Immunisation Handbook 2006
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Foreword

Immunisation is a highly effective strategy for the prevention of infectious disease throughout life. The results of the 2005 National Coverage Survey (as summarised in the Introduction) have shown we have made progress in improving immunisation coverage in New Zealand since the previous survey in 1991. The implementation of the National Immunisation Register and the Meningococcal B Immunisation Programme have focused health professionals and the public on the benefits of immunisation. We will be able to build on these successes to use the National Immunisation Register to improve immunisation coverage so that children whose parents wish to immunise their children receive their age appropriate immunisations.

The Immunisation Handbook 2006 provides information for health professionals on vaccine preventable diseases, the vaccines available, and the updated National Immunisation Schedule, as well as practical advice and strategies for health professionals immunising children and adults in New Zealand. A new chapter identifies new vaccines likely to be available in New Zealand during the time this edition of the handbook is current.

The 2006 National Immunisation Schedule introduces a pertussis containing vaccine to be offered at the age of 11 years to protect adolescents and young adults against pertussis. This new vaccine provides an opportunity to decrease the impact of pertussis in young people and reduce the size of pertussis epidemics. The meningococcal B vaccine will continue to be offered to infants and children under the age of five years until it is no longer necessary to control the disease.

I would like to thank the members of the Immunisation Technical Working Group who have contributed to rewriting the Immunisation Handbook 2006, and to thank all those who acted as peer reviewers. I trust this edition, like its predecessors, will prove a valuable resource for health professionals.

Karen O Poutasi (Dr)
Director-General of Health
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Preface

Welcome to the *Immunisation Handbook 2006*.

This Handbook provides information on the National Immunisation Schedule 2006 for children and recommendations for adult immunisation. There is information on the immunisation programme and on vaccines that may be available and used in New Zealand. Since the last edition of the Handbook, New Zealand health professionals have delivered a nation-wide Meningococcal B Immunisation Programme, offered to all children and young adults age 0–19 years. The National Immunisation Register was used for the Meningococcal B Immunisation Programme and is now recording immunisation information on all infants born in New Zealand, with parental consent. We shall now be able to record children’s immunisations and follow-up children who do not receive immunisation and measure coverage.

The new National Immunisation Schedule (Schedule) began on 1 February 2006, and all children will transfer to the new Schedule. In 2006, children at age 11 years will be offered the dTap-IPV vaccine (tetanus, adult dose of diphtheria and adult dose of pertussis vaccines and inactivated polio vaccine). This pertussis containing vaccine will offer protection to adolescents against pertussis. At the age of 15 months MMR (measles, mumps, and rubella vaccine) and Hib vaccine will be given. The Meningococcal B Immunisation Programme will continue for infants and the programme will be reviewed regularly until the vaccine can be discontinued. From 2006 pneumococcal vaccine is available for a small group of children at high risk of pneumococcal disease and for adults or children pre- or post-splenectomy.

The Ministry of Health’s Immunisation Technical Working Group (ITWG) provided advice on the National Immunisation Schedule 2006, and have re-written this Handbook. The ITWG was assisted by a number of health professionals and individuals who all contributed their expertise to chapter writing or peer review of the chapters.

Because of the rapid developments and availability of new vaccines, the Schedule will be reviewed, though not necessarily changed, every two years. This will allow New Zealand children to receive the most appropriate, safe and effective vaccines.
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Main source books

*Adis International*, MIMS. Adis International.


Information on New Zealand epidemiology is sourced from data collated by the Institute of Environmental Science and Research (ESR), on behalf of the Ministry of Health, or from the New Zealand Health Information Services (NZHIS).


Commonly used abbreviations

ACC  Accident Compensation Corporation
AEFI  adverse event following immunisation
AFP  acute flaccid paralysis
AIDS  acquired immunodeficiency syndrome
BCG  Bacillus Calmette-Guérin vaccine
BSE  bovine spongiform encephalopathy
CARM  Centre for Adverse Reactions Monitoring
CRS  congenital rubella syndrome
CSF  cerebrospinal fluid
DHB  district health board
DNA  deoxyribonucleic acid
DT  diphtheria tetanus vaccine
DTaP  diphtheria, tetanus and acellular pertussis vaccine
DTaP/Hib  diphtheria, tetanus, acellular pertussis and Haemophilus influenzae type b vaccine
DTaP-IPV  diphtheria, tetanus, acellular pertussis and inactivated polio vaccine
dTap-IPV  adult dose diphtheria, tetanus, acellular pertussis and inactivated polio vaccine
DTwP  diphtheria, tetanus and whole cell pertussis vaccine
DTwPH  diphtheria, tetanus, whole cell pertussis and Haemophilus influenzae type b vaccine
ESR  Institute of Environmental Science and Research
GBS  Guillain-Barré Syndrome
HAV  hepatitis A virus
Hep B  hepatitis B vaccine
HBIG  hepatitis B immunoglobulin
HBsAg  hepatitis B surface antigen
HHE  hypotonic, hyporesponsive episode
Hib  Haemophilus influenzae type b
HIV  human immunodeficiency virus
HPV  human papilloma virus
IG  immunoglobulin
<table>
<thead>
<tr>
<th>Acronym</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>IM</td>
<td>intramuscular</td>
</tr>
<tr>
<td>IMAC</td>
<td>Immunisation Advisory Centre</td>
</tr>
<tr>
<td>IPV</td>
<td>inactivated polio vaccine</td>
</tr>
<tr>
<td>IV</td>
<td>intravenous</td>
</tr>
<tr>
<td>IVIG</td>
<td>intravenous immunoglobulin</td>
</tr>
<tr>
<td>LMC</td>
<td>lead maternity carer</td>
</tr>
<tr>
<td>MeNZB™</td>
<td>meningococcal B vaccine</td>
</tr>
<tr>
<td>MMR</td>
<td>measles, mumps and rubella vaccine</td>
</tr>
<tr>
<td>NIR</td>
<td>National Immunisation Register</td>
</tr>
<tr>
<td>NZPSU</td>
<td>New Zealand Paediatric Surveillance Unit</td>
</tr>
<tr>
<td>OMP</td>
<td>outer membrane protein</td>
</tr>
<tr>
<td>OPV</td>
<td>oral polio vaccine</td>
</tr>
<tr>
<td>PCR</td>
<td>polymerase chain reaction</td>
</tr>
<tr>
<td>PCV7</td>
<td>seven valent pneumococcal conjugate vaccine</td>
</tr>
<tr>
<td>PHO</td>
<td>primary health organisation</td>
</tr>
<tr>
<td>23PPV</td>
<td>23 valent pneumococcal polysaccharide vaccine</td>
</tr>
<tr>
<td>PRP</td>
<td>polyribosylribitol phosphate</td>
</tr>
<tr>
<td>RCT</td>
<td>randomised control trial</td>
</tr>
<tr>
<td>RIG</td>
<td>rabies immunoglobulin</td>
</tr>
<tr>
<td>SC</td>
<td>subcutaneous</td>
</tr>
<tr>
<td>SIDS</td>
<td>sudden infant death syndrome or cot death</td>
</tr>
<tr>
<td>Td</td>
<td>adult tetanus diphtheria vaccine</td>
</tr>
<tr>
<td>TIG</td>
<td>tetanus immunoglobulin</td>
</tr>
<tr>
<td>TT</td>
<td>tetanus toxoid</td>
</tr>
<tr>
<td>TB</td>
<td>tuberculosis</td>
</tr>
<tr>
<td>UK</td>
<td>United Kingdom</td>
</tr>
<tr>
<td>US</td>
<td>United States of America</td>
</tr>
<tr>
<td>VAPP</td>
<td>vaccine associated paralytic poliomyelitis</td>
</tr>
<tr>
<td>vCJD</td>
<td>variant Creutzfeldt-Jakob disease</td>
</tr>
<tr>
<td>VZV</td>
<td>varicella zoster virus</td>
</tr>
<tr>
<td>WHO</td>
<td>World Health Organization</td>
</tr>
<tr>
<td>ZIG</td>
<td>varicella-zoster immunoglobulin</td>
</tr>
</tbody>
</table>
Introduction

The National Immunisation Schedule 2006

The new National Immunisation Schedule (Schedule) commenced on 1 February 2006. This edition of the Handbook provides information on the new Schedule, vaccines available and the epidemiology of the vaccine preventable diseases in New Zealand.

To assist immunisation coverage and disease prevention in New Zealand the Schedule will be reviewed every two years and may change as new, safer and more effective vaccines and combinations become available.

Table 1: National Immunisation Schedule commencing 1 February 2006

<table>
<thead>
<tr>
<th>Age</th>
<th>Immunisation given</th>
<th>Special programme**</th>
</tr>
</thead>
<tbody>
<tr>
<td>6 weeks</td>
<td>DTaP-IPV</td>
<td>Hib-Hep B</td>
</tr>
<tr>
<td>3 months</td>
<td>DTaP-IPV</td>
<td>Hib-Hep B</td>
</tr>
<tr>
<td>5 months</td>
<td>DTaP-IPV</td>
<td>Hep B</td>
</tr>
<tr>
<td>10 months***</td>
<td></td>
<td></td>
</tr>
<tr>
<td>15 months</td>
<td>Hib</td>
<td>MMR</td>
</tr>
<tr>
<td>4 years</td>
<td>DTaP-IPV</td>
<td>MMR</td>
</tr>
<tr>
<td>11 years</td>
<td>dTap-IPV*</td>
<td></td>
</tr>
<tr>
<td>45 years</td>
<td>Td</td>
<td></td>
</tr>
<tr>
<td>65 years</td>
<td>Td</td>
<td>Influenza (annually)</td>
</tr>
</tbody>
</table>


* IPV will be given until the end of 2007 for those who have not previously had four doses.

** MeNZB™ vaccine will be available providing provisional consent is extended. See also Table 1.2 for additional individuals eligible for MeNZB™ vaccine.

*** Infants who receive their 3rd dose between 5 and 6 months of age, have the 4th at a minimum of 10 months of age. Infants who receive their 3rd dose after 6 months of age or older, have the 4th dose at a minimum of four months after the 3rd dose.

Babies of HBsAg positive mothers need hepatitis B immunoglobulin (HBIG) and vaccine at birth. Household and sexual contacts of hepatitis B cases and carriers should be offered hepatitis B immunisation.

Neonatal BCG should be offered to infants at increased risk of tuberculosis defined as those who:

1. will be living in a house or family/whānau with a person with either current tuberculosis or a past history of tuberculosis
2. have one or both parents who identify as being Pacific people
3. have parents or household members who have within the last five years lived for a period of six months or longer in countries where there is a high incidence of tuberculosis†
4. during their first five years will be living for three months or longer in a high incidence country†
5. live in specific geographical areas as defined by the medical officer of health after consultation with the Ministry of Health (see chapter 12).
+ All countries except Australia, Austria, Belgium, Canada, Czech Republic, Denmark, Finland, France, Germany, Greece, Holland, Iceland, Ireland, Israel, Italy, Luxembourg, Malta, Monaco, New Zealand, Norway, Slovakia, Sweden, Switzerland, the UK, and the US.

- All children transfer to the new Schedule on 1 February 2006.

- At age 11 years, the dTap-IPV vaccine (adult diphtheria, tetanus, acellular pertussis and inactivated polio vaccine) will be offered in 2006 and 2007 so that children receive four doses of polio vaccine. From 2008 the vaccine offered at age 11 years will be dTap.

- Hib and MMR will be given at age 15 months. The fourth dose of a pertussis containing vaccine will be given at age four years as DTaP-IPV.

- The Meningococcal B Immunisation Programme is completed on 30 June 2006. However children and young people, aged 5 to 19 years should complete a course of MeNZB™ up to 31 December 2006, after that the vaccine is not available to them.

- From 1 July 2006 MeNZB™ vaccine will be available to infants as a four dose course at age six weeks, three, five and 10 months. Children under the age of five years should complete a course of MeNZB™ vaccine whilst the vaccine is available. The Ministry of Health will communicate with practitioners if there are changes or additions to this programme.

- Pneumococcal conjugate vaccine is funded and available for a specified group of children at high risk of pneumococcal disease, on recommendation of a paediatrician or other secondary care specialist (such as haematologist, infectious diseases physician). These are children:
  - on immunosuppressive therapy or radiation therapy, when there is expected to be sufficient immune response
  - with primary immune deficiencies
  - with HIV infection
  - with renal failure, or nephrotic syndrome
  - immune suppressed following organ transplantation
  - with cochlear implants or intracranial shunts
  - with chronic cerebrospinal fluid leaks
  - receiving corticosteroid therapy for more than two weeks, who are on an equivalent daily dosage of prednisone of 2 mg/kg per day or greater, or a total daily dosage of 20 mg or greater.

- A vaccine programme for adults and children pre- or post-splenectomy will be funded from 2006. Pneumococcal, meningococcal polysaccharide A,C,Y,W135, MeNZB™ and Hib vaccines are now funded for children pre- and post-splenectomy or with functional asplenia, and for adults pre- and post-splenectomy.
• Adult tetanus boosters will be offered at 45 and 65 years of age.
• Influenza vaccine is funded for adults over the age of 65 years and adults and children with chronic medical conditions.

Changes in the Immunisation Handbook 2006
There is a Key Points section for each of the chapters that focus on a particular disease (chapters 3–17) to assist health professionals.

The Western Pacific Region remains poliomyelitis free but polio reappears in some countries
In October 2000 the World Health Organization (WHO) declared the Western Pacific Region to be polio free. New Zealand and other countries of the Western Pacific continue to provide high coverage polio vaccine programmes, disease surveillance programmes, laboratory testing and diagnosis of cases of acute flaccid paralysis (AFP). The reappearance of poliomyelitis in countries such as Indonesia and across Africa has put back the WHO goal of eradication of poliomyelitis from the world for at least another two years.

Influenza and the risk of a pandemic influenza
Emergence and spread in South East Asia and beyond, of a highly pathogenic avian influenza H5N1 virus able to infect humans has led to fears of an influenza pandemic arising through change in the virus. Vaccine manufacturers are developing a vaccine against an H5N1 strain and countries around the world have developed emergency plans.

Information on new vaccines which are available or in development
• Meningococcal B vaccine and the New Zealand immunisation programme (see chapter 15).
• Meningococcal C conjugate vaccine, results from the programmes in the United Kingdom and Australia.
• Pneumococcal conjugate vaccine –this vaccine is now funded for a specific group of children at special risk (see chapter 16). It is hoped this programme can be extended to other children at risk of pneumococcal disease when funds are available.
• Funded immunisation programme for adults and children pre- and post-splenectomy (see chapters 16,15,7).
• MMRV (measles, mumps, rubella and varicella vaccine) is likely to be licensed in New Zealand within the next year (see chapters 9 and 17).
• Adult dose pertussis vaccine combined with adult dose diphtheria, tetanus and inactivated polio vaccine is now on the National Immunisation Schedule at age
11 years. It is expected that recommendations for use of the adult pertussis containing vaccine will be extended as results of clinical trials become available (see chapter 6).

- Human papilloma virus vaccines are now in stage III clinical trials. Applications to license the vaccine have or will be submitted in many countries, including New Zealand, in the next one to two years (see chapter 19). This vaccine is best given to girls before the onset of sexual activity.
- New rotavirus vaccines are in stage III clinical trials (see chapter 19).
- Combination typhoid and hepatitis A vaccines are licensed in New Zealand (see chapter 14).

Other recommendations

Adult immunisation: These recommendations are unchanged.

The following vaccines are recommended and are publicly funded.

- Adults should have received a primary series of vaccines against tetanus and diphtheria. Boosters of tetanus-diphtheria (Td) are recommended at 45 and 65 years of age. These recommendations that boosters are given at a specific age may increase uptake as it is expected Td immunisation will be linked with other preventive health visits (see chapter 5).
- Adult females of childbearing age should know whether or not they are immune to rubella. Combined MMR vaccine is available for susceptible adults (see chapter 11).
- Hepatitis B vaccine is available for household and sexual contacts of known hepatitis B carriers (see chapter 3).
- IPV is available for adults who have not received a primary course of polio vaccine (see chapter 8).

Varicella vaccine

For these recommendations see chapter 17.

Safe delivery and assessing contraindications

- For updated recommendations see chapter 1.
- Emergency equipment and management of anaphylaxis; see chapter 2, and the inside of the Handbook's back cover.
- The questions likely to be asked, concerns, and information about the latest research and assessments of vaccine safety have been updated. (See chapter 20).
- For the updated standards for immunisation see Appendix 3.
Immunisation programme changes

Outreach immunisation services
Outreach immunisation services have been set up in 16 District Health Boards (DHBs). Outreach services are primary health care providers who are referred children according to a local protocol, for tracing and follow up of missed or delayed immunisations. The aim is to either immunise the child or to ensure they are linked back to a primary health care service for immunisation and other health services.

Cold chain accreditation
Cold chain accreditation (CCA) is a process that allows primary care practices to demonstrate their management of vaccine stocks in the cold chain, as required by existing national cold chain standards. The demonstration is through a self audit that is reviewed by the local immunisation co-ordinator/facilitator. The CCA process minimises the levels of vaccine wastage and ensures the provision of effective vaccines for the National Immunisation Schedule vaccines.

For a practice to achieve CCA they must meet all the essential requirements for their cold chain management. CCA is valid for up to three years (see chapter 2).

National Immunisation Register
The National Immunisation Register (NIR) is aimed at benefitting individuals by facilitating the delivery of immunisation services and providing an accurate record of their immunisation history. It will also provide national and regional level information on the immunisation coverage of a specified population, and assist in achieving New Zealand coverage targets (ie, 95 percent of children fully immunised by two years of age), thus improving individual and population health through the control or elimination of vaccine preventable diseases.

The NIR was implemented during 2004/05 to collect immunisation information for the Meningococcal B Immunisation Programme. During 2005 the NIR began collecting immunisation information on all individuals born after a specified date (ie, a birth cohort). In the future the NIR may also collect other immunisation information (eg, 11 year immunisation event or adult immunisations).

Immunisation Research Strategy
The Ministry of Health and the Health Research Council (HRC) jointly fund an Immunisation Research Strategy. Further information is found on the HRC website www.hrc.govt.nz.

National Serosurvey
The Ministry of Health has contracted with the University of Otago for a National Serosurvey. This is currently under way.
Immunisation coverage in New Zealand

It is important to know the level of immunisation coverage in New Zealand children, that is, the proportion of children who have either been immunised with a specific vaccine or who have completed an immunisation series.

This information is used to assist programme planning and to target disease control interventions. It is also used to assess the risk of epidemics of vaccine preventable diseases, for measuring vaccine efficacy, monitoring the frequency of adverse events, and assessing acceptability of the National Immunisation Schedule. More detailed information is useful at a regional level to assist with targeting services.

Up until 2000 ESR provided estimates of national immunisation coverage using immunisation benefit claims and information from capitated practices. The denominators were based on census data and population projections. Table 2 below is an estimate of coverage in 2000, based on claims from January to June 2000.

Table 2: National immunisation coverage for 2000 based on benefit claim data

<table>
<thead>
<tr>
<th>Vaccination*</th>
<th>Recommended timing</th>
<th>National coverage levels (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>DTwPH/DTaP 1</td>
<td>6 weeks</td>
<td>89</td>
</tr>
<tr>
<td>DTwPH/DTaP 2</td>
<td>3 months</td>
<td>87</td>
</tr>
<tr>
<td>DTwPH/DTaP 3</td>
<td>5 months</td>
<td>90</td>
</tr>
<tr>
<td>DTwPH/DTaP/Hib</td>
<td>15 months</td>
<td>86</td>
</tr>
<tr>
<td>Hep B/Hib-Hep B</td>
<td>6 weeks</td>
<td>89</td>
</tr>
<tr>
<td>Hep B/Hib-Hep B</td>
<td>3 months</td>
<td>87</td>
</tr>
<tr>
<td>Hep B</td>
<td>5 months</td>
<td>90</td>
</tr>
<tr>
<td>OPV1</td>
<td>6 weeks</td>
<td>84</td>
</tr>
<tr>
<td>OPV2</td>
<td>3 months</td>
<td>81</td>
</tr>
<tr>
<td>OPV3</td>
<td>5 months</td>
<td>82</td>
</tr>
<tr>
<td>MMR 1</td>
<td>15 months</td>
<td>85</td>
</tr>
</tbody>
</table>


* D=diphtheria, T=tetanus, wP = whole cell pertussis, aP= acellular pertussis, Hib= *Haemophilus influenzae* type b, Hep B= hepatitis B, OPV= oral polio vaccine, MMR= measles, mumps and rubella.

National Immunisation Coverage Survey 2005

The last national immunisation coverage survey completed in 1992 showed inadequate levels of fully immunised coverage at age 2 years (<60 percent), and disproportionately lower levels for Māori (42 percent) and Pacific (45 percent)\(^1\). A follow-up survey was undertaken in the North health region\(^2\) in 1996 that suggested

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\(^1\) Note that the references quoting these figures did not indicate whether these differences were statistically significant.

\(^2\) North Health included the sub-regions Northland, and North, West, Central, and South Auckland.
little improvement with 63 percent of children fully immunised at age 2 years, and Māori significantly lower at 45 percent.

A National Childhood Immunisation Coverage Survey was undertaken between January and March 2005 that showed improvement over previous coverage estimates. Fully immunised coverage at age 2 years had improved from less than 60 percent in 1992 to 77.4 percent in 2005. However, Māori were significantly less likely to be fully immunised at age 2 years (69 percent) compared with European/Other ethnicity (80.1 percent) (Figure 1).

**Figure 1: Fully immunised coverage at different time periods by ethnicity**

![Immunisation coverage level (%)](image)

Although there were no significant differences between the four health regions³ the Southern region tended to have better coverage overall, and have the best coverage rates for Māori (although this was not statistically significant). The DHBs with significantly better coverage than total New Zealand coverage were South Canterbury, Southland, and the West Coast (which had significantly better coverage than all other DHBs⁴)(Figure 2). Whanganui DHB⁵ coverage was significantly lower than West Coast, South Canterbury, Southland, Canterbury, and MidCentral DHBs, and the total New Zealand coverage. Northland coverage was significantly less than

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³ Northern, Central-Northern, Central-Southern, Southern.

⁴ Although the survey contained only 6 children within the West Coast DHB increasing the possibility that chance may have explained the survey result.

⁵ The survey included only 10 children in the Whanganui DHB and therefore results should be interpreted with caution.
the first three DHBs as for Whanganui. These survey results have highlighted the priority that needs to be given to improving immunisation coverage for Māori and for predominantly North Island DHBs.

Figure 1 shows results for coverage at age 1 year, and at the time of the survey\(^6\), in addition to coverage at age two years. Coverage rates drop at two years of age but return to similar levels at the time of the survey indicating a catch-up of late vaccination occurring after age two years. Late vaccination results in a vulnerable population increasing the chances for epidemics (especially of measles). Improving on-time coverage (within four weeks of recommended due date) is an important control measure for vaccine preventable diseases. Coverage rates for individual vaccines at age two years are shown in Table 3. The trend is for decreasing coverage for each sequential dose; however the greatest (and significant) decline in coverage is for the 15 month DTaP and Hib vaccinations. For these 15 months immunisations, the coverage levels in Māori children are significantly lower than European/Other and Pacific ethnic groups for the DTaP4, Hib3, and MMR (see Figure 3). Priority needs to be given to improving coverage for the 15 month vaccinations and above all for Māori.

**Figure 2: Coverage at age 2 years by DHB including 95 percent confidence intervals (CI)**

<table>
<thead>
<tr>
<th>Immunisation coverage level (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>100</td>
</tr>
<tr>
<td>90</td>
</tr>
<tr>
<td>80</td>
</tr>
<tr>
<td>70</td>
</tr>
<tr>
<td>60</td>
</tr>
<tr>
<td>50</td>
</tr>
<tr>
<td>40</td>
</tr>
<tr>
<td>30</td>
</tr>
<tr>
<td>20</td>
</tr>
<tr>
<td>10</td>
</tr>
<tr>
<td>0</td>
</tr>
</tbody>
</table>

* Count ≤10

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\(^6\) Coverage at the time of the survey does not place time restrictions on when a child receives a vaccine and covers the age ranges represented in the survey of 2–3-year-olds.
### Table 3: Vaccination coverage level (95% confidence intervals (CI)) at age 2 years

<table>
<thead>
<tr>
<th>Vaccine Dose*</th>
<th>Coverage Level %</th>
<th>(95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>DTaP dose 1</td>
<td>92.1</td>
<td>(90.9, 93.4)</td>
</tr>
<tr>
<td>DTaP dose 2</td>
<td>90.6</td>
<td>(89.3, 92.0)</td>
</tr>
<tr>
<td>DTaP dose 3</td>
<td>88.6</td>
<td>(87.0, 90.3)</td>
</tr>
<tr>
<td>DTaP dose 4</td>
<td>79.3</td>
<td>(77.2, 81.5)</td>
</tr>
<tr>
<td>Oral Polio or DTaP-IPV dose 1</td>
<td>92.1</td>
<td>(90.8, 93.4)</td>
</tr>
<tr>
<td>Oral Polio or DTaP-IPV dose 2</td>
<td>90.4</td>
<td>(89.0, 91.8)</td>
</tr>
<tr>
<td>Oral Polio or DTaP-IPV dose 3</td>
<td>88.5</td>
<td>(86.8, 90.1)</td>
</tr>
<tr>
<td>Hib dose 1</td>
<td>91.3</td>
<td>(89.9, 92.6)</td>
</tr>
<tr>
<td>Hib dose 2</td>
<td>90.0</td>
<td>(88.5, 91.4)</td>
</tr>
<tr>
<td>Hib dose 3</td>
<td>79.6</td>
<td>(77.5, 81.6)</td>
</tr>
<tr>
<td>Hep B dose 1</td>
<td>90.6</td>
<td>(89.2, 91.9)</td>
</tr>
<tr>
<td>Hep B dose 2</td>
<td>88.9</td>
<td>(87.4, 90.4)</td>
</tr>
<tr>
<td>Hep B dose 3</td>
<td>86.5</td>
<td>(84.8, 88.3)</td>
</tr>
<tr>
<td>MMR dose 1</td>
<td>82.0</td>
<td>(79.8, 84.1)</td>
</tr>
<tr>
<td>Neonatal Hep B + HBIG</td>
<td>72.0</td>
<td>(53.5, 90.5)</td>
</tr>
</tbody>
</table>


The results from the National Childhood Immunisation Coverage Survey 2005 can be used as a baseline measure with which to compare coverage rates following implementation of the National Immunisation Register (NIR). Monitoring and evaluation of immunisation coverage rates and targets can contribute to improved immunisation coverage. Individual primary care practices within New Zealand with high coverage rates have attributed their success to the use of enrolled populations, good recall systems and outreach services to high-risk children. In addition to the use of the NIR, the development of Primary Health Organisations (PHOs) with enrolled populations is likely to result in an improvement of coverage levels from the 2005 survey. The impact of the NIR, PHOs, and other interventions with the potential to increase childhood immunisation coverage can be assessed when the NIR has sufficient data for analysis of coverage levels and then compared with the 2005 survey results.
Introduction

**Figure 3: Immunisation coverage at age 2 years by ethnicity**

**Immunisation coverage level (%)**

- **All**
- **Asian**
- **Māori**
- **European/Other**
- **Pacific**

**Influenza immunisation coverage**

The New Zealand target for influenza vaccine coverage in adults over the age of 65 years is 75 percent. The influenza vaccine coverage for the population eligible for funded vaccine is calculated from benefit claims data for those over 65 years attending a PHO. At the present time the coverage data for those with chronic medical conditions is not robust.

The coverage for those over 65 years enrolled in a PHO was 58 percent in 2004 and 61 percent in 2005. This increase was achieved in spite of a delay in arrival of influenza vaccine and the pressures on health care workers delivering the Meningococcal B Immunisation Programme at the same time.

The influenza vaccine coverage by DHB in adults over the age of 65 years is shown in Figure 4.
Figure 4: Influenza vaccination coverage in adults over 65 enrolled in Primary Health Organisations
Key points
Following are the key points from each of the chapters that focus on a particular disease (chapters 3–17). See page xvi for an explanation of the abbreviations. For catch up schedules for unimmunised or partially immunised children see Appendix 2.

Hepatitis B key points  (see chapter 3)

Illness or risks of infection
• Hepatitis B is mainly transmitted by infected blood, or the exchange of bodily fluids during sexual intercourse/activity.
• Vertical transmission occurs from mother to infant.
• Asymptomatic infection occurs in 60 percent of individuals.
• The host immune response leads to death of the infected liver cell.

Disease complications
• Fulminant hepatitis.
• The chronic carrier state leads to chronic active hepatitis or cirrhosis, hepatocellular carcinoma and death. Chronic carriers are the most common source of hepatitis B infection.

New Zealand epidemiology
• New Zealand overall has a low endemic level (≤ 2 percent) of hepatitis B carriage, but there are areas with medium (2–7 percent) and high (≥ 8 percent) endemic levels.
• In 2004 the case notification rate was 1.6 per 100,000 population.
• In 2005 there were no new cases identified in the 0–15 years age group, and one case in the 15–19 years age group.

National Immunisation Schedule

<table>
<thead>
<tr>
<th>Age*</th>
<th>Immunisation given</th>
<th>Special Programme</th>
</tr>
</thead>
<tbody>
<tr>
<td>6 weeks</td>
<td>DTaP-IPV</td>
<td>Hib-Hep B</td>
</tr>
<tr>
<td>3 months</td>
<td>DTaP-IPV</td>
<td>Hib-Hep B</td>
</tr>
<tr>
<td>5 months</td>
<td>DTaP-IPV</td>
<td>Hep B</td>
</tr>
<tr>
<td>10 months</td>
<td></td>
<td></td>
</tr>
<tr>
<td>15 months</td>
<td>Hib</td>
<td>MMR</td>
</tr>
<tr>
<td>4 years</td>
<td>DTaP-IPV</td>
<td>MMR</td>
</tr>
<tr>
<td>11 years</td>
<td>dTap-IPV</td>
<td></td>
</tr>
<tr>
<td>45 years</td>
<td>Td</td>
<td></td>
</tr>
<tr>
<td>65 years</td>
<td>Td</td>
<td>Influenza (annually)</td>
</tr>
</tbody>
</table>

* Hep B and HBIG are offered at birth to babies of HBsAg positive mothers
**Vaccine and dosage**

- Hep B – hepatitis B vaccine (HBvaxPRO®, MSD), 0.5 mL dose, intramuscular injection.

- Hib-Hep B – *Haemophilus influenzae* type b-hepatitis B vaccine (COMVAX®, MSD), 0.5 mL dose, intramuscular injection.

**Vaccine efficacy**

- The protective level of antibodies is $\geq 10$ mIU/mL.

- After three doses of vaccine, 95 percent of infants, children and adolescents develop protection.

- In high risk groups vaccine efficacy is 85–95 percent.

- The response rate declines with age and other risk factors such as smoking, obesity, HIV infection and chronic disease.

**Vaccine composition**

- HBvaxPRO® – 5 µg hepatitis B surface antigen (without preservative).

- COMVAX® – 5 µg hepatitis B surface antigen, 7.5 µg *Haemophilus influenzae* type b purified capsular polysaccharide, 125 µg *Neisseria meningitidis* (without preservative).

**Expected responses and AEFI**

- Expected responses: local soreness and redness, nausea, diarrhoea, general malaise and fever are more common in adults than in children, and are similar to placebo except for local reactions.

- AEFI: rarely thrombocytopenia, myalgia and arthralgia. Allergic reactions are reported but rare. Anaphylaxis has been reported in adults but is extremely rare.

**Vaccine contraindications**

- Anaphylaxis following a previous dose.
Diphtheria key points (see chapter 4)

Illness or risks of infection

- A serious, often fatal disease, diphtheria causes a membranous inflammation of the upper respiratory tract, and it can also cause infection at other sites, notably the skin.

- The organism is not usually invasive, but produces a powerful toxin that damages the myocardium, peripheral nerves, kidneys and other organs.

Disease complications

- These include myocarditis and heart failure, nerve demyelination and paralysis and kidney failure.

- The case fatality rate is 2–10 percent.

New Zealand epidemiology

- The antibody decline apparent with age suggests there is likely to be a large and increasing pool of adults susceptible to diphtheria in New Zealand.

- This was the reason for the introduction of adult tetanus diphtheria (Td) vaccination in 1994.

National Immunisation Schedule

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</tr>
</thead>
<tbody>
<tr>
<td>6 weeks</td>
<td>DTaP-IPV</td>
<td>MeNZB™</td>
</tr>
<tr>
<td>3 months</td>
<td>DTaP-IPV</td>
<td>MeNZB™</td>
</tr>
<tr>
<td>5 months</td>
<td>DTaP-IPV</td>
<td>MeNZB™</td>
</tr>
<tr>
<td>10 months</td>
<td>DTaP-IPV</td>
<td>MeNZB™</td>
</tr>
<tr>
<td>15 months</td>
<td>Hib</td>
<td>MeNZB™</td>
</tr>
<tr>
<td>4 years</td>
<td>DTaP-IPV</td>
<td>MMR</td>
</tr>
<tr>
<td>11 years</td>
<td>dTap-IPV</td>
<td></td>
</tr>
<tr>
<td>45 years</td>
<td>Td*</td>
<td></td>
</tr>
<tr>
<td>65 years</td>
<td>Td*</td>
<td>Influenza (annually)</td>
</tr>
</tbody>
</table>

* Administration is not funded.

Vaccine and dosage

- DTaP-IPV – diphtheria-tetanus-acellular pertussis-inactivated polio vaccine (INFANRIX™-IPV, GSK), 0.5 mL dose, intramuscular injection.

- dTap-IPV – adult diphtheria-tetanus-acellular pertussis-inactivated polio vaccine (BOOSTRIX®-IPV, GSK), 0.5 mL dose, intramuscular injection.
• DT – diphtheria-tetanus vaccine (CDT™, CSL), 0.5 mL dose, intramuscular injection for children under seven years of age requiring an alternative to pertussis containing vaccine.

