

Should all Australian children be vaccinated against influenza?

Questions of cost-effectiveness, vaccine efficacy and feasibility are yet to be answered

In the United States, routine immunisation of all healthy children aged 6–23 months against influenza has recently been introduced. The principal justification for this is the relatively high morbidity and mortality from this disease in very young children.¹ The United States is also considering routine influenza immunisation of all children aged over 6 months, in view of the herd protection it would provide to the adult population.

Currently, Australian guidelines recommend immunisation of children in groups considered at high risk of severe influenza.² Should Australia introduce universal childhood immunisation?

There is no doubt that children have an extremely high incidence of influenza. It is estimated that, on average, 20%–43% of children are infected during typical influenza seasons.^{3–5} The incidence is highest in young children less than 2 years old, who are often hospitalised.^{1,3–5} The mortality due to influenza in infancy is second only to that in the most elderly patients.¹ In the severe 2003–04 influenza season, 143 children died from influenza in the United States, of whom 58 (41%) were less than 2 years old and 65 (45%) had no underlying condition.¹ These data emphasise the importance of protecting children with annual influenza immunisation, if feasible.

Another reason to consider universal childhood influenza immunisation is herd protection. In what turned out to be an illuminating natural experiment, 50%–85% of Japanese schoolchildren were immunised annually against influenza from 1962 to 1987, but there was no routine immunisation of the elderly. When mandatory immunisation of schoolchildren was relaxed in 1987 and repealed in 1994 (because of doubts about safety and effectiveness), influenza immunisation rates dropped to very low levels. A retrospective study comparing excess mortality from pneumonia and influenza in Japan and the United States concluded that the vaccination of Japanese schoolchildren prevented about 37 000 to 49 000 deaths *per year*, mostly of elderly people. (This represented about one death for every 420 children vaccinated.)⁶

In considering the feasibility of universal childhood vaccination, vaccine efficacy is one of the factors that needs to be taken into account. In healthy adults under 65 years of age, inactivated influenza vaccine is 70%–90% effective when the match between vaccine and circulating viruses is close.¹ However, the same vaccine may be less immunogenic in children. Studies in children aged 6 months to 15 years show a vaccine efficacy of 31%–91% against influenza A and 45% against influenza B.^{7,8} However, very few of the studies have examined children aged 6–23 months,^{9,10} the age group currently recommended for routine influenza vaccination in the United States.

An alternative form of vaccine administration is on the horizon — live attenuated influenza vaccines. A recent systematic review¹⁰ suggested that live vaccines may be more effective than inactivated vaccines in children over 2 years of age (79% versus 65%). Live attenuated influenza vaccines have been licensed in the United States, and might be more acceptable because they are given intranasally.¹¹ However, live vaccines cost a lot more and are not licensed for use in children under 5 years in the United States (because of limited safety data). They are not yet licensed in Australia for use in any age group.

The high morbidity of influenza in children and the likely benefits due to herd immunity do make annual childhood influenza immunisation appear economically attractive. However, against this must be weighed the need to immunise with a new influenza vaccine each year, because of antigenic drift in influenza strains, and the need to give two doses of vaccine to children under 9 years in the first year they are immunised.^{1,2} In addition, the severity of influenza seasons varies unpredictably from mild to severe, and it costs as much to immunise in a mild year as in a severe one.

In the United States, indirect costs (mainly days of work lost by parents) dominate economic analyses supporting the use of influenza vaccines in children.¹² In Australia, by contrast, the Pharma-

ceutical Benefits Advisory Committee considers only direct costs of illness, so it is unlikely that a universal, publicly funded childhood immunisation program could be justified using such cost-effectiveness criteria.

There may also be practical problems with attempts to introduce routine childhood immunisation. In 2004–05, the uptake of influenza vaccine for children aged 6–23 months in the United States, when the vaccine was recommended universally, was estimated to be only 48%.¹³ In Ontario, Canada, where all residents aged over 6 months have been offered free annual influenza immunisation since 2000,¹⁴ the 2003 uptake in children was only 27%.¹⁵ Parents of unimmunised children were more likely to believe that immunisation resulted in a flu-like illness, caused adverse effects more severe than the disease, or weakened the immune system.¹⁵ Such immunisation myths are common, although studies have repeatedly shown inactivated influenza vaccine to be safe, with low rates of adverse events and the benefits clearly outweighing the risks.^{1,2,9}

Another practical issue is the question of how to fit the vaccine into an already crowded childhood vaccination schedule. In general, annual immunisation against influenza is recommended in autumn at the start of the influenza season; there is no fixed age of administration of vaccine. Implementing universal influenza vaccination would place a substantial extra burden on primary care practices.¹⁶

Considering all the available information, I believe that there is currently insufficient reason for introducing universal childhood vaccination for this disease in Australia. There are too many unanswered questions about the cost-effectiveness, efficacy and feasibility of universal immunisation of healthy children, whether infants or school-aged.

