

13 Influenza

13.1 Introduction

Influenza continues to be a major threat to public health world wide because of its ability to spread rapidly through populations. Epidemics of influenza typically occur during the winter months in New Zealand, affecting all age groups. The greatest burden is among children, but people at increased risk of complications and death from influenza are those 65 years of age or older, and those aged under 65 who have certain medical conditions. Influenza viruses can also cause pandemics, during which the rates of illness and mortality can rise dramatically.

Influenza vaccination is the primary method for preventing influenza and its severe complications.

13.2 The illness

Influenza remains an important cause of morbidity and mortality in New Zealand in all age groups, particularly in the elderly.

Three types of influenza virus are recognised: A, B and C. Type A viruses include a number of subtypes, three of which (H1N1, H2N2, H3N2) have caused epidemics and pandemics of human disease. Type B is associated with widespread outbreaks and epidemics, and C causes only sporadic cases. The virus type is determined by the antigenic properties of the relatively stable internal structural proteins, the nucleoprotein and the matrix protein. Influenza A subtypes are classified on the basis of two surface antigens: haemagglutinin (H) and neuraminidase (N). Both influenza A and B viruses are further separated on the basis of their antigenic characteristics, with new variants arising from frequent antigenic change (antigenic drift). Newly emerged variants are described by the geographic site of isolation, culture number and year of isolation, for example, the H3N2 virus: A/Wellington/1/2004.

The occasional emergence of completely new subtypes occurs only with influenza A viruses. They are responsible for pandemics and result from the adaptation of an avian influenza virus to humans, or the reassortment of human and avian influenza virus genes (antigenic shift). The frequent minor changes (antigenic drift) of A and B viruses are the virologic basis for seasonal epidemics and necessitate the annual reformulation of influenza vaccines.

Influenza is very contagious. The virus is primarily spread from person to person by the aerosol route, via inhalation of droplets formed during coughing and sneezing, or by direct contact with articles contaminated with respiratory secretions. Inhaled virus particles initiate infection in the respiratory tract, although infection can also occur through the mucous membranes of the eyes, nose and mouth. The incubation period can range from one to seven days but is commonly one to three days, during

which time the virus replicates in the ciliated columnar epithelial cells of the upper and lower respiratory tract. An infected person is contagious from one to two days before symptoms start until about day five of illness. Peak viral shedding occurs one to three days after the development of symptoms, diminishing to a low level by five days. Children shed more virus and remain infectious for considerably longer.

In older children and adults, the illness usually begins abruptly with fever, chills, malaise, headache, myalgia, non-productive cough, rhinitis, sore throat and mild conjunctivitis. In children, but less often in adults, vomiting and diarrhoea may be present. Children younger than five years of age most commonly have fever, cough and rhinitis, while in infants only rhinitis may be present. Influenza virus may result in cases of croup and bronchiolitis. The accuracy of the clinical diagnosis of influenza is limited, even during peak influenza activity, because other co-circulating respiratory pathogens can cause similar symptoms. Studies, predominantly in adults, report positive predictive values ranging from 18–87 percent for clinical diagnosis compared with laboratory confirmed influenza.^{1,2,3,4} A definitive diagnosis requires laboratory confirmation. Influenza typically resolves after several days in most people, although cough and malaise may persist for two or more weeks.

In some people influenza can exacerbate underlying medical conditions (eg, pulmonary, cardiac or metabolic disease), and in this group, as well as in previously healthy individuals may lead to secondary bacterial or primary viral pneumonia. Some of the many reported complications associated with influenza include myositis, encephalopathy, myocarditis, pericarditis and Reye syndrome (associated with aspirin use in children), and death.

Avian influenza associated with human cases

Human infections and outbreaks following interspecies transmission of avian influenza viruses have been reported since 1997. Most cases have been associated with direct or indirect contact with infected birds. In 1997 the infection of 18 humans – of whom six died – with an avian H5N1 virus raised the level of global concern of a possible pandemic. In 1999 H9N2 avian influenza infected two children in Hong Kong with other cases in Mainland China. In 2003 H5N1 and H9N2 infections were confirmed in Hong Kong, while in the Netherlands a large avian influenza outbreak involved an H7N7 virus; up to 1000 cases among farmers and poultry workers occurred.