• Td – adult diphtheria-tetanus vaccine (ADT®, CSL), 0.5 mL dose, intramuscular injection for children over seven years of age requiring an alternative to pertussis containing vaccine, and adults.

Vaccine efficacy
• Efficacy is 87–98 percent protection.
• Immunised cases have been shown to have less severe disease.

Vaccine composition
• INFANRIX™-IPV – not less than 30 IU of adsorbed diphtheria toxoid, not less than 40 IU of adsorbed tetanus toxoid, 25 µg of PT, 25 µg of FHA, 8 µg of pertactin, 40 D antigen units of type 1 (Mahoney), 8 D antigen units of type 2 (MEF1), and 32 D antigen units of type 3 (Saukett) of the polio virus; inactivated by formaldehyde, and containing traces of neomycin and polymyxin.

• BOOSTRIX®-IPV – not less than 2 IU of adsorbed diphtheria toxoid, not less than 20 IU of adsorbed tetanus toxoid, 8 µg of PT, 8 µg of FHA, 2.5 µg of pertactin, 40 D antigen units of type 1 (Mahoney), 8 D antigen units of type 2 (MEF1), and 32 D antigen units of type 3 (Saukett) of the polio virus; inactivated by formaldehyde and containing traces of neomycin and polymyxin.

• CDT™ – see diphtheria and tetanus components of INFANRIX™-IPV.

• ADT® – see diphtheria and tetanus components of BOOSTRIX®-IPV.

Expected responses and AEFI
• DTaP-IPV and dTap-IPV – local and systemic reactions do occur, especially when infant vaccine is used in older children and adults. (See Pertussis key points.)

• Td – fever, headache and malaise; serious adverse events in 2.1 events per million doses.

Vaccine contraindications
• DTaP-IPV and dTap-IPV – see Pertussis key points.

• Td and DT – serious reaction to a previous dose.
Tetanus key points (see chapter 5)

Illness or risks of infection

- Infection may follow even a trivial wound.
- Tetanus is a clinical diagnosis, and is characterised by muscular rigidity and very painful contraction spasms.
- Initial symptoms include weakness, stiffness or cramps, and difficulty chewing or swallowing food.
- Reflex muscle spasms usually occur within one to four days of the initial symptoms.

Disease complications

- When severe tetanus is associated with a characteristic facial grimace (risus sardonicus) and arching of the back (opisthotonus).
- The patient suffering from tetanus remains alert unless they become severely hypoxic.
- Respiratory failure can occur.

New Zealand epidemiology

- Eight cases were notified from 2001 to 2004, and among these was an unimmunised child aged one year diagnosed with tetanus in 2001.
- The single case notified in 2004 was a female age 60–65 years with an unknown immunisation history.
- However, there were five cases hospitalised with tetanus in 2004 (not all cases are notified).

National Immunisation Schedule

<table>
<thead>
<tr>
<th>Age</th>
<th>Immunisation given</th>
<th>Special Programme</th>
</tr>
</thead>
<tbody>
<tr>
<td>6 weeks</td>
<td>DTaP-IPV</td>
<td>Hib-Hep B MeNZB™</td>
</tr>
<tr>
<td>3 months</td>
<td>DTaP-IPV</td>
<td>Hib-Hep B MeNZB™</td>
</tr>
<tr>
<td>5 months</td>
<td>DTaP-IPV</td>
<td>Hep B MeNZB™</td>
</tr>
<tr>
<td>10 months</td>
<td></td>
<td>MeNZB™</td>
</tr>
<tr>
<td>15 months</td>
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<td>MMR</td>
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</tr>
<tr>
<td>65 years</td>
<td>Td*</td>
<td>Influenza (annually)</td>
</tr>
</tbody>
</table>

* Administration is not funded.
Vaccine and dosage
- See Table 5.1 for vaccine and immunoglobulin recommendations for wound care.
- See Diphtheria key points.

Vaccine efficacy
- The tetanus vaccine was 100 percent effective when given to pregnant women to protect against neonatal tetanus in a randomised controlled trial.
- In most studies, 100 percent of infants have protective levels of tetanus antibody after three doses of vaccine given at intervals of one month or longer.

Vaccine composition
- See Diphtheria key points.

Expected responses and AEFI
- Local reactions such as pain, redness and swelling around the injection site have been reported in 0–95 percent of recipients.
- Sterile abscesses and persistent nodules at the injection site may develop if the injection is not given deeply enough into the muscle.
- Brachial plexus neuropathy from tetanus vaccine occurs at a rate of 0.5 to 1 per 100,000 doses within one month of immunisation.
- See also Pertussis key points.

Vaccine contraindications
- Immunisation with Td (or tetanus toxoid) should not be repeated in individuals who have had previous severe hypersensitivity reactions.
Pertussis key points (see chapter 6)

Illness or risks of infection

- This is a highly infectious bacterial disease spread by droplets.
- The initial catarrhal stage, which is the most infectious period, is of insidious onset with rhinorrhoea and an irritating cough that can progress to severe paroxysms of coughing, characterised by a series of short expiratory bursts, followed by an inspiratory gasp or typical whoop and/or vomiting.
- Risk of infection is nearly universal without immunisation.

Disease complications

- Secondary infections include otitis media and pneumonia, and the physical sequelae of paroxysmal coughing (eg, subconjunctival haemorrhages, petechiae, epistaxes, central nervous system haemorrhages, pneumothoraces and herniae).
- Prolonged periods of apnoea may result in cyanosis, anoxic encephalopathy, convulsions and death.

New Zealand epidemiology

- The most recent epidemic was in 2004/05.
- The population case rate in 2004 was 93.4 per 100,000, with 3.4 percent of cases hospitalised.
- Infants less than one year of age had the highest disease rate (327.5 per 100,000), although rates were high up to age 19 years.

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<tr>
<td>10 months</td>
<td></td>
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</tr>
<tr>
<td>15 months</td>
<td>Hib</td>
<td>MMR</td>
</tr>
<tr>
<td>4 years</td>
<td>DTaP-IPV</td>
<td>MMR</td>
</tr>
<tr>
<td>11 years</td>
<td>dTap-IPV</td>
<td></td>
</tr>
<tr>
<td>45 years</td>
<td>Td</td>
<td></td>
</tr>
<tr>
<td>65 years</td>
<td>Td</td>
<td>Influenza (annually)</td>
</tr>
</tbody>
</table>

Vaccine

- See Diphtheria key points.
- It is recommended that for students who have recently received a tetanus diphtheria (Td) vaccine booster, eg, at the time of an injury, the age 11 (year 7), dTap-IPV immunisation should be delayed until two years after the dose of Td,
and offered before the student reaches the age of 16 years. Students who would normally receive the year 7 event at school should be referred to their general practitioner for follow up and recall.

**Vaccine efficacy**
- The acellular pertussis vaccine is 76–90 percent effective in the first two years of life.
- Protection lasts at least six years, and immunity gradually wanes if not boosted with vaccine or natural infection.
- Adolescents and adults are known to pass infection on to babies and infants.
- Pertussis containing vaccine given at age 11 years from 1 February 2006 is expected to prevent outbreaks of pertussis in young adults.

**Vaccine composition and dosage**
- See Diphtheria key points.

**Expected responses and AEFI**
- Redness at site of injection (33 percent) and mild fever (20 percent) after a dose of acellular pertussis. The frequency increases with increasing number of doses. (See section 6.6.)
- Persistent (> 3 hours) inconsolable screaming (44 per 100,000 doses); seizures (7 per 100,000); hypotonic, hyporesponsive episode (0–26 per 100,000 doses); anaphylaxis is very rare. (See section 6.6.)

**Vaccine contraindications**
- These include a severe reaction following a previous dose of pertussis vaccine (ie, immediate severe anaphylactic reaction to the vaccine, or any component of the vaccine), or an encephalopathy within seven days.
- Those with an evolving neurological disorder should not be immunised until stabilised (eg, uncontrolled epilepsy or a deteriorating neurological state).
**Haemophilus influenzae type b (Hib) key points** (see chapter 7)

**Illness or risks of infection**
- Before immunisation, Hib was the commonest cause of life threatening bacterial infection, usually meningitis, in children under five years of age.

**Disease complications**
- Hib causes meningitis, pneumonia, epiglottitis, septic arthritis, bacteraemia, cellulitis, and empyema in infants and young children, particularly under the age of two years but up to four years.

**New Zealand epidemiology**
- Since the introduction of Hib vaccine there has been a greater than 90 percent reduction in the incidence of Hib disease in children less than five years of age.
- Of the small numbers of children who have developed Hib infection in New Zealand since the change to conjugated Hib vaccine in 2000, most were incompletely vaccinated for their age.

**National Immunisation Schedule**

<table>
<thead>
<tr>
<th>Age</th>
<th>Immunisation given</th>
<th>Special Programme</th>
</tr>
</thead>
<tbody>
<tr>
<td>6 weeks</td>
<td>DTaP-IPV</td>
<td>Hib-Hep B</td>
</tr>
<tr>
<td></td>
<td></td>
<td>MeNZB™</td>
</tr>
<tr>
<td>3 months</td>
<td>DTaP-IPV</td>
<td>Hib-Hep B</td>
</tr>
<tr>
<td></td>
<td></td>
<td>MeNZB™</td>
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<tr>
<td>5 months</td>
<td>DTaP-IPV</td>
<td>Hepatitis B</td>
</tr>
<tr>
<td></td>
<td></td>
<td>MeNZB™</td>
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<tr>
<td>10 months</td>
<td></td>
<td></td>
</tr>
<tr>
<td>15 months</td>
<td>Hib</td>
<td>MMR</td>
</tr>
<tr>
<td>4 years</td>
<td>DTaP-IPV</td>
<td>MMR</td>
</tr>
<tr>
<td>11 years</td>
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<tr>
<td>45 years</td>
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<td></td>
</tr>
<tr>
<td>65 years</td>
<td>Td</td>
<td>Influenza (annually)</td>
</tr>
</tbody>
</table>

**Vaccine and dosage**
- Hib-Hep B – *Haemophilus influenzae* type b-hepatitis B vaccine (COMVAX®, MSD), 0.5 mL dose, intramuscular injection.
- Hib – monovalent Hib vaccine (Hib-PRP-T, Hiberix™, GSK), intramuscular injection.

**Vaccine composition**
- COMVAX® – see Hepatitis B key points.
- Hiberix™ – when reconstituted each dose contains 10 µg of purified polyribosyl-ribitol-phosphate capsular polysaccharide (PRP) of Hib covalently bound to approximately 30 µg tetanus toxoid.
Vaccine efficacy

- A primary course of Hib-OMP at two and four months of age and a booster dose at 12 months had an efficacy of 100 percent in 2588 Navajo children less than 15 months of age, who had received either one or two doses.
- Disease following a full course of Hib vaccine is rare.
- In the US, 15 cases per year are expected in children who have completed their Hib immunisation.

Expected responses and AEFI

- COMVAX® – sleepiness and irritability; local reactions.
- Hiberix™ – local reactions (up to 32 percent of children) and a fever higher than 38°C (5–10 percent).

Vaccine contraindications

- Known hypersensitivity or anaphylaxis to any component of the vaccine, or those who develop symptoms of hypersensitivity after a previous Hib injection.
Poliomyelitis (Polio) key points (see chapter 8)

Illness or risks of infection
- Polio is transmitted by the faecal-oral route, or by pharyngeal secretions.
- Infection is more common in young children.
- Symptoms include fever, headache, gastrointestinal disturbances, malaise, stiffness of the neck and back, and pain in the limbs, back and neck, with or without paralysis.
- Infection may be clinically inapparent in up to 95 percent of infections.

Disease complications
- These include viral meningitis and flaccid paralysis (paralysis is more common in adults), and post-polio syndrome.

New Zealand epidemiology
- New Zealand was certified polio free in 2000, with no indigenous cases since 1997.
- Since the change from OPV to IPV in 2002 there have been no cases of VAPP.

National Immunisation Schedule

<table>
<thead>
<tr>
<th>Age</th>
<th>Immunisation given</th>
<th>Special Programme</th>
</tr>
</thead>
<tbody>
<tr>
<td>6 weeks</td>
<td>DTaP-IPV</td>
<td>Hib-Hep B</td>
</tr>
<tr>
<td>3 months</td>
<td>DTaP-IPV</td>
<td>Hib-Hep B</td>
</tr>
<tr>
<td>5 months</td>
<td>DTaP-IPV</td>
<td>Hep B</td>
</tr>
<tr>
<td>10 months</td>
<td></td>
<td></td>
</tr>
<tr>
<td>15 months</td>
<td>Hib</td>
<td>MMR</td>
</tr>
<tr>
<td>4 years</td>
<td>DTaP-IPV</td>
<td>MMR</td>
</tr>
<tr>
<td>11 years</td>
<td>dTap-IPV*</td>
<td></td>
</tr>
<tr>
<td>45 years</td>
<td>Td</td>
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</tr>
<tr>
<td>65 years</td>
<td>Td</td>
<td>Influenza (annually)</td>
</tr>
</tbody>
</table>

* dTap-IPV is given in 2006/07 so that children receive 4 doses of polio vaccine.

Vaccine and dosage
- DTaP-IPV – see Diphtheria key points.
- dTap-IPV – see Diphtheria key points.
- IPV – inactivated polio vaccine (IPOL, Sanofi Pasteur), 0.5 mL dose, subcutaneous injection.
Vaccine efficacy

- IPV – virtually all infants seroconvert after three doses of IPV; over 85 percent seroconvert after two doses. Efficacy of IPV is over 90 percent.

- DTaP-IPV and dTap-IPV – one month after the three-dose primary vaccination series with DTaP-IPV the overall seropositivity for poliovirus serotypes 1, 2 and 3 was 99.5 percent. One month after dTap-IPV the immune responses to poliovirus were similar to the responses to IPV alone.

Vaccine composition

- IPOL – 40 D antigen units of type 1 (Mahoney), 8 D antigen units of type 2 (MEF1), and 32 D antigen units of type 3 (Saukett) of the polio virus; inactivated by formaldehyde, and containing 2-phenoxyethanol (5 percent v/v) as a preservative, and traces of streptomycin and/or polymyxin B.

- INFANRIX™-IPV and BOOSTRIX®-IPV – see Diphtheria key points.

Expected responses and AEFI

- IPV – erythema (33 percent); induration (1 percent); pain (13 percent); sleepiness, fussiness, crying and change in feeding (5 percent).

- DTaP-IPV and dTap-IPV – see Pertussis key points.

Vaccine contraindications

- IPV – previous history of an anaphylactic reaction to a previous dose of IPV or to the antibiotics streptomycin, neomycin or polymixin.

- DTaP-IPV and dTap-IPV – see Pertussis key points.
Measles key points (see chapter 9)

Illness or risks of infection
- Measles is an acute, highly communicable viral illness usually transmitted via exposure to infected respiratory secretions.
- The characteristic maculopapular rash appears on day three to seven, spreads over three to four days from the head over the trunk to the extremities, and lasts for up to one week.

Disease complications
- These include otitis media, pneumonia, croup or diarrhoea in 1 out of 10 cases.
- Encephalitis has been reported in 1 per 1000 cases.
- Death occurs in 1 per 1000 cases.

New Zealand epidemiology
- In 2003 there were 67 cases of measles notified, of which 11 were laboratory confirmed; and in 2004 33 were notified, of which nine were laboratory confirmed.
- It has been calculated that to prevent future measles epidemics (and possibly to eradicate measles) in New Zealand, there needs to be over 90 percent coverage of both doses of MMR at 15 months and four years of age.

National Immunisation Schedule

<table>
<thead>
<tr>
<th>Age</th>
<th>Immunisation given</th>
<th>Special Programme</th>
</tr>
</thead>
<tbody>
<tr>
<td>6 weeks</td>
<td>DTaP-IPV</td>
<td>MeNZB™</td>
</tr>
<tr>
<td>3 months</td>
<td>DTaP-IPV</td>
<td>MeNZB™</td>
</tr>
<tr>
<td>5 months</td>
<td>DTaP-IPV</td>
<td>MeNZB™</td>
</tr>
<tr>
<td>10 months</td>
<td></td>
<td>MeNZB™</td>
</tr>
<tr>
<td>15 months</td>
<td>Hib</td>
<td>MMR</td>
</tr>
<tr>
<td>4 years</td>
<td>DTaP-IPV</td>
<td>MMR</td>
</tr>
<tr>
<td>11 years</td>
<td>dTap-IPV</td>
<td></td>
</tr>
<tr>
<td>45 years</td>
<td>Td</td>
<td></td>
</tr>
<tr>
<td>65 years</td>
<td>Td</td>
<td>Influenza (annually)</td>
</tr>
</tbody>
</table>

Vaccine and dosage
- MMR – live attenuated measles, mumps and rubella vaccine (M-M-R® II, MSD), 0.5 mL, subcutaneous injection.

Vaccine efficacy
- Seroconversion to all three viruses of MMR vaccine occurs in 85–100 percent of recipients, with 90–95 percent efficacy against measles.
• Primary vaccine failure occurs in 5–10 percent of recipients after the first dose and is rare after a second dose.

Vaccine composition
When reconstituted, the vaccine contains $\geq 1000$ CCID$_{50}$ (50 percent cell culture infectious dose) of measles virus (Enders’ Edmonston [Moraten] strain); 12,500 CCID$_{50}$ of mumps virus (Jeryl Lynn strain); and 1000 CCID$_{50}$ of rubella virus (RA 27/3 strain); 25 µg neomycin (no preservative).

Expected responses and AEFI
• Rash in 1.6 percent of children and high fever in 1.4 percent could be attributed to MMR in a placebo controlled study.
• Febrile convulsions occur in 1 in 3000 children, 6–12 days after immunisation.
• Thrombocytopenia occurs in approximately 1 in 30,000 doses, 15–35 days after immunisation.
• Central nervous system symptoms following measles vaccine are reported to occur in 1 in 1 million children.

Vaccine contraindications
• Anaphylaxis following a previous dose of measles vaccine or MMR is a contraindication to a further dose of MMR.
• Other contraindications are: individuals with proven anaphylaxis (but not contact dermatitis) to neomycin; children with immune suppression; children who have received another live vaccine, including BCG, within the previous month; pregnant women; women of childbearing age, who should be advised to avoid pregnancy for the next 28 days after the MMR or measles vaccines; individuals who have received immunoglobulin or a blood transfusion during the preceding 11 months; children with HIV infection who are severely immune compromised.
Mumps key points (see chapter 10)

Illness or risks of infection

- An acute viral illness, mumps is characterised by fever, headache, and swelling and tenderness of one or more salivary glands.
- At least 30 percent of mumps infections in children are asymptomatic.

Disease complications

- Aseptic meningitis occurs in 15 percent of cases, orchitis (usually unilateral) in up to 20 percent of post-pubertal males, and oophoritis in 5 percent of post-pubertal females.
- Encephalitis occurs in 1 in 6000 cases. The case fatality for mumps encephalitis is 1.4 percent.
- The overall mumps case fatality rate is 1.8 per 10,000 cases.

New Zealand epidemiology

- There have been no mumps epidemics since 1994, due to the introduction of the MMR vaccine.

National Immunisation Schedule

<table>
<thead>
<tr>
<th>Age</th>
<th>Immunisation given</th>
<th>Special Programme</th>
</tr>
</thead>
<tbody>
<tr>
<td>6 weeks</td>
<td>DTaP-IPV, Hib-Hep B</td>
<td>MeNZB™</td>
</tr>
<tr>
<td>3 months</td>
<td>DTaP-IPV, Hib-Hep B</td>
<td>MeNZB™</td>
</tr>
<tr>
<td>5 months</td>
<td>DTaP-IPV, Hep B</td>
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<tr>
<td>15 months</td>
<td>Hib</td>
<td>MMR</td>
</tr>
<tr>
<td>4 years</td>
<td>DTaP-IPV</td>
<td>MMR</td>
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<tr>
<td>11 years</td>
<td>dTap-IPV</td>
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<td>45 years</td>
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<tr>
<td>65 years</td>
<td>Td</td>
<td>Influenza (annually)</td>
</tr>
</tbody>
</table>

Vaccine and dosage

- MMR – see Measles key points.

Vaccine efficacy

- See Measles key points.
- The protective efficacy of the Jeryl Lynn strain of mumps is 95–96 percent.

Vaccine composition

- See Measles key points.
Expected responses and AEFI
• See Measles key points.

Vaccine contraindications
• See Measles key points.
Rubella key points (see chapter 11)

Illness or risks of infection

- Rubella is a common childhood disease that can affect adults, and often occurs in epidemics.
- It is most common in children of early school age.
- Clinical features include a transient erythematous rash, lymphadenopathy (particularly in the posterior auricular and suboccipital nodes), without respiratory symptoms.
- In adults, arthritis or arthralgia may occur.

Disease complications

- These include encephalitis, arthritis or arthralgia, and neonatal death.
- Congenital rubella syndrome (CRS) is associated with cataracts, nerve deafness, cardiac malformations, microcephaly, mental retardation and behavioural problems. Inflammatory changes may also be found in the liver, lungs and bone marrow.

New Zealand epidemiology

- Outbreaks continue to occur and emphasise the need to immunise both boys and girls to reduce the risk of exposure in pregnant women, as well as to reduce illness in men.
- No new cases of CRS have been reported between 1998 and 2004.

National Immunisation Schedule

<table>
<thead>
<tr>
<th>Age</th>
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<th>Special Programme</th>
</tr>
</thead>
<tbody>
<tr>
<td>6 weeks</td>
<td>DTaP-IPV</td>
<td>MeNZB™</td>
</tr>
<tr>
<td>3 months</td>
<td>DTaP-IPV</td>
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</tr>
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<td>5 months</td>
<td>DTaP-IPV</td>
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<tr>
<td>10 months</td>
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<tr>
<td>15 months</td>
<td>Hib</td>
<td>MMR</td>
</tr>
<tr>
<td>4 years</td>
<td>DTaP-IPV</td>
<td>MMR</td>
</tr>
<tr>
<td>11 years</td>
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<tr>
<td>45 years</td>
<td>Td</td>
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</tr>
<tr>
<td>65 years</td>
<td>Td</td>
<td>Influenza (annually)</td>
</tr>
</tbody>
</table>

Vaccine and dosage

- MMR – see Measles key points.
- Note – there is no single antigen rubella vaccine available in New Zealand.
Vaccine efficacy
- The rubella vaccine is 90–97 percent effective in an outbreak after a single dose.
- One dose of rubella at $\geq 12$ months induces an antibody response in $\geq 95$ percent of recipients.
- In 90 percent of recipients antibodies persist for longer than 16 years.
- See Measles key points.

Vaccine composition
- See Measles key points.

Expected responses and AEFI
- See Measles key points.

Vaccine contraindications
- See Measles key points.
**Tuberculosis (TB) key points** (see chapter 12)

**Illness or risks of infection**
- TB most commonly causes disease in the lungs, but any part of the body may be affected.
- The lifetime risk for infected people progressing from the latent phase to active TB disease is ~5–15 percent, but this risk is strongly affected by the size of the infecting dose and the strength of the infected person’s immunity.

**Disease complications**
- A small proportion of those infected progress directly to pulmonary TB, or by lympho-haematogenous dissemination of bacilli to miliary, meningeal or other extrapulmonary involvement.
- Complications are greater in infants, young children, older people and the immune compromised.

**New Zealand epidemiology**
- The overall incidence rate is low compared with many other countries, but there are high rates among population groups from Asia, Africa and the Pacific, particularly recent immigrants from these areas.
- Extrapulmonary TB continues to occur in New Zealand, and Pacific, African and Asian children are disproportionately affected.

**National Immunisation Schedule**

<table>
<thead>
<tr>
<th>Age</th>
<th>Vaccine</th>
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</thead>
<tbody>
<tr>
<td>Birth*</td>
<td>BCG**</td>
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</tbody>
</table>

* Offered to babies at risk of TB if: they live in a house with either current TB or a past history of TB; they have household members who within the past 5 years have lived for a period of 6 months or longer in countries where TB is common; one or both parents identify as being Pacific people; in their first 5 years they will be living for 3 months or more in a country where TB is common; live in geographical area as defined by the medical officer of health after consultation with the Ministry of Health.

** Only gazetted vaccinators may give BCG immunisations.
- See chapter 12 for more details.

**Vaccine and dosage**
- BCG – freeze-dried Bacillus Calmette-Guérin vaccine (CSL), 0.05–0.1 mL, intradermal injection.

**Vaccine efficacy**
- BCG is regarded as efficacious in preventing serious extrapulmonary disease in neonates, and young children.
• BCG may protect individuals at high risk of intensive exposure, but it does not have a significant impact on the incidence of disease.

Vaccine composition
• Contains a live attenuated strain of *Mycobacterium bovis* as freeze-dried material, with a diluent in a separate ampoule.

Expected responses and AEFI
• Expected responses: a local reaction, followed by healing and scar formation within three months (90–95 percent of recipients); minor adenitis.
• AEFI: local subcutaneous abscess; regional lymphadenopathy; musculoskeletal lesions; multiple lymphadenitis; non-fatal disseminated lesions; fatal disseminated lesions.

Vaccine contraindications
• Immune compromised or receiving immunosuppressive therapy; malignant conditions; HIV; positive Mantoux reaction; significant fever; generalised septic skin conditions; pregnancy.
Influenza key points (see chapter 13)

Illness or risks of infection

- Influenza is very contagious, and the virus is primarily spread from person to person by the aerosol route.
- 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 under five years of age most commonly have fever, cough and rhinitis, while in infants only rhinitis may be present.

Disease complications

- These include exacerbation of underlying medical conditions, leading to secondary bacterial or primary viral pneumonia.
- Other complications included myositis, encephalopathy, myocarditis, pericarditis and Reye syndrome (associated with aspirin use in children), and death.

New Zealand epidemiology

- Peak incidence is usually during the winter months, between May and October.

National Immunisation Schedule

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<tr>
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<th>Immunisation given</th>
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</tr>
</thead>
<tbody>
<tr>
<td>6 weeks</td>
<td>DTaP-IPV</td>
<td>MeNZB™</td>
</tr>
<tr>
<td>3 months</td>
<td>DTaP-IPV</td>
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<td>5 months</td>
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<td>65 years</td>
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</tbody>
</table>

* See chapter 13 for schedule and dosage for influenza vaccination to those under 65 years with chronic medical conditions.

- Influenza vaccine is funded for those over 65 years and all persons under 65 years with chronic medical conditions including children.

Vaccine

- Trivalent split virion or purified antigen vaccine.
**Vaccine efficacy**
- Efficacy 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 composition**
- 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.

**Expected responses and AEFI**
- Local reactions occur in 10–64 percent of recipients, systemic reaction in 1 percent of adults (higher in children not previously immunised).

**Vaccine contraindications**
- Contraindications are anaphylactic allergy to egg or egg protein, and anaphylactoid hypersensitivity to polymyxin or neomycin, or any other vaccine component or previous influenza vaccine dose.
Note: For the following non-Schedule vaccines (with the exception of Meningococcal and Pneumococcal Key Points), refer to the relevant chapters for more information.

**Hepatitis A key points** (see chapter 14)

**Illness or risks of infection**
- Infection is characterised by an acute febrile illness with jaundice, anorexia, nausea, abdominal discomfort, malaise and dark urine.
- The virus is usually transmitted by the faecal-oral route, either from person to person contact or through contaminated food or drink.

**Disease complications**
The case fatality rate is 1.8 percent in adults over the age of 50 years.

**New Zealand epidemiology**
- Viral spread occurs in households and early childhood services leading to community outbreaks.
- Sewage contaminated shellfish can lead to epidemics.

**National Immunisation Schedule**
Hepatitis A vaccine is not publicly funded, but is recommended for the following groups:
- individuals with chronic liver disease
- travellers to countries with high or intermediate endemicity
- certain occupational groups – see chapter 14
- other at-risk groups – see chapter 14.

**Vaccine information**
- See chapter 14.
Meningococcal Invasive Disease key points (see chapter 15)

**Illness or risks of infection**

- There is usually a sudden onset, with fever, malaise, prostration and a variety of other possible symptoms including nausea, vomiting and headache.
- Approximately two-thirds of cases have a rash, which may be petechial, purpuric or (less commonly) maculopapular and urticarial.
- Those particularly at risk of meningococcal disease are children under five years of age, although all age groups may be infected and there is a higher case fatality rate in adults.

**Disease complications**

- In fulminant cases, disseminated intravascular coagulation, shock, coma and death can occur in a few hours despite appropriate treatment.
- Invasive meningococcal infection can also give rise to arthritis, myocarditis, pericarditis, endophthalmitis and pneumonia.
- Other presentations include primary pneumonia, occult bacteraemia, conjunctivitis and chronic meningococcaemia.

**New Zealand epidemiology**

- Since 1991 there has been a New Zealand wide epidemic of serogroup B disease with the B:4:P1.4 strain.
- The rate of *Neisseria meningitidis* serogroup B disease in 2004 was 11.6 per 100,000 total population in the northern region, compared with 9.7 per 100,000 in the midland region, and 7.0 per 100,000 in both the central and southern regions.
- Rates are consistently higher in Māori and Pacific children compared with the total population.
- Outbreaks of serogroups A and C disease have occurred in New Zealand over the past 20 years.
### National Immunisation Schedule – Special Programme

<table>
<thead>
<tr>
<th>Age</th>
<th>Immunisation given</th>
<th>Special Programme*</th>
</tr>
</thead>
<tbody>
<tr>
<td>6 weeks</td>
<td>DTaP-IPV Hib-Hep B</td>
<td>MeNZB™</td>
</tr>
<tr>
<td>3 months</td>
<td>DTaP-IPV Hib-Hep B</td>
<td>MeNZB™</td>
</tr>
<tr>
<td>5 months</td>
<td>DTaP-IPV Hep B</td>
<td>MeNZB™</td>
</tr>
<tr>
<td>10 months**</td>
<td>Hib</td>
<td>MeNZB™</td>
</tr>
<tr>
<td>15 months</td>
<td></td>
<td></td>
</tr>
<tr>
<td>4 years</td>
<td>DTaP-IPV MMR</td>
<td></td>
</tr>
<tr>
<td>11 years</td>
<td>dTap-IPV</td>
<td></td>
</tr>
<tr>
<td>45 years</td>
<td>Td</td>
<td></td>
</tr>
<tr>
<td>65 years</td>
<td>Td</td>
<td>Influenza (annually)</td>
</tr>
</tbody>
</table>

* MeNZB vaccine will be available providing provisional consent is extended. For other individuals who are eligible for MeNZB™, see chapter 15: Meningococcal Invasive Disease.

** Infants who receive their 3rd dose between 5 to 6 months of age, have the 4th at a minimum of 10 months of age. Infants who receive their 3rd dose after 6 months of age or older, have the 4th dose at a minimum of four months after the 3rd dose.

### Vaccine and dosage
- **MeNZB™** – meningococcal group B outer membrane vesicle (OMV) vaccine (Chiron), 0.5 mL dose, intramuscular injection.
- See chapter 15 for publicly funded vaccines against serogroups A, C, Y and W135, offered to adults pre- and post-splenectomy; and to children (upon secondary care specialist recommendation) pre- and post-splenectomy or with functional asplenia.

### Vaccine efficacy
**MeNZB™** – 55 percent of infants (aged 6–10 weeks), 74 percent of older infants (aged 6–8 months), 75 percent of toddlers (aged 16–24 months), 76 percent of children (aged 8–12 years), and 93 percent of adults developed a four-fold rise (compared with pre-vaccination values) in serum bactericidal assay titres four to six weeks after the third dose.

### Vaccine composition
- 25 µg of *N. meningitidis* group B outer membrane protein.

### Expected responses and AEFI
- Very common (> 10 percent): injection site reactions (all age groups), crying (infants), irritability, sleepiness, change in eating habits, diarrhoea and vomiting, and fever of at least 38.0°C (infants, toddlers).
- In children and adults, very common (> 10 percent): headache, malaise, nausea and myalgia.

### Vaccine contraindications
- Anaphylaxis to a prior dose of MeNZB™ is a contraindication to a further dose.
- Fever > 38°C.
Pneumococcal Disease key points (see chapter 16)

Illness or risks of infection

- Transmission of the pneumococcus is from person to person, usually by droplet contact.

- The pneumococcus is the most common bacterial cause of otitis media in children and a frequent cause of sinusitis and pneumonia in all age groups.

Disease complications

- Meningitis and bacteraemia are complications, especially in the very young, and pneumococcal disease is often the cause of bacteraemia with no obvious primary site of infection.

- The pneumococcus may also cause endocarditis, and, less commonly, sites such as joints, the peritoneal cavity and the fallopian tubes are affected.

- The mortality rate is 10–20 percent, but may exceed 50 percent in high risk groups.

New Zealand epidemiology

- The incidence of pneumonia caused by *Streptococcus pneumoniae* may be under reported.