For the time being, we should maintain a watching brief. Future data emanating from Ontario and the United States may provide us with a clearer answer as to whether large-scale programs of routine childhood influenza immunisation are feasible and effective. Further, if the US experience with live vaccines shows consistent immunogenicity and improved ease and acceptability of administration, live vaccines may yet prove to be a cost-effective way to implement universal childhood influenza immunisation in Australia.

One thing is clear: influenza vaccination is most cost-effective for children considered at high risk of severe influenza, such as those with chronic cardiopulmonary and other chronic illness. These children should clearly be vaccinated annually against influenza.^{1,2} Yet vaccine coverage of high-risk groups aged 2–17 years is only 35% in the United States,¹³ and probably lower in Australia, although we lack age-specific data. Australian immunisation providers should redouble their efforts to ensure that children at high risk are immunised annually.² Also, it should be remembered that the *Australian immunisation handbook*² does not preclude vaccinating others who are not at high risk. It states that “influenza vaccine should be administered to any person who wishes to reduce the likelihood of becoming ill”.

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- 1 Harper SA, Fukuda K, Uyeki TM, et al; Centers for Disease Control and Prevention (CDC) Advisory Committee on Immunization Practices (ACIP). Prevention and control of influenza: recommendations of the Advisory Committee on Immunization Practices (ACIP). *MMWR Recomm Rep* 2004; 53(RR-6): 1-40.
- 2 National Health and Medical Research Council. The Australian immunisation handbook. 8th ed. Canberra: NHMRC, 2003: 166-175.
- 3 Neuzil KM, Mellen BG, Wright PF, et al. Effect of influenza on hospitalization, outpatient visits and courses of antibiotics in children. *N Engl J Med* 2000; 342: 225-231.
- 4 Izurieta HS, Thompson WW, Kramarz P, et al. Influenza and the rates of hospitalization for respiratory disease among infants and young children. *N Engl J Med* 2000; 342: 232-239.
- 5 Neuzil KM, Wright PF, Mitchel EF Jr, Griffin MR. The burden of influenza illness in children with asthma and other chronic medical conditions. *J Pediatr* 2000; 137: 856-864.
- 6 Reichert TA, Sugaya N, Fedson DS, et al. The Japanese experience with vaccinating schoolchildren against influenza. *N Engl J Med* 2001; 344: 889-896.
- 7 Hoberman A, Greenberg DP, Paradise JL, et al. Effectiveness of inactivated influenza vaccine in preventing acute otitis media in young children: a randomized controlled trial. *JAMA* 2003; 290: 1608-1616.
- 8 Ruben FL. Inactivated influenza virus vaccines in children. *Clin Infect Dis* 2004; 38: 678-688.
- 9 Zangwill KM, Belshe RB. Safety and immunogenicity of trivalent inactivated influenza vaccine in young children: a summary for the new era of routine vaccination. *Pediatr Infect Dis J* 2004; 23: 189-200.
- 10 Jefferson T, Smith S, Demichelli V, et al. Assessment of the efficacy and effectiveness of influenza vaccines in healthy children: systematic review. *Lancet* 2005; 365: 773-780.
- 11 Harper SA, Fukuda K, Cox NJ, Bridges CB; Advisory Committee on Immunization Practices. Using live attenuated influenza vaccine for prevention and control of influenza: supplemental recommendations of the Advisory Committee on Immunization Practices (ACIP). *MMWR Recomm Rep* 2003; 52(RR-13): 1-8.
- 12 Meltzer MI, Neuzil KM, Griffin MR, Fukuda K. An economic analysis of annual influenza vaccination of children. *Vaccine* 2005; 23: 1004-1014.
- 13 Centers for Disease Control and Prevention (CDC). Estimated influenza vaccination coverage among adults and children — United States, September 1, 2004—January 31, 2005. *MMWR Morb Mortal Wkly Rep* 2005; 54: 304-307.
- 14 Langley JM, Faughnan ME. Prevention of influenza in the general population. *CMAJ* 2004; 171: 1213-1222.
- 15 Grant VJ, Le Saux N, Plint AC, et al. Factors influencing childhood influenza immunization. *CMAJ* 2003; 168: 39-41.
- 16 Szilagyi PG, Iwane MK, Schaffer S, et al. Potential burden of universal influenza vaccination of young children on visits to primary care practices. *Pediatrics* 2003; 112: 821-828. □