Since late 2003 outbreaks of avian H5N1 have been reported among poultry in South East Asia. Human infections and deaths were initially reported in Viet Nam and Thailand, but with the widespread presence of this virus in Asia, human infections in an increasing number of countries are being reported. Clusters of human infection are small, suggesting that if human to human transmission is occurring it is very inefficient. Because this H5N1 virus continues to circulate in and be spread by avian species there is an ongoing risk of human infection, and the threat of the emergence of a human pandemic virus remains. During 2004/05 the

circulating H5N1 pathogenic avian influenza virus was able to infect humans and therefore has the potential for recombination with a human influenza virus to form a novel influenza virus to which humans would have little, if any, protective immunity. Vaccine trials in humans started in mid-2005, with a vaccine developed against a currently circulating H5N1 strain. In New Zealand, illness due to highly pathogenic avian influenza virus (HPAI) is a notifiable disease, and this will assist in early identification and use of legislation in the event of an outbreak. Further information may be found on the Ministry of Health website (www.moh.govt.nz/influenza).

Pandemic influenza

New Zealand has a pandemic influenza action plan (as an appendix of the National Health Emergency Plan), which the Ministry of Health continues to update.⁵ The plan includes surveillance, health service planning, and the development of policies for the use of antiviral medication and a vaccine (if available).

13.3 Epidemiology

New Zealand experiences the typical temperate climate epidemiology of influenza, and although influenza activity can occur throughout the year, the peak incidence is usually during the winter months, between May and October (Figure 13.1). Ongoing surveillance of influenza is carried out by the four regional virus diagnostic laboratories, and by the Institute of Environmental Science and Research (ESR) virology laboratory. The regional virus diagnostic laboratories report all respiratory virus diagnoses, largely from hospital inpatients and outpatients, to ESR. Sentinel general practice surveillance, as part of the World Health Organization (WHO) Global Programme for Influenza Surveillance, operates nationally during the ‘influenza season’ from May through September each year. Each sentinel practice records the daily number of consultations that fit a case definition for an influenza like illness (ILI), and collects respiratory samples for virus culture from patients with an ILI. Weekly consultation data, along with virus isolation data, are forwarded by local co-ordinators to ESR. The influenza surveillance data and the virology laboratory data are available weekly on the ESR website (see Appendix 11).

The national weekly consultation rate is used to describe the overall level of ILI activity using a set of threshold values: a weekly rate of 50–249 consultations per 100,000 patients is considered indicative of normal seasonal influenza activity; 250–399 indicates higher than expected activity; while 400 and over indicates an epidemic level of disease.^{6,7}

Figure 13.2 shows the weekly consultation rates for ILI from 1992–2005. In 1996 influenza was considered to be at epidemic levels. Rates were highest in infants under one year of age (776 per 100,000) and lowest in those 60 years and over (193 per 100,000). All other years were considered normal seasonal influenza activity.

Figure 13.1: Weekly consultation rates for influenza-like illness in New Zealand, 2003–2005