- Incidence rates are high for children under five years of age and in those 65 years of age and over, and higher in Māori and Pacific compared to the total population.
# Recommendations and Funding for Pneumococcal Vaccine

<table>
<thead>
<tr>
<th>Funded vaccine* recommendations</th>
<th>Not funded but recommended</th>
</tr>
</thead>
<tbody>
<tr>
<td>Splenectomy or functional asplenia</td>
<td>Children with high risk conditions (&lt; 5 years):</td>
</tr>
<tr>
<td></td>
<td>Children with other risk conditions (≥ 16 years):</td>
</tr>
<tr>
<td>Children with high risk conditions (&lt; 5 years):</td>
<td>Adults at higher risk (≥ 16 years):</td>
</tr>
<tr>
<td>Adults pre- or post-splenectomy</td>
<td>Healthy children (&lt; 5 years):</td>
</tr>
<tr>
<td>On immunosuppressive therapy or radiation therapy</td>
<td></td>
</tr>
<tr>
<td>Primary immune deficiencies</td>
<td></td>
</tr>
<tr>
<td>HIV</td>
<td></td>
</tr>
<tr>
<td>Renal failure or nephrotic syndrome</td>
<td></td>
</tr>
<tr>
<td>Organ transplants</td>
<td></td>
</tr>
<tr>
<td>Cochlear implants or intracranial shunts</td>
<td></td>
</tr>
<tr>
<td>With chronic CSF leaks</td>
<td></td>
</tr>
<tr>
<td>On corticosteroid therapy for more than 2 weeks, at daily dose of prednisone of 2mg/kg or greater, or a total daily dosage of 20mg or more</td>
<td></td>
</tr>
<tr>
<td>Preterm infants, born at under 28 weeks gestation</td>
<td></td>
</tr>
<tr>
<td>Preterm infants with chronic lung disease discharged home on oxygen</td>
<td></td>
</tr>
<tr>
<td>Cardiac disease with cyanosis or failure</td>
<td></td>
</tr>
<tr>
<td>Bronchiectasis</td>
<td></td>
</tr>
<tr>
<td>Insulin dependent diabetes</td>
<td></td>
</tr>
<tr>
<td>Down’s syndrome</td>
<td></td>
</tr>
<tr>
<td>Children over age 5 years with a high risk condition</td>
<td></td>
</tr>
<tr>
<td>Particularly Ma¯ori and Pacific children</td>
<td></td>
</tr>
<tr>
<td>All children attending early childhood services</td>
<td></td>
</tr>
</tbody>
</table>

* Vaccine administration is also funded.

- The funded vaccines are available upon the recommendation of a paediatrician or other secondary care specialist (such as haematologist or infectious diseases physician).
### Schedule for pneumococcal vaccines for eligible children under five years of age with no prior history of pneumococcal vaccines

<table>
<thead>
<tr>
<th>Age of child at start of course</th>
<th>Conjugate pneumococcal vaccine, Prevenar® (PCV7)</th>
<th>Polysaccharide pneumococcal vaccine, Pneumovax®23 (23PPV)</th>
</tr>
</thead>
<tbody>
<tr>
<td>6 weeks to 6 months</td>
<td>3 doses PCV7 at least 6–8 weeks apart, or at same time as the usual schedule; plus a 4th dose at age 15 months</td>
<td>One dose of 23PPV at age 2 years and a second dose at age 4–5 years</td>
</tr>
<tr>
<td>7–11 months</td>
<td>2 doses of PCV7 at least 6–8 weeks apart; plus a 3rd dose at age 15 months</td>
<td>One dose of 23PPV at age 2 years and a second dose at age 4–5 years</td>
</tr>
<tr>
<td>12–59 months</td>
<td>2 doses of PCV7 given at 6–8 weeks apart</td>
<td>One dose of 23PPV at age 2 years and a second dose at age 4–5 years</td>
</tr>
</tbody>
</table>

### Schedule for pneumococcal vaccines for adults pre- and post-splenectomy and children pre- and post-splenectomy or with functional asplenia

<table>
<thead>
<tr>
<th>Age of child at start of course</th>
<th>Conjugate pneumococcal vaccine (PCV7)</th>
<th>Polysaccharide pneumococcal vaccine (23PPV)</th>
</tr>
</thead>
<tbody>
<tr>
<td>6 weeks to 6 months</td>
<td>3 doses PCV7 at least 6–8 weeks apart, or at same time as the usual schedule; plus a 4th dose at age 15 months</td>
<td>One dose of 23PPV at age 2 years and a second dose at age 4–5 years Booster dose of 23PPV 5 yearly</td>
</tr>
<tr>
<td>7–11 months</td>
<td>2 doses of PCV7 at least 6–8 weeks apart; plus a 3rd dose at age 15 months</td>
<td>One dose of 23PPV at age 2 years and a second dose at age 4–5 years Booster dose of 23PPV 5 yearly</td>
</tr>
<tr>
<td>12–59 months</td>
<td>2 doses of PCV7 given at 6–8 weeks apart</td>
<td>One dose of 23PPV at age 2 years and a second dose at age 4–5 years Booster dose of 23PPV 5 yearly</td>
</tr>
<tr>
<td>5–9 years</td>
<td>One dose of PCV7</td>
<td>One dose of 23PPV 6–8 weeks after PCV7 Booster dose of 23PPV 5 yearly</td>
</tr>
<tr>
<td>10–16 years</td>
<td>(A dose of PCV7 may be recommended for some children)</td>
<td>One dose of 23PPV Booster dose of 23PPV 5 yearly</td>
</tr>
<tr>
<td>Adults &gt; 16 years</td>
<td></td>
<td>One dose of 23PPV Booster dose of 23PPV 5 yearly</td>
</tr>
</tbody>
</table>

Key: PCV7 – Prevenar®; 23PPV – Pneumovax®23.
Vaccine and dosage

- **PCV7** – pneumococcal conjugate vaccine, 7-valent (Prevenar®, Wyeth), 0.5 mL, intramuscular injection.

- **23PPV** – pneumococcal polysaccharide vaccine, 23-valent (Pneumovax®23, MSD), 0.5 mL, intramuscular or subcutaneous injection.

Vaccine efficacy

- **PCV7** – 97.4 percent efficacy against *Streptococcus pneumoniae* invasive disease in children who had completed a four-dose vaccine course at 2, 4, 6 and 12–15 months of age, and 85.7 percent efficacy in partially vaccinated children who had received one dose or more of vaccine, against the seven vaccine serotypes. (See chapter 16: Pneumococcal Disease.)

- **23PPV** – the efficacy depends on whether immune competent or immune compromised patients are compared, and whether the end point is pneumococcal pneumonia or bacteraemia. (See chapter 16: Pneumococcal Disease.)

Vaccine composition

- **Prevenar®** – 2 µg of saccharide for serotypes 4, 9V, 14, 18C, 19F, and 23F, and 4 µg of serotype 6B per dose (16 µg total saccharide) conjugated to CRM197 carrier protein and adsorbed on aluminium phosphate (0.5 mg).

- **Pneumovax®23** – 25 µg of each capsular polysaccharide antigen (1, 2, 3, 4, 5, 6B, 7F, 8, 9N, 9V, 10A, 11A, 12F, 14, 15B, 17F, 18C, 19A, 19F, 20, 22F, 23F and 33F), dissolved in isotonic saline solution with phenol (0.25 percent) added as preservative and no adjuvant.

Expected responses and AEFI

- **PCV7** – local reactions (redness and swelling). Rare events (≥ 0.01 percent and < 0.1 percent) include: febrile seizures and hypotonic, hyporesponsive episode. Very rare events (< 0.01 percent) include: urticaria, angioneurotic oedema, erythema multiforme, and hypersensitivity including anaphylaxis.

- **23PPV** – local discomfort, erythema and induration in 1–10 percent of recipients; side effects requiring a general practitioner consultation occur in 8 per 1000 vaccinations, and more severe side effects in 1 per 100,000.

Vaccine contraindications

- Contraindications include a severe reaction to a previous dose, or known hypersensitivity to any components of either vaccine.

- Deferral of immunisation in pregnancy is recommended unless the risk of infection is substantial.
Varicella (chickenpox) key points (see chapter 17)

Illness or risks of infection

- Varicella is a highly infectious disease.
- A maculo-papular rash, which becomes vesicular, appears first on the face and scalp, later spreading to the trunk and abdomen and eventually to the limbs.
- The rash is pruritic and is usually associated with mild fever, malaise, anorexia and listlessness.

Disease complications

- These include bacterial superinfection of the skin lesions, leading to hospitalisation; varicella pneumonia, acute cerebellar ataxia, and rarely encephalitis with permanent neurological disability or fatal outcome.
- Transverse myelitis, thrombocytopenia, and rarely, involvement of the viscera and joints may also occur.
- Congenital varicella syndrome.
- Herpes zoster (shingles) can occur in later life.

New Zealand epidemiology

- Per year in New Zealand it is estimated there are 50,000 chickenpox infections, of which 150–200 result in hospitalisation, one to two cases result in residual long term disability or death, and 0.5–1 cases result in severe congenital varicella syndrome.
- About two-thirds of this burden is borne by otherwise healthy children, and less than one-tenth by children with a disease associated with immune suppression.

National Immunisation Schedule

Varicella vaccine is not publicly funded but is recommended for the following groups:

- adults and adolescents who were born and resident in tropical countries if they have no history of varicella infection
- children with chronic liver disease who may in future be candidates for transplantation
- children with deteriorating renal function, as early as possible before transplantation
- children likely to undergo solid organ transplant
- children with HIV infection at CDC stage N1 or A1.

For further information and recommendations for health care workers, immune suppressed, and healthy infants, adolescents, and adults, see chapter 17: Varicella.

Vaccine information

- See chapter 17: Varicella.
General Considerations

1.1 Immunity

The immune system is a complex network of interacting cells and molecules. One of its primary purposes is to identify and remove infectious organisms and their by-products and thereby prevent infection. The immune system works by recognising small parts of microbes or their products, which are called antigens. Microorganisms contain many antigens and the immune system has an almost infinite capacity to recognise them.

Immunity to a variety of bacterial and viral antigens may be induced either actively by the disease or vaccination, or passively by antibody transfer \textit{in utero} and through breastmilk, or by injecting serum containing antibodies.

Active immunity

Natural active immunity occurs when the immune system responds to a foreign antigen (eg, exposure to a bacterium or virus). The antigens contained within the microorganisms are processed in local antigen presenting cells to optimise their interactions with lymphocytes. Lymphocytes are then stimulated to multiply, produce cytokines, and develop into cytotoxic cells, or into antibody producing cells.

This specific immune response amplifies and co-ordinates with other arms of the immune system, such as phagocytes and the complement system. The process takes from days to weeks to develop and fully mature, which usually results in control of the infection. In some situations there is long lasting protection against organisms and viruses of a similar type. The relative importance of cellular (T lymphocyte) and humoral (antibody) responses varies from organism to organism. Natural, active immunity depends on an individual having a relatively intact immune system to mount a full response.

Vaccine induced immunity follows a similar process, although vaccines contain either attenuated (weakened) living organisms, or components selected to produce maximum protective immunity with minimal systemic or local reactions. The response of the immune system to vaccination is essentially the same as to a ‘wild type’ infection. The essential goal of vaccination is to prime and prepare the immune system so that it can rapidly respond to the wild type organism, thereby preventing disease and ideally infection.

Passive immunity

An infant naturally receives passive immunity from its mother via antibodies, which are actively and selectively transported across the placenta during the last three months of pregnancy. These antibodies provide some disease specific protection for the infant (for a few months) from the same diseases to which the mother is immune. As a result, a premature baby has a lower concentration of antibodies, and therefore a shorter duration of protection, than a full term infant.
The major antibody contained in breast milk is secretory immunoglobulin A (IgA), which is not absorbed by the baby but remains in the intestine to protect the mucosal surfaces. Some of these secretory IgA antibodies are directed against the bacterial and viral infections often present in the intestine. The protection from secretory IgA is passive and does not rely on the infant’s immune system or stimulate immunologic memory.

Passive immunity can be provided by the injection of human immunoglobulin (IG), which contains high titres of antibodies to hepatitis B, cytomegalovirus, varicella, tetanus, etc. In addition, there are specific high titre globulins, such as hepatitis B immunoglobulin (HBIG), zoster immunoglobulin (ZIG), rabies immunoglobulin (RIG) and tetanus immunoglobulin (TIG). The protection provided by these injections is immediate, but lasts only a few months.

Note that passive immunity does not depend on the recipient’s immune response for protection.

Recommendations for the use of immunoglobulins are outlined in the relevant specific disease sections, and in chapter 18.

### 1.2 Principles of immunisation

**What is the difference between vaccination and immunisation?**

The terms ‘vaccination’ and ‘immunisation’ are often used interchangeably, but their meanings are not equivalent.

Vaccination originally referred to the inoculation of vaccinia virus to render individuals immune to smallpox. These days the term ‘vaccination’ means the administration (by injection, mouth or any other route) of a vaccine. Vaccination (or indeed suffering from the disease) does not always result in immunity. Immunisation is the process of converting an individual to an immune state in which the individual is protected from disease with that microbe.

**How does immunisation work?**

There are many types of vaccines, but they all work in the same general way, by preparing the immune system to attack the infection. A vaccine contains components that look like the infecting organism, and so the immune system responds as it would to an infection with that organism. The most important consequence of successful vaccination is that long lived memory lymphocytes are produced. These respond more quickly and in a more co-ordinated way to subsequent infections so that the infectious microbe is destroyed more quickly. Protection is not always complete, infection may not be prevented but the severity of the illness is usually reduced.
The first exposure to a vaccine stimulates the immune response (known as priming). The immune system takes time to respond to the antigen by producing antibodies and immune cells. Initially immunoglobulin M (IgM) antibody is produced but this is in small amounts and does not bind very strongly to the antigen. After a few days the immune response begins to make immunoglobulin G (IgG) antibody, which is more specific to the microbe. Priming can take more than one dose. For example, many infants will need at least two doses of pertussis vaccine for priming to occur.

Subsequent administration of the same vaccine stimulates the secondary response. The secondary response is much faster than the primary response and produces predominantly IgG rather than IgM. The aim is to generate enough immune cells and antibodies, specific to the infectious microbe, to provide long lasting protection against the disease. The primary and secondary responses constitute the primary series of a vaccine.

If a further dose (a booster) is given some months or years later, a greater and longer lasting secondary response is stimulated, reinforcing and extending the immunologic memory for that microbe.

In assessing the immune response to vaccines, it is easier to measure circulating antibodies in the laboratory rather than cellular responses. One exception is the tuberculosis vaccine Bacillus Calmette-Guérin (BCG), where antibodies are not protective against infection. Here immunity is measured by the tuberculin skin test (Mantoux test), which reflects an active cellular immune response to tuberculin and not the level of antibodies.
1.3 National Immunisation Schedule

The National Immunisation Schedule (Schedule) from February 2006 is shown in Table 1.1.

Table 1.1: National Immunisation Schedule from 1 February 2006

<table>
<thead>
<tr>
<th>Age</th>
<th>Immunisation given</th>
<th>Special programme**</th>
</tr>
</thead>
<tbody>
<tr>
<td>6 weeks</td>
<td>DTaP-IPV</td>
<td>Hib-Hep B</td>
</tr>
<tr>
<td>3 months</td>
<td>DTaP-IPV</td>
<td>Hib-Hep B</td>
</tr>
<tr>
<td>5 months</td>
<td>DTaP-IPV</td>
<td>Hep B</td>
</tr>
<tr>
<td>10 months***</td>
<td></td>
<td></td>
</tr>
<tr>
<td>15 months</td>
<td>Hib</td>
<td>MMR</td>
</tr>
<tr>
<td>4 years</td>
<td>DTaP-IPV</td>
<td>MMR</td>
</tr>
<tr>
<td>11 years</td>
<td>dTap-IPV*</td>
<td></td>
</tr>
<tr>
<td>45 years</td>
<td>Td</td>
<td></td>
</tr>
<tr>
<td>65 years</td>
<td>Td</td>
<td>Influenza****</td>
</tr>
<tr>
<td></td>
<td></td>
<td>(annually)</td>
</tr>
</tbody>
</table>


*  IPV will be given until the end of 2007 for those who have not previously had four doses.

**  MeNZB™ vaccine will be available providing provisional consent is extended. See also Table 1.2 for additional individuals eligible for MeNZB™ vaccine.

***  Infants who receive their 3rd dose between 5 to 6 months of age, have the 4th at a minimum of 10 months of age. Infants who receive their 3rd dose after 6 months of age or older, have the 4th dose at a minimum of four months after the 3rd dose.

****Influenza vaccine is also recommended and funded for those under 65 years of age with chronic medical conditions.
### Table 1.2: Other publicly funded vaccines

<table>
<thead>
<tr>
<th>Vaccine</th>
<th>Individuals eligible for publicly funded vaccine</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Hepatitis B vaccine and hepatitis B immunoglobulin (HBIG)</strong></td>
<td>Babies of hepatitis B surface antigen (HBsAg) positive mothers need both hepatitis B vaccine and HBIG at birth (see chapter 3).</td>
</tr>
<tr>
<td><strong>Hepatitis B vaccine</strong></td>
<td>Household and sexual contacts of hepatitis B cases and carriers should be offered hepatitis B vaccine (see chapter 3).</td>
</tr>
<tr>
<td><strong>BCG (Bacillus Calmette-Guérin)</strong></td>
<td>Neonatal BCG should be offered to infants at increased risk of tuberculosis, defined as those who:</td>
</tr>
<tr>
<td></td>
<td>1. will be living in a house or family/whānau with a person with either current tuberculosis or a past history of tuberculosis</td>
</tr>
<tr>
<td></td>
<td>2. have one or both parents who identify as being Pacific people</td>
</tr>
<tr>
<td></td>
<td>3. have parents or household members who have within the last 5 years lived for a period of 6 months or longer in countries where there is a high incidence of tuberculosis</td>
</tr>
<tr>
<td></td>
<td>4. during their first 5 years will be living for 3 months or longer in a high incidence country†</td>
</tr>
<tr>
<td></td>
<td>5. live in specific geographical areas as defined by the medical officer of health after consultation with the Ministry of Health (see chapter 12).</td>
</tr>
<tr>
<td><strong>MeNZB™ vaccine</strong></td>
<td>Children under 5 years should continue to be offered MeNZB™ vaccine opportunistically from 1 July 2006, until there is clinical or epidemiological evidence to warrant cessation.</td>
</tr>
<tr>
<td></td>
<td>Individuals aged 5–19 years who have had their first dose of MeNZB™ vaccine before 30 June 2006 as part of the Meningococcal B Immunisation Programme should be encouraged to complete the course by 31 December 2006.</td>
</tr>
<tr>
<td></td>
<td>MeNZB™ will also be available and funded for microbiologists and laboratory workers routinely exposed to <em>Neisseria meningitidis</em> isolates.</td>
</tr>
<tr>
<td></td>
<td>Adults and children pre- or post-splenectomy.</td>
</tr>
<tr>
<td></td>
<td>(See chapter 15.)</td>
</tr>
<tr>
<td>Vaccine Type</td>
<td>Recommendations</td>
</tr>
<tr>
<td>-------------------------------------------------</td>
<td>-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------</td>
</tr>
<tr>
<td>MMR vaccine</td>
<td>Women of childbearing age who are susceptible to rubella should be offered MMR vaccine (see chapter 11).</td>
</tr>
<tr>
<td>Influenza vaccine</td>
<td>This should be offered annually to individuals with certain chronic medical conditions (see chapter 13).</td>
</tr>
</tbody>
</table>
| Pneumococcal vaccine***                         | Pneumococcal immunisation is available on the recommendation of a paediatrician or other secondary care specialist for children under 5 years of age at high risk of pneumococcal disease. Children eligible for publicly funded pneumococcal immunisation are children:  
  - on immunosuppressive therapy or radiation therapy, when there is expected to be sufficient immune response  
  - with primary immune deficiencies  
  - with HIV infection  
  - with renal failure, or nephrotic syndrome  
  - immune suppressed following organ transplantation  
  - with cochlear implants or intracranial shunts  
  - with chronic cerebrospinal fluid leaks  
  - receiving corticosteroid therapy for more than two weeks, who are on an equivalent daily dosage of prednisone of 2 mg/kg per day or greater, or children on a total daily dosage of 20 mg or greater.  
  For further information refer to chapter 16.  

| Pneumococcal vaccine, Hib vaccine, meningococcal A, C, Y, W135 vaccine | Upon recommendation of a secondary care specialist:  
Adults pre- and post-splenectomy should be offered pneumococcal, Hib and meningococcal A, C, Y, W135 vaccines.  
Children under 5 years of age pre- and post-splenectomy or with functional asplenia.  
See section 1.8 plus individual vaccine chapters for more information. |

* MeNZB™ will continue, providing provisional consent is extended.  
** All countries with high incidence of tuberculosis, except Australia, Austria, Belgium, Canada, Czech Republic, Denmark, Finland, France, Germany, Greece, Holland, Iceland, Ireland, Israel, Italy, Luxembourg, Malta, Monaco, New Zealand, Norway, Slovakia, Sweden, Switzerland, United Kingdom and the United States of America.  
*** It is expected that the group of eligible children for the pneumococcal vaccine will be expanded over time. Information will be sent to health practitioners and will be available on the Ministry of Health website when there are changes in pneumococcal immunisation programme eligibility.
Review of the National Immunisation Schedule

The Schedule will be reviewed by the Ministry of Health and may change every two years. This is because of the rapid advances in vaccinology, the increased availability of combination vaccines, and the need to introduce new antigens to the Schedule. The Schedule review is also based on the epidemiology of vaccine preventable diseases in New Zealand.

Every effort should be made to ensure that all children are vaccinated, even if they are older than the recommended age (see Appendix 2: Immunisation Catch Up Schedules). An alternative vaccine may be necessary for older children; for example, children seven years and older require Td because it has a reduced dose of diphtheria toxoid to avoid severe local reactions (see section 4.5).

When an epidemic occurs, it may be appropriate to vaccinate a child at an earlier age than is usually recommended (see section 9.8).

Eligibility for publicly funded vaccines

See Table 1.3 below.

Only vaccines given according to the National Immunisation Schedule are available free of charge, unless there is a specific funded programme in response to a recognised need.

The Ministry of Health funds providers:

- for the administration of all childhood vaccines
- for eligible adults the hepatitis B, MMR, influenza, IPV, pneumococcal, Hib and meningococcal vaccines.

Currently there is no funding provided for the administration of Td boosters or any other vaccines (see also section 1.6).
### Table 1.3: Vaccines available free of charge

<table>
<thead>
<tr>
<th>Age</th>
<th>Vaccines</th>
</tr>
</thead>
</table>
| <16 years| • diphtheria  
• tetanus  
• pertussis  
• hepatitis B  
• *Haemophilus influenzae* type b vaccine for all children up to the 5th birthday and for individuals pre- or post splenectomy (see section 1.8 and chapter 7)  
• MMR  
• IPV  
• influenza for those meeting the chronic medical condition criteria  
• BCG for high risk individuals or groups (see Ministry of Health *Guidelines for Tuberculosis Control in New Zealand 2003*, www.moh.govt.nz)  
• Pneumococcal for those meeting the eligibility criteria  
• MeNZB™ (see chapter 15 for eligibility) |
| > 16 years| • tetanus diphtheria boosters  
• MMR for any individual susceptible to any one of the three diseases  
• hepatitis B for household and sexual contacts of known hepatitis B carriers  
• influenza vaccine for those ≥ 65 years  
• influenza for those < 65 years meeting the chronic medical condition criteria  
• IPV  
• BCG for high risk individuals or groups (see Ministry of Health *Guidelines for Tuberculosis Control in New Zealand 2003*, www.moh.govt.nz)  
• Hib, pneumococcal, meningococcal A, C, Y, W135 for pre- or post-splenectomy individuals only; MeNZB™ for post-splenectomy individuals while the vaccine is available |

### Timing of doses

The immune response to a series of vaccines is time dependent. In particular, the time interval between doses is important. A second dose of the same vaccine given less than four weeks from the first dose may result in a reduced immune response. Therefore, the general rule is for a minimum interval of four weeks between doses,
unless there are specific recommendations for rapid schedule by the manufacturer. It is not necessary to repeat prior doses.

**Vaccination of children with inadequate vaccination records**

Research indicates that parents tend to overestimate their child’s immunisation history. For this reason, children without a documented history of vaccination should be given a full course of vaccination appropriate for their age. In cases of doubt it is much safer to provide an unnecessary dose than to miss out a needed dose.

The National Immunisation Register (NIR) will assist parents and primary health care providers by providing an accurate immunisation history for a child registered on the NIR (see section 2.3).

**Catch-up programmes for unimmunised or partially immunised children for the usual childhood schedule**

The objective of a catch-up programme is to complete a course of vaccination and provide adequate protection. Catch-up programmes should be based on documented evidence of previous vaccination. It is not necessary to repeat a vaccine dose. (See Appendix 2: Immunisation catch-up schedules.)

When children have missed vaccine doses, it is important to bring them up to date as quickly as possible. This may require more than two injections at some visits. If the vaccine provider (general practitioner or practice nurse) is uncertain about how to plan the catch-up programme, they should contact the local immunisation co-ordinator/facilitator, medical officer of health, Public Health Service or the Immunisation Advisory Centre (IMAC).

Use the following instructions to help decide what doses need to be given. Where more than one vaccine is overdue, it is preferable to give the maximum possible at the first visit. For children over 15 months of age, MMR should be the priority. (See examples of catch-up programmes in Appendix 2.) For information on the Meningococcal B Immunisation Programme see chapter 15.

For children and young people up to 16 years of age:

1. determine the total number of antigens required
2. subtract the number of previous documented doses
3. complete the primary programme using the minimum interval of one month between doses
4. when a fourth dose is required, give it not less than six months after the third dose (for the booster response to occur).
1.4 Notifiable diseases in New Zealand

Medical practitioners who suspect or diagnose a person with certain infectious diseases are required under the Health Act 1956 to notify the local medical officer of health, so that public health prevention and control activities can occur. All diseases prevented by vaccines on the National Immunisation Schedule are notifiable. Notification should be on clinical suspicion and should not necessarily await laboratory confirmation.

The case definitions in Table 1.4 are used by the medical officer of health to classify the notified case for surveillance purposes and to assist in identifying appropriate prevention and control activities. Table 1.5 lists the laboratory tests that confirm the diagnosis.

When cases of measles are clinically diagnosed, practitioners should notify on suspicion, and obtain laboratory confirmation of the diagnosis. Similarly, when rubella is suspected, laboratory confirmation for diagnosis should be sought, especially for any decisions involving a pregnant woman. This is because diagnosis of rash in children or adults may be confusing, and it is important to identify a vaccine preventable disease with epidemic potential. Also, the World Health Organization (WHO) is moving towards world eradication of measles, and this places a greater emphasis on laboratory confirmation of the disease.

Table 1.4: Case definitions for vaccine preventable diseases

<table>
<thead>
<tr>
<th>Disease</th>
<th>Clinical description</th>
<th>Probable case</th>
<th>Confirmed case</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diphtheria</td>
<td>An upper respiratory tract illness characterised by pharyngitis or laryngitis, low grade fever, with or without an adherent membrane of the tonsils, pharynx and/or nose, and/or toxic (cardiac or neurological) symptoms. Cutaneous diphtheria is not notifiable, but should be discussed with the medical officer of health.</td>
<td>A clinically compatible illness that is not laboratory confirmed.</td>
<td>A clinically compatible illness that is laboratory confirmed.</td>
</tr>
<tr>
<td>Disease</td>
<td>Clinical description</td>
<td>Probable case</td>
<td>Confirmed case</td>
</tr>
<tr>
<td>---------------------------------------------</td>
<td>--------------------------------------------------------------------------------------</td>
<td>--------------------------------------------------------------------------------</td>
<td>--------------------------------------------------------------------------------</td>
</tr>
<tr>
<td><em>Haemophilus influenzae</em> type b (Hib)</td>
<td>Invasive disease due to Hib may cause septicaemia, meningitis, epiglottitis, cellulitis, septic arthritis, pneumonia or osteomyelitis.</td>
<td>A clinically compatible illness or a confident diagnosis of epiglottitis by direct vision, laryngoscope or X-ray.</td>
<td>A clinically compatible illness with isolation of Hib from a normally sterile site.</td>
</tr>
<tr>
<td>Hepatitis B</td>
<td>(The acute illness but not the carrier state is to be notified.)</td>
<td>A clinically compatible illness with a positive HBsAg test.</td>
<td>A clinically compatible illness that is laboratory confirmed with a positive anti-HBc IgM test.</td>
</tr>
<tr>
<td>Measles</td>
<td>Cases must meet all the following criteria:</td>
<td>A clinically compatible illness.</td>
<td>A clinically compatible illness that is epidemiologically linked to a confirmed case, or is laboratory confirmed.</td>
</tr>
<tr>
<td></td>
<td>• fever 38˚C or higher</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>• generalised maculopapular rash lasting three or more days</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>• cough or coryza or conjunctivitis or Koplik spots.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Neisseria meningitidis invasive disease</td>
<td>The disease presents as an acute illness with fever, nausea, vomiting and headache, and may progress rapidly to shock and death.</td>
<td>A clinically compatible illness.</td>
<td>A clinically compatible illness with one of the laboratory tests positive.</td>
</tr>
<tr>
<td>Disease</td>
<td>Clinical description</td>
<td>Probable case</td>
<td>Confirmed case</td>
</tr>
<tr>
<td>---------</td>
<td>----------------------</td>
<td>---------------</td>
<td>---------------</td>
</tr>
<tr>
<td>Mumps</td>
<td>An illness with acute onset of fever and unilateral or bilateral tender, self limited swelling of the parotid or other salivary glands, lasting more than two days, and without other apparent cause.</td>
<td>A clinically compatible illness.</td>
<td>A case with laboratory confirmation or a clinically compatible illness that is epidemiologically linked to another case.</td>
</tr>
<tr>
<td>Pertussis</td>
<td>A disease characterised by a cough lasting longer than two weeks, and one or more of the following: • paroxysms of cough • cough ending in vomiting or apnoea • inspiratory whoop.</td>
<td>Cough lasting longer than two weeks and one or more of the following: paroxysmal cough, cough ending in vomiting or apnoea, inspiratory whoop, for which there is no other known cause.</td>
<td>A clinically compatible illness that is laboratory confirmed or that is epidemiologically linked to a confirmed case.</td>
</tr>
<tr>
<td>Rubella</td>
<td>An illness with a generalised maculopapular rash and fever and one or more of the following: • arthralgia/arthritis • lymphadenopathy • conjunctivitis. Rubella often presents atypically and is difficult to diagnose clinically with certainty. If accurate diagnosis is important it must be laboratory confirmed.</td>
<td>A case that meets the clinical case definition.</td>
<td>A clinically compatible illness that is laboratory confirmed or has a close epidemiological link to a laboratory confirmed case.</td>
</tr>
<tr>
<td>Disease</td>
<td>Clinical description</td>
<td>Probable case</td>
<td>Confirmed case</td>
</tr>
<tr>
<td>------------------</td>
<td>---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------</td>
<td>------------------------------------------------------------------------------</td>
<td>-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------</td>
</tr>
<tr>
<td>Rubella (congenital)</td>
<td>A live or stillborn infant with clinically compatible defects (cataracts, congenital heart disease, hearing defects, microcephaly, mental retardation, purpura, hepatosplenomegaly).</td>
<td>A clinically compatible illness.</td>
<td>A clinically compatible illness that is laboratory confirmed.</td>
</tr>
</tbody>
</table>
| Poliomyelitis    | A disease, with no other apparent cause, characterised by:  
  - acute flaccid paralysis of one or more limbs with decreased or absent deep tendon reflexes in affected limbs  
  - no sensory or cognitive loss  
  - may affect bulbar muscles.                                                                                                                                 | A clinically compatible illness.                                              | A clinically compatible illness in which the neurological deficit persists 60 days after the onset of symptoms or the individual has died, with no other cause.                                          |
| Tetanus          | Acute onset of hypertonia and/or painful muscular contractions, most commonly of the jaw and neck, which may proceed to generalised muscle spasms. The clinical presentation of tetanus may be subtle.                                                                 | Nil.                                                                         | A clinically compatible case.                                                                                                                                                                                   |

Table 1.5: Microbiological and serological tests used in the diagnosis of vaccine preventable disease

<table>
<thead>
<tr>
<th>Disease</th>
<th>Laboratory basis for diagnosis</th>
<th>Specimen</th>
<th>When to take specimens</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diphtheria</td>
<td>Isolation of toxigenic <em>Corynebacterium diphtheriae</em> from a clinical specimen.</td>
<td>Swab from area of the lesion (e.g., throat swab, or skin in case of ulcer).</td>
<td>At presentation of illness: must state ‘query diphtheria’ to ensure appropriate laboratory testing.</td>
</tr>
<tr>
<td><em>Haemophilus influenzae</em> type b (Hib)</td>
<td>Isolation of Hib from a normally sterile site OR detection of a positive antigen test in cerebrospinal fluid (CSF).</td>
<td>CSF and/or blood culture or aspirate from normally sterile site.</td>
<td>At presentation of illness.</td>
</tr>
<tr>
<td>Hepatitis B (acute)</td>
<td>Serology (HBsAg positive and anti-HBc IgM positive) and abnormal liver function tests (LFTs).</td>
<td>Blood.</td>
<td>At presentation of illness, but may need a second specimen one week after presentation.</td>
</tr>
<tr>
<td>Disease</td>
<td>Laboratory basis for diagnosis</td>
<td>Specimen</td>
<td>When to take specimens</td>
</tr>
<tr>
<td>------------------------------</td>
<td>-----------------------------------------------------------------------------------------------</td>
<td>---------------------------</td>
<td>----------------------------------------------------------------------------------------</td>
</tr>
<tr>
<td>Measles</td>
<td>Demonstration of measles specific IgM antibody*</td>
<td>Blood</td>
<td>Single specimen taken 3–4 days after onset of rash (the preferred test; if negative a repeat test may be required).</td>
</tr>
<tr>
<td></td>
<td>OR</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>a significant rise in measles antibody titre (IgG)</td>
<td>Blood</td>
<td>One specimen taken at onset of illness and a second taken at least 14 days later.</td>
</tr>
<tr>
<td></td>
<td>OR</td>
<td>Urine; nasopharyngeal swab/saliva swab for virus.</td>
<td>At initial presentation of illness (note: culture of virus takes up to 35 days and viral transport medium is required). Serology is preferred.</td>
</tr>
<tr>
<td>Neisseria meningitidis</td>
<td>Isolation of <em>Neisseria meningitidis</em> from blood, CSF, or other normally sterile site OR detection of gram negative intracellular diplococci in blood or CSF or skin petechiae OR detection of meningococcal antigen in CSF OR positive polymerase chain reaction (PCR).</td>
<td>Blood, CSF, other sterile site.</td>
<td>At presentation of illness.</td>
</tr>
<tr>
<td>invasive disease</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Chapter 1: General Considerations
<table>
<thead>
<tr>
<th>Disease</th>
<th>Laboratory basis for diagnosis</th>
<th>Specimen</th>
<th>When to take specimens</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mumps</td>
<td>A positive serologic test for mumps IgM antibody except following vaccine OR a significant rise in mumps antibody level by any standard serological assay, except following vaccination OR isolation of mumps virus from a clinical specimen.</td>
<td>Blood.</td>
<td>At initial presentation of illness.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Blood.</td>
<td>One specimen taken at onset of illness and a second taken at least 14 days later.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Saliva or viral swab taken from mouth or throat.</td>
<td>At presentation. Note: viral transport medium is required.</td>
</tr>
<tr>
<td>Pertussis</td>
<td>Isolation of <em>Bordetella pertussis</em> from a pernasal swab** OR PCR.</td>
<td>Isolation: pernasal swab.</td>
<td>At initial presentation of clinically compatible illness.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>PCR: nasopharyngeal swab; for PCR ensure correct swab is used (ie, not wooden handle and not cotton tipped).</td>
<td></td>
</tr>
<tr>
<td>Poliomyelitis</td>
<td>Two faecal specimens collected at least 24 hours apart 0–14 days after the onset of paralysis are to be collected and sent to ESR.*** (Acute poliomyelitis titres may assist diagnosis, but viral isolation and identification are required to confirm a case of poliomyelitis.)</td>
<td>Faeces.</td>
<td>At initial presentation of illness and a second specimen collected at least 24 hours later.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Blood.</td>
<td>At initial presentation and 14 days later.</td>
</tr>
<tr>
<td>Disease</td>
<td>Laboratory basis for diagnosis</td>
<td>Specimen</td>
<td>When to take specimens</td>
</tr>
<tr>
<td>----------</td>
<td>------------------------------------------------------------------------------------------------</td>
<td>------------------------</td>
<td>----------------------------------------------------------------------------------------</td>
</tr>
<tr>
<td>Rubella</td>
<td>Demonstration of rubella specific IgM antibody, except following immunisation OR a four-fold rise in rubella antibody titre between acute and convalescent sera OR isolation of rubella virus from a clinical specimen.</td>
<td>Blood.</td>
<td>Four days after onset of illness.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Blood.</td>
<td>One specimen at onset of illness and second specimen 14 days later.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Nasopharyngeal swab.</td>
<td>Taken within three days of initial presentation of illness. (Note: rubella virus isolation rate is poor and takes four weeks. Viral transport medium is required. Serology is the preferred test.)</td>
</tr>
</tbody>
</table>
### Disease | Laboratory basis for diagnosis | Specimen | When to take specimens |
--- | --- | --- | --- |
**Rubella** (congenital) | Isolation of rubella virus from a clinical specimen from the infant | Throat swab. | At birth. (Note: rubella virus isolation rate is poor and takes four weeks. Viral transport medium is required. Serology is preferred test.) |
| OR demonstration of rubella specific antibody (IgM) in the infant’s serum | Blood. | Cord blood specimen. |
| OR persistence of rubella specific IgG antibody of titre higher than expected from passive transfer of maternal antibody | Blood. | One specimen at birth and second specimen 14–21 days later. |
| OR laboratory confirmed maternal rubella infection in the first trimester of pregnancy. | Blood. | Two maternal blood tests in first trimester of pregnancy (see rubella diagnosis). |
**Tetanus** | None. | None. |

* Measles IgM is needed to initiate public health action but viral isolation or change in IgG or PCR is needed to confirm diagnosis.

