{13,14} It is apparent that the risk of Guillain–Barré syndrome after influenza, while very low, is much higher than the risk after vaccination, and vaccination has even been proposed as a means to protect against the syndrome.^{15–17}

“I think I had the infection in 2009 anyway.” Clinically, it is impossible to distinguish confidently between novel H1N1 infection, seasonal influenza and other viral upper respiratory tract infections, including infections with rhinoviruses, respiratory syncytial virus and adenoviruses. Only about 20% of those who think they might have been infected with H1N1 in 2009 actually were infected, leaving a larger proportion of young people (age, < 65 years) still susceptible to severe infection in 2010.

“I am fit and well and not at risk.” A third of those who required ICU admission because of H1N1 in 2009 were fit and well with no comorbidities, and 16.2% died.¹ All health professionals are at risk.

“I’ll wait until the 2010 vaccine is available.” The 2009/H1N1 virus [A/California/7/2009 (H1N1)] will be included in the 2010 seasonal vaccine, along with an A/Perth/16/2009 (H3N2)-like virus and a B/Brisbane/60/2008-like virus.⁸ The 2010 seasonal influenza vaccine will not be available until after February 2010, which may be too late to ensure protection against a second wave of 2009 H1N1 virus, and only 4 million doses will be produced (as usual for seasonal flu), compared with 21 million doses of the pandemic H1N1 vaccine.^{18,19} The 2010 vaccine will be free only to those aged over 65 years and specified high-risk groups, whereas the current pandemic vaccine is free to all. There is no harm in having *both* the pandemic H1N1 vaccine now and the 2010 seasonal vaccine in due course — indeed, initial trials of the H1N1 vaccine assessed the response to two doses of 15 µg antigen before confirming that the response to one dose was adequate in both adults and children.^{7,20}

All doctors and nurses who care for patients are at risk of 2009 H1N1 influenza, particularly as the 2010 influenza season begins, but even earlier as virus is imported again from the northern hemisphere. Although the disease is mild in most people, and there are specific risk groups, there is potential for critical illness and even death in previously well young people, including doctors and nurses. The risk of vaccination is very small, and significantly less than the risk of acquiring influenza. The vaccine is administered using strict protocols by trained personnel, and furthermore it is free!

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References

- 1 The ANZIC Influenza Investigators. Critical care services and 2009 H1N1 influenza in Australia and New Zealand. *N Engl J Med* 2009; 361: 1925–34.
- 2 The Australia and New Zealand Extracorporeal Membrane Oxygenation (ANZ ECMO) Influenza Investigators. Extracorporeal membrane oxygenation for 2009 Influenza A(H1N1) acute respiratory distress syndrome. *JAMA* 2009; 302: 1888–95.
- 3 Webb SAR, Seppelt IM. Pandemic (H1N1) 2009 influenza (“swine flu”) in Australian and New Zealand intensive care. *Crit Care Resusc* 2009; 11: 170–2.
- 4 Speers DJ, Williams SH, Pinder M, et al. Oseltamivir-resistant pandemic (H1N1) 2009 influenza in a severely ill patient: the first Australian case. *Med J Aust* 2010; Jan 11. [Epub ahead of print]. http://www.mja.com.au/public/issues/192_03_010210/spe11148_fm.html (accessed Jan 2010).
- 5 Australian Government Department of Health and Ageing, Communicable Diseases Intelligence. Vaccine preventable diseases and vaccine coverage in Australia, 2003–2005. *Commun Dis Intell* 2007; 31 (Jun Suppl). <http://www.nhrc.org.au/internet/main/publishing.nsf/Content/cda-cdi31suppl.htm> (accessed Jan 2010).
- 6 Clark TW, Pareek M, Hoschler K, et al. Trial of influenza A (H1N1) 2009 monovalent MF59-adjuvanted vaccine. *N Engl J Med* 2009; 361: 2424–35.
- 7 Greenberg ME, Lai MH, Hartel GF, et al. Response to a monovalent influenza A (H1N1) 2009 vaccine. *N Engl J Med* 2009; 361: 2405–13.
- 8 CSL Biotherapies. Fluvax ® for the season 2010. Product information. http://www.csllbiotherapies.com.au/s1/cs/aucb/1196562673365/Web_Product_C/1196562642777/ProductDetail.htm (accessed Jan 2010).

EDITORIALS

- 9 Centers for Disease Control and Prevention. Seasonal influenza vaccine supply for the US 2009-10 influenza season. <http://www.cdc.gov/flu/about/qa/vaxsupply.htm> (accessed Jan 2010).
- 10 Centers for Disease Control and Prevention. Updated guidance for the use of CSL™ 2009 H1N1 monovalent vaccine. http://www.cdc.gov/H1N1flu/vaccination/csl_guidance.html (accessed Jan 2010).
- 11 Schonberger LB, Bregman DJ, Sullivan-Bolyai JZ, et al. Guillain-Barré syndrome following vaccination in the National Influenza Immunization Program, United States, 1976-1977. *Am J Epidemiol* 1979; 110: 105-23.
- 12 Kaplan JE, Katona P, Hurwitz ES, Schonberger LB. Guillain-Barré syndrome in the United States, 1979-1980 and 1980-1981: lack of an association with influenza vaccination. *JAMA* 1982; 248: 698-700.
- 13 Tam CC, O'Brien SJ, Petersen I, et al. Guillain-Barré syndrome and preceding infection with campylobacter, influenza and Epstein-Barr virus in the general practice research database. *PLoS One* 2007; 2: e344.
- 14 Stowe J, Andrews N, Wise L, Miller E. Investigation of the temporal association of Guillain-Barré syndrome with influenza vaccine and influenzalike illness using the United Kingdom General Practice Research Database. *Am J Epidemiol* 2009; 169: 382-8.
- 15 Price LC. Should I have an H1N1 flu vaccination after Guillain-Barré syndrome? *BMJ* 2009; 339: b3577.
- 16 Ellis O. Swine flu vaccine is a "thousandfold" safer than the infection, say experts. *BMJ* 2009; 339: b3802.
- 17 Sivadon-Tardy V, Orlikowski D, Porcher R, et al. Guillain-Barré syndrome and influenza virus infection. *Clin Infect Dis* 2009; 48: 48-56.
- 18 CSL Biotherapies, Panvax@H1N1 vaccine and seasonal flu vaccine. <http://www.h1n1vax.com.au/s1/cs/auvx/1247066992580/content/1247066992420/content.htm> (accessed Jan 2010).
- 19 Sharp A. Swine flu warning: don't delay on vaccine. *The Age* 2010; 8 Jan. <http://www.theage.com.au/national/swine-flu-warning-dont-delay-on-vaccine-20100107-lwqb.html> (accessed Jan 2010).
- 20 Nolan T, McVernon J, Skeljo M, et al. Immunogenicity of a monovalent 2009 influenza A(H1N1) vaccine in infants and children: a randomized trial. *JAMA* 2010; 303: 37-46. □