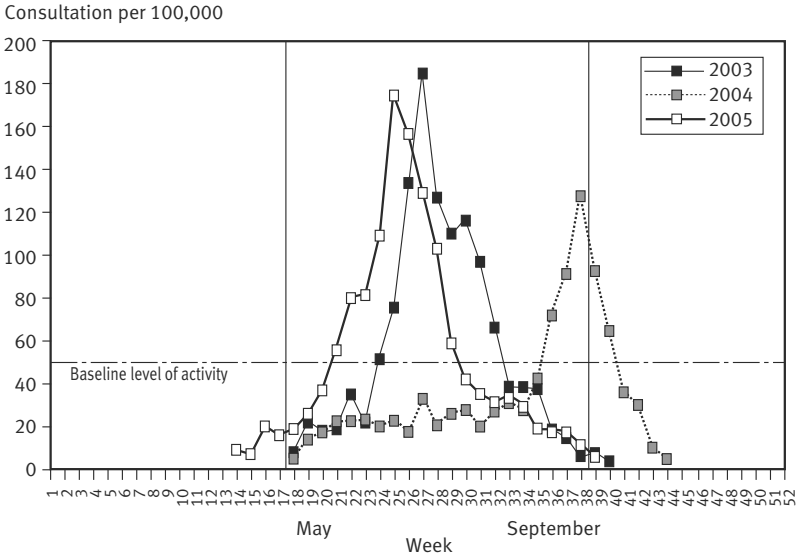
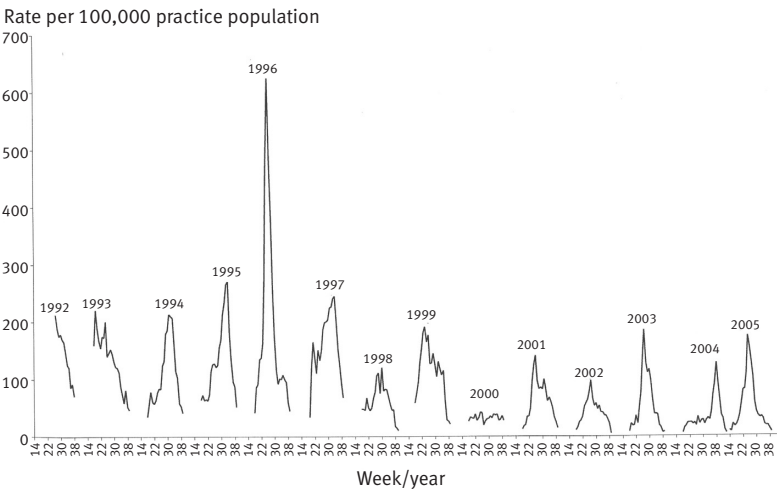
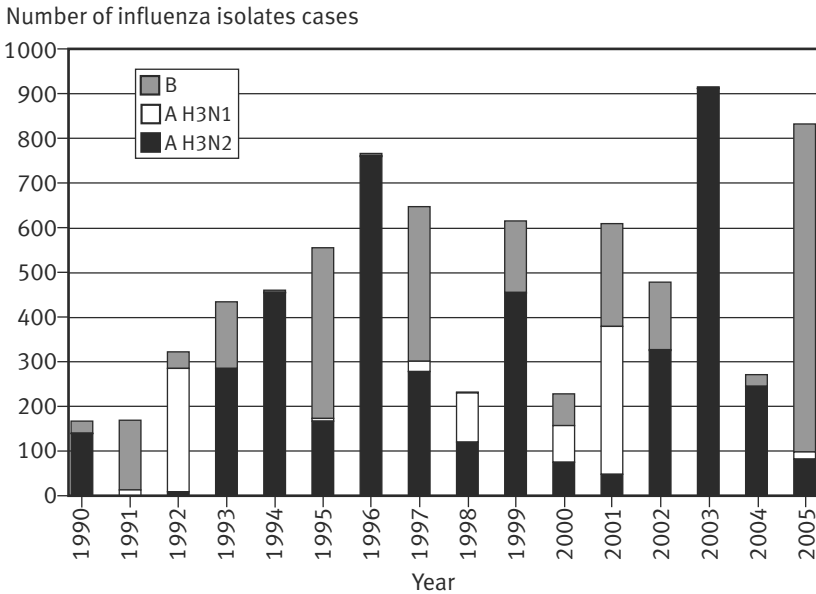


Figure 13.2: Weekly consultation rates for influenza-like illness, 1992–2005



During 2005 there were large outbreaks of influenza B especially in school aged children resulting in some school closures in Wellington. There were three deaths associated with influenza B in school-age children. This was the largest outbreak of influenza B since surveillance began in 1990. Other large outbreaks of influenza B occurred in 1995 and 1997, whereas the annual influenza epidemics are predominantly influenza A, as in Figure 13.3.