** When testing for pertussis, alternative serological tests may be available. Serology is not accepted as a confirmatory test for surveillance in the *Communicable Disease Control Manual 1998* (Ministry of Health). A case diagnosed from clinical findings and positive serology would be classified as ‘probable’ and not ‘confirmed’. Blood should be taken at the initial clinical presentation and a second specimen taken at least four days later. A positive serological test for pertussis IgA and/or IgM or rising titres would be indicative of recent infection.

*** ESR – Institute of Environmental Science and Research.
1.5 Vaccine types and composition

Vaccines are an antigenic preparation used to produce active immunity to a disease. There are two basic types:

- vaccines that use living, attenuated (weakened) strains of viruses or bacteria
- vaccines that use the killed whole virus or bacterial organism, or purified products derived from them.

**Live vaccines**

To produce a live vaccine, such as MMR or varicella, the ‘wild’ or disease causing virus is attenuated or modified through repeated culture in the laboratory. This process reduces the virulence (ability to produce disease) properties of the virus so that it does not cause disease. It does, however, still generate an immune response that is protective against the wild virus. The attenuated vaccine virus multiplies to a limited extent in host tissue and induces the same immune response as the wild virus infection in the majority of subjects. Live vaccines are generally very effective and induce long lived immunity.

In some instances (eg, varicella vaccine in adults), more than one dose may be needed because replication of the vaccine virus, and hence immunity, does not always result from the first dose. Booster doses may be needed to maintain antibody levels.

**Inactivated vaccines**

Whole cell, toxoid, subunit, recombinant and conjugate vaccines all come under the category of inactivated vaccines, in that they are non-infectious but retain the ability to stimulate the immune system. These are explained below.

**Whole cell vaccines**

Growing whole bacteria or viruses (eg, inactivated influenza or inactivated poliomyelitis vaccine) in culture media, then treating them with heat and/or chemicals, produces an inactivated, non-viable vaccine. These micro-organisms cannot cause an infection because they are dead.

**Toxoid vaccines**

In some bacterial infections (eg, diphtheria, tetanus) the clinical manifestations of disease are caused not by the bacteria themselves but by the toxins they secrete. Toxoid vaccines are produced by purifying the toxin and altering it chemically (usually with formaldehyde). While no longer toxic, the toxoid is still capable of inducing a specific immune response protective against the effects of the toxin.

**Subunit vaccines**

The whole organism is grown in culture media and then the organism is further treated to purify only those components to be included in the vaccine (eg, acellular
pertussis and the meningococcal B vaccine, MeNZB™). The use of subunit vaccines has greatly reduced the number of antigens given to children. Despite an increase in the number of vaccines given to children in the last two to three decades, the total number of antigens has significantly decreased.

**Recombinant vaccines**

For example, the hepatitis B vaccine is made by inserting a segment of the hepatitis B virus gene into a yeast cell. The modified yeast cell produces large amounts of hepatitis B surface antigen, which is purified and harvested and used to produce the vaccine. The recombinant hepatitis B vaccine is identical to the natural hepatitis B surface antigen, but does not contain virus DNA, and is therefore unable to produce infection.

**Conjugated vaccines**

Children under two years of age do not respond well to antigens such as polysaccharides, which produce antibodies via a T-cell independent mechanism. If these polysaccharide antigens are chemically linked (conjugated) to a protein that T-cells recognise, then these conjugate vaccines can elicit strong immune responses and immune memory in young children. For example, the *H. influenzae* type b (Hib) vaccine is made from combining the bacterial polysaccharide cell coat (PRP, which is poorly immunogenic in children) with a protein carrier – either tetanus toxoid (hence PRP-T), or an outer membrane protein from *N. meningitidis* (hence PRP-OMP). Conjugating the polysaccharide to the protein in this way makes them more easily recognised by the immune system of young children, and therefore produces long lasting immunity from an earlier age than would otherwise be possible.

The different types of vaccines are summarised in Tables 1.6 and 1.7.
Table 1.6: Bacterial vaccines

<table>
<thead>
<tr>
<th>Inactivated</th>
<th>Live attenuated</th>
</tr>
</thead>
<tbody>
<tr>
<td>Toxoid:</td>
<td>tuberculosis – BCG</td>
</tr>
<tr>
<td>• diphtheria</td>
<td></td>
</tr>
<tr>
<td>• tetanus.</td>
<td></td>
</tr>
<tr>
<td>Conjugate:</td>
<td></td>
</tr>
<tr>
<td>• <em>Haemophilus influenzae</em> type b</td>
<td></td>
</tr>
<tr>
<td>• meningococcal C (conjugate)</td>
<td></td>
</tr>
<tr>
<td>• pneumococcal conjugate.</td>
<td></td>
</tr>
<tr>
<td>Subunits:</td>
<td></td>
</tr>
<tr>
<td>• acellular pertussis</td>
<td></td>
</tr>
<tr>
<td>• pneumococcal polysaccharide</td>
<td></td>
</tr>
<tr>
<td>• meningococcal A, C, Y &amp; W135</td>
<td></td>
</tr>
<tr>
<td>• MeNZB™</td>
<td></td>
</tr>
</tbody>
</table>

Table 1.7: Viral vaccines

<table>
<thead>
<tr>
<th>Inactivated</th>
<th>Live attenuated</th>
</tr>
</thead>
<tbody>
<tr>
<td>Whole cell:</td>
<td></td>
</tr>
<tr>
<td>• inactivated poliomyelitis – IPV Salk</td>
<td></td>
</tr>
<tr>
<td>• hepatitis A.</td>
<td></td>
</tr>
<tr>
<td>Recombinant:</td>
<td></td>
</tr>
<tr>
<td>• hepatitis B.</td>
<td></td>
</tr>
<tr>
<td>Subunit:</td>
<td></td>
</tr>
<tr>
<td>• influenza A and B.</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• measles</td>
</tr>
<tr>
<td></td>
<td>• mumps</td>
</tr>
<tr>
<td></td>
<td>• rubella</td>
</tr>
<tr>
<td></td>
<td>• varicella zoster</td>
</tr>
<tr>
<td></td>
<td>• oral polio (OPV)</td>
</tr>
</tbody>
</table>

Other compounds in vaccines

Other compounds may be added to vaccines as part of their preparation as *inactivating agents* (eg, formaldehyde), as *preservatives* (eg, phenoxyethanol), as *stabilisers* (eg, human serum albumin, lactose, sorbitol, hydrolysed gelatin, neomycin, magnesium chloride), or as *adjuvants* to enhance the immune response (eg, aluminium hydroxide or phosphate). These additives are present in very small quantities and comply with WHO guidelines.

*Inactivating agents* are chemical agents used in the manufacture of certain vaccines made from components of bacteria or viruses (eg, formaldehyde is used to inactivate the tetanus toxin protein used to manufacture the tetanus vaccine). The product is then further purified to remove any contaminants and any excess formaldehyde. The resulting vaccine may contain minute traces of formaldehyde. The vaccines used in New Zealand contain well below the standard limit for traces of formaldehyde set by the WHO.
Preservatives are added to vaccines to prevent bacterial growth where there is risk of contamination (eg, when the vaccine is prepared in multidose vials). As a precaution, thiomersal is no longer used as a preservative in vaccines on the usual National Immunisation Schedule even though there is no evidence that it represented a danger. However, thiomersal is found in both child and adult doses of the combination diphtheria tetanus vaccines (CDT™ and ADT™; 0.01 percent w/v), and in some influenza vaccines.

Stabilisers are added to vaccines to maintain their effectiveness and thermal stability, because the storage and transportation of vaccines can be easily compromised. Examples are human serum albumin, lactose and sorbitol. There is no risk of transmitting blood borne viruses from human serum albumin in vaccines.

Adjuvants are added to vaccines to enhance the protective response. The main functions of adjuvants such as aluminium hydroxide or phosphate are to keep the antigen near the injection site and to activate the special antigen presenting cells of the immune system. The amount of adjuvant varies from 0.25 mg to 0.5 mg per dose, depending on the vaccine. There is no evidence that aluminium hydroxide or phosphate given intramuscularly causes toxic effects. They do, however, enhance the local immune response, which is essential for the induction of a good immune response. Thus a localised injection reaction may occur. They are not adverse events (AEFI). (See section 20.2c for further information on vaccine content.)

Transfer of biological products: minimising the risk from animal products
The development of a rapidly progressive neurological disease (variant Creutzfeldt-Jakob disease, vCJD) in people presumed to be infected by exposure to tissue from cows with bovine spongiform encephalopathy (BSE) has raised concern about exposure to bovine products. The estimated risk of acquiring vCJD as a result of vaccination is generally agreed to be extremely small (or infinitesimal). (See also chapter 20: Vaccination Questions and Concerns.)

Animal products: vaccine manufacturers are required to source bovine products from BSE free countries. New Zealand is one of the few countries in the world certified BSE free.

Blood products: there is a theoretical risk of transfer of prion protein in a vaccine made using blood products. Human serum albumin is currently used during MMR manufacture. However, donors are carefully selected, and in future years synthetic human albumin will be used.

Concurrent administration of vaccines
In general, it is not recommended that the schedule of vaccines or the timing of visits be changed to avoid giving multiple injections at a visit (see chapter 2). Increasing the number of visits may lead to incomplete immunisation.
Vaccines, including live virus vaccines, may be given concurrently, unless the manufacturer makes a specific recommendation against it. *Where a number of different injectable vaccines are given on the same day, they must be administered in separate syringes, at different sites.*

Some combination vaccines have a liquid and lyophilised component and are specifically designed to be mixed just prior to administration.

There are concerns about impaired immune responses to other vaccines shortly after exposure to live viral vaccines. For this reason it is suggested that other vaccines should not be administered within a four-week period after vaccination with live viral vaccines. In particular, if a live attenuated viral vaccine is given within four weeks of another viral vaccine it may result in unexpected adverse reactions due to this lowered state of immunity.

**Use of unapproved vaccines**

*Vaccines unlicensed for distribution in New Zealand*

It is possible for authorised prescribers and medical practitioners to use products that are not yet licensed for distribution in New Zealand under the terms that are set out in sections 25 and 29 of the Medicines Act 1981. For further information on the risks and benefits of using an unlicensed product in New Zealand, refer to the Medsafe website: www.medsafe.govt.nz.

*Other vaccines licensed for distribution in New Zealand*

There are vaccines licensed for distribution in New Zealand but not publicly funded by the Ministry of Health. Health professionals can, however, purchase vaccines directly from the manufacturer. Manufacturer’s contact details can be found in the back of the *MIMS New Ethicals*.

### 1.6 Adolescent and adult vaccination

An important proportion of vaccine preventable disease now occurs in adolescents and adults. People who escaped natural infection as children, or were not vaccinated against hepatitis B, pertussis, measles, mumps, rubella, diphtheria, tetanus and poliomyelitis, are at risk of these diseases and their complications.

**Adolescent and adult vaccination**

When adolescents and adults are seen in general practice or by vaccination providers, there is an opportunity to ensure that they have been adequately protected against the following diseases and have received at least a primary immunisation course of:

- tetanus 3 doses
- diphtheria 3 doses
- hepatitis B 3 doses (depending on age and other health factors)
• polio  3 doses
• measles  1 dose (all people born between 1969 and 1990 should have received 2 doses of measles containing vaccine, see chapter 9: Measles)
• mumps  1 dose
• rubella  1 dose.

If the requisite number of doses has not been received, catch-up vaccination should be offered. The vaccines and the administration of all Schedule vaccines are available free of charge up to the 16th birthday. Females should be offered testing to ensure that they are immune to rubella. All should be reminded of the necessity for age appropriate boosters against tetanus and diphtheria.

**Checklist for adult vaccination**

The following vaccines are recommended and publicly funded:

• Td vaccine at 45 and 65 years of age (note: the administration charge for the Td booster is not publicly funded; see section 5.5).

• Influenza vaccine for those 65 years of age and over, and those under 65 years who meet the chronically ill criteria (see chapter 13: Influenza).

• MMR for any individual susceptible to any one of these three diseases (see relevant chapters).

• Hepatitis B vaccine for household and sexual contacts of known hepatitis B carriers (see chapter 3: Hepatitis B).

• Pneumococcal, Hib, meningococcal A, C, Y, W135 vaccines for individuals pre- and post-splenectomy (see relevant chapters).

Adult females of childbearing age should know whether or not they are immune to rubella.

The following vaccines are recommended but not publicly funded (although they may be available through hospitals):

• pneumococcal polysaccharide vaccine for those 65 years of age and over and those at risk (this includes immune competent persons at risk because of chronic illness, individuals with chronic CSF leaks and immune compromised individuals) (see chapter 16)

• hepatitis B for adults at risk (see chapter 3)

• varicella, if susceptible (see chapter 17).

All travellers should be encouraged to consider vaccination requirements well in advance of overseas travel. Information on vaccination for adults is included in the appropriate sections of this Handbook. Information can also be obtained in the Ministry of Health publication *Health Advice for Overseas Travellers 1996*. 
1.7 Special groups: immigration, work and pregnancy

Immigrant and refugee children

Adults and children who enter New Zealand as refugees or immigrants require assessment in regard to their vaccination requirements.

Assess the immunisation status of the presenting child and determine which catch-up vaccinations the child should receive. Children who have been previously immunised in a non-industrialised country may have received BCG, three doses of DTwP and OPV in the first six months of life, and a dose of measles vaccine between 9 and 15 months of age. However, they are unlikely to have received Hib or MMR vaccine, unless they have come from an industrialised country. Increasing numbers of countries have hepatitis B vaccine included in their national childhood immunisation schedule.

If a refugee or immigrant child has no valid documentation of vaccination, an age appropriate catch-up programme should be commenced (see Appendix 2).

If there is a valid record of vaccination, the history of prior doses should be taken into account when planning a vaccination catch-up that complies with the New Zealand programme.

Tuberculosis is an important public health problem for refugees. Figures from the United States (US) show that approximately 1–2 percent of refugees are suffering from active tuberculosis on arrival, and about half have positive tuberculin skin tests. The number who have received BCG immunisation is unknown. It is important that all refugee children be skin tested with the Mantoux tuberculin test at the time of the first visit and, if negative, tested again three months later to identify recently acquired infection. Previous BCG immunisation should be considered when interpreting Mantoux results. A chest X-ray is recommended if the Mantoux is > 10 mm following BCG, or > 5 mm without a previous history of BCG.

In New Zealand the policy is to provide BCG vaccination to newborns at increased risk of tuberculosis (see section 1.3 and chapter 12 for more details on the neonatal BCG eligibility criteria).

The prevalence of chronic hepatitis B infection in refugees from eastern Asia is estimated to be 10–15 percent. If a member of the family is found to have chronic hepatitis B infection, it is recommended all the family be screened and immunisation offered to all susceptibles. If no one in the family is a carrier, all children under 16 years of age should be offered immunisation against hepatitis B.

For details of immunisation schedules of other countries, contact your local immunisation co-ordinator/facilitator, medical officer of health or IMAC.
Immunisation of those at occupational risk

Certain occupations are at increased risk of contracting some of the vaccine preventable diseases. Immunisation is recommended and may not be publicly funded. It may be employer funded. The following vaccines should be considered for certain occupational groups.

Table 1.8: Recommended vaccines, by occupational group

<table>
<thead>
<tr>
<th>Occupation</th>
<th>Recommended vaccines</th>
<th>Vaccines to consider</th>
</tr>
</thead>
<tbody>
<tr>
<td>Early childhood services staff</td>
<td>Hepatitis B, MMR, influenza, varicella (if susceptible)</td>
<td>Hepatitis A; dTap</td>
</tr>
<tr>
<td>Medical, nursing, other health professionals and students</td>
<td>Hepatitis B, MMR, influenza</td>
<td>Varicella (if susceptible and those working in high risk areas); BCG and hepatitis A; dTap for paediatric ward staff</td>
</tr>
<tr>
<td>Laboratory staff</td>
<td>Hepatitis B, MMR, influenza; MeNZB™ (while the vaccine is available)</td>
<td></td>
</tr>
<tr>
<td>Health care assistants, long term facility carers</td>
<td>Hepatitis B, MMR, influenza</td>
<td></td>
</tr>
<tr>
<td>Police</td>
<td>Influenza, hepatitis B</td>
<td></td>
</tr>
<tr>
<td>Sewerage workers</td>
<td>IPV, hepatitis B</td>
<td></td>
</tr>
</tbody>
</table>

Vaccination during pregnancy

Because of the theoretical possibility of harm to the fetus, live vaccines should not be administered to a pregnant woman. In some circumstances where there is increased risk of exposure to the micro-organism, the need for immunisation may outweigh any possible risk to the fetus. Women who are to receive the rubella vaccine (as MMR) are advised to ensure they are not pregnant at the time of immunisation and for at least 28 days afterwards. There is no current evidence that rubella vaccine is teratogenic (see section 11.7). The influenza vaccine is recommended for at risk pregnant women, and may be offered to women in the second and third trimester of pregnancy (see chapter 13).

1.8 Special risk groups: medical conditions

Some conditions increase the risk from infectious diseases, and children with such conditions should be immunised as a matter of priority. These conditions include chronic diseases, and immune deficient and immune compromised individuals. Special care is required with some live vaccines. When considering immunising children at risk, seek advice from the child’s paediatrician.
**Preterm infants**

Preterm infants and other infants with low birthweight should be immunised at the usual chronological age with the usual vaccine dosage.

If an infant is still in hospital when immunisations are due, the DTaP-IPV and Hib-Hepatitis B vaccines should be given at the scheduled chronological age. Babies who weigh under 2 kg have a sub-optimal response to hepatitis B vaccine, so immunisation may need to be deferred (see section 3.5). In New Zealand, some neonatal units give Hib-Hepatitis B at six weeks of age (chronological age); others when the baby weighs 2 kg. However, all pre-term infants born to HBsAg positive mothers should receive immune prophylaxis (HBIG and hepatitis B vaccine) as soon as possible after birth. Available data suggests very low birthweight infants have a less adequate antibody response to Hib-OMP vaccine and an extra dose is recommended at age five months, (see chapter 7). The response may be decreased in chronically sick infants.

Preterm infants who develop chronic respiratory disease should be given influenza vaccine at six months of age, and a second dose one month later (influenza vaccine is usually available from March to June each year). Further protection of infants with these and other chronic conditions should be ensured by immunising the family and caregivers, including hospital personnel.

**Immune deficient children**

For information on the pneumococcal immunisation programme for high risk children, see chapter 16: Pneumococcal Disease.

Diagnosis of immune deficient children is often not made before children start their immunisation schedules. However, no live virus vaccines are given in the first year of life. For children with immune suppression, consult their specialist about a suitable immunisation schedule.

The safety and effectiveness of vaccines in people with immune deficiency are determined by the nature and degree of immune suppression. Immune deficiency conditions may be divided into primary and secondary. Primary immune deficiencies that present in childhood are generally inherited, and include antibody deficiency (disorders of B lymphocytes or antibody production), defects of cell mediated immunity (disorders of T lymphocytes, which most often present as combined defects affecting antibody production as well), and defects of complement and phagocytic function. Secondary disorders of the immune system are acquired, and occur in people with human immunodeficiency virus (HIV), malignant neoplasms or transplantation, and in people receiving immune suppressive treatment or radiotherapy (see Table 1.9).

Experience with vaccine administration in immune suppressed children is limited.
**Live vaccines** (these include MMR, varicella and BCG) should not in general be given to people who are severely immune suppressed, either viral or bacterial, because of the risk of disease from vaccine strains.

**Inactivated vaccines** (IPV, DTaP, hepatitis B, Hib, pneumococcal and influenza) may be administered since the risk of adverse reactions is not increased in immune suppressed children. However, the response of immune suppressed children to these inactivated vaccines may be inadequate. In children with a secondary immune deficiency, their ability to develop an adequate immunological response depends on when immune suppression occurs. In children in whom immune suppressive therapy is discontinued, an adequate response usually occurs between three months and one year after discontinuation. Influenza vaccine should be given to immune suppressed children before each influenza season, and to children receiving chemotherapy for malignant neoplasm three to four weeks after chemotherapy is discontinued, when both the peripheral granulocyte and lymphocyte counts are > 1.0 x 10⁹/L.

**Primary immune deficiencies**

Live vaccines are contraindicated for most children with B lymphocyte defects (except IgA deficiency), and for all children with T lymphocyte mediated disorders of immune function. Most of these children will be on intravenous immunoglobulin (IVIG) replacement therapy, which provides passive protection against most vaccine preventable infections. Seek specialist paediatric advice. (See Table 1.9.)

**Secondary (acquired) immune deficiencies**

Factors to consider when immunising children with secondary immune deficiency include the underlying disease, the dose and schedule of the immune suppressive drugs, the infectious disease, and the immunisation history of the child. Live vaccines, generally, are contraindicated because of the risk of serious adverse effects. Exceptions are children with HIV infection who are not severely immune compromised, in whom MMR is recommended. Varicella vaccine is recommended for children with HIV infection with CD4+ T lymphocyte values of 25 percent or greater. Live virus vaccines should be withheld until at least three months after cessation of immune suppressive cancer chemotherapy, and tests of immune function may be used to guide safe timing. Recommendations for children on corticosteroids are given below. Seek specialist paediatric advice.

**Other considerations**

Children with a primary or secondary immune deficiency may not respond adequately to an immunising agent. Specific serum antibody titres should be determined to guide future management of exposures and vaccine.
People with certain immune deficiencies may benefit from specific vaccines to prevent diseases to which they are particularly susceptible. Pneumococcal and meningococcal vaccine are indicated to those with splenic dysfunction, asplenia and complement deficiencies, who are at increased risk of infection from encapsulated bacteria. Influenza vaccine is indicated for children with splenic dysfunction, asplenia, and phagocyte function deficiencies to prevent influenza and reduce risk of secondary bacterial infections.

**Household contacts**

Immunologically competent siblings and household contacts may receive all the National Immunisation Schedule vaccines, particularly IPV and MMR. There is no risk of transmission of the IPV or MMR vaccine viruses to the immune compromised individual. However, it is important to ensure that close household contacts are immune for the added protection of the immune suppressed individual. Varicella vaccine can be given safely to household contacts of immune suppressed children.

Oral polio vaccine, which was contraindicated in households where immune suppressed individuals lived, is no longer available in New Zealand.

A summary of the appropriate immunisation for children with primary and secondary immune deficiencies is given in Table 1.9.

**Table 1.9: Immunisation of children with primary and secondary immune deficiencies**

<table>
<thead>
<tr>
<th>Category</th>
<th>Specific immune deficiency</th>
<th>Vaccine contraindications</th>
<th>Efficacy and comments</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Primary</strong></td>
<td></td>
<td></td>
<td>---------------------------------------------------------------------------------------</td>
</tr>
<tr>
<td>B lymphocyte (humoral)</td>
<td>X-linked and common variable immune deficiency</td>
<td>Live bacterial vaccines, MMR and varicella</td>
<td>The efficacy of any vaccine dependent on humoral response is doubtful; IVIG interferes with the response to live vaccines and provides passive protection.</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>---------------------------------------------------------------------------------------</td>
</tr>
<tr>
<td>Selective IgA deficiency</td>
<td>Nil</td>
<td></td>
<td>All vaccines are probably effective.</td>
</tr>
<tr>
<td>T lymphocyte (cell mediated and humoral)</td>
<td>Severe combined immune deficiency</td>
<td>All live vaccines(^{a,b})</td>
<td>The efficacy of any vaccine dependent on humoral or cellular response is doubtful.</td>
</tr>
<tr>
<td>Category</td>
<td>Specific immune deficiency</td>
<td>Vaccine contraindications</td>
<td>Efficacy and comments</td>
</tr>
<tr>
<td>--------------------------</td>
<td>---------------------------------------------------------------------------------------------</td>
<td>---------------------------</td>
<td>-------------------------------------------------------------------------------------------------------------------------------------------------------</td>
</tr>
<tr>
<td>Complement</td>
<td>Deficiency of early components (C1, C4, C2, C3)</td>
<td>None</td>
<td>All routine vaccines are probably effective; pneumococcal and meningococcal are recommended.</td>
</tr>
<tr>
<td></td>
<td>Deficiency of late components (C5–9), properdin, factor B</td>
<td>None</td>
<td>All routine vaccines are probably effective; meningococcal vaccine is recommended.</td>
</tr>
<tr>
<td>Phagocytic function</td>
<td>Chronic granulomatous disease, leukocyte adhesion defect, myeloperoxidase deficiency</td>
<td>Live bacterial vaccines</td>
<td>All routine vaccines are probably effective; consider influenza vaccine.</td>
</tr>
<tr>
<td>Secondary</td>
<td>HIV/AIDS</td>
<td>BCG; withhold MMR and varicella in severely immunocompromised children</td>
<td>MMR, varicella and all inactivated vaccines may be effective.</td>
</tr>
<tr>
<td></td>
<td>Malignant neoplasm, transplantation, immune suppressive or radiation therapy</td>
<td>Live viral and bacterial, depending on immune status</td>
<td>The effectiveness of any vaccine depends on the degree of immune suppression.</td>
</tr>
</tbody>
</table>

Key: IVIG: intravenous immunoglobulin; IgA: immunoglobulin A; HIV: human immunodeficiency virus; AIDS: acquired immunodeficiency syndrome; BCG: Bacille Calmette-Guérin; MMR: measles, mumps and rubella.

a  Live viral vaccines (MMR, varicella).

b  Live bacterial vaccines (BCG).

c  HIV infected children should receive IG after exposure to measles and may receive varicella vaccine if CD4+ count ≥ 25 percent.

*Children receiving corticosteroids*[^2^]

Children who receive corticosteroid therapy can become immune suppressed. The minimal amount of corticosteroid and duration of administration sufficient to cause immune suppression is not well defined, and is dependent on dose, duration and underlying disease. Many clinicians consider a daily dosage equivalent to 2 mg/kg...
prednisone or greater, or a total daily dosage of 20 mg or greater, particularly when given for 14 days or more, is sufficient to raise concern about the safety of live virus vaccines.

This guide may be used for safe live virus vaccine administration to children on corticosteroids.

- Topical therapy or local injections of corticosteroids, including on skin or respiratory tract (by aerosol) or intra-articular, bursal or tendon injections, usually do not result in immune suppression, and live virus vaccines may be given after topical therapy.

- Children on maintenance physiologic doses of corticosteroids can receive live virus vaccine while on treatment.

- Children on low to moderate doses of systemic steroids given daily or on alternate days can receive live virus vaccines. This includes children receiving less than 2 mg/kg per day prednisone or less than 20 mg/day if they weigh more than 10 kg, or an equivalent dose of another short acting systemic corticosteroid.

- Children receiving high dose corticosteroids daily or on alternate days for fewer than 14 days (eg, children receiving 2 mg/kg of prednisone, or up to 20 mg if the child weighs more than 10 kg) can receive live virus vaccines immediately on discontinuation of treatment. Some experts would delay immunisation for two weeks if possible.

- Children receiving high dose corticosteroids daily or on alternate days for more than 14 days (eg, children receiving 2 mg/kg of prednisone, or 20 mg or more if the child weighs more than 10 kg) should not receive live virus vaccines until the corticosteroid therapy has been discontinued for at least one month.

- Children who have a disease process which causes immune suppression, and who are being treated with either systemic or locally administered corticosteroids, should not be offered live virus vaccines except in special circumstances.

Note: these guidelines are made to ensure safety of administration of the live virus vaccine and may not achieve optimal vaccine immunogenicity.

**Hodgkin’s disease**

Patients suffering from Hodgkin’s disease should be immunised with Hib and pneumococcal vaccines (see chapters 7 and 16) according to age specific recommendations, and have their routine childhood vaccines and MeNZB™ updated as required. Quadrivalent meningococcal vaccine should also be considered. The antibody response is best if immunisation is undertaken 10–14 days prior to the initiation of any chemotherapy. If given during chemotherapy or shortly after its cessation, the antibody response will be sub-optimal. The immune system recovers quickly and immunisation can be carried out three months after chemotherapy.
ceases. For children who received immunisation during therapy, the vaccines should be re-administered three months after discontinuation of therapy.

**Children and adults receiving chemotherapy or immune suppressive therapy**

Live virus vaccines (see chapters 9–11 and 17) are generally contraindicated because of the risk of serious adverse effects. An exception appears to be the judicious use of live varicella vaccine in children with acute lymphocytic leukaemia in continuous remission of at least one year, whose total lymphocyte count is $> 0.7 \times 10^9/L$ and in whom the risk of natural varicella far outweighs the risk from attenuated vaccine virus. Inactivated vaccines may be used where appropriate, but the immune response is likely to be sub optimal and following exposure passive immunisation with IG is likely to be required.

After cessation of immune suppressive therapy, live virus vaccines are generally withheld for an interval of not less than three months. The interval may need to be extended according to the intensity and type of the immune suppressive therapy, radiation therapy, underlying disease and other factors.

**Bone marrow transplant**

Many factors can affect transplant recipients’ immunity to vaccine preventable diseases following a successful marrow transplant. These include the donor’s immunity, the type of transplant, the interval since the transplant, the continuing use of immune suppressive drugs, and graft versus host disease (GVHD). Some recipients acquire the immunity of the donor, but others lose all serological evidence of immunity. Serological tests should be carried out to establish immunological status 12 months after bone marrow transplant and prior to immunisation. If tests are not available, the patient should be reimmunised according to the appropriate catch-up schedule (see Appendix 2).

One study suggests that three doses of tetanus toxoid are required after bone marrow transplant to achieve adequate immunity. Information regarding the response to diphtheria toxoid is not available, but at least three doses will be required. As noted above, the usual childhood immunisations should be given for under seven years of age, and after the seventh birthday Td should be given. No data is available about the other inactivated bacterial vaccines (pneumococcal, meningococcal or Hib), but for maximum benefit all should be delayed for at least one year after transplant.

Healthy survivors of bone marrow transplant can be given MMR vaccine two years after transplant, but the vaccine should not be given to individuals suffering from GVHD, because of a risk of a resulting chronic latent virus infection leading to central nervous system sequelae. It is important to ensure that household contacts are immune to infectious diseases wherever possible. Household contacts may be safely given MMR (see chapter 9). IPV can be given to transplant recipients and their household contacts (see chapter 8).
**Solid organ transplants**

Children older than 12 months who have been scheduled for solid organ transplantation should receive the MMR vaccine at least one month before the transplant. Measles antibody titres should be measured one to two years after the transplant; immunisation may be repeated if titres are low. It may be advisable to check other antibody titres and reimmunise where indicated. The use of passive immunisation with IG should be based on the documentation of negative antibody titres and a positive history of exposure to the disease. See chapter 16 for further information regarding pneumococcal immunisation for these children.

**HIV infection**

For children with HIV infection, discuss with their specialist the recommendations for immunisation. HIV positive children (CD4+ > 14 percent), whether symptomatic or asymptomatic, should follow the routine immunisation schedule, including MMR. No ill effects have been reported following administration of MMR vaccines to HIV positive individuals, who are at increased risk from these three diseases.

The efficacy of any vaccine may be reduced in HIV positive individuals. Serological testing and the need for additional doses should be discussed with the child’s specialist.

Passive immunisation with IG should be considered in HIV positive individuals exposed to measles, even if they have received measles immunisation (see section 9.8). Zoster immunoglobulin (ZIG) should be offered to HIV positive individuals who have not been infected with clinical chickenpox or who can be shown to be non-immune following exposure to chickenpox or shingles. ZIG should be given within 72 hours of exposure but may still have some effects up to seven days later (see section 17.8). For information on varicella vaccine see chapter 17. In general varicella vaccine may be safely given to children at CDC A1 or N1 ie, CD4+ ≥ 25 percent.

Since influenza has not caused excessive morbidity in HIV infected individuals, this vaccine is not routinely recommended for HIV positive individuals.

For other vaccines, see specific disease chapters (chapter 15 for meningococcal invasive disease, chapter 16 for pneumococcal disease).

**Asplenic children**

There are three general reasons why individuals may not have a functioning spleen:

- surgical removal (eg, post trauma)
- disease (eg, sickle cell disease, thalassaemia)
- congenital asplenia.

All asplenic individuals are at increased risk of fulminant bacteraemia, which is associated with a high mortality rate. The risk is greatest for infants, and probably
declines with age and with the number of years since onset of asplenia. The degree of risk of mortality from sepsis is also influenced by the nature of the underlying disease, being increased 50 times (compared with healthy children) in asplenia after trauma, 350 times in asplenia with sickle cell disease, and even higher in asplenia with thalassaemia.

The organisms that most commonly cause fulminant sepsis in these individuals are *Streptococcus pneumoniae* (most frequent), *N. meningitidis*, *H. influenzae* type b, and *Escherichia coli*. Less commonly, infection may be caused by other streptococci, *Staphylococcus aureus* and gram-negative coliforms (eg, *Klebsiella*, *Salmonella* sp and *Pseudomonas aeruginosa*). There is an increased fatality from malaria for asplenic individuals.

If possible, splenectomy should be avoided or delayed, accessory spleens should be preserved, hemisplenectomy should be performed during staging for Hodgkin’s disease, and partial splenectomy should be performed for benign splenic tumours.

The following vaccines are recommended in addition to the normal National Immunisation Schedule:

- pneumococcal vaccine – for recommendations for pneumococcal conjugate vaccine (PCV 7) and polysaccharide pneumococcal vaccine (23 PPV) for all asplenic children and adults see also below, and chapter 16.
- quadrivalent meningococcal polysaccharide vaccine for all asplenic children two years of age or older (see chapter 15 for adult recommendations); conjugate meningococcal group C vaccine may be given to children under two years of age.

Because of an increased risk of infection it is particularly important that asplenic children, whatever their age, receive the Hib vaccine schedule as per the National Immunisation Schedule.

Pneumococcal vaccine appears to reduce the risk of fulminant pneumococcal bacteraemia in asplenic children. The efficacy of other bacterial vaccines (eg, Hib) in these circumstances is not clearly established, but they are probably as effective as pneumococcal vaccine.

**Antimicrobial prophylaxis**

The effectiveness of antimicrobial prophylaxis in asplenic children was proven only for sickle cell disease, but should be strongly considered for all children under five years of age and for at least one year after splenectomy. Monthly benzathine penicillin injections have been shown to reduce episodes of pneumococcal bacteraemia in asplenic children as compared with rates observed in untreated children. Oral penicillin daily also reduces the incidence of severe bacterial infection by 84 percent in asplenic children, compared with rates observed in placebo treated controls.
It is reasonable to extrapolate these data to other asplenic children with a high risk of bacteraemia (eg, asplenic children with malignancies, thalassaemia, etc). There is less agreement regarding the use of chemoprophylaxis in children who have been splenectomised following trauma.

Chemoprophylaxis should be recommended for:
- asplenic children five years of age and under
- for older asplenic children at least two years post-splenectomy.

There are no studies that help decide the age at which chemoprophylaxis should be discontinued. This decision has to be made according to clinical judgement.

The dosage given is as follows:
- under five years of age: 125 mg bd oral penicillin
- five years of age and older: 250 mg bd oral penicillin.

An alternative recommended by some experts is amoxycillin 20 mg/kg per day.

Parents/caregivers should be advised that all febrile illnesses are potentially serious and that they should seek immediate medical help in these circumstances. Patients should be hospitalised if bacteraemia is a possibility. In hospital, the usual treatment would be cefotaxime, ceftriaxone, or another regimen effective against *S. pneumoniae, H. influenzae type b* and *N. meningitis*.

### 1.9 Contraindications

No child should be denied immunisation without serious consideration of the consequences, both for the individual child and for the community. Where there is any doubt, seek advice from the child’s general practitioner, a public health medicine specialist, medical officer of health, or consultant paediatrician. If there is concern about the risk of anaphylaxis, the child may be vaccinated in a controlled environment.

#### General contraindications

*Acute febrile illness*

Minor infections without significant fever or systemic upset are not contraindications to immunisation. The decision to administer or delay immunisation because of a current or recent acute illness depends on the severity of the illness and the aetiology of the disease. All vaccines can be administered to persons with minor acute illness (eg, diarrhoea or mild upper respiratory tract infections), but should be postponed if the subject has a significant fever over 38°C.


Table 1.10: Examples of vaccine specific contraindications

<table>
<thead>
<tr>
<th>Vaccine</th>
<th>Contraindications</th>
</tr>
</thead>
<tbody>
<tr>
<td>Any vaccine</td>
<td>• Anaphylaxis/allergy to any vaccine component</td>
</tr>
<tr>
<td></td>
<td>• Anaphylaxis reaction to a prior dose or to any vaccine component</td>
</tr>
<tr>
<td></td>
<td>• Moderate or severe acute illness (T &gt; 38.0°C)</td>
</tr>
<tr>
<td>DTaP, dTap</td>
<td>• Previous encephalopathy within seven days after DTwPH, DTwP or DTaP</td>
</tr>
<tr>
<td></td>
<td>• Evolving (undiagnosed) neurological problem</td>
</tr>
<tr>
<td>MMR</td>
<td>• Live vaccine within 4 weeks</td>
</tr>
<tr>
<td></td>
<td>• Immune suppressed individuals</td>
</tr>
<tr>
<td></td>
<td>• If blood, plasma or immunoglobulin was given within the last 11 months (see Table 1.11)</td>
</tr>
<tr>
<td>Influenza, yellow fever</td>
<td>• Anaphylaxis to egg or chickens</td>
</tr>
</tbody>
</table>

Precautions

Reaction to a previous dose

Careful consideration will be needed depending on the nature of the reaction. If in doubt about the safety of future doses, seek specialist advice. An anaphylactic reaction to a previous dose is a contraindication to further doses of that vaccine.

Allergy to vaccine components

Delayed type hypersensitivity to the traces of antibiotics (eg, neomycin in MMR) is not a contraindication to the vaccine. If an individual has had anaphylaxis to an antibiotic contained in the vaccine, seek specialist advice.

Egg allergy is not a contraindication to the measles or MMR vaccines. Large studies have confirmed these children can be vaccinated safely. Other components of the vaccine (eg, gelatin) may be responsible for allergic reactions. Anaphylaxis to a prior dose of MMR is a contraindication to a further dose.

It is therefore recommended that any child who has a history of anaphylaxis with cardiorespiratory symptoms should be vaccinated under close supervision, with adrenaline and age appropriate resuscitation equipment immediately available. Vaccinators must be aware of the possibility that allergic reactions, including anaphylaxis, may occur after vaccination without any apparent risk factors (see chapter 2).

Recent receipt of another vaccine, blood or immunoglobulin product

There are theoretical concerns about impaired immune responses if two live virus vaccines are given within four weeks of each other, and there is evidence to substantiate these concerns. If two live virus vaccines are not given concurrently, doses should be separated by four weeks, where possible.
Live virus vaccines should be given at least three weeks before, or up to six months after, doses of human normal immunoglobulin. This is because immunoglobulin may interfere with the response to live viral vaccines. This interference may extend beyond three months for the measles vaccine, depending on the dose given. MMR should be given three weeks before or up to six months after receipt of blood or immunoglobulin, according to Table 1.11.

**Table 1.11: Suggested intervals between immunoglobulin (IG) product administration or blood transfusion and measles vaccination (MMR or monovalent measles vaccine)**

<table>
<thead>
<tr>
<th>Indication for IG</th>
<th>Route</th>
<th>Dose U or mL</th>
<th>mg IgG/kg</th>
<th>Interval (mths)*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tetanus (as TIG)</td>
<td>IM</td>
<td>250 U</td>
<td>≥10</td>
<td>3</td>
</tr>
<tr>
<td>Hepatitis A prophylaxis (as IG) for contact prophylaxis</td>
<td>IM</td>
<td>0.02 mL/kg</td>
<td>3.3</td>
<td>3</td>
</tr>
<tr>
<td>Hepatitis B prophylaxis (as HBig)</td>
<td>IM</td>
<td>0.06 mL/kg</td>
<td>10</td>
<td>3</td>
</tr>
<tr>
<td>Rabies prophylaxis (as RIG)</td>
<td>IM</td>
<td>20 IU/kg</td>
<td>22</td>
<td>4</td>
</tr>
<tr>
<td>Measles prophylaxis (as IG):</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>• standard</td>
<td>IM</td>
<td>0.25 mL/kg</td>
<td>40</td>
<td>5</td>
</tr>
<tr>
<td>• immune comprised host</td>
<td>IM</td>
<td>0.50 mL/kg</td>
<td>80</td>
<td>6</td>
</tr>
<tr>
<td>Varicella prophylaxis (as ZIG)</td>
<td>IM</td>
<td>125 U/10kg</td>
<td>20–39</td>
<td>5</td>
</tr>
<tr>
<td></td>
<td></td>
<td>(maximum 625 U)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Blood transfusion:</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>• washed RBCs</td>
<td>IV</td>
<td>10 mL/kg</td>
<td>Negligible</td>
<td>0</td>
</tr>
<tr>
<td>• RBCs, adenine saline added</td>
<td>IV</td>
<td>10 mL/kg</td>
<td>10</td>
<td>3</td>
</tr>
<tr>
<td>• packed RBCs</td>
<td>IV</td>
<td>10 mL/kg</td>
<td>20–60</td>
<td>5</td>
</tr>
<tr>
<td>• whole blood</td>
<td>IV</td>
<td>10 mL/kg</td>
<td>80–100</td>
<td>6</td>
</tr>
<tr>
<td>• plasma/platelet products</td>
<td>IV</td>
<td>10 mL/kg</td>
<td>160</td>
<td>7</td>
</tr>
<tr>
<td>Replacement (or therapy) of immune deficiencies (as IGIV)</td>
<td>IV</td>
<td></td>
<td>300–400</td>
<td>8</td>
</tr>
<tr>
<td>ITP (as IGIV)</td>
<td>IV</td>
<td></td>
<td>400</td>
<td>8</td>
</tr>
<tr>
<td>ITP</td>
<td>IV</td>
<td></td>
<td>1000</td>
<td>10</td>
</tr>
<tr>
<td>ITP or Kawasaki disease</td>
<td>IV</td>
<td></td>
<td>1600–2000</td>
<td>11</td>
</tr>
<tr>
<td>RSV-IGIV</td>
<td>IV</td>
<td></td>
<td>750</td>
<td>9</td>
</tr>
</tbody>
</table>

Key:

TIG = tetanus immunoglobulin, IG = immunoglobulin, HBIG = hepatitis B immunoglobulin, RIB = rabies immunoglobulin, ZIG = zoster immunoglobulin, IV = intravenous, RBC = red blood cells, ITP = immune (formerly termed ‘idiopathic’) thrombocytopenic purpura, RSV = respiratory syncytial virus.

* These intervals should provide sufficient time for decreases in passive antibodies in all children to allow for an adequate response to measles vaccine. Physicians should not assume that children are fully protected against measles during these intervals. Additional doses of IG or measles vaccine may be indicated after exposure to measles.
References


2 Processes for Safe Immunisation

2.1 Vaccinator training

As vaccines are prescription medicines, they can only be administered by the following persons:

- a medical practitioner
- a registered midwife
- a designated prescriber (which includes registered nurses fulfilling the designated prescriber criteria)
- a person authorised to administer the medicine in accordance with a standing order

And, in the case of an approved immunisation programme:

- a person who is authorised by either the Director-General of Health or a Medical Officer of Health under Regulation 44D of the Medicines Regulations 1984 (‘independent vaccinator’).

Vaccinator training courses

All nurses who provide immunisation services are recommended to attend a vaccinator training course (VTC) before or as soon after commencing their vaccinator role as possible. The VTC is set to meet the ‘Immunisation Standards’ (see Appendix 3) to ensure that vaccinators have the appropriate knowledge and skills to competently deliver immunisation services. To remain up to date on immunisation practice and policy, vaccinators should attend an immunisation update course every two years or self directed learning (to be a minimum of four hours).

The VTC educates nurses to a level that allows them to seek authorisation as an independent vaccinator (see below). VTCs are provided regularly in all regions. Contact the local immunisation co-ordinator/facilitator, Immunisation Advisory Centre (IMAC), or Well Women’s Nursing Service (WONS, in Auckland) for details.

Authorisation as an independent vaccinator

For a vaccinator to be authorised as an independent vaccinator they must meet the requirements in the ‘Protocol for Authorisation of Vaccinators in New Zealand’ (see Appendix 4) and apply to their local medical officer of health for authorisation.

The Medicines Regulations 1984, clause 44A (2), state:

*The Director-General or a medical officer of health may authorise any person to administer a vaccine for the purposes of an approved immunisation programme if that person, following written application, provides documentary evidence satisfying the Director-General or medical officer of health as the case may be, that that person:*
i) Can carry out basic emergency techniques including resuscitation and the treatment of anaphylaxis and;

ii) Has knowledge of the safe and effective handling of immunisation products and equipment and;

iii) Can demonstrate clinical interpersonal skills and;

iv) Has knowledge of the relevant diseases and vaccines in order to be able to explain the vaccination to the patient, parent or guardian of the patient who is to consent to the vaccination on behalf of the patient, to ensure that the patient or parent or guardian of the patient can give informed consent to the vaccination.

An authorised independent vaccinator may administer either all or specific vaccines on the National Immunisation Schedule, and any other vaccine as authorised by the medical officer of health or Director-General; for example, public health nurses deliver the age 11 years immunisation event as the annual Year 7 School Immunisation Programme in the North Island and Nelson-Marlborough District Health Boards.

Since 2002, schedule 3, clause 2.1(s) of the section 88 Notice to General Practitioners requires all primary care practices to have at least one nurse authorised as an independent vaccinator, although all nurses should be encouraged to seek authorisation. Authorisation as an independent vaccinator is valid for a period of two years.

For further information about authorisation as an independent vaccinator, contact the local medical officer of health.

2.2 Informed consent

What is consent?

Consent is a fundamental concept in the provision of health care services, including immunisation. It is based on ethical obligations, which are, in part, supported by legal provisions (eg, Health and Disability Commissioners Act 1994, Code of Health and Disability Services Consumers’ Rights 1996, and Privacy Act 1994). Seeking informed consent is an external expression of a health care practitioner’s pivotal ethical duty to uphold and enhance their patient’s autonomy, by respecting the patient’s personhood in every aspect of their relationship with that individual.

The right to authorise or to exert some control over the collection and disclosure of personal information about oneself is a right closely allied to that of consent to treatment and is also relevant to personal integrity and autonomy.

Consent is a process whereby the individual and/or their representative (if the patient does not have the capacity to consent) are appropriately informed and willing and able to agree to what is being suggested without coercion. It also includes the
right to be honestly and openly informed about one’s personal health matters. The right to agree to treatment carries with it the right to refuse treatment.

Regardless of age, an individual and/or their parent/guardian must be able to understand:

• that they have a choice
• why they are being offered the treatment
• what is involved in what they are being offered
• the probable benefits, risks, side effects, failure rates and alternatives.

The essential elements of the informed consent process are effective communication, full information and freely given competent consent. The Code of Health and Disability Services Consumers’ Rights that represent these three elements are:

• Right 5: Right to effective communication
• Right 6: Right to be fully informed
• Right 7: Right to make an informed choice and give informed consent.¹

For example, section 7(1) of the Code states that ‘services may be provided to a consumer only if that consumer makes an informed choice and gives informed consent, except where any enactment, or the common law, or any other provision of the Code provides otherwise.’ Information on the Code of Health and Disability Services Consumers’ Rights can be found on the Health and Disability Commissioner website: www.hdc.org.nz.

Health professionals have legal obligations to obtain informed consent. Unless there are specific legal exceptions to the need for consent, the health professional who acts without consent potentially faces the prospect of a civil claim for exemplary damages, criminal prosecution for assault (sections 190 and 196 of the Crimes Act 1961), complaints to the Health and Disability Commissioner, and professional disciplining.

Ensuring an individual has made an informed choice regarding treatment options has been included in the Health Practitioners Competence Assurance Act 2003, whereby each health practitioner must practise within the scope of practice within which he or she is competent to practise. For example, the Nursing Council of New Zealand competencies for the Registered Nurse Scope of Practice, Competency 2.4, ‘Ensures the client has adequate explanation of the effects, consequences and alternatives of proposed treatment options.’ (See the Nursing Council of New Zealand website www.nursingcouncil.org.nz.)

The patient or parent/guardian needs to understand the risks and benefits of vaccination, including risks to the child and community, in order to give informed consent.
Immunisation consent in primary care

Parents should be prepared in the antenatal period for the choice they will have to make about their child’s vaccination. This information should be given to parents by the 28 weeks antenatal visit. The Health Funding Authority Notice Issued Pursuant to Section 51 of the Health and Disability Services Act 1993, and continued under Section 88 Notice by Section 112(3) of the New Zealand Public Health and Disability Act 2000 for the provision of Maternity Services (otherwise known as the Maternity Section 88), state that these are the requirements of the lead maternity carer (LMC) in relation to immunisation.

Health professionals should offer information without individuals/parents/guardians having to ask for it. The depth of information offered/required will differ, but the minimum will ensure that the individual/parent/guardian understands what the vaccine is for and the possible side effects.

Every effort should be made to ensure that the need for information is met, including extra discussion time, use of an interpreter and alternative language pamphlets (e.g., Ministry of Health immunisation pamphlets are available in Pacific translations). Issues to discuss with patients/parents/guardians about immunisation include:

- the vaccine preventable diseases
- the vaccines used on the National Immunisation Schedule
- how vaccines work
- the collection of immunisation information on the National Immunisation Register (NIR) from birth, or following the MeNZB™ vaccine (e.g., the information that will be collected, who will have access to it and how will it be used; for more information on the NIR see section 2.3)
- the choice to vaccinate
- the publicly funded vaccines available free to children under 16 years of age.

Consent is required for each immunisation episode or dose. Individuals and parents/guardians have the right to change their mind at any time. Where consent is obtained formally but not in writing, it is good practice to document what was discussed, that consent was obtained and by whom. Note that presentation for an immunisation event should not be interpreted as implying consent.

Further information for parents and health providers may be found in:

- *Immunising Your Children* leaflet (Ministry of Health) – available in English and 12 language translations
- *National Immunisation Register* leaflet (Ministry of Health) – available in English and 12 language translations
- *Childhood Immunisation* health education booklet (Ministry of Health)
Chapter 2: Processes for Safe Immunisation

- the Immunisation Standards 2006 (see Appendix 3)
- *What Every Parent Should Know about Vaccines*, by Paul A Offit and Louis M Bell, Macmillian, New York, 1998 (available at public libraries)
- manufacturer's data sheets on the Medsafe website (www.medsafe.govt.nz)
- other immunisation related websites (see Appendix 11)
- contact IMAC on freephone 0800 IMMUNE or 0800 466863 or see the IMAC website (www.immune.org.nz).

Immunisation consent in other settings (eg, schools)

In mass immunisation campaigns, such as those undertaken at schools, the consent requirements are different from those that apply to the vaccination of individuals in primary care. The parent/guardian may not be with the child on the day of immunisation, so immunisation should proceed only after the parent/guardian has had the opportunity to read the immunisation information and discuss any areas of concern. Written consent must be obtained if the parent/guardian will not be present at the time of immunisation.

Consent and children

Under the Code of Health and Disability Services Consumers' Rights 1996 (Code of Rights), every consumer, including a child, has the right to the information they need to make an informed choice or give informed consent. The law relating to the ability of children to consent to medical treatment is complex. There is no one particular age at which all children can consent to all health and disability services. The presumption that parental consent is necessary in order to give health care to those under 16 years of age is inconsistent with common law developments and the Code of Rights.

The Code of Rights makes a presumption of competence (to give consent) in relation to children, and New Zealand is unusual in this respect (ie, the obligations regarding consent of minors are greater in New Zealand than in many other jurisdictions). A child under 16 years of age has the right to consent for minor treatment, including immunisation, providing he or she understands fully the benefits and risks involved. In 2001, the Health and Disability Commissioner provided an opinion of a child’s consent to a vaccine, whereby the Commissioner was satisfied that a 14 year old was competent to give informed consent for an immunisation event. More details of this opinion can be found on the Health and Disability Commissioner website www.hdc.org.nz (Case: 01HDC02915).
Further information on informed consent may be found in:

- Health and Disability Commissioner website

**Safety for vaccinators**

All vaccinators should carry indemnity insurance. Most employers have indemnity cover, but vaccinators do not have automatic right to claim under that cover. Indemnity insurance should cover vaccinators/health professionals for disciplinary proceedings, coroner’s inquiries, and claims of negligence or error which may lead to injury, death or damage.

**2.3 Vaccine administration**

The Immunisation Standards identify the roles and responsibilities for all those involved in immunisation. The vaccinator is responsible for the delivery and administration of the vaccines on the National Immunisation Schedule. Further details on these standards can be found in Appendix 3.

Information on vaccine presentation, preparation and disposal can be found in Appendix 6. It is expected that vaccinators will know and observe standard occupational health and safety guidelines in order to minimise the risk of spreading infection and needle stick injury.

**Pre-vaccination checklist**

Prior to immunisation with *any* vaccine, the vaccinator should ascertain if the vaccinee (child or adult):

- is well today
- has ever had a severe reaction to any vaccine
- has any severe allergies to vaccine components (eg, gelatin, egg protein, neomycin)
- has a history of a severe allergic reaction from any cause
- is not pregnant (if applicable)
- does not have an undiagnosed or evolving neurological condition
- has appropriate spacing between doses of the same vaccine.

The vaccinator will also need to determine which vaccines the vaccinee is due to have and assess the vaccinee’s overall current vaccination status.
Additional precautions for live vaccines
Prior to immunisation with a live vaccine, the vaccinator should ascertain that the vaccinee (child or adult):

- does not have lowered immunity (eg, due to leukaemia, cancer, AIDS)
- is not taking corticosteroids (eg, prednisone) or other immune suppressive drugs
- has not had a vaccine containing a live virus within the last month (eg, measles, mumps, rubella, MMR)
- has not had an injection of immunoglobulin or blood transfusion in the last 11 months (see Table 1.11)
- does not live with someone with a disease or treatment which lowers immunity.

False beliefs about contraindications to immunisation
The following conditions or circumstances are not contraindications to immunisation of children:

- mildly unwell, but afebrile (temperature less than 38°C)
- asthma, hayfever, eczema, ‘snuffles’, allergy to house dusts
- treatment with antibiotics or locally acting steroids
- pregnancy in the child’s mother or other household contact
- the breastfed child
- neonatal jaundice
- low weight in an otherwise healthy child
- the child being over the usual age for immunisation (use age appropriate vaccines as per the catch up schedules in Appendix 2)
- family history of vaccine reactions
- family history of seizures
- family history of sudden infant death syndrome (SIDS)
- clinical history of pertussis, measles, mumps or rubella infection (clinical history without laboratory confirmation cannot be taken as proof of immunity, and even when proven to be immune to one or two of either measles, mumps or rubella, there is still the need for immunisation against the other(s); immunisation with MMR does not pose any extra risks to those already immune to one or all of the three diseases)
- prematurity in an otherwise well infant – it is particularly important to immunise these children who are likely to suffer severe illness if infected; immunisation should be given at the usual chronological age (see section 1.8 on pre-term infants)
• static neurological conditions, such as cerebral palsy or Down’s syndrome
• contact with an infectious disease
• belief in the value of homoeopathy.

See section 1.9 for information on general contradictions to immunisation, or the relevant chapter section for more specific vaccine contraindications.

Preparing for vaccine administration
Correct vaccine administration is vitally important, and vaccinators have a responsibility to see that vaccines are given in the optimal site, using the appropriate needle size for vaccine effectiveness and patient safety. The use of alternative sites will be based on professional judgement, including knowledge of the potential risks at each site.

Following the guidelines below will help to make the experience less distressing for vaccinator, vaccinee and parent/caregiver.

• Administer the vaccination in a private and appropriate clinical setting.
• Be familiar with the vaccines (eg, their correct preparation, administration and the management of adverse events).
• Be aware of the vaccinee’s immunisation history.
• Ensure the individual/parent or caregiver has the opportunity to discuss any concerns and has given informed consent.
• Be prepared to include other family members in discussion, and explain to older children accompanying infants why the injections are being given and what will happen.
• Ensure there are plenty of distractions available.
• Draw up injections out of sight, if possible. While needles, syringes and other medical paraphernalia are commonplace to vaccinators, they may heighten the anxiety of some individuals/parents/caregivers (and older vaccinees).
• Talk quietly to the infant before immunisation. Make eye contact and explain what is going to happen. Even when a child is unable to understand the words, an unhurried quiet approach has a calming effect and reassures the parent/caregiver.
• Give written and verbal instructions to the individual/parent/caregiver. These should cover what may be expected after immunisation, and what to do in the event of an adverse reaction, including the use of cold compresses, paracetamol dosage and advice on when to notify the vaccinator.
• Inform the individual/parent/caregiver that the information will be collected on the National Immunisation Register (NIR), if applicable (refer to the NIR Privacy Policy on the Ministry of Health website www.moh.govt.nz).
It is important to note that MMR (prior to and following reconstitution) and reconstituted Bacillus Calmette-Guérin (BCG) must be protected from exposure to heat and light, and if not used immediately should be refrigerated at +2°C to +8°C and discard if not used within eight hours (MMR) or within four hours for BCG (BCG must be stored at 4°C). (See the vaccine datasheets.)

Table 2.1: Route of administration for the 2006 National Immunisation Schedule vaccines and special programme

<table>
<thead>
<tr>
<th>Age</th>
<th>National Immunisation Schedule</th>
<th>Special programme**</th>
</tr>
</thead>
<tbody>
<tr>
<td>Birth</td>
<td>DTaP-IPV, Hep B, Hib, MMR, dTap-IPV, Td, Influenza</td>
<td>MeNZB™</td>
</tr>
<tr>
<td>6 weeks</td>
<td>IM, IM</td>
<td>IM</td>
</tr>
<tr>
<td>3 months</td>
<td>IM, IM</td>
<td>IM</td>
</tr>
<tr>
<td>5 months</td>
<td>IM, IM</td>
<td>IM</td>
</tr>
<tr>
<td>10 months</td>
<td>IM</td>
<td>IM</td>
</tr>
<tr>
<td>15 months</td>
<td>IM, SC</td>
<td>MeNZB™</td>
</tr>
<tr>
<td>4 years</td>
<td>IM, IM</td>
<td>IM</td>
</tr>
<tr>
<td>11 years</td>
<td>IM</td>
<td>SC</td>
</tr>
<tr>
<td>45 years</td>
<td>IM</td>
<td>IM</td>
</tr>
<tr>
<td>65 years</td>
<td>IM, IM/SC</td>
<td></td>
</tr>
</tbody>
</table>

Key:

* Refer to chapter 3 for the hepatitis B immunisation criteria for infants of HBsAg (hepatitis B surface antigen) positive mothers.

** MeNZB™ vaccine will be available providing provisional consent is extended. For information on the Meningococcal B Immunisation Programme, see www.immunise.moh.govt.nz. See also chapter 15 for additional individuals eligible for the MeNZB™ vaccine.

**Skin preparation**

Skin preparation or cleansing when the injection site is clean is no longer considered necessary. However, if an alcohol swab is used it must be allowed to dry, otherwise alcohol may be tracked into the muscle, causing local irritation. Alcohol may also inactivate a live attenuated vaccine such as MMR.

**Needle angle, gauge and length**

When administering an intramuscular injection the choice of needle angle used (in a range of 60–90 degrees) is part of the overall injection technique. This is determined by the size of the vaccinee, whether the tissue is bunched or stretched, needle length (16 mm–25 mm) and the vaccinator’s professional judgement.
## Table 2.2: Needle gauge and length, by site and age

<table>
<thead>
<tr>
<th>Age</th>
<th>Site</th>
<th>Needle gauge and length</th>
<th>Rationale</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>Intramuscular injection</em></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Birth</td>
<td>Vastus lateralis</td>
<td>23–25 G × 16 mm</td>
<td></td>
</tr>
<tr>
<td>6 weeks</td>
<td>Vastus lateralis</td>
<td>23–25 G × 16 or 25 mm</td>
<td>Choice of needle length will be based on the vaccinator's professional judgement.</td>
</tr>
<tr>
<td>3–14 months</td>
<td>Vastus lateralis</td>
<td>23–25 G × 25 mm</td>
<td>A 25 mm needle will ensure deep IM vaccine deposition.</td>
</tr>
<tr>
<td>15 months – 3 years (optional)</td>
<td>Deltoid</td>
<td>23–25 G × 16 mm</td>
<td>The vastus lateralis site remains an option in young children while the deltoid muscle bulk is small and multiple injections are necessary.</td>
</tr>
<tr>
<td></td>
<td>Vastus lateralis</td>
<td>23–25 G × 25 mm</td>
<td></td>
</tr>
<tr>
<td>3–7 years</td>
<td>Deltoid</td>
<td>23–25 G × 16 mm</td>
<td>A 16 mm needle should be sufficient to effect deep IM deposition in most children</td>
</tr>
<tr>
<td>Older children (7 years and over), adolescents and adults</td>
<td>Deltoid</td>
<td>23–25 G × 16 mm or 23–25 G × 25 mm</td>
<td>Most adolescents and adults will require a 25 mm needle to effect deep IM deposition. NB: a 21–23 G 38 mm needle may be required for a deltoid injection in an obese male or female.</td>
</tr>
<tr>
<td></td>
<td>Vastus lateralis*</td>
<td>21–22 G × 38 mm</td>
<td></td>
</tr>
<tr>
<td><em>Subcutaneous injection</em></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Subcutaneous injection</td>
<td>Deltoid</td>
<td>25–26 G × 16 mm</td>
<td>While an insertion angle of 30 degrees is recommended, the needle should never be longer than 16 mm or inadvertent IM administration could result.</td>
</tr>
</tbody>
</table>

* Consideration may be given to vastus lateralis as an alternative site, providing it is not contraindicated by the manufacturer’s information sheet.
Intramuscular injection sites
Injectable vaccines should be administered in healthy, well developed muscle, in a site as free as possible from the risk of local, neural, vascular and tissue injury. Incorrectly administered vaccines (incorrect sites and poor administration techniques) contribute to vaccine failure and injection site nodules or lumps, and local reactions. Careful use of a longer needle will cause less damage than a shorter needle.

The recommended sites for intramuscular (IM) vaccines (based on proven uptake and safety) are:

- the vastus lateralis muscle on the lateral thigh for infants under 15 months of age
- for young children, both the vastus lateralis and deltoid sites may be used – the choice will be based on the vaccinator’s professional judgement
- the deltoid muscle for older children, adolescents and adults.

In infants and young children under 15 months of age, the deltoid muscle does not provide a safe IM injection site due to the superficiality of the radial nerve and the deltoid muscle being insufficiently developed to absorb medication adequately.

Use of the anterior thigh or rectus femoris muscle in children is not recommended, because what appears to be a bulky muscle anteriorly is predominantly subcutaneous fat. Immediately underlying the rectus femoris muscle is a neurovascular bundle, and depositing vaccine within that bundle will increase the potential for local reactions and chronic injection site nodules. Injecting at a point halfway between the anterior and lateral sites will have the same outcome.

The buttock should not be used for the administration of vaccines in infants or young children, because the buttock region is mostly subcutaneous fat until the child has been walking for at least 9–12 months. Use of the buttock is not recommended for adult vaccinations either, as the buttock subcutaneous layer can vary from 1–9 cm and IM deposition may not occur.

Consideration may be given to using the vastus lateralis as an alternative site to the deltoid, providing it is not contraindicated by the manufacturer’s information sheet.