Figure 13.3: Influenza isolates by type, 1990–2005



Influenza disease burden surveillance from 1989 to 2004 showed there were 5226 hospitalisations, an average of 327 hospitalisations per year, and 414 deaths directly attributed to influenza in the 16-year period (Figure 13.4). More detailed analysis of data from 1990–99 found the average annual hospitalisation rate for the total population was 7.5 per 100,000, and the rates were high for infants under five years of age, and rates increased from 55 years of age, with a rate of 33.7 per 100,000 in those 65 years and over.⁸ Overall, 21.5 percent of hospitalisations were in this age group. Rates were higher for Māori and Pacific peoples (9.5 per 100,000 and 8.0 per 100,000, respectively) than for Europeans (7.3 per 100,000).

From 1990–99 there were 307 influenza fatalities, an average annual rate of 0.9 per 100,000. Deaths from influenza peaked in 1996 during an influenza A (H3N2) epidemic. The death rate was markedly higher in those 65 years of age and older (10.5 per 100,000), and this age group accounts for the majority (94.1 percent) of the deaths from influenza. The mortality rate was higher for Māori than for Europeans (1.6 per 100,000 compared with 0.9).

Figure 13.4: Hospitalisations for influenza, 1989–2004, and mortality 1989–2002



Modelling for the 13-year period 1980–92 suggested that for every death diagnosed as being due to influenza (primary or secondary diagnosis) a further 7.7 deaths are attributable to influenza but not diagnosed as such.⁹ In some years over 1000 deaths were attributable to influenza, with an average of over 400 deaths per year (5650 over the 13-year period). Overseas modelling has found a similar rate of under diagnosis, with a factor of 3.7 for the Netherlands,¹⁰ and 10 for the United Kingdom (UK).¹¹

Influenza related illness

Hospital data for pneumonia and influenza includes both those cases coded as influenza and cases diagnosed with pneumonia that are secondary to, or a complication of, influenza but the primary diagnosis coded is pneumonia. This underestimates the burden of disease associated with influenza. In 2001/02 there were 12,282 hospitalisations from pneumonia and influenza.

Influenza vaccine in 2005

In 2005 the vaccine programme was delayed due to an influenza vaccine manufacturing failure. The vaccine contained 10 micrograms (µg) of antigen for

the A/Wellington (H3N2) strain instead of 15 µg. Vaccines of full strength (15µg) of the three viruses were purchased for all eligible (publicly funded) individuals from other manufacturers. A study on the lower antigen content vaccine suggested that it offered similar protection to a 15 µg dose. However, the influenza virus circulating early in the 2005 influenza season was predominantly B/Hong Kong, and this virus caused high absenteeism in school children.

13.4 Vaccine

The trivalent influenza vaccines available in New Zealand are split virion or purified antigen vaccines prepared from virus grown in the allantoic cavity of embryonated eggs. The virus is purified, disrupted and inactivated with beta-propiolactone, or formaldehyde. The final product contains 15 µg of the surface haemagglutinins of each component strain (H1N1, H3N2, B) as recommended in September/October each year by the WHO following the WHO southern hemisphere strain selection meeting.

Developments in influenza vaccines

Live attenuated influenza vaccines

Live attenuated influenza virus vaccines are licensed for use in North America for healthy individuals aged 5–49 years. The viruses in these vaccines replicate in the upper respiratory tract with minimal symptoms, producing a specific immune response. Studies in the United States (US) support their safety and efficacy^{12,13} and their potential as an alternative to current inactivated vaccines in healthy individuals. However, unpublished data from one pre-licensure study showed increased airway reactivity in children under the age of five years, and there is not yet sufficient evidence to endorse their use in the elderly and immune compromised.

Other vaccine developments

Research to improve influenza vaccines includes the development of recombinant vaccines, and DNA vaccines, using mammalian cells rather than eggs to grow the influenza virus, and improvements in the efficacy of influenza vaccines by using different parenteral and mucosal adjuvants.¹⁴

Dosage and administration

The vaccine should be administered by intramuscular or subcutaneous injection. The contents of the syringe must be shaken thoroughly before use. Adults receive one dose of 0.5 mL vaccine (see Table 13.1 and the manufacturer's data sheet for the dose in children).

Children younger than nine years of age who have not previously received influenza vaccine require two doses of vaccine one month apart to produce a satisfactory immune response. Children 6–35 months of age are given a 0.25 mL dose to reduce antigen load and reactogenicity. (See section 2.3 for needle sites and sizes.)