Infant vaccination episode (vastus lateralis)
Infants six months of age and under do not need to be grasped or restrained as firmly as toddlers. At this age excessive restraint increases their fear as well as muscle tautness. An infant can be placed lying on his or her back on the bed, or in the cuddle (semi-recumbent) position on the parent’s/caregiver’s lap. Placing the infant on the bed minimises delay between injections and makes the injection process easier, although some vaccinators believe the cuddle position offers better support for both the infant and the parent/caregiver.
Ideally the parent/caregiver should be asked if they wish to hold the infant or child for the injections. Some will prefer not to be involved with the procedure – some do not even wish to be present. If the parent/caregiver is helping to hold the infant or child, ensure they understand what is expected of them and what will take place. Most vaccinators choose to administer the injections quickly and soothe the infant or child afterwards.

The vastus lateralis is a large, thick, well developed muscle in infants, wrapping slightly onto the anterior thigh and extending posteriorly to the biceps femoris.

**Figure 2.1: Diagram showing how to locate the vastus lateralis site**

Have the infant on their back or in the cuddle position with the napkin undone. Gently adduct the flexed leg and then (see Figure 2.1):

1. find the greater trochanter
2. find the lateral femoral condyle
3. section into thirds and run an imaginary line from the centre of the lower marker to the centre of the upper marker (look for the dimple along the lower portion of the fascia lata)
4. The injection site is on that imaginary line, proximal to the junction of the upper and middle thirds.
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Figure 2.2: Photo showing the infant lateral thigh injection technique

Immobilise the limb, as above (see Figure 2.2). The anatomical landmarks are located, and the injection site determined.

The needle should be inserted at a 60–70 degree angle (or 90 degree World Health Organization (WHO) technique) towards the long axis of the leg (towards the patella) and at the junction of the upper and middle thirds. Inject the vaccine at a controlled rate. To avoid tracking, make sure all the vaccine has been injected before withdrawing the needle.

Do not massage or rub the injection site afterwards as this can cause vaccine leakage back along the needle track, leading to tissue irritation.

*Multiple injections in the same muscle*

In general the best practice recommendation is only one injection per site (eg, vastus lateralis), although with the introduction of new vaccines and the need for protection (catch-up), two injections in one muscle may be required. This is considered safe and acceptable, but the vaccinator's injection technique does need to be more precise.

When necessary, two vaccines can be given in the same limb at a single visit. The anterolateral aspect of the thigh is the preferred site for two simultaneous IM injections because of its greater muscle mass. Injection sites should be separated by at least 2–3 cm so that local reactions will not overlap.
Multiple vaccines should not be mixed in a single syringe unless specifically licensed and labelled for administration in one syringe. A different needle and syringe should be used for each injection.²

If the vaccinator is right handed, two injections can be more easily given into the left thigh, and if left handed, into the right thigh. Administering these vaccines into whichever thigh the vaccinator finds the easier facilitates smooth penetration of the muscle and reduces tissue trauma. A well prepared and confident vaccinator will reassure the parent/caregiver that giving concurrent vaccines is a safe and appropriate practice, avoiding multiple visits.

When preparing multiple vaccines, the vaccinator needs to be aware that once drawn up, the vaccines can be visually very similar (eg, MeNZB™ and Hib-Hep B or hepatitis B vaccines). Ensure careful placement of the drawn up vaccines with their corresponding vials.

If all scheduled vaccines are not administered concurrently, there is no minimum interval necessary between visits (ie, it could be the next day). However, there must be four weeks between doses of the same vaccine.

**Young child immunisation episode (vastus lateralis or deltoid)**

The choice between the two sites for IM injections from 15 months of age will be based on the vaccinator’s professional judgement, such as knowledge of the child and ease of restraint. Some vaccinators consider the vastus lateralis preferable for young children because of the size of the deltoid muscle and superficiality of the radial nerve. Discuss the options with the parent/caregiver when making your decision.

The principles for a young child IM lateral thigh and deltoid injection are the same as for an infant lateral thigh injection and for an older child or adult deltoid injection, except the young child will be sitting on the parent’s/caregiver’s lap. The easiest and safest way to position and restrain a young child is to sit the child sideways on their parent’s/caregiver’s lap. Alternatively, the child may face their parent/caregiver, while straddling the parent’s/caregiver’s legs.

If sitting sideways, the child’s right arm should be placed behind their parent’s/caregiver’s back. The parent’s left arm is placed over the child’s left arm and chest and their right arm should lie across the child’s legs and be tucked under the child’s knee.

If the child is in the straddle position, both the child’s arms should be placed behind the parent’s/caregiver’s back and the parent then wraps their arms around the child’s body. It should be noted that if using the straddle position, both the deltoid and vastus lateralis muscle are likely to be more tense or taut, and the injection may therefore be more painful (see Figures 2.3 and 2.5).
Older child, adolescent and adult vaccination episode (deltoid)

The deltoid muscle is located in the lateral aspect of the upper arm. The entire deltoid muscle must be exposed to avoid the risk of radial nerve injury (an injection at the junction of the middle and upper thirds of the lateral aspect of the arm may damage the nerve) (see Figures 2.4 and 2.5).

The volume injected into the deltoid should not exceed 0.5 mL in children and 1.0 mL in adults.
With the vaccinee’s arm removed from the garment sleeve (see Figure 2.4):
1. Find the acromion process
2. Find the deltoid tuberosity, in line with the axilla
3. Draw an imaginary triangle pointing downwards from the acromion.

The injection site is in the centre of the triangle, or the point halfway between the markers (from one to four finger widths from the acromion, depending on the size of the arm).
Insert the needle at a 60–70 degree angle towards the acromion, as this follows the natural path of the muscle fibres and deposits the vaccine at the bulkiest part of the muscle. Inject the vaccine at a controlled rate. To avoid tracking, make sure all the vaccine has been injected before withdrawing the needle.

**Subcutaneous injection sites**

A subcutaneous (SC) injection should be given into healthy tissue, which is away from bony prominences and free of large blood vessels or nerves. SC tissue is found all over the body, but the most commonly used site is the upper arm (ie, deltoid), based on its accessibility and proven vaccine uptake. The lateral thigh may be an alternative site (check the manufacturer’s information sheet).

The principles for locating the deltoid site for a SC injection are the same as for an IM injection. While an insertion angle of 30–45 degrees is recommended, the needle should never be longer than 16 mm, otherwise inadvertent IM administration could result (see Figure 2.6). Some vaccinators choose the thigh for SC vaccines.
Key points for administering injectable vaccines

- Vaccines should not be mixed in the same syringe, unless the prescribing information sheet specifically states it is permitted.
- Careful use of a longer needle will cause less damage than a short needle.
- Needles should be changed routinely after drawing up and prior to administration of the vaccine.
- Do not prime the new needle, because vaccine at the needle tip will cause irritation as it is tracked through the muscle.
- Use of a smaller volume syringe (eg, 1 mL tuberculin) allows for greater control of the rate of plunger depression.

Post-vaccination advice

Post-vaccination advice should be given both verbally and in writing. The advice should include:

- what vaccines have been given and the injection site, and whether the injection was IM or SC (see Table 2.1)
- potential vaccine responses and what to do if these occur (eg, measures for relieving fever, see Table 2.3)
• potential expected responses and adverse events and what to do if these occur (ie, when to seek medical advice) (see section 2.4)

• the weight related paracetamol dosage and how frequently it may be administered (prophylactic paracetamol administered with triple antigen during the primary immunisation series in a dose of 15 mg/kg reduces the incidence of fever, pain and fussiness in infants for the next 6-12 hours)\textsuperscript{3,4}

• when the individual or parent/caregiver should contact the vaccinator if they are worried or concerned

• contact phone numbers.
Table 2.3: Common vaccine responses and relieving measures

<table>
<thead>
<tr>
<th>Vaccine</th>
<th>Common vaccine responses following immunisation</th>
<th>Relieving measures</th>
</tr>
</thead>
</table>
| DTaP containing vaccine and IPV | • Localised pain, redness and swelling at injection site  
• Low grade temperature (fever)  
• Being grizzly, unsettled and generally unhappy – may persist for 24–48 hours  
• Drowsiness  
• Extensive limb swelling after 4th and 5th dose of a DTaP containing vaccine | • Give extra fluids to drink (eg, more breast feeds or water).  
• Do not overdress the baby if hot.  
• Placing a cold, wet cloth on the injection site will help relieve some discomfort.  
• Give paracetamol if needed for pain or to lower fever. |
| Hepatitis B              | • Very occasionally soreness, redness at the injection site  
• Low grade temperature |                                                                                  |
| Hib                      | • Localised pain, redness and swelling at the injection site  
• Low grade temperature |                                                                                  |
| MMR                      | • Discomfort at injection site  
• 5 to 12 days after vaccination:  
  – low grade temperature  
  – faint rash (not infectious)  
  – head cold and/or runny nose  
  – cough and/or puffy eyes  
  – swelling of salivary glands |                                                                                  |
| Adult Td dTap-IPV        | • Localised discomfort, redness and swelling at the injection site |                                                                                  |
| Influenza                | • Low grade temperature  
• Occasional discomfort, redness and swelling at the injection site |                                                                                  |
| Pneumococcal             | • Pain at the injection site  
• Low grade temperature |                                                                                  |
| MeNZB™                   | • Pain at the injection site  
• Fever  
• Headache, malaise |                                                                                  |

**Alternative soothing measures**

Some parents/caregivers, vaccinators and non-vaccinating health professionals may have experience of using other products (eg, topical medications, arnica and bonjela) for relieving vaccination pain and discomfort. However, some of these products are being used outside the manufacturer’s recommendations. Because of
possible medico-legal implications, vaccinators are advised to be cautious when undertaking this practice.

Documentation / record keeping
Accurate documentation is essential. If the vaccinator has not kept accurate clinical records, it is difficult to prove what action/care was or was not taken/delivered when the patient notes are held up for legal scrutiny.

National Immunisation Register
The National Immunisation Register (NIR) is aimed at benefiting individuals by facilitating the delivery of immunisation services and providing an accurate record of their immunisation history. It will also provide national and regional level information on the immunisation coverage of a specified population, and assist in achieving New Zealand coverage targets (ie, 95 percent of children fully immunised by two years of age), thus improving individual and population health through the control or elimination of vaccine preventable diseases.

The NIR was implemented during 2004/05 to collect immunisation information for the Meningococcal B Immunisation Programme. During 2005 the NIR began collecting immunisation information on all individuals born after a specified date (ie, a birth cohort). In the future the NIR may also collect other immunisation information (eg, 11 year immunisation event or adult immunisations).

Further information about the NIR can be found on the Ministry of Health website: www.moh.govt.nz.

Key points about the NIR
The NIR has been developed to ensure that the management of health information (eg, collection, holding, use and disclosure) is governed by the Health Information Privacy Code 1994. The NIR Privacy Policy can be found on the Ministry of Health website.

Individuals or their parents/caregivers may choose at any time not to have any further health information collected on the NIR (ie, they opt off the further collection of immunisation data). However, the NIR will retain the patient’s National Health Index number (NHI), date of birth, district health board they are resident in, date of opt off and any immunisation information recorded before opt off. The reason for retaining this information is to provide an accurate denominator for immunisation coverage calculations and to prevent inappropriate recall and referral.

It is not possible to opt off the NIR for any meningococcal B vaccinations or any immunisation events given concurrently with a meningococcal B vaccine. This information must be recorded on the NIR for safety monitoring purposes.
An individual's immunisation information will be retained on the NIR for their whole life, plus a period of 10 years after their death. Only authorised users will have access to the information held on the NIR. Such a person will be authorised to use and disclose NIR information in accordance with their function.

Information collected on the NIR includes:

- date
- patient name
- patient NHI
- patient date of birth
- vaccine type and number in the series
- batch number and expiry date
- dose, injection site and injection route
- provider name
- vaccinator's name and title
- recall date (when applicable).

Additional information, which may be collected in the patient’s clinical notes, includes:

- confirmation that consent was given
- needle length used
- that the patient was observed for the recommended time and no adverse events occurred during the observation period. If an adverse event does occur, it is important to document the action and treatment given and inform the Centre for Adverse Reactions Monitoring (CARM) (see section 2.4).

The vaccinator should also complete the relevant sections in the *Well Child Tamariki Ora Health Book*, the child's Immunisation Certificate (see Appendix 5), the Ministry of Health payment claim form (where applicable), and, where applicable, the NIR manual form.

**School based vaccination system**

The school based vaccination system (SBVS) was developed to assist in the collection and management of data for immunisation programmes (eg, school immunisation programmes).
The SBVS was first used to collect immunisation information for the Meningococcal B Immunisation Programme School Campaign and this information was transferred to the NIR. From 2006 the SBVS will be used in district health boards (DHBs) where public health nurses deliver the annual Year 7 School Immunisation Programme, ie, all North Island DHBs and Nelson-Marlborough DHB. Currently the information that will be collected on the SBVS for the Year 7 School Immunisation Programme will not be transferred to the NIR. However, it is anticipated that this may change in the future and students and parents will be informed on the Year 7 consent form when this will occur.

**Recommendations following a needle stick injury**

In the event of a needle stick injury, follow the guidelines below.

- The recipient should stop what they are doing and attend to the injury.
- Wounds and skin sites should be washed with soap and water. There is no evidence that encouraging bleeding or applying antiseptic reduces the risk of infection, but these actions are not contraindicated.
- The injury should be immediately reported to the medical advisor, who should consider what immediate action is advised.
- When the needle stick injury involves exposure to a vaccinee’s (or other person’s) blood, serological testing of that source individual should be sought and undertaken as soon as possible.
- Blood should be withdrawn from the affected individual within a few days after the injury and counselling arranged. Testing for hepatitis B, hepatitis C and HIV serology should be undertaken.
- Depending on the infection status of the vaccinee and the immune status of the injured vaccinator, it may be appropriate to start anti-HIV medications within the next few hours or to administer hepatitis B immunoglobulin within the next few days.

The blood borne viruses of main concern in needle stick injuries are hepatitis B, hepatitis C and HIV. All vaccinators should be immunised against hepatitis B and their antibody status known. Currently in New Zealand most HIV infected children (or their parents/caregivers) are likely to know their status at the time of immunisation, so HIV testing in case of needle stick injuries is not routinely advocated. If there is a possibility that the child could be HIV infected, the informed consent of the child or parent/guardian is required before blood is drawn for testing.

Blood borne virus exposures after vaccination are rarely of high risk – because of the small needle size there is seldom visible blood, and there is low risk of blood borne viruses in the community.
2.4 Expected responses and adverse events following immunisation (AEFI)

Expected responses
A vaccine provokes an immune response in the recipient and is most often accompanied by a local or systemic response to the vaccine. This response may include pain, redness and swelling at the injection site, and/or systemic responses such as fever, nausea, headache, malaise, muscle or joint pain depending on the vaccine. These reactions can be expected, and parents should be given information about these ‘expected responses’.

Attenuated live virus vaccines such as measles or rubella induce immunity by causing a mild infection. It is to be expected, therefore, that some vaccinees will develop symptoms such as mild fever, rash or, in the case of rubella, joint pains. These are expected responses, and therefore not regarded as unexpected adverse events. Similarly, toxoid vaccines such as tetanus or diphtheria must introduce sufficient antigen to induce a satisfactory antibody response, so some local reactions and fever are to be expected.

For information on the severe and unexpected reactions that should be reported to the Centre for Adverse Reactions Monitoring (CARM), see Table 2.4, Figure 2.7 and below.

Adverse events following immunisation
An adverse event following immunisation (AEFI) is any adverse event that follows immunisation. The vaccine is not responsible for all of these events. A vaccine reaction is an event that is likely to have been caused by the vaccine. Any serious, unexpected events and events causing clinical concern should be reported to CARM (see Table 2.4 and below). CARM assesses events to establish whether they are vaccine linked. Reports are welcome even when there is uncertainty about the causal relationship to the vaccine.

Before a vaccine is approved for supply in New Zealand, the manufacturer must demonstrate the quality, efficacy and safety of the product to the satisfaction of Medsafe, a division of the Ministry of Health. In addition, the manufacturer is required to extensively test each lot (‘batch’) for quality, potency and safety prior to distribution.

Surveillance for AEFI is an integral part of a national immunisation programme. Through surveillance, it is hoped to detect changes in the rates of known adverse events, and also to detect any adverse events that were previously undocumented or that result from incorrect vaccine delivery.

Information codes will be collected on the NIR for any AEFI for the National Immunisation Schedule events once validated by CARM. This information will merely
provide an alert for the vaccinator to seek further information from the individual or parent/caregiver prior to the administration of a vaccine.

**Notification to the Centre for Adverse Reactions Monitoring (CARM)**

An unexpected or serious AEFI should be reported to:

The Medical Assessor  
Centre for Adverse Reactions Monitoring (CARM)  
PO Box 913 (Freepost no. 112002)  
Dunedin  
Phone 03 479 7247  

or via online reporting at [http://carm.otago.ac.nz](http://carm.otago.ac.nz)

Information should include:

- patient details
- vaccine used
- vaccine batch number
- onset date
- type and duration of adverse event
- treatment required
- outcome.
Figure 2.7: Copy of HP3442 Form for Reporting Adverse Reactions to Medicines, Vaccines and Devices and all Clinical Events for IMMP

**PATIENT DETAILS**

<table>
<thead>
<tr>
<th>Surname:</th>
<th>First Name(s):</th>
<th>NHF No:</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Address:</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Date of Birth:</th>
<th>Sex:</th>
<th>Ethncity:</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**ALL MEDICINES IN USE “ASTERISK SUSPECT MEDICINE/S”** Include over-the-counter (OTC) and alternative medicines

<table>
<thead>
<tr>
<th>Medicine or Vaccine+batch no. (and brand name if known)</th>
<th>Daily Dose</th>
<th>Route</th>
<th>Date Started</th>
<th>Date Stopped</th>
<th>Reason for Use</th>
</tr>
</thead>
<tbody>
<tr>
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<td></td>
</tr>
</tbody>
</table>

**DESCRIPTION OF ADVERSE REACTION OR EVENT**

Date of onset: ________________

**OTHER FACTORS - Please tick or specify as appropriate**

- [ ] Renal disease
- [ ] Hepatic disease
- [ ] Nutritional Suppl or OTC use
- [ ] Allergy
- [ ] Other Medical Conditions: __________________________
- [ ] Industrial Chemicals: __________________________

**REPORTER - Please tick as appropriate:**

- [ ] Doctor
- [ ] Pharmacist
- [ ] Dentist
- [ ] Nurse
- [ ] Other

Name: __________________________

Address: __________________________

Signature: __________________________

Phone: __________________________

Date: __________________________

Send completed form to CARM

Freepost 112002, CARM, PO Box 913, Dunedin or Fax: (03) 479 7150
A reply paid postcard (HP3442) is supplied in each edition of the *MIMS New Ethicals Catalogue* and issues of the Ministry of Health Prescribers Update (see Medsafe website in Appendix 11). Supplies of HP3442 can be obtained from the CARM website (http://carm.otago.ac.nz), the local immunisation co-ordinator/facilitator, or photocopied from Figure 2.7.

If the individual or parent/caregiver does not consent to being identified, the report should be made without personal identification.

Medical practitioners and other health professionals, including vaccinators, are professionally and ethically responsible for reporting *serious or unexpected* adverse events that occur after all medicines, including vaccines. Serious reactions are defined as those that significantly affect a patient’s management, including reactions suspected of causing:

- death
- danger to life
- hospitalisation
- prolongation of hospitalisation
- interruption of productive activity in an adult recipient
- increased investigational or treatment costs
- birth defects.

**What should be reported?**

In order to further enhance the AEFI Reporting Programme, the attending practitioner is asked to report all severe events that occur following immunisation, such as those described in Table 2.4.

Individuals or parents/caregivers must be encouraged to notify vaccinators of any AEFI, in children or adults, which they consider may have been caused by the vaccination. Alternatively, individuals/parents/caregivers may wish to notify CARM themselves, or contact the local immunisation co-ordinator/facilitator, or IMAC (0800 IMMUNE/0800 466 863) to notify on their behalf.

Health professionals/vaccinators should report any serious or unexpected AEFI, regardless of whether or not they consider the event to have been caused by the vaccination. The reporter will receive a letter of response from CARM commenting on the adverse effect, the causal relationship, the number of other similar events and advice about future use of the vaccine in this individual. Also where applicable, CARM will provide a validated AEFI code to be noted on the NIR.

The information provided will help to identify those children who should receive follow up vaccination in a controlled environment, such as a hospital.
Table 2.4: AEFIs to be reported

<table>
<thead>
<tr>
<th>Time frame</th>
<th>Event</th>
</tr>
</thead>
<tbody>
<tr>
<td>Within 24 hours of vaccination</td>
<td>• anaphylactic reaction (acute hypersensitivity reaction)</td>
</tr>
<tr>
<td></td>
<td>• anaphylaxis</td>
</tr>
<tr>
<td></td>
<td>• persistent inconsolable screaming (more than 3 hours)</td>
</tr>
<tr>
<td></td>
<td>• hypotonic/hyporesponsive episodes (HHE)</td>
</tr>
<tr>
<td></td>
<td>• fever &gt; 40°C</td>
</tr>
<tr>
<td>Within 5 days of vaccination</td>
<td>• severe local reaction</td>
</tr>
<tr>
<td></td>
<td>• sepsis</td>
</tr>
<tr>
<td></td>
<td>• injection site abscess</td>
</tr>
<tr>
<td>Within 12 days of vaccination</td>
<td>• seizures, including febrile seizures</td>
</tr>
<tr>
<td></td>
<td>• encephalopathy</td>
</tr>
<tr>
<td>Within 3 months of vaccination</td>
<td>• acute flaccid paralysis (AFP)*</td>
</tr>
<tr>
<td></td>
<td>• brachial neuritis (usually occurs 2–28 days after tetanus containing vaccine)</td>
</tr>
<tr>
<td></td>
<td>• thrombocytopenia (usually occurs 15–35 days after measles/MMR)</td>
</tr>
<tr>
<td>Between 1 and 12 months after BCG vaccination</td>
<td>• lymphadenitis</td>
</tr>
<tr>
<td></td>
<td>• disseminated BCG infection</td>
</tr>
<tr>
<td></td>
<td>• osteitis/osteomyelitis</td>
</tr>
<tr>
<td>No time limit</td>
<td>• any death, hospitalisation, or other severe and unusual events of clinical concern that are thought by health workers or the public to be related to vaccination</td>
</tr>
</tbody>
</table>

* AFP, including Guillain-Barré syndrome, should be reported to CARM.

Note: AFP in children is also monitored by the New Zealand Paediatric Surveillance Unit (NZPSU) as part of polio eradication surveillance (see chapter 8 Poliomyelitis and section 13.6 on influenza).

**Anaphylaxis**

All vaccinators must be able to distinguish anaphylaxis from fainting, anxiety, breath holding spells and convulsions.

Anaphylaxis is a very rare, unexpected and occasionally fatal allergic reaction. Anaphylaxis develops over several minutes and usually involves multiple body systems. Unconsciousness is rarely the sole manifestation, and it only occurs as a late event in severe cases. A strong central pulse (eg, carotid) is maintained during a faint (vasovagal syncope), but not in anaphylaxis.
In general, the more severe the reaction, the more rapid the onset. Most life threatening adverse events begin within 10 minutes of vaccination. The intensity usually peaks at around one hour after onset.

Symptoms limited to only one system can occur, leading to delay in diagnosis. Biphasic reactions, where symptoms recur 8 to 12 hours after onset of the original attack and prolonged attacks lasting up to 48 hours, have been described. All patients with anaphylaxis should be hospitalised.

**Signs of anaphylaxis**

Anaphylaxis is a severe adverse event of rapid onset, characterised by circulatory collapse. In its less severe (and more common) form, the early signs are generalised erythema and urticaria with upper and/or lower respiratory tract obstruction. In more severe cases, limpness, pallor, loss of consciousness and hypotension become evident in addition to the early signs.

Vaccinators should be able to recognise all of the signs and symptoms of anaphylaxis given in Table 2.5.

**Table 2.5: Signs and symptoms of anaphylaxis**

<table>
<thead>
<tr>
<th>Time scale</th>
<th>Signs and symptoms</th>
<th>Severity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Early warning signs (within a few minutes)</td>
<td>Dizziness, perineal burning, warmth, pruritis</td>
<td>Mild</td>
</tr>
<tr>
<td></td>
<td>Flushing, urticaria, nasal congestion, sneezing, lacrimation, angioedema</td>
<td>Mild to moderate</td>
</tr>
<tr>
<td></td>
<td>Hoarseness, nausea, vomiting, substernal pressure</td>
<td>Moderate to severe</td>
</tr>
<tr>
<td></td>
<td>Laryngeal oedema, dyspnoea, abdominal pain</td>
<td>Moderate to severe</td>
</tr>
<tr>
<td>Late life threatening symptoms</td>
<td>Bronchospasm, stridor, collapse, hypotension, dysrhythmias</td>
<td>Severe</td>
</tr>
</tbody>
</table>

There is no place for conservative management of anaphylaxis. Early administration of adrenaline is essential. (For more details see Table 2.8.)

Misdiagnosis of fainting and other common causes of collapse as anaphylaxis can lead to inappropriate use of adrenaline. Vaccinators should be able to distinguish anaphylaxis from fainting (vasovagal syncope), anxiety and breath holding spells (see Table 2.6). However, infants and babies rarely faint. Sudden loss of consciousness, limpness, pallor and vomiting (signs of severe anaphylaxis in children) should be presumed to be an anaphylactic reaction.
In adults and older children, the most common adverse event is a syncopal episode (fainting), either immediately or soon after vaccination. During fainting the individual suddenly becomes pale, loses consciousness and if sitting or standing will slump to the ground. Recovery of consciousness occurs within a minute or two. Fainting is sometimes accompanied by brief clonic seizure activity, but this generally requires no specific treatment or investigation if it is a single isolated event.

Table 2.6: Distinguishing anaphylaxis from a faint (vasovagal reaction)

<table>
<thead>
<tr>
<th></th>
<th>Faint</th>
<th>Anaphylaxis</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Onset</strong></td>
<td>Usually at the time or soon after the injection</td>
<td>Usually a delay of 5–30 minutes after injection</td>
</tr>
<tr>
<td><strong>System</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Skin</strong></td>
<td>Pale, sweaty, cold and clammy</td>
<td>Red, raised and itchy rash; swollen eyes and face; generalised rash</td>
</tr>
<tr>
<td><strong>Respiratory</strong></td>
<td>Normal to deep breaths</td>
<td>Noisy breathing from airways obstruction (wheeze or stridor); respiratory arrest</td>
</tr>
<tr>
<td><strong>Cardiovascular</strong></td>
<td>Bradycardia; transient hypotension</td>
<td>Tachycardia; hypotension; dysrrhythmias; circulatory arrest</td>
</tr>
<tr>
<td><strong>Gastrointestinal</strong></td>
<td>Nausea/vomiting</td>
<td>Abdominal cramps</td>
</tr>
<tr>
<td><strong>Neurological</strong></td>
<td>Transient loss of consciousness; good response once prone</td>
<td>Loss of consciousness; little response once prone</td>
</tr>
</tbody>
</table>

Distinguishing a hypotonic, hyporesponsive episode (HHE) from anaphylaxis

Hypotonic, hyporesponsive episode (HHE)\(^5\) is defined as ‘an episode of acute diminution in sensory awareness or loss of consciousness accompanied by pallor or cyanosis and muscle hypotonicity’. Different studies have found an incidence varying between 3.5 and 291 per 100,000 immunisations. This wide variation probably reflects lack of an ideal case definition and difficult case recognition, as well as different vaccine formulations.

Collapse reactions, often called an HHE or shock like syndrome, are seen occasionally in infants and very young children following vaccination. Note that:
- onset is sudden, occurring within 48 hours of vaccination
- duration of the episode usually ranges from 1–30 minutes, but may last longer.
All of the following must be present:
- limpness or hypotonia
- reduced responsiveness or hyporesponsiveness
- pallor or cyanosis (no urticaria or angioedema).

The child recovers spontaneously but may remain drowsy for 24–48 hours. Any child who has an HHE should be referred to a paediatrician for review as soon as possible.

In contrast to HHE, an episode of anaphylaxis in infants or small children usually occurs shortly after vaccination, and respiratory (bronchospasm and laryngeal oedema), circulatory (hypotension and tachycardia) problems, and vomiting and diarrhoea will develop rapidly.

Adrenaline is not recommended for HHE as these children do not have respiratory and circulatory problems.

An HHE is no longer a contraindication to further doses of a pertussis vaccine, but rather a precaution (see also sections 6.6 and 6.7).

**Avoidance of anaphylaxis**

To help avoid anaphylaxis, before immunisation:
- ensure there are no contraindications to immunisation
- ask the vaccinee or parent/caregiver about known hypersensitivity
- ask the vaccinee or parent/caregiver about previous AEFIs
- if in doubt as to the advisability or otherwise of administering the vaccine, consult the vaccinee’s general practitioner or a paediatrician.

Vaccinees should remain under observation for 20 minutes to ensure they are observed if they experience an immediate adverse event and they can be appropriately treated.

Be prepared by:
- ensuring emergency procedures are known by all staff
- practising emergency procedures regularly
- having an emergency kit (see Table 2.7) and adrenaline in every room where vaccinations/medications are given
- checking emergency kits regularly
- not giving vaccines when working alone.
Table 2.7: Emergency equipment

Emergency kit
An emergency kit should contain:

- adrenaline* 1:1000 and dosage chart
- syringes: 1.0 mL (tuberculin not insulin, as the insulin needle is non-removable)
- needles: a range of needle lengths and gauges, including 23 or 25 G × 25 mm,
  22 G × 38 mm
- a range of airways, including paediatric.

Other emergency equipment required
It is also necessary to have on hand:

- an oxygen cylinder
- an ambubag, oxygen tubing and a range of oxygen mask sizes (adult and paediatric)
- access to a telephone.

* The expiry date of the adrenaline and other medicines should be written on the outside of the emergency kit, and the kit should be checked monthly. Adrenaline is heat and light sensitive and should be stored appropriately. Adrenaline that has a brown tinge must be discarded.

Remember: events happen without warning. Appropriate emergency equipment must be immediately at hand whenever immunisations are given, and all vaccinators must be familiar with the practical steps necessary to save life following an anaphylactic reaction (see Tables 2.7 and 2.8).

The following drugs are used only under the direction of a medical practitioner:

- antihistamine injection
- hydrocortisone injection (available on Medical Practitioner Supply Order).
Table 2.8: Initial anaphylaxis response/management

- **CALL FOR HELP** – send for professional assistance (ambulance, doctor). Never leave the recipient alone.

- **ASSESS** – if unconscious, place in the recovery position and institute standard procedures for basic life support (airway, breathing, circulation). If cardiorespiratory arrest occurs, administer age appropriate CPR and life support measures.

- **ADMINISTER ADRENALINE** – dosage: 1:1000 (adrenaline 1:1000 = 0.01 mg per 0.01 mL).

  Adrenaline dosage for 1:1000 formulation is 0.01 mL/kg up to a maximum of 0.5 mL.

  If weight unknown use the following guidelines:

  - Infants less than 1 year: 0.05–0.10 mL
  - Infants less than 2 years: 0.10 mL
  - Children 2–4 years: 0.20 mL
  - Children 5–10 years: 0.30 mL
  - Adolescents over 11 years: 0.30–0.50 mL
  - Adults: 0.50 mL

  Route: deep IM. Where possible administer in a non-injected limb.

  You can expect to see some response to the adrenaline within 1–2 minutes. If necessary, adrenaline can be repeated at 5–15 minute intervals, to a maximum of three doses, while waiting for assistance. Use alternate sites/limbs for additional doses.

- **ADMINISTER OXYGEN** at high flow rates where there is respiratory distress, stridor or wheeze.

- **IF HYPOTENSIVE, ELEVATE LEGS.**

- **IF STRIDOR IS PRESENT, ELEVATE HEAD AND CHEST.**

- **RECORD VITAL SIGNS** every 5–10 minutes and document fully all symptoms and treatment given.

- **ADMIT TO HOSPITAL** – all cases of anaphylaxis should be admitted to hospital for observation. Rebound anaphylaxis can occur 12–24 hours after the initial episode.

  Note: Only medical practitioners should administer IV adrenaline, and then only 1:10,000 dilution at a dose of 0.01 mg/kg and volume of 1:10,000 of 0.1 mL/kg.
Adrenaline

Intramuscular injection of 1:1000 adrenaline is the preferred treatment of anaphylaxis and it should be universally available when vaccinating. A tuberculin syringe should be used to improve the accuracy of measurement when drawing up small doses.

Adrenaline is the mainstay of the treatment of anaphylaxis. It stimulates the heart and reverses vasoconstriction and bronchospasm, and reduces oedema and urticaria, thus countering the anaphylaxis. However, adrenaline is a very potent agent, and if used in inappropriate doses can cause dysrrhythmias, severe hypertension, left ventricular failure and tissue necrosis. Intravenous adrenaline should be administered by a medical practitioner with extreme caution, in small boluses, and under careful monitoring, and it is not appropriate as the first line of treatment of anaphylaxis (see the note in Table 2.8).

Ongoing management in hospital or by a medical practitioner

All patients who have experienced anaphylaxis should be admitted to hospital. The attending medical practitioner should accompany patients who are in an unstable or deteriorating condition, so that treatment can be continued during transfer.

Hydrocortisone and antihistamine may be used as adjunctive medication. Nebulised salbutamol is helpful for bronchospasm. Additional drugs that may be administered include:

- phenergan: 0.5 mg/kg orally or 0.25 mg intravenous, to inhibit delayed histamine reactions
- adrenaline: nebulised adrenaline for laryngeal oedema
- bronchodilators: salbutamol 5 mg nebulised, to help reverse bronchospasm
- corticosteroids: prednisone 2 mg/kg (up to 40 mg) orally, or hydrocortisone 4 mg/kg IV, to help resolve tissue swelling (for young children and infants prednisolone syrup 5 mg/mL may be more appropriate).

Observation for a period of up to 24 hours after stabilisation of the patient’s condition is recommended due to the risk of late deterioration from delayed and biphasic reactions.