Table 13.1: Recommended influenza vaccine doses in children

Age	Dose	Number of doses
6–35 months	0.25 mL	1 or 2*
3–8 years	0.5 mL	1 or 2*
> 9 years	0.5 mL	1

* Two doses separated by at least four weeks if the vaccine is being used for the first time.

The recommended dosages for young children at different ages may vary between vaccine manufacturers, so check the manufacturer’s data sheet before administering. There are limited data on which to base the recommendations, but the aim is to reduce reactions, particularly febrile reactions, which are increased in young children. For this reason, children should be given paracetamol with immunisation at a dose of 15 mg/kg every four hours, up to four doses per 24 hours.

When to vaccinate

The optimal time to vaccinate people in high risk groups is usually during March to April. This is in advance of the usual May to October period of influenza activity. The vaccine can be given even when influenza virus activity has been identified, as protective antibody levels develop from four days to two weeks after immunisation.¹⁵ Immunity lasts about one year¹⁶ and the vaccine should be administered annually.

Efficacy

The effectiveness of influenza vaccine depends primarily on the age and immune competence of the vaccine recipient and the degree of similarity between the virus strains in the vaccine and those in circulation. Vaccine efficacy is 60 to 95 percent against laboratory confirmed influenza when there is a good match. In a study of healthy children aged 6–24 months, vaccines reduced culture confirmed influenza by 66 percent when the vaccine strains matched the predominant circulating strains.¹⁷

Although less effective in preventing clinical illness in older people,¹⁸ the vaccine does reduce hospitalisation and deaths. A 1995 meta-analysis of 20 cohort studies in older people estimated that influenza vaccine prevented 56 percent of respiratory illnesses, 53 percent of pneumonias, 50 percent of all hospitalisations, and 68 percent of deaths.¹⁹ Effectiveness in studies where the epidemic strain had ‘drifted’ was similar to that in studies where the vaccine and epidemic strain were identical. However, if the epidemic strain had ‘shifted’, effectiveness was nil.²⁰

Large case control studies in diabetics and in older people with chronic lung disease have found similar results.²¹ Randomised controlled trials have shown influenza immunisation to reduce illness and days of sick leave in health care workers^{22,23} and to be cost effective for the employer.^{24,25} There is some evidence that immunising health care workers not only reduces illness in the workers, but also reduces mortality in long stay patients.^{26,27} Pregnant women are at increased risk of hospitalisation for selected cardiorespiratory disorders during the second and third trimesters, and it is estimated one to two hospitalisations could be prevented for every 1000 pregnant women vaccinated.²⁸

13.5 Recommended immunisation schedule

Publicly funded influenza immunisation was introduced in 1997 for people 65 years of age and over. From 1999 the vaccine became publicly funded for younger people at increased risk of influenza complications.

To encourage early uptake of the vaccine, free immunisation is available only until the end of June each year. Immunisation is recommended, and free of charge, for the following groups:

Table 13.2: Eligibility criteria for funded influenza immunisation

A – all people 65 years of age and over
<p>B – people under 65 years of age, including children with:</p> <ul style="list-style-type: none"> – cardiovascular disease (ischaemic heart disease, congestive heart failure, rheumatic heart disease, congenital heart disease, cerebrovascular disease) – chronic respiratory disease (asthma if on regular preventive therapy; other chronic respiratory disease with impaired lung function) – diabetes – chronic renal disease – any cancer, excluding basal and squamous skin cancers if not invasive – other conditions (autoimmune disease, immune suppression, human immunodeficiency virus (HIV), transplant recipients, neuromuscular and central nervous system diseases, haemaglobinopathies, children on long term aspirin).

The following conditions are excluded from funding:

- asthma not requiring regular preventive therapy
- hypertension and/or dyslipidaemia without evidence of end organ disease
- pregnancy in the absence of another risk factor.

Pregnant women

Influenza vaccine should be offered, and is funded, for pregnant women with a medical condition (as above in Table 13.2). The vaccine should be given before the influenza season. Although the inactivated influenza vaccine is considered by many experts to be safe at any stage of pregnancy, others prefer to administer the influenza vaccine in the second trimester to avoid a coincidental association with spontaneous abortion.²⁹ Practitioners should assess the risks for individual women.

Although the publicly funded vaccine is not yet available for pregnant women (without a risk condition) the Immunisation Technical Working Group to the Ministry of Health makes the following recommendation for pregnant women:

Influenza vaccination is recommended for women who are beyond the first trimester of pregnancy (ie, greater than 14 weeks gestation) during the influenza season.

Other adults

Health care workers

It is recommended (but not publicly funded) that health care workers should receive influenza immunisation for personal protection against illness, to reduce the risk of transmission within services³⁰ and to reduce the chances of transmitting influenza to family members.

Other healthy adults

Healthy individuals should also consider the use of the vaccine, especially if they are in close contact with individuals at high risk of complications. Employers should consider providing influenza vaccine to avoid illness in their employees, especially those engaged in health care and other essential community services. Immunising healthy individuals has been shown to be cost effective.

Influenza immunisation and travel

People travelling outside New Zealand who are in the at risk groups should consider immunisation, depending on the season and their destination. In tropical countries influenza activity can occur throughout the year but is more likely during the monsoon, while in the northern hemisphere activity is commonest between the months of December and March.

Children

Influenza vaccine is funded for children with chronic illnesses (see Table 13.2). At particular risk are children with the following conditions, who should be prioritised to be recalled to receive influenza vaccine:

- all asthmatics on preventive therapy
- other children with chronic respiratory disorders (eg, cystic fibrosis, non-cystic fibrosis bronchiectasis, and chronic lung disease of infancy).

Special considerations apply to children, as follows.

- In children 6–24 months of age with significant chronic medical conditions, influenza immunisation is occasionally associated with fever between six and 24 hours after administration, which may cause an exacerbation of the underlying condition. Because of the increased risk of fever, regular doses of paracetamol should be given.
- Immune suppressed children receiving cancer chemotherapy respond poorly to influenza vaccine. The optimal time for immunisation is three to four weeks after the last dose of chemotherapy, when the neutrophil and lymphocyte counts are each $\geq 1.0 \times 10^9/L$. Children who are no longer receiving chemotherapy can be expected to show seroconversion three months after the cessation of chemotherapy.
- In children with unstable heart disease (who are a priority group for immunisation), the immune response and safety of influenza vaccine appears to be comparable with that of normal children.
- Infants under six months of age with high risk conditions may be at greater risk from influenza than older children, but there is limited evidence on the efficacy of vaccine in this age group, so alternative methods of protection should be considered.

Other measures to prevent morbidity, particularly in children

In order to optimise the protection of high risk infants and toddlers (including those younger than six months of age):

- all household contacts should receive influenza vaccine
- avoid exposure of the infant to cigarette smoke
- use simple infection control measures such as tissues and hand washing
- avoid contact with those with an acute respiratory infection.

Improving uptake

A randomised controlled trial in Auckland found that making immunisation free to people 65 years of age and over doubled the uptake.³¹ For this age group, national uptake increased from an estimated 25 to 39 percent in 1997, the year the vaccine

was first provided free. Vaccine uptake has further increased to 44 percent in 1998, 55 percent in 1999 and 58 percent in 2000.³² In 2005 the uptake of influenza vaccine in those over 65 years was 61 percent.

The attitude of the practice nurse and general practitioner is important in determining coverage, as was shown by a survey of people 65 years of age or older in Georgia, in the US. Patient attitude had little effect on uptake, but a provider recommendation increased uptake from 8 percent to 75 percent.³³ A further large US survey confirmed previous data that the main reasons for lack of uptake were lack of knowledge, misconceptions about vaccines and vaccine associated illnesses, and lack of recommendations from physicians.³⁴

A review of interventions to improve influenza vaccine uptake found that provider and system oriented interventions were more effective than patient oriented interventions.³⁵ The interventions were: a reminder to the health professional, the existence of a standing order to vaccinate, and the use of a patient reminder by letter/phone call, respectively. Organised registers for recall and opportunistic immunisation are likely to be the key factors to achieving high coverage.