Report the reaction to CARM, PO Box 913, Dunedin, using the prepaid postcard HP3442, or via online reporting at http://carm.otago.ac.nz.

2.5 Vaccine storage, transportation and disposal

Cold chain

The ‘cold chain’ is the system of transporting and storing vaccine at +2°C to +8°C from the place of manufacture to the point of vaccine administration (the patient).
The success of an immunisation programme depends on maintaining vaccine potency. To achieve this, the recommended temperature +2°C to +8°C must be maintained during storage and distribution to avoid cumulative irreversible loss of potency from thermal insult (heat or freezing). Immunisation service providers should maintain their vaccine refrigerators as close as possible to 5°C, which gives a safety margin of plus or minus 3°C.

The distribution of the publicly funded vaccines throughout New Zealand is through a direct delivery system, with only one distributor for each region in order to minimise the number of links in the cold chain. (Note: there may be more than one distributor depending on the specific immunisation programme, eg, Meningococcal B Immunisation or Influenza Programmes.) This system reduces the potential for vaccine damage to occur.

Vaccines are distributed by courier, in either a cardboard box or chilly bin, with delivery occurring within the predetermined ‘window’ period. On receipt of vaccines the vaccinator is required to sign for the vaccines from the courier with the date and the time.

**Vaccine storage**

Part 5 of the Medicines Regulations 1984 sets out legal requirements in relation to the packaging, storage and handling of medicines in general. Section 47 of the Medicines Act 1981 sets out some specific requirements relating to the storage and delivery of prescription and restricted medicines, including vaccines:

(1) No person who is in possession or charge of any prescription medicine or restricted medicine shall put it:

   a) In any cupboard, box, shelf, or other place of storage in which articles of food or drink are stored or kept for ready use

In this case, food is not to be stored in the vaccine refrigerator (see Appendix 7 for details on section 47).

All persons using vaccines have a responsibility to report and correct any problems relating to cold chain storage.

Vaccine Storage and Distribution National Standards (2nd edition), May 2002, and the Annual Cold Chain Management Guide are available from your local immunisation co-ordinator/facilitator or IMAC.

**Cold chain accreditation**

Cold chain accreditation (CCA) is a process that allows primary care practices to demonstrate their management of vaccine stocks in the cold chain, as required by existing national cold chain standards. The demonstration is through a self audit that is reviewed by the local immunisation co-ordinator/facilitator. The CCA process aims to minimise the levels of vaccine wastage and ensures the provision of effective vaccines for the National Immunisation Schedule vaccines.
The CCA is based on the following five assessment sections:
1. practice policies
2. vaccine reference information
3. vaccine stock management
4. temperature monitoring and performance
5. refrigerator details.

Each of these sections has been divided into two categories:
• essential requirements – considered essential for effective cold chain management
• desirable requirements – an important component of cold chain management, which may not be attained at the first practice review.

Achievement of both the essential and desirable requirements are considered the ‘Gold Standard’.

The CCA review measures performance against the criteria as follows:
• met – fully meets the essential requirement in this area, as per national standards
• partially met – meets critical aspects of the requirement, but some aspects need improvement before CCA is achieved
• not met – fails to meet the requirement in a way that places vaccines at risk.

For a practice to achieve CCA they must meet all the essential requirements for their cold chain management. CCA is valid for up to three years.

In the future it is hoped the CCA process will align with the Royal New Zealand College of General Practice accreditation programme, Aiming for Excellence.

CCA practice assessment

1) Practice policies

Each practice should have an individualised and documented cold chain management policy. This should include details of the designated staff member, vaccine requirement estimations, vaccine ordering process, refrigerator operation, maintenance and management processes, and an emergency procedure for dealing with equipment failure.

One person should assume responsibility for the cold chain management policy. It is essential, however, that a second person is familiar with the workplace cold chain management, in the event of sickness, annual leave, staff movement, etc.
The cold chain management policy should be dated and signed by the relevant staff, and reviewed on an annual basis.

2) **Vaccine reference information**

All immunisation providers should have easy access to copies of the current New Zealand *Immunisation Handbook*.

In the event of any sudden variations in refrigerator temperature, or recordings outside the recommended +2˚C to +8˚C range, or equipment failure, the local immunisation co-ordinator/facilitator, medical officer of health, Public Health Service or IMAC should be contacted for advice and support.

The following table provides guidelines for use of the National Immunisation Schedule vaccines following exposure to temperatures outside the recommended range.

**Table 2.9: Recommendations for the use of vaccines exposed to temperatures outside +2˚C to +8˚C**

<table>
<thead>
<tr>
<th>Vaccine</th>
<th>Exposure to temperatures below 0˚C</th>
<th>Exposure to temperatures between 8˚C and 25˚C</th>
</tr>
</thead>
<tbody>
<tr>
<td>MMR</td>
<td>Use</td>
<td>&lt; 24 hours: Use</td>
</tr>
<tr>
<td></td>
<td></td>
<td>24–72 hours: Use within 3 months</td>
</tr>
<tr>
<td></td>
<td></td>
<td>≥ 3 days: Do not use</td>
</tr>
<tr>
<td>BCG</td>
<td>Use</td>
<td>&lt; 5 days: Use</td>
</tr>
<tr>
<td></td>
<td></td>
<td>≥ 5 days: Do not use</td>
</tr>
<tr>
<td>DTaP-IPV, dTap-IPV</td>
<td>Do not use</td>
<td>&lt; 5 days: Use</td>
</tr>
<tr>
<td></td>
<td></td>
<td>≥ 5 days: Do not use</td>
</tr>
<tr>
<td>Td, Hib-Hepatitis B, Hib, IPV, influenza and PPD</td>
<td>Do not use</td>
<td>&lt; 5 days: Use</td>
</tr>
<tr>
<td></td>
<td></td>
<td>≥ 5 days: Do not use</td>
</tr>
<tr>
<td>MeNZB™</td>
<td>Do not use</td>
<td>&lt; 5 days: Use</td>
</tr>
<tr>
<td></td>
<td></td>
<td>≥ 5 days: Do not use</td>
</tr>
<tr>
<td>PCV7, 23PPV, MenA,C,Y,W135</td>
<td>Do not use</td>
<td>Information not available</td>
</tr>
</tbody>
</table>
Consult with the local immunisation co-ordinator/facilitator, medical officer of health or Public Health Service before discarding any vaccines. If the vaccines are to be destroyed contact the distributor and arrange for their return. Discarded vaccines should be returned to the supplier, clearly labelled:

‘Vaccines for destruction Return to Supplier’, supplier details, address and phone number.

The vaccines for destruction should be packed in a cardboard box with all needles removed and the reason for destruction included. Vaccines for destruction must be correctly disposed of as required under the Resource Management Act 1991. (See also the section on the ‘National Cold Chain Audit’ below.)

For advice on the return of non-Immunisation Schedule and travel vaccines, contact the supplier directly (eg, ProPharma).

3) Vaccine stock management
All practices should have a system to record vaccine stock levels (ie, a stock management plan). The plan may include the ordering of vaccines, stock rotation, and the use of a log/register to document the date, name and batch numbers of vaccines arriving from the supplier, vaccine expiry dates, and date of transfer to the refrigerator.

On receipt of vaccines, the vaccinator or workplace should check the cardboard box or chilly bin contents against the order form. Check that the vaccine delivery is within the stated delivery window. Also check for monitor cards and record their status (see ‘National Cold Chain Audit’ below for more detail on monitor cards). If the vaccinator has reason to believe the vaccines have not been kept at the required temperature (eg, the vaccines are warm to touch, or the time is over the delivery window period (see Table 2.9)), the distributor and local immunisation co-ordinator/facilitator should be notified. If the vaccines need to be destroyed contact the supplier and arrange for their return. The order should be clearly labelled ‘vaccines for destruction’ so the vaccines do not re-enter the system. Once satisfied with the vaccine order, the vaccinator should sign for the vaccines.

4) Temperature monitoring and performance
Each vaccine specific refrigerator must have a refrigerator temperature recording device that measures the current temperature as well as the minimum and maximum temperatures reached at any given time, eg, minimum maximum thermometer or data logger. This reading should be read and recorded daily, preferably at the same time each day. These recordings should be reviewed monthly to identify cyclical fluctuations and climatic changes. For further information on refrigerator temperature recording devices contact the local immunisation co-ordinator/facilitator.

Temperature records need to be retained for a minimum of 10 years.
Once CCA has been achieved, six monthly/annually electronic monitoring will be undertaken by the local immunisation co-ordinator/facilitator.

5) Refrigerator details

*Pharmaceutical refrigerators*

The refrigerator should be of sufficient size to accommodate vaccine storage requirements without exceeding the manufacturer’s recommendations for maximum storage capacity.

As a result of the implementation of the CCA, most primary care practices now have dedicated vaccine pharmaceutical refrigerators. These refrigerators are more reliable for vaccine storage than domestic refrigerators as they are programmed to maintain an internal temperature between +2°C to +8°C. They have an external temperature reading with continuous minimum/maximum recording display, and most practices have availed themselves of the accompanying data logger technology.

There are several brands available in New Zealand. Contact the local immunisation co-ordinator/facilitator or manufacturing distributors for further advice.

*Domestic refrigerators*

The refrigerator should be of sufficient size to accommodate vaccine storage requirements without exceeding 50 percent of the refrigerator’s storage capacity (see Figure 2.8). Where a pharmaceutical refrigerator is not available, frost free or manual defrost model refrigerators are recommended for vaccine storage. Frost free refrigerators do not have heating cycles, but remain frost free with low levels of frequent warming temperatures.

Cyclic type domestic refrigerators *are not* recommended because they produce wide fluctuations in the internal temperature, with regular internal heating.

Multi-flow type (known as fan forced or sensor flow) domestic refrigerators *are not* recommended because the multi-flow cooling system directs air from the freezer compartment into the main refrigerator compartment. This type of refrigerator always has two thermostat controls (one controlling the freezer temperature and the other the volume of freezing air that enters the main refrigerator compartment). The air in the middle section of the main refrigerator compartment routinely falls below 0°C and may even fall as low as –7°C.

*Refrigerator placement*

The refrigerator should have an independent power point, and the plug should be taped over or permanently wired into the outlet to overcome the risk of deliberate or accidental disconnection. The refrigerator must be in a reasonably sized, well ventilated room and not in direct sunlight or against a heat source, because the efficiency of refrigeration equipment declines with high ambient temperatures.
There should be sufficient ventilation around the condenser of the refrigerator (eg, the Rollex recommendations are at least 50 cm from the sides and 75 cm from the back) to allow air to circulate, as this will assist in reducing cyclical fluctuations.

It is advisable to contact the manufacturer of a vaccine specific refrigerator before moving the refrigerator.

Refrigeration maintenance
The following actions should be taken to ensure the efficient refrigeration of vaccines.

- Temperature charts/logs should be reviewed monthly to determine if there are any cyclical fluctuations.

- The door seal should be checked six monthly using the paper check and self closing methods. To perform the paper check, use an ordinary piece of paper (approximately 7 cm by 4 cm wide). Take the paper and, starting at the top of the refrigerator (hinge side), open the door wide enough to place the paper between the door seal rubber and refrigerator surface, then shut the door and try to remove the paper. If the paper cannot be removed easily the door seal is intact. Repeat this procedure at 7–10 cm intervals around the entire door seal. Leave the door open to perform the self closing door check. The door should close automatically. To ensure this, alter the height adjusters underneath the refrigerator so that the door hinge side of the refrigerator is set slightly higher than the non-hinge side.

- Monitor the effectiveness of the refrigerator at least six monthly/annually using an electronic monitoring device such as a Temprecord or similar. (Contact the local immunisation co-ordinator/facilitator for more information.)

- Although pharmaceutical refrigerators do not require defrosting, check for any visible ice on the back plate inside the refrigerator on a fortnightly basis.

- Defrost the domestic refrigerator regularly, if it has a freezer compartment/rear ice plate, once the ice layer is 5–10 mm thick. While doing so store the vaccines in another monitored refrigerator or chilly bin.

- Service the refrigerator annually, according to the manufacturer’s instructions, or if the temperature fluctuates.

- All interior and exterior surfaces of the refrigerator should be cleaned at least every six months, with a solution of 0.03 percent hypochlorite solution (1 part domestic bleach to 99 parts water).

- The top of the refrigerator should remain clear.

- During a power failure of up to four hours, the refrigerator door should be left closed. If the power fails for more than four hours, vaccines should be transferred to an appropriately sized chilly bin with the correct number and size of icepacks to ensure the vaccines will remain at +2°C to +8°C. A min/max thermometer will
assist with temperature monitoring. If the power is not restored, the vaccines will need to be transferred to an alternative refrigerator. (See the information on vaccine transportation below.)

- In domestic refrigerators, vaccines should not be stored near the ice plate, in the drawers or door, or on the top shelf of the refrigerator. When space is limited (eg, during the influenza vaccine season), the least freeze sensitive vaccines may be stored near the ice plate (eg, MMR). The diluent for MMR can be stored at room temperature.

**Key points for vaccine storage**

- All National Immunisation Schedule vaccines should be stored between +2°C and +8°C.
- The refrigerator temperature needs to be monitored and documented at the same time each working day (ideally by the same person) and entered in the temperature log or annual cold chain management guide.
- The refrigerator temperature recording device must measure the current temperature as well as the minimum and maximum temperature (eg, minimum maximum thermometer or data logger).
- Vaccines should be left in their original packaging, as this acts as insulation.
- Vaccines should be refrigerated immediately on arrival from the distributor.
- Air should be able to circulate in the refrigerator (ie, do not store vaccines against the walls, to the top of each shelf, or in the bottom or door of the refrigerator). There should be 25–30 mm between vaccines at the back of the refrigerator and the shelf above.
- Stock with the shortest expiry date should be used first. Vaccines should be stored with the batch number and expiry date label showing. Record this in the vaccine stock log/register.
- To avoid overcrowding and to ensure stock rotation, a maximum of six weeks of stock should be held at any given time.
- Opening of the refrigerator door should be minimised in order to reduce temperature fluctuations.
Figure 2.8: How to stock a domestic refrigerator being used as a vaccine refrigerator

Keep lower shelf of freezer filled with ice packs or plastic bottles of plain water.

Upper shelf: MMR, BCG (gazetted vaccinators only).

Middle shelves: DTap, DTaP-IPV, dTap-IPV, dTap, IPV, Hib-Hep B, Hep B, Td, Hib, influenza, meningococcal and pneumococcal vaccines, ie all freeze sensitive vaccines.

Lower shelf: Emergency drugs, vaccine diluents. (Diluents may be stored at room temperature.)

Bottles of salt water.

Keep vaccines in trays on the safe upper shelves.

Fill the empty space on the door and in the lower drawers with bottles/bladders filled with salt water and keep the temperature steady.

National Cold Chain Audit

The Ministry of Health has commissioned an ongoing National Cold Chain Audit to monitor National Immunisation Schedule vaccines. When the vaccine arrives at the national vaccine store (Institute of Environmental Science and Research, ESR), monitor cards are packed with randomly selected packs of schedule vaccines. See Figure 2.9. These monitor cards monitor storage and transport conditions and remain with the vaccine until it has been administered. Recordings are documented at vaccine arrival and departure points.

The monitor cards have two temperature indicators attached to a record card: the ColdMark™ indicates if the temperature has been below 0°C (freezing) and the WarmMark™ tracks cumulative temperatures over 10°C. If at any time the temperature has been outside the accepted range, contact the immunisation co-ordinator/facilitator for advice. Following are guidelines on how to deal with a monitor card included with a vaccine pack as part of the cold chain audit.
### Temperature-Sensitive Monitor Record Card

<table>
<thead>
<tr>
<th>Date in</th>
<th>Warm Mark Index</th>
<th>Cold Mark Status</th>
<th>Location</th>
<th>Date out</th>
<th>Warm Mark Index</th>
<th>Cold Mark Status</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

#### WarmMark™ Monitor

- If no colour or partial colour is visible, record index as 0.

#### ColdMark™ Monitor

- If the bulb is clear in colour, record status as C.
- If the bulb is purple in colour, record the status as V (see overlay).

Index greater than 2 (see overlay): DTaP-IPV 30 Nov 2005

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Keep the monitor with the vaccine that it arrives with.

When the monitor arrives, complete the top part of the card:
- Fill in the ‘Date in’
- Fill in the ‘Warm Mark Index’ (0, 1, 2, 3 and/or 4). If the index is greater than 2 consult your local coordinator.
- Fill in the ‘Cold Mark Status’ (C or V). If V do not use. Consult your local coordinator.
- Fill in the ‘Location’ with your organization’s name and town.

When the monitor leaves your store or the last vaccine in the pack is used, complete the top part of the card:
- Fill in the ‘Date out’
- Fill in the ‘Warm Mark Index’ (0, 1, 2, 3 and/or 4). If the index is greater than 2 consult your local coordinator.
- Fill in the ‘Cold Mark Status’ (C or V). If V do not use. Consult your local coordinator.

Return the completed card to:
- National Vaccine Store
- ESR
- PO Box 50-348
- PORTUA

Please direct any enquiries to:
- Pamela Raynel
- National Vaccine Store, ESR
- phone: (04) 914 0727
- fax: (04) 914 0770
- email: pamela.raynel@esr.cri.nz

Extra envelopes used for the return of monitors are available from ESR.

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**Notes:**

1. Yellow label on vaccine packs indicates monitors are included and must be read.
2. A record card that regional and local providers fill in to show when vaccines are received and despatched. The status of the monitors is also recorded.
3. An indicator that is a heat-sensitive strip, WarmMark™ with four windows, marked 1, 2, 3, and 4.
4. An indicator that is freeze-sensitive at 0°C indicator, ColdMark™, a colour change occurs from clear to violet.
5. Instructions on how to read and record the temperature indicators when vaccine is received.
6. Instructions on how to read and record the temperature indicators when vaccine is despatched or the last dose is used.
7. Instructions on where to send the completed monitor card.
1. A yellow sticker will be on the vaccine pack if there is a monitor card (see Figure 2.9) inside the pack.

2. Record the date of arrival, clinic name, town/city and the ColdMark™ and WarmMark™ in the space provided on the card.
   - The ColdMark™ changes if the temperature drops below 0°C: enter C for a clear bulb, or V for a violet bulb.
   - The WarmMark™ tracks cumulative temperatures over 10°C: enter 0 if there are no completely red windows, or 1, 2, 3 or 4 to indicate which windows are completely red.

3. Keep the monitor card with the vaccines it arrived with – secure the card to the pack and ensure it remains with the vaccines in the refrigerator.

4. If the temperature has gone outside the acceptable range (ie, the ColdMark™ bulb has turned violet or the WarmMark™ window 3 has started to go red), then do not use the vaccines. Contact the local immunisation co-ordinator/facilitator for advice.

5. Every time a vaccine is used that arrived with a monitor card, check the ColdMark™ and WarmMark™ for any changes in colour that have occurred while it is in the refrigerator.

6. When the last dose of the vaccine is being prepared for administration, record the date and note the ColdMark™ and WarmMark™ status.

7. Return the completed monitor card to ESR in the envelope provided.

Vaccine transportation

The chilly bin and cardboard box are reliable and tested methods for transporting vaccines for vaccinating off site (eg, school immunisation programme, or storing vaccines while defrosting the refrigerator or in the event of a power or equipment failure). When transporting vaccines, the temperature needs to be maintained between +2°C to +8°C at all times. A temperature monitoring device should be placed with the vaccines during this time.

Ice packs need to be frozen at least two days before being used for transporting vaccines. When placing ice packs in the freezer, set them on their edge and allow space between the ice packs, to ensure even freezing.
Key points for vaccine transportation

- Use a solid wall chilly bin with a clip on lid.
- Use a chilly bin of a size suitable for the amount of vaccine to be transported.
- Use the appropriate number and sizes of ice packs for the chilly bin size to ensure the vaccines will remain at +2°C to +8°C throughout their journey.
- Monitor the chilly bin with either a min/max thermometer or data logger.
- Before placing the ice packs in the chilly bin, warm them until frost no longer forms on their surface.
- Place shredded paper in the bottom of the chilly bin, then place the vaccines so that the most heat sensitive are nearest the ice packs and the most freeze sensitive are furthest away.
- Separate the ice packs from the vaccine by using shredded paper or a sheet of 10 mm thick polystyrene foam. This will prevent contact with the ice packs and thus ensure they will not freeze the vaccines.
- Tape the chilly bin lid in place.

Following these recommendations will keep the temperature within +2°C to +8°C for up to five hours and allows for the chilly bin to be opened briefly, up to four times.

In a school based immunisation programme, when vaccines are likely to be stored in chilly bins for longer periods and more frequent opening will occur, extra care must be taken with cold chain maintenance. An extra chilly bin of frozen slicker pads or Environfreeze should be carried to top up the vaccine carrying chilly bin to keep the temperature between +2°C to +8°C. Use of a data logger rather than a min/max thermometer is advisable.
References


3 Hepatitis B

3.1 Introduction
Hippocrates described episodes of jaundice, likely to have been viral hepatitis caused by various viruses. In 1883 hepatitis transmitted through blood or blood products was first documented in Germany during a smallpox immunisation campaign. McCallum proposed the term hepatitis B for ‘serum’ hepatitis in 1947. The Australia antigen, now called the hepatitis B surface antigen (HBsAg), was first identified in 1967 and is the basis of the vaccine.

Hepatitis B virus (HBV) has a high impact on morbidity and mortality throughout the world. In New Zealand, HBV causes more deaths than any other vaccine preventable disease apart from influenza. The long latency period of the virus and the importance of lifestyle factors (in particular, alcohol intake) mean that the impact of HBV is largely invisible. HBV is believed to be second only to tobacco as a cause of human cancers. Superinfection of hepatitis B infected patients with hepatitis D (delta) virus is common in some Pacific peoples and injecting drug users, and can result in exacerbation of liver disease.

When New Zealand introduced universal infant hepatitis B immunisation it was one of the first countries to do so. The World Health Organization (WHO) recommends hepatitis B immunisation, and at least 90 countries have included the vaccine on their immunisation programmes.

In 2005, the countries of the Western Pacific Region of WHO agreed to the target that by 2012 the rate of carriage of HBV in five-year-old children will be reduced to 2 percent. The long-term aim is to reduce carriage of hepatitis B to below 1 percent at the age of five years. New Zealand has had a universal infant immunisation programme for hepatitis B vaccine since 1988 and therefore should have already reached this target. This may be confirmed by the result of the serosurvey being carried out in New Zealand in 2005/06.

3.2 The illness
HBV is a partially double stranded DNA virus, composed of a nucleocapsid core (HBcAg) surrounded by an outer lipoprotein coat that contains the surface antigen (HBsAg). A third antigen, HBeAg, is soluble and is released from liver cells with active HBV infection. The presence of HBeAg in the blood indicates a high degree of infectivity (ie, an actively replicating virus). The antigens are identified as indicated above, while their respective antibodies are designated anti-HBc, anti-HBs and anti-HBe.

HBV is usually transmitted by infected blood or exchange of body fluids during sexual intercourse/activity. Although HBV can be found in all body fluids, the blood has most and saliva least. Bond et al\(^1\) have shown that desiccated blood was still
infective after one week (and the antigen remained detectable for several years). Before the immunisation programme in New Zealand, HBV transmission occurred commonly in school aged children. The exact mode of transmission is not clear but could be related to contact with impetigo, or surfaces such as mats or playgrounds that contain crusts from sores. Vertical transmission from mother to infant also occurs, particularly if the mother is HBeAg positive.

The incubation period varies between six weeks and six months (average two to three months). HBsAg may appear within two weeks, but in rare instances may not be apparent until six to nine months. The variation is related to the dose of virus in the inoculum, the mode of transmission and host factors. Blood from experimentally inoculated volunteers has been shown to be infectious many weeks before the onset of the first symptoms, and it remains infective through the acute clinical course of the disease and during the chronic carrier state.

The virus infects liver cells, multiplying there and releasing large amounts of HBsAg, which may be detected in blood during active infection. The virus is not cytopathic itself; rather, the host immune response leads to death of the infected liver cell. There is a spectrum of clinical illness, which includes asymptomatic infection in approximately 60 percent of individuals; sub-acute illness with jaundice, anorexia, nausea and malaise; and fulminant hepatitis, which may be fatal, especially in those over 40 years of age. Acute hepatitis occurs rarely in infants, in approximately 6 percent of infected children and in approximately 33 percent of infected adults. Arthralgias, macular rashes and polyarteritis nodosa may occur early in the course of the illness. Papular acrodermatitis has been noted in children. Because jaundice is not always present with these conditions, the true aetiology of symptoms may not be obvious. Following the acute illness there is a prolonged convalescent phase, often lasting many weeks. Rarely (2 percent) acute hepatitis B may be fatal.

A chronic carrier state (see section 3.3) may develop if infection does not stimulate an effective immune response, and the virus survives in the body and continues to replicate, often for many years. This chronic carrier state is more frequent after infection during infancy and early childhood. The risk of carriage following infection drops from about 90 percent in the first six months of life,2 to 25–50 percent by five years of age and to 6–10 percent of acutely infected older children and adults. It is unusual for adults to become chronic carriers unless they are immune suppressed. The chronically infected individual often has no history of an acute illness.

Viral antigens remain present for many years in carriers, although 1–6 percent of carriers per year will clear the virus spontaneously. The presence of HBeAg in the blood of a chronic carrier indicates a high degree of infectivity, while the disappearance of HBsAg and the appearance of anti-HBs generally indicate the individual is immune and no longer infectious.
Screening for carriers

Once detected, carriers can be offered counselling, screening and long term follow-up to detect chronic liver disease and the early stages of hepatocellular carcinoma. Vaccination is offered to susceptible household and sexual contacts of carriers to limit the spread of disease. Treatment with antiviral drugs such as interferon and/or lamivudine are options currently available, although neither is ideal.

Although there remains uncertainty about the population benefit of screening, it is likely that in some individuals the serious outcomes of carriage will be prevented by early detection. In 1999 a screening programme for Māori, Pacific and Asian peoples over 15 years of age was started in the North Island. The programme also enrolled people of other ethnic groups and included follow-up of individuals under the age of 15 years found to carry the HBV. Up to 30 June 2005 there were more than 12,000 clients with chronic hepatitis B actively enrolled on the surveillance programme (with the Hepatitis Foundation as the national provider – see below for contact details) for long term follow-up. If they are identified as carriers, participants are assessed and followed-up by the programme to detect and manage liver disease.

All pregnant women should be screened for hepatitis B carriage antenatally. Administration at birth of hepatitis B immunoglobulin (HBIG) and hepatitis B vaccine prevents mother to infant transmission of hepatitis B virus in 92–95 percent of infants (see section 3.4).

A surveillance and advice service is available from:

The Hepatitis Foundation
PO Box 647
Whakatane
Phone 07 307 1259 or 0800 332 010.

3.3 Epidemiology

Chronic carriers, defined as individuals having HBsAg detectable in their blood for more than six months, are the most common source of hepatitis B infection. The world can be divided into areas of high (8 percent and over), middle (2–7 percent) and low (less than 2 percent) levels of carriage (or endemicity), with 45 percent, 43 percent and 12 percent of the world’s population living in those areas, respectively. In areas of high endemicity, the lifetime risk of infection with hepatitis B virus is over 60 percent, and most infections are in the first years of life. The Pacific countries and most of Asia (except Japan and India) are high endemicity countries. In areas of low endemicity, the lifetime risk of infection is less than 20 percent, and most infections are in adult at risk populations (see Figure 3.1).
New Zealand is defined overall as a country with a low endemic level of hepatitis B carriage, but there are areas with medium and high endemic levels (see New Zealand epidemiology below).

**Figure 3.1: WHO geographic pattern of Hepatitis B prevalence, 2001**

![WHO geographic pattern of Hepatitis B prevalence, 2001](www.who.int/vaccines-documents/DocsPDF01/www613.pdf)

Source: www.who.int/vaccines-documents/DocsPDF01/www613.pdf

The highest risk of transmission is during the perinatal period. If no prophylaxis is given to the infant, the baby of an HBeAg positive carrier mother has a 70–90 percent risk of infection, while the baby of an HBeAg negative, HBsAg positive carrier mother has a 5–20 percent risk of infection.

**New Zealand epidemiology**

The 1985 National Serum Survey found evidence of past infection in 15 percent of New Zealand children, with generally higher rates in the north and east of the North Island. Milne, Moyes and others showed that in the eastern Bay of Plenty almost half of the population (60 percent of Māori and 30 percent of Europeans) were infected by 15 years of age. Prior to vaccination, the lifetime risk of acute icteric hepatitis in this region was 10 percent and the risk of developing the chronic carrier state 9 percent.
According to estimates from New Zealand data, chronic carriers have a 5 percent risk of developing chronic active hepatitis or cirrhosis, with perhaps a 2 percent risk of death. The risks are doubled if hepatitis D (delta) virus infection is also present. Hepatocellular carcinoma is estimated to occur in approximately 10 percent of male and 5 percent of female HBsAg carriers. Hepatitis B notifications have declined from about 600 per year in the mid-1980s, when immunisation was introduced, to 61 cases notified in 2003 and 39 cases in 2004 (1.6 per 100,000 population) (see Figure 3.2). The change in the number of notifications of hepatitis B may also be because earlier notifications of hepatitis B included chronic carrier states, whereas only acute cases are under surveillance now. In 2005 there were no cases notified who were less than 15 years of age, and only one case was in the 15–19 years age group.

History of the New Zealand Immunisation Schedule

Hepatitis B vaccine was added to the Immunisation Schedule gradually, starting in September 1985, when it was offered to newborn babies of HBeAg positive mothers. Three 10 µg doses of plasma derived vaccine were given, as recommended by the manufacturer. In March 1987 the immunisation programme was extended to newborns of mothers with HBsAg and children born in certain high risk districts (Northland, Takapuna, Auckland, South Auckland, Rotorua, Napier and Gisborne).

The demonstration that low dose vaccination was immunogenic enabled the extension of hepatitis B immunisation to everyone born after 29 February 1988. From this date four doses of 2 µg of plasma derived vaccine were given at birth, six
weeks, three months and 15 months of age. There was a catch-up campaign for all preschoolers. The households and sexual contacts of HBsAg positive women identified during antenatal screening were also entitled to free immunisation.

The plasma derived vaccine (H-B-Vax®) was replaced by a genetically engineered recombinant vaccine (ENGERIX-B) from 1 December 1989. This was given at the manufacturer’s recommended dose at six weeks, three months and 15 months of age. Babies of carrier mothers also received a dose of vaccine plus HBIG at birth. From February 1990 free hepatitis B immunisation was extended to all children under 16 years of age.

In February 1996 the third dose of hepatitis B vaccine was brought forward from 15 to five months of age to give early protection to infants and to complete the hepatitis B vaccine schedule in the first year of life, when compliance is high. This schedule continues in 2006 with hepatitis B vaccine at age six weeks, three months and five months, plus hepatitis B vaccine and hepatitis B immunoglobulin at birth for a baby whose mother is a carrier of the hepatitis B virus.

3.4 Vaccines

All the hepatitis B vaccines currently available are preparations of HBsAg. The vaccines in New Zealand are the yeast and Escherichia coli derived vaccines HBvaxPRO® (MSD) and ENGERIX-B (GSK), which have been developed using recombinant DNA technology. Hepatitis B (HBvaxPRO®) vaccine and the combination Haemophilus influenzae type b and hepatitis B vaccine (Hib-Hepatitis B, COMVAX®, MSD) are publicly funded for the National Immunisation Schedule.

At the end of 2005, in addition to COMVAX®, the following hepatitis B containing combination vaccines are licensed for distribution in New Zealand:

- HAV-Hep B (hepatitis A and hepatitis B vaccine, TWINRIX and TWINRIX JUNIOR, GSK) (see also section 14.4)
- DTwP-Hib-Hep B (TRITANRIX-HB+Hib, GSK)
- DTaP-Hep B (INFANRIX™-HepB, GSK)
- DTaP-IPV-Hep B (INFANRIX®-penta, GSK)
- DTaP-IPV-Hep B/Hib (INFANRIX®-hexa, GSK).

(Key: D: diphtheria, T: tetanus, wP: whole cell pertussis, aP: acellular pertussis, Hep B: hepatitis B, Hib: Haemophilus influenzae type b, IPV: inactivated polio vaccine)

Efficacy

Clinical trials in high risk groups have shown a vaccine efficacy of 85 to 95 percent, and virtually complete protection in those who develop antibody levels of ≥ 10 mIU/mL (the protective level). At least 95 percent of infants, children and adolescents develop protection after three doses of vaccine.
The response rate drops with age: from 90 percent for adults under 40 years of age, to about 70 percent for those 60 years of age. Smoking, obesity, HIV (human immunodeficiency virus) infection and chronic disease all reduce the response rate, but age is the primary factor affecting response. Some non-responders to the initial vaccination course will produce adequate antibody levels after a further booster dose of vaccine, or a second course. However, persistent non-responders occur, especially those with impaired immune systems or undergoing haemodialysis.

For babies of HBeAg positive mothers, controlled trials have shown that vaccine at birth provides 65–95 percent protection from infection, and correct administration of HBIG with vaccination provides 80–97 percent protection against infection. Although the height of the antibody titre determines the length of time the antibody can be detected in the blood, it does not seem important for long term protection. It is probable that once a seroprotective level is reached (a titre of ≥ 10 mIU/mL), booster doses of vaccine are unnecessary. Children who are given booster doses up to 12 years after the primary series show strong anamnestic responses, and follow-up studies of vaccinees have shown evidence of wild virus infection (anti-HBc) without any clinical illness and without HBsAg. This is despite the fact that a large proportion will lose detectable antibodies (30 to 50 percent after seven years).