A study³⁶ of the knowledge and attitudes about influenza vaccination among general practitioners, practice nurses and people aged 65 years or over was carried out in four regions of New Zealand during 2001/02. The study found that the health professionals were generally well informed, and 64–68 percent had received influenza immunisation that year. Among the people 65 years and over, 76 percent had received influenza vaccine that year. The commonest reason for receiving the vaccine was that it protects against influenza, followed by they were concerned about getting influenza and its complications, and they believed influenza vaccine prevents serious disease. The reasons for not getting vaccinated were: they believed they did not need it as they rarely get sick, they were unlikely to get influenza, and they had a concern about the side effects. Just over 50 percent of respondents who were not vaccinated erroneously believed they could get influenza from the vaccine, or they could get sick from it. Provider recommendation was important in the participants being immunised against influenza: 67 percent of participants could recall a recommendation from their general practitioner or practice nurse. Among those who could recall such a reminder, 83 percent were immunised, whereas only 63 percent of those who did not recall a reminder had received influenza immunisation.

13.6 Expected responses and adverse events following immunisation (AEFI)

Expected responses

Influenza vaccine is well tolerated. Placebo controlled trials have shown that influenza vaccine may cause systemic reactions in only 1 percent of adults.^{37,38,39}

Systemic reactions (eg, fever, malaise, myalgia) are more likely in children not previously exposed to the vaccine or virus, starting six to 12 hours after immunisation and persisting for one to two days.⁴⁰

Vaccinators need to emphasise to recipients that:

- it is an inactivated vaccine and cannot cause influenza
- many other viruses are present during the autumn, and coincidental infection is likely after immunisation
- local reaction and mild systemic symptoms may occur within a day or two of immunisation.

Local reactions, including redness and induration at the injection site, may persist for one to two days in 10–64 percent of recipients, but these effects are usually mild. Analysis by gender of 14 studies has revealed that females (both young and elderly) report significantly more local reactions.⁴¹ There were no gender differences in seroconversion.

Many individuals will develop a viral infection coincidentally following immunisation and these may be falsely attributed to the vaccine.

See section 13.7 for information on egg allergy.

Asthma

There have been concerns that influenza vaccine causes exacerbation of asthma, based on evidence of increased bronchial reactivity and case reports. However, the reported exacerbations are likely to be coincidental, due to other viral infections that are common at the time of influenza immunisation. Recent studies of inactivated influenza vaccine have failed to find a risk of asthma exacerbation.^{42,43}

Adverse events following immunisation

Guillain-Barré syndrome

There was a statistically significant association between the US 1976 swine influenza vaccine (no longer used) and Guillain-Barré syndrome (GBS) in older adults. A study by the Centers for Disease Control (CDC), Atlanta, defined the risk for that vaccine as 4.9 to 5.9 per million up to eight weeks after immunisation.⁴⁴ It is possible there was a small excess risk of GBS in influenza vaccinees between 18 and 64 years of age in the 1990/91 vaccine season in the US.⁴⁵ In the US between 1976 and 1990 there were no overall increases in GBS among 15–18 million vaccine recipients per year. A study in the US of the 1992/93 and 1993/94 influenza seasons combined found an increased GBS risk of borderline statistical significance (relative risk 1.7; 95 percent confidence interval 1.0–2.8) during the six weeks after vaccination: an excess risk of one to two per million people vaccinated.⁴⁶ The risk was limited to those over 45 years of age.

New Zealand hospitalisations for GBS showed no increase during the 1990s despite the marked increase in vaccine use during this period, but did show a marked year to year variation. In particular, the doubling of vaccine use in 1997 was not associated with any increase in GBS hospitalisations.

No excess risk for GBS following influenza vaccine in children has been documented. No association between influenza vaccines and any other neurological disease has been substantiated.

Any severe or unexpected reactions should be reported to CARM, PO Box 913, Dunedin, using the prepaid postcard HP3442 (see section 2.4) or via online reporting at www.carm.otago.ac.nz. If the patient or parent/caregiver does not consent to being identified, the report should be made without personal identification.

13.7 Contraindications

See section 1.9 for general contraindications for all vaccines.

Individuals who have had an anaphylactoid reaction to hens' eggs or egg protein should not be given influenza vaccine, because it contains minute quantities of residual egg protein. Anaphylactoid hypersensitivity to polymyxin or neomycin or any other vaccine component is a contraindication, because traces of these antibiotics may also be present in the vaccine.

There is no evidence that influenza vaccine prepared from inactivated virus causes damage to the fetus, but as with other vaccines it should not be given during the first trimester of pregnancy (see section 13.5 for recommendations for influenza vaccination of pregnant women).

13.8 Control measures

Transmission of influenza involves person to person spread from the respiratory tract. Therefore one method of limiting an outbreak is to interrupt the chain of infection by persuading those with symptoms to avoid contact with others in the community. In particular, infected individuals should avoid contact with the elderly and chronically ill.

Every effort should be made, during March and April, to immunise all people 65 years of age and over, those under 65 years including children who have certain medical conditions (see Table 13.2), and health care workers. A decision to offer immunisation in winter, during an influenza epidemic, to those who were not immunised in the autumn will depend on the circumstances of the outbreak or epidemic and other factors. Availability of an appropriate vaccine is the most pertinent of these factors.

Immunisation of contacts during an outbreak is not immediately effective because the incubation period of influenza of one to three days is shorter than the time to mount an immune response following vaccination (up to two weeks). Antiviral drugs are approximately 80 percent effective in preventing influenza and should be considered for the prevention of influenza in unimmunised or recently immunised contacts at high risk. When used to limit the size of an institutional outbreak, antiviral drugs are usually given for a period of two weeks after immunisation or until one week after the end of the outbreak.

Rapid diagnostic tests may be useful in identifying outbreaks or deciding whether to start antiviral drugs. During known periods of influenza activity, antiviral therapy should be given to high risk patients with an influenza like illness within 48 hours of symptom onset, even without laboratory confirmation, because rapid diagnostic tests vary in sensitivity and confirmation by PCR (polymerase chain reaction) or culture may not be available, or may take several days.^{47,48}

Pandemics

At the time of a pandemic the priority groups and the timing of vaccination may be quite different from those during inter-pandemic periods. The Ministry of Health is continuing work on updating the New Zealand Pandemic Plan (see www.moh.govt.nz).

The Ministry of Health will provide recommendations for immunisation in the event of a pandemic.

Antiviral drugs

The neuraminidase inhibitors, zanamivir (RELENZA™, taken by inhalation) and oseltamivir (Tamiflu®, taken orally), are effective against both influenza A and B, unlike amantadine and rimantadine, which are only effective against influenza A. The drugs are compared in Table 13.3.

Table 13.3: Influenza antivirals

	Amantadine	Zanamivir	Oseltamivir
Common name	Symmetrel® Novartis	Relenza™ GlaxoSmithKline	Tamiflu® Roche
Route	Oral	Inhaled	Oral
Dose	100 mg bid (5 mg/kg/day 1–9 years)	10 mg bid 5 days	75 mg bid 5 days; 2mg/kg in children
Viruses inhibited	Influenza A	Influenza A & B	Influenza A & B
Resistance	Develops rapidly	In vitro – yes In vivo – ?	In vitro – yes In vivo – yes
Side effects	Central nervous system side effects	Few side effects	Nausea, vomiting; take with food
Age treatment available	≥1 year	≥ 12 years	≥ 1 year
Cost	~ \$10	~ \$50 not available in NZ	~ \$70

The antiviral drugs have been shown to shorten the duration of illness by one to two days, to reduce complications if given within 48 hours of symptoms, and to prevent infection in adults if given appropriately.^{49,50}

Universal influenza immunisation of infants

Universal influenza immunisation of all healthy infants, six to 24 months of age, has recently been introduced in the US.⁵¹ This is because young children have the highest rates of infection and mortality secondary only to the elderly. There is also some evidence from Japan that immunisation in children protects the elderly from influenza related deaths by a herd immunity effect.⁵² However, in an already crowded immunisation schedule, more information is required on the efficacy of influenza vaccines in the very young, whether such a strategy is clinically cost effective, if parents will accept the need for annual vaccination, and whether primary health care has the capacity to deliver such a programme.^{53,54} Cost–benefit analysis identifies the greatest returns from vaccinating children identified as high risk.⁵⁵

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