Evidence is accumulating that boosters of hepatitis B vaccine are unnecessary provided that the seroprotective level is reached (a titre of ≥ 10 mIU/mL). Follow-up of vaccinees in Taiwan who were immunised at birth has shown that protection against hepatitis B infection persisted for at least 15 years, and the programme reduced both perinatal transmission and subsequent horizontal transmission. A follow-up study was undertaken in Alaska on 841 Alaskan natives, 53 percent of a cohort of 1578 individuals, who had been vaccinated with three doses of hepatitis B vaccine starting at age six months or older, including adults. The study found that overall 84 percent had protective levels of antibody after 15 years and the vaccine protected against infection. Both the participants who received hepatitis B vaccine as adults and those who received vaccine in infancy remained protected. Antibody levels decreased most in individuals who received vaccine before the age of four years. Out of the original cohort there were 16 asymptomatic infections which were more frequent in those who had not responded to the original course of vaccine. Only one individual was HBV DNA positive over at least a three year follow-up.

In all populations where it has been measured, immunisation has led to a dramatic drop in HBV carriage. For example, in Alaska carriage dropped from 16 percent to zero as a result of 96 percent immunisation coverage. In Taiwan the incidence of hepatocellular carcinoma also decreased in children as a result of the immunisation programme.

It is important that vaccination against hepatitis B does not encourage relaxation of good infection control procedures. Hepatitis B immunisation does not protect against HIV, hepatitis C or other blood borne viruses.
Dosage
Follow the manufacturer’s recommended dosage for the vaccines in current use (hepatitis B vaccine, HBvaxPRO®, or Hib-Hepatitis B, COMVAX®). It is important that the injection is given intramuscularly, not into dermal fat. In special circumstances hepatitis B vaccine may be given intradermally to increase the immune response (see section 3.5).

The hepatitis B vaccine may be given at the same time as all other vaccines on the schedule, including measles, mumps and rubella (MMR) vaccine. If a course of vaccine is interrupted, it may be resumed without repeating prior doses. (See section 2.3 for needle sites and sizes.)

3.5 Recommended immunisation schedule

Babies of HBsAg positive mothers
Follow the flow chart in Figure 3.3 below.

These children are at high risk of infection (almost certain if the mother is HBeAg positive) and of becoming carriers. At birth, or as soon as possible after (preferably within 12 hours), the first dose of 5 µg of hepatitis B vaccine is given at the same time as HBIG 100 IU, using a separate syringe and different limb. A vitamin K injection may be given at the same time, in the same limb as the HBIG but not at the same site. If administration is inadvertently delayed it should be given as soon as the delay is identified, because such delays are associated with increased risk of infection.

All women should be tested for their HBsAg status during the antenatal period. If a woman’s HBsAg status is unknown at the time of delivery, the infant should be given hepatitis B vaccine at the time of delivery while waiting for the result of an urgent HBsAg test on the mother. If she is found to be HBsAg positive, the infant should be given HBIG as soon as possible (preferably within two days). The use of HBIG confers a small additional benefit in preventing carriage, and is recommended given the serious consequences of carriage. The recommended dose of HBIG for neonates is 100 IU.

Subsequent doses are given as per the National Immunisation Schedule: H. influenzae type b with hepatitis B vaccine is given at six weeks and three months of age, and the hepatitis B vaccine is given at five months.

At five months of age, as well as giving the hepatitis B vaccine (and the other schedule vaccines), it is essential to take blood to confirm the infant is protected and to identify the 2–3 percent of children who are infected (either from prenatal infection or from failure of prophylaxis), and the similar number of children who are not infected (ie, HBsAg negative) and who have failed to seroconvert. The protective level for adults and children is generally accepted as ≥ 10 mIU/mL. However,
for the babies of HBsAg positive mothers who have received HBlG at birth the immunoglobulin may interfere with a test result at five months (see Appendix 8).

The following recommendations for babies of HBsAg positive mothers at five months of age are:

- Babies with serology of $\geq 100$ mIU/mL are considered protected.
- Babies with serology of $< 100$ mIU/mL at five months have an indeterminate result, and a further two doses of vaccine at six and seven months should be given and the serology repeated to test for a protective level of $\geq 10$mIU/mL at eight months of age (see also Appendix 8).

If the blood test at five or eight months confirms the carrier state, the parents should be advised accordingly (see Figure 3.3 below).

**Figure 3.3:** Recommended screening for hepatitis B of women in early pregnancy and management of a baby of a HBsAg positive woman

All other vaccines are given as on the usual National Immunisation Schedule.

<table>
<thead>
<tr>
<th>At age</th>
<th>Give</th>
</tr>
</thead>
<tbody>
<tr>
<td>Delivery</td>
<td>Hepatitis B immunoglobulin 100 IU and hepatitis B vaccine 5 μg</td>
</tr>
<tr>
<td>6 weeks</td>
<td>Hib-Hepatitis B (COMVAX®) plus DTaP-IPV</td>
</tr>
<tr>
<td>3 months</td>
<td>Hib-Hepatitis B (COMVAX®) plus DTaP-IPV</td>
</tr>
<tr>
<td>5 months</td>
<td>Hepatitis B vaccine (HBvaxPRO®) plus DTaP-IPV and</td>
</tr>
<tr>
<td></td>
<td>take a blood test to check for antibody levels (anti-HBs) of $\geq 100$</td>
</tr>
<tr>
<td>6 months</td>
<td>Hepatitis B vaccine (HBvaxPRO®)</td>
</tr>
<tr>
<td>7 months</td>
<td>Hepatitis B vaccine (HBvaxPRO®)</td>
</tr>
<tr>
<td>8 months</td>
<td>Repeat blood test on the baby and advise the parents of result</td>
</tr>
</tbody>
</table>

The National Immunisation Register (NIR) will collect data on those infants who receive HBlG and hepatitis B vaccine at birth.
All other children
The recommended immunisation schedule is for three doses of 5 µg of hepatitis B vaccine at six weeks, three months and five months of age. At six weeks and three months of age the combination vaccine Hib-Hepatitis B is given, and at five months of age the hepatitis B vaccine is used.

Adolescents and adults
It is recommended (and publicly funded) that adolescents between 11 and 15 years of age who have not previously received a full hepatitis B vaccine course receive two doses of 10 µg hepatitis B vaccine (HBvaxPRO®), with the second dose four to six months after the first.

For adults, the vaccine manufacturers recommend three doses of 10 µg hepatitis B vaccine spaced at zero, one and six months. Shorter intervals between the second and third doses lead to lower antibody levels but adequate protection. In healthy adults a two dose schedule separated by six months, a three dose schedule given over three weeks, and various other accelerated schedules have led to seroconversion rates equivalent to those obtained when following the manufacturer’s usual recommended schedule. In general, three doses separated by four-week intervals are recommended, but the doses may be delivered at weekly intervals if more rapid protection is needed.

Other recommendations
Hepatitis B immunisation is recommended and publicly funded for the following groups:

- all children up to their 16th birthday – if the hepatitis B vaccine is not given during the first year, three doses of vaccine are recommended (follow the manufacturer’s recommendations); a two-dose regime of 10 µg of HBvaxPRO® is recommended for adolescents (from 11 to 15 years of age)
- household and sexual contacts of known carriers – these individuals may be offered hepatitis B immunisation, at monthly intervals at the recommended dosage, unless testing indicates they are already infected or immune
- participants and family members in the hepatitis B screening programme.

Hepatitis B immunisation is also recommended, but not publicly funded, for the following groups (note that employers should fund hepatitis B vaccine for employees at occupational risk):

- adults at risk because of their occupation – including dentists, medical practitioners, nurses, laboratory technologists, physiotherapists, students entering the health professions, orderlies, and other emergency, educational or health care workers who may come into contact with blood or body fluids in the course of their work
• other adults at risk, including:
  – those undergoing renal dialysis, who require a higher dose of vaccine (check manufacturer’s recommendation for this group)
  – adults with chronic liver disease, and prior to liver transplant, who should receive hepatitis B vaccine early in the course of their illness
  – adults with hepatitis C infection, who should receive hepatitis A and B vaccine
  – individuals with haemophilia and other regular recipients of blood products
  – persons (staff and patients) in institutions caring for intellectually disabled individuals
  – prison inmates
  – men who have sex with men
  – injecting drug users
  – people with a high number of sexual partners
  – commercial sex workers.

Preterm infants
In infants of carrier mothers, early protection is vital and these infants must receive HBIG within 12 hours of birth and the vaccine at birth, with subsequent doses of hepatitis B vaccine at the recommended chronological ages (see ‘Babies of HBsAg positive mothers’ section above).

One small study\(^\text{17}\) suggests that in very premature infants born to carrier mothers, adequate protection is maintained for up to 59 days by giving HBIG within 12 hours of birth. A decision as to whether to immunise at that stage or give a further dose of HBIG will be made according to the clinical condition of the infant, but the same study indicated that an immune response to hepatitis B vaccine can be mounted by infants with birth weights as low as 1000 grams.

For babies of non-carrier mothers, some studies indicate a reduced response to hepatitis B vaccine in infants less than 37 weeks gestation or less than 2000 grams.\(^\text{18}\) In infants of non-carrier mothers, the first dose is normally given at six weeks of age. It is recommended, in the case of neonates born at less than 31 weeks gestation, that the first dose of hepatitis B vaccine be postponed until just before discharge from hospital. (See also section 1.8.)

Pregnancy
Hepatitis B infection in pregnant women may result in severe disease for the mother and active infection of the newborn. Vaccination should not be withheld from a susceptible pregnant woman at increased risk of acquiring hepatitis B (eg, the sexual partner of an injecting drug user or partner of an infectious male).
Testing post immunisation

For the testing schedule for babies of HBsAg positive mothers, see Figure 3.3. Routine testing is not recommended for infants born to non-carrier mothers because almost all will seroconvert.

All those who are likely to be at increased risk of infection should have a blood test one to six months after the last dose of vaccine to ensure they have seroconverted. This includes households and sexual contacts of carriers and those occupationally exposed.

Vaccinees who have anti-HBs levels $\geq 10$ mIU/mL are protected and will not need boosters. If the level is $< 10$ mIU/mL one to six months after the last dose is given, an additional dose of vaccine should be given, and another blood sample taken to confirm adequate antibody levels. If negative, complete the course of two further doses and check the blood test at least one month after completion of the course. A study of 76 adults who had not developed protective antibodies after three doses of hepatitis B vaccine found that 75 percent developed specific cellular immune responses that may protect them against viral infection.$^{19}$

For those vaccinated some time ago, and for whom it is unknown whether three doses of hepatitis B vaccine were given, it is recommended that a booster dose be given and serology repeated one month after that dose. If $\geq 10$ mIU/mL, no further doses should be given; if $< 10$ mIU/mL, complete the course of three doses of vaccine.

Those who have reached levels of 10 mIU/mL or more do not need any booster doses, even if antibodies subsequently wane to undetectable levels. If exposed, they will have a secondary anamnestic immune response that will prevent replication of the virus.$^{20,21}$

For adults at particular risk of exposure to hepatitis B virus (such as health care workers) who fail to respond to a course of hepatitis B vaccine and do not reach a serology of $\geq 10$ mIU/mL, a fourth dose of hepatitis B vaccine should be given and serology repeated. This is followed by two further doses at one-month and six-month intervals to complete a second course. Individuals who fail to respond to this second course of vaccine should be considered for a further course of three doses of hepatitis B vaccine given by the intradermal route.

In a small study from Queensland, intradermal hepatitis B vaccine was given to 43 health care workers who had failed to respond to intramuscular hepatitis B vaccine. Thirty-nine individuals (90 percent) developed protective immunity following intradermal vaccination.$^{22}$ In another study in Canterbury District Health Board,$^{23}$ 27 health care workers who had not responded to previous courses of hepatitis B vaccine were given a further booster dose of hepatitis B vaccine. If they remained non-responders they were given intradermal hepatitis B vaccine at each of four visits, with two intradermal injections given at each visit. Both the GSK and the MSD
vaccine were used in the study; the dose of the MSD (10 µg/mL) vaccine was given as two injections of 1.25 µg, and the dose of the GSK (20 µg/mL) vaccine as two intradermal injections of 2.5 µg. There were local reactions at the injection sites. Following the intradermal course of hepatitis B vaccine, 20 out of the 27 participants had seroconverted, reaching an anti-HBs level of > 10 mIU/mL. The mean level was 126 mIU/mL (with a range of 12–1000 mIU/mL).

Pre-vaccination screening
A discussion on pre-vaccination screening should be part of the informed consent procedure before administering hepatitis B vaccine (see section 2.2). The purpose of pre-vaccination screening is to avoid giving vaccine to those who are carriers or already immune. In particular, vaccination of those who do not know they are carriers may produce a false sense of security about their hepatitis B status. In general, those at higher risk of being a carrier should be encouraged to undergo pre-vaccination screening, while those at low risk may be vaccinated without prior screening. Vaccinating a person who is a carrier does not prevent the future detection of the carrier state, nor cause an increase in adverse reactions.

3.6 Expected responses and adverse events following immunisation (AEFI)

Expected responses
Minor side effects – including local soreness and redness, nausea, diarrhoea, general malaise and fever – are more common in adults than children and, except for local reactions, occur at rates close to those seen with a placebo. Minor reactions reported after the receipt of the vaccine include a temperature > 37.7°C in 1–6 percent, pain in 3–29 percent, and erythema, headache or swelling in 3 percent.

Adverse events following immunisation
A number of studies have looked for and failed to find disease events linked to hepatitis B immunisation, including any links with multiple sclerosis,24,25 diabetes, chronic fatigue syndrome,26 encephalomyelitis, or hair loss.27 Rarely, thrombocytopenia28 and myalgia and arthralgia29,30 have been reported after hepatitis B vaccine.

Allergic reactions have been reported but appear rare. Anaphylaxis has been reported extremely rarely in adults.

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 http://carm.otago.ac.nz. If the patient or parent/caregiver does not consent to being identified, the report should be made without personal identification.
3.7 Contraindications
The general contraindications to all vaccines apply to hepatitis B vaccine (see section 1.9).

The only true specific contraindication to hepatitis B vaccine is anaphylaxis following a previous dose. This is uncommon. Immunisation of previously infected subjects is wasteful, but not harmful, apart from giving a false reassurance to carriers, who remain unaware of their condition and may subsequently assume they are immune.

3.8 Control measures
All cases of hepatitis B infection should be notified to the local medical officer of health.

HBIG is available for passive protection and should be used in combination with the hepatitis B vaccine to confer both passive and active immunity after exposure.

Whenever immediate protection is required, immunisation with a vaccine should be combined with simultaneous administration of HBIG at a different site. It has been shown that passive immunisation with HBIG does not suppress an active immune response. A single dose of HBIG (usually 400 IU for adults, 100 IU for the newborn) is sufficient for healthy individuals (see Table 3.1). If infection has already occurred at the time of the first immunisation, virus replication is unlikely to be inhibited completely, but severe illness and, more importantly, the development of the carrier state may be prevented, particularly in the infants of carrier mothers.

Table 3.1: Hepatitis B immunoglobulin (HBIG) doses

<table>
<thead>
<tr>
<th>Age</th>
<th>HBIG dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Neonates (under 1 month)</td>
<td>100 IU</td>
</tr>
<tr>
<td>1 month to 4 years</td>
<td>200 IU</td>
</tr>
<tr>
<td>5 to 9 years</td>
<td>300 IU</td>
</tr>
<tr>
<td>10 years to adult</td>
<td>400 IU</td>
</tr>
</tbody>
</table>

Those who should receive HBIG and the hepatitis B vaccine, apart from infants born to carrier mothers (see section 3.5), are:

- non-immune persons who have been accidentally inoculated, or who have contaminated the eye, mouth, fresh cuts or abrasions of the skin with blood from a known HBsAg positive person – individuals who suffer such accidents should wash the contaminated area thoroughly and seek medical advice from the local medical officer of health, the local hospital infection control officer or an occupational health service

- susceptible households and sexual contacts of those with acute hepatitis B, if they are not already carriers or immune. HBIG should be given within seven days of the onset of clinical disease in the index case. Commence vaccination at the
same time. The local medical officer of health can assist with contact tracing and HBIG administration.

Sexual and household contacts of carriers should be immunised but need not receive HBIG.

For more details on control measures, refer to *Control of Communicable Diseases Manual*.31

References


4 Diphtheria

4.1 Introduction
Diphtheria has been known since ancient times, although in the pre-microbiological age it was not clearly distinguished from streptococcal infections. The first accurate description of the disease was by Bretonneau in 1826. Epidemics of diphtheria occurred in France, Norway and Denmark during the early part of the 19th century. In 1858 there was a sudden widespread appearance of severe diphtheria, and within a year it had spread all over the world, including New Zealand. Very young children were most at risk, with few cases being reported in individuals over 10 years of age. Klebs described the morphological appearance of the organism in a diphtheritic membrane in 1883, and a year later Loeffler isolated the organism.

The incidence of diphtheria had been declining before the introduction of immunisation, which accelerated the decline. Although immunisation is more effective at preventing disease than preventing infection, it does create herd immunity and reduces carriage and therefore transmission.1 To prevent major community outbreaks it has been suggested that 70 percent or more of the childhood population must be immune to diphtheria.2,3 This may explain the control of diphtheria in New Zealand despite relatively poor coverage. A larger dose of diphtheria vaccine is recommended for children (signified by capital D, eg, DTaP) than for adults (signified by a small d, eg Td) (see section 4.5).

4.2 The illness
Diphtheria is a serious, often fatal disease caused by Corynebacterium diphtheriae, a non-sporulating, non-encapsulated, non-motile, pleomorphic gram-positive bacillus. This disease causes a membranous inflammation of the upper respiratory tract, and it can also cause infection at other sites, notably the skin, where disease tends to be less serious. The organism is not usually invasive but produces a powerful toxin that damages the myocardium (leading to myocarditis and heart failure), peripheral nerves (resulting in demyelination and paralysis), the kidneys (resulting in tubular necrosis) and other organs. The neuropathy begins two to eight weeks after disease onset, while the myocarditis can be early or late.

C. diphtheriae may be toxin producing (toxigenic) or non-toxin producing (non-toxigenic). Immunisation leads to the disappearance of toxigenic strains, but toxigenicity can be rapidly conferred on non-toxigenic strains via phage conversion.4 This makes the return of epidemic diphtheria a real threat when there is insufficient herd immunity, as happened in the states of the former Soviet Union during 1990–97.

The incubation period is usually from one to five days, but can be up to 10 days. The disease remains communicable for up to four weeks, but carriers of diphtheria may continue to shed the organism and be a source of infection for much longer periods.
The clinical illness has a gradual onset over one to two days, characterised by the development of a mildly painful tonsillitis or pharyngitis with an associated greyish membrane. Diphtheria should be suspected particularly if the membrane extends to the uvula and soft palate. The nasopharynx may also be obstructed by a greyish membrane, which leaves a bleeding area if disturbed. It is stated that the breath of a patient with diphtheria has a characteristic mousy smell.

The majority of diphtheria deaths are due to the effects of toxin on the myocardium, and the earlier the electrocardiographic changes occur, the worse the prognosis. The case fatality rate in the United States (US) for pharyngeal diphtheria has remained at about 10 percent since 1920. The mortality in the recent Russian outbreak was much lower, at just over 2 percent, but was variable by age and region.

4.3 Epidemiology
Humans are the only known host for diphtheria, and the disease is spread by close personal contact with a case or carrier. In the pre-immunisation era diphtheria was predominantly a disease of children under 15 years of age, and most adults acquired immunity without experiencing clinical diphtheria. Asymptomatic carriage was common (3–5 percent) and important in perpetuating both endemic and epidemic diphtheria. Immunisation appears to reduce carriage, and therefore reduces exposure to infection (herd immunity).

The incidence of diphtheria dropped dramatically during the 20th century. Although immunisation played a large part in this reduction it may not be wholly responsible. Diphtheria is rare in industrialised countries like New Zealand, although small outbreaks may occur. A Swedish outbreak in 1984–86 was caused by a single strain and occurred mainly in a group of destitute alcoholics and drug users. It occurred after more than 25 years without indigenous diphtheria, and was notable for not spreading to the general population, despite 70 percent of women and 50 percent of men having no detectable antibody against diphtheria (ie, an antibody titre < 0.01 IU/mL). Limited contact between affected individuals and the general population, as well as outbreak control measures such as immunising hospital personnel, may have accounted for the lack of spread.

In June 1995 the World Health Organization (WHO) declared the diphtheria epidemic affecting the former Soviet Union to be an international health emergency. The epidemic began in Russia in 1990 and had affected almost all states of the former Soviet Union by 1994. Although other factors (ie, social disruption, mass population movements, inadequate immunisation coverage among children and the introduction of a new strain) were relevant, the importance of waning immunity and/or lack of immunity among adults were highlighted by the epidemiology. More than 115,000 cases and 3000 deaths were reported between 1990 and 1997 in the Russian Federation. Most of the cases and deaths occurred in adults, although the incidence rate for diphtheria was higher among children. Mass immunisation of adults and improved childhood immunisation controlled the epidemic, but has not
yet eliminated the circulation of diphtheria in the region. A case control study in the Ukraine found that three doses of vaccine were 98 percent effective in preventing disease in children under 15 years of age, thus showing that poor vaccine efficacy was not responsible for the epidemic.

Diphtheria remains endemic in many parts of the non-industrialised world but is being controlled by immunisation. In industrialised countries diphtheria has become increasingly rare; for example, in the US there were 853 notifications of non-cutaneous diphtheria during the 1970s, but only 41 cases between 1980 and 1995. However, continuing endemic cutaneous diphtheria in indigenous communities has been reported from the US, Canada and Australia.

The virtual disappearance of diphtheria in industrialised countries has removed the opportunity for infection to either produce or boost immunity. In all developed countries that have undertaken surveys, many adults have been shown to lack diphtheria antibodies. In Australia, where infant vaccination against diphtheria was introduced from 1940 to 1945, a report from the national serosurvey using samples taken during 1996–99 showed that about 99 percent of children aged five to nine years had diphtheria antitoxin levels ≥0.01 IU/mL and were considered immune or partially immune. Eighty-one percent of those aged 20–29 years were considered immune or partially immune, whereas in subjects aged 50–59 years, who were born between 1937 and 1948, only 59 percent had antitoxin levels considered immune or partially immune to diphtheria.

Despite these findings there has been minimal disease in developed countries, suggesting that antibody levels may not be a reliable guide to protection and that other factors may be operating. For example, a high proportion of the adult German population have antibody levels indicating susceptibility yet this has not led to diphtheria outbreaks despite Germany’s relative proximity to the former Soviet Union.

Diphtheria continues to occur each year in less developed countries in Asia and the Western Pacific Region. For sources of further information see Appendix 11.

**New Zealand epidemiology**

Between 1917 and 1921 there were 794 reported deaths in non-Māori from diphtheria. Regular epidemics of infection occurred in New Zealand until 1950, and further outbreaks occurred in Milton and the Waikato in the 1960s. In 1998 the first case of diphtheria was reported in New Zealand since 1979, and this was the first toxigenic isolate since 1987. In 2002 a four-year-old child was reported after a toxigenic strain was isolated from a hip aspirate. The child had no toxin related symptoms and had been fully vaccinated for age; this would not be regarded as a vaccine failure. (See Figure 4.1.)
There is no current data on the proportion of New Zealand adults susceptible to diphtheria. The 1985 National Serum Survey found that 73 percent of five year olds, 65 percent of 10 year olds and 53 percent of 15 year olds had protective levels of diphtheria antibody. The decline apparent with age suggests that there is likely to be a large and increasing pool of adults susceptible to diphtheria in New Zealand. This was the reason for the introduction of adult tetanus diphtheria (Td) vaccination in 1994.

Figure 4.1: Number of cases of diphtheria and diphtheria mortality, 1909–2004

History of the New Zealand Immunisation Schedule

During the 1920s the Department of Health, at the instigation of individual school medical officers or medical officers of health, began delivering diphtheria immunisation in a few selected schools and orphanages, but there was no national policy. By 1941 diphtheria immunisation was offered routinely to children under seven years of age through the School Medical Service and the Plunket Society. From 1960 the Department of Health programme was delivered by general practitioners using three doses of non-adsorbed triple vaccine (diphtheria, tetanus and whole cell pertussis vaccine – DTwP) at three, four and five months of age, and a dose of double (diphtheria and tetanus – DT) vaccine before school entry at five years of age. In 1964 a DT booster at 18 months was added to the schedule. There was a change in 1971 to an adsorbed (ie, adjuvant added) vaccine that was more immunogenic, and the dose given at four months of age was dropped. In 1980 the dose of DT given at five years of age was replaced by the monovalent tetanus toxoid (TT) given at 15 years of age, as part of a move from 10-yearly to 20-yearly boosters for tetanus.
There was a return to a three dose primary series for DTwP (by the addition of a dose at six weeks of age) in 1984, because two doses of DTwP had been inadequate to control pertussis.

Emerging concerns about the lack of adult immunity to diphtheria, prompted by outbreaks and epidemics overseas, led to the introduction of Td in 1994. Td replaced the TT vaccine given to 15 year olds and as adult boosters. The recommendation for boosters was changed from 20-yearly to 10-yearly in the hope this would increase uptake. In 1996 the timing of the adolescent booster of Td was changed from age 15 years to age 11 years. Td was continued at age 11 years until the introduction of the adult diphtheria, tetanus, acellular pertussis and inactivated polio vaccine (dTaP-IPV) in February 2006. From 2002 Td boosters for adults have been recommended at age 45 and 65 years, as a pragmatic attempt to improve the uptake of adult booster doses.

From 1996 the vaccine used for infants was the combination vaccine of diphtheria, tetanus, whole cell pertussis and *Haemophilus influenzae* type b vaccine (DTwPH). In August 2000 the vaccines were changed to diphtheria, tetanus and acellular pertussis (dTaP) during the first year, and diphtheria, tetanus, acellular pertussis and *H. influenzae* type b (dTaP/Hib) at age 15 months. In 2002, with the change to inactivated polio vaccine (IPV), dTaP-IPV was given during the first year of life at age six weeks, and at three and five months. A booster of dTaP-IPV was added at the age of four years before school entry to improve pertussis control and boost diphtheria immunity.

From 2006 the schedule is three doses of a diphtheria containing vaccine (dTaP-IPV) in the first year of life, and a fourth dose at age four years. At age 11 years (school year 7) dTap-IPV will be given, and adult boosters will continue to be recommended at age 45 and 65 years. The diphtheria, tetanus and acellular pertussis vaccine dose at 15 months has been dropped. However, it is expected that young children will have adequate protection from diphtheria from the end of the first year and the dose at age four years (see chapter 6: Pertussis for further details).

### 4.4 Vaccines

Diphtheria toxoid is prepared from cell free purified diphtheria toxin treated with formaldehyde. It is a relatively poor immunogen, which, to improve its efficacy, is usually adsorbed onto an adjuvant – either aluminium phosphate or aluminium hydroxide.

The diphtheria vaccine is only available as a component of combination vaccines. From 2006 the publicly funded vaccine for the infant series and the booster at age four years is diphtheria, tetanus, acellular pertussis and inactivated polio vaccine (dTaP-IPV – INFANRIX™-IPV, GSK). A smaller adult dose of diphtheria and pertussis vaccine together with tetanus and inactivated polio vaccine (dTaP-IPV – BOOSTRIX®-IPV, GSK) is given at age 11 years (school year 7) (see section 4.5 below, and sections 6.4 and 8.4).
There are other diphtheria vaccines available that are publicly funded for children requiring an alternative to a pertussis containing vaccine. These vaccines include adsorbed diphtheria tetanus (DT–CDT™, CSL) for children six years of age and under, and the adult tetanus-diphtheria vaccine (Td–ADT®, CSL), with a reduced dose of diphtheria toxoid for individuals seven years of age and over (see section 4.5). Because the age cut off for changing from the childhood to the adult vaccine varies between countries, the manufacturer’s inserts may suggest different age cut offs. The Australian guidelines use a cut off age of eight years, the British 10 years and the American guidelines seven years.

**Efficacy of vaccine**

Although there are no randomised controlled studies on the efficacy of the vaccine, between 87 and 98 percent protection has been demonstrated. Immunised cases have been shown to have less severe disease, as highlighted during the outbreak in the former Soviet Union.

**Dosage**

The dose of DTaP-IPV, dTap-IPV, DT or Td is 0.5 mL given by intramuscular injection. (See section 2.3 for needle sites and sizes.)

### 4.5 Recommended immunisation schedule

**Primary immunisation**

From 2006 the diphtheria containing vaccine for infants and children up to and including six years of age is DTaP-IPV, which is given at six weeks, three months and five months of age. A further dose of DTaP-IPV is given at four years of age, prior to school entry, and at age 11 years (school year 7) a dose of dTap-IPV is given. The dTap-IPV vaccine will be given to children aged 11 years in 2006/07, because these children have not received four doses of polio vaccine. Children receiving a fifth dose of a polio (IPV) containing vaccine are unlikely to experience adverse events. After this it is expected dTap will be given.

If a course of immunisation is interrupted for any reason, it may be resumed, without repeating prior doses, to complete four doses of diphtheria toxoid. The fifth dose is given at age 11 years.

**Maximum number of doses for children**

Children who did not receive the pertussis vaccine (DTwPH, DTaP or DTaP-IPV) as infants, but subsequently wish to have pertussis vaccine, will receive additional doses of diphtheria and tetanus vaccine because pertussis is only available in the DTaP-IPV combination. In general, children should not have more than six doses of tetanus and diphtheria vaccines by their fourth birthday. For an individual child, the vaccinator may be guided by the extent of any local reaction in determining whether to give future doses. The only danger from the additional doses is a local reaction, and this needs to be balanced against the need to protect against pertussis.
Immunisation of individuals seven years of age and over, including adults

When immunising individuals seven years of age and over the adult tetanus diphtheria (Td) vaccine should be used. This is because of the risk of severe local reactions if the larger dose of diphtheria toxoid contained in the childhood vaccines (DTaP-IPV, DT and other combinations) is administered to partially immune individuals seven years of age and over. For full primary immunisation in this age group, three doses of 0.5 mL Td vaccine should be given by intramuscular injection at not less than monthly intervals. For previously unimmunised adults a course of three doses of Td at zero, one and six months is recommended.

As at 2006, dTap and dTap-IPV are licensed for distribution for booster doses only. However, there are expected to be no safety concerns to giving three doses of dTap-IPV to previously unimmunised older children and adults. Therefore, using dTap should be considered for all catch up and adult schedules for primary and booster immunisation.

Dose intervals between Td and dTap-IPV

It is recommended that for students who have recently received a tetanus diphtheria (Td) vaccine booster, eg, at the time of an injury, the age 11 (year 7), dTap-IPV immunisation should be delayed until two years after the dose of Td, and offered before the student reaches the age of 16 years. Students who would normally receive the year 7 event at school should be referred to their general practitioner for follow up and recall.

Booster doses for adults

Studies overseas show that many adults lack protective levels of the antibody, and this has led to concern about waning immunity and recommendations for booster doses beyond childhood. Most authorities recommend maintenance of diphtheria immunity by periodic reinforcement using Td.¹⁸

In New Zealand, following the dose of dTap-IPV at age 11 years, booster doses of Td are recommended at 45 and 65 years of age. The age specific recommendations may facilitate the linkage of adult immunisation to the delivery of other preventive health measures.

Booster doses before travel

If someone is travelling to an area endemic for diphtheria, or there is another reason to ensure immunity, a booster dose should be given if it is more than 10 years since the last dose. If adults have not received a primary series of diphtheria containing vaccine, a course of three doses should be given (at zero, one and six months). For website sources of further information see Appendix 11.
4.6 Expected responses and adverse events following immunisation (AEFI)

Expected responses
There is limited data on reactions to the diphtheria toxoid because it is usually given in combination with tetanus, pertussis and other vaccines. The 1994 Institute of Medicine review of vaccine reactions did not identify any reaction where the evidence favoured or established a causal relation for diphtheria toxoid. However, local and systemic reactions do occur with diphtheria vaccine, especially when the infant vaccine is used in older children and adults.

Adverse events following immunisation
For further information on adverse events following a vaccine containing diphtheria/tetanus/pertussis antigens (DTaP, DTaP-IPV, dTap-IPV) and events following the fourth and fifth dose of a DTaP containing vaccine, see chapter 6: Pertussis.

There was an increase in the number of reports (although the rates are not known) of AEFI in adults following the change from TT to Td in New Zealand, and the majority of these were local reactions. Studies in the US have found that booster doses of Td are associated with fever in 0.5 to 7 percent of recipients, but that temperatures above 39°C are rare. Other systemic symptoms such as headache or malaise are reported less frequently, and severe adverse events are reported in 2.1 events per million doses of Td.

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 http://carm.otago.ac.nz. If the patient or parent/caregiver does not consent to being identified, the report should be made without personal identification.

4.7 Contraindications
See section 1.9 for general contraindications for all vaccines. There are no specific contraindications to diphtheria vaccine (or Td/DT), except for a serious reaction to a previous dose. See also section 6.7 for contraindications to a pertussis containing vaccine.

Td must be used for individuals seven years of age and over because of the increased risk of local reactions with the higher dose of diphtheria toxoid contained in the childhood formulation.

4.8 Control measures
All cases of diphtheria should be notified immediately on suspicion to the local medical officer of health. Alert the laboratory that culture for C. diphtheriae is requested. If C. diphtheriae is isolated it should be sent to the Institute of
Environmental Science and Research (ESR) reference laboratory to determine whether it is a toxigenic strain. All patients with *C. diphtheriae* isolated from a clinical specimen should be discussed with the medical officer of health.

Household and close contacts of a case of diphtheria or a carrier should be given a complete course of vaccine or a booster dose according to the following schedule.

- Fully immunised children up to and including six years of age who have not received a booster dose of diphtheria containing vaccine within the last five years: give one injection of DTaP-IPV.
- Fully immunised individuals seven years of age and over who have not received a booster dose of a diphtheria containing vaccine within the last five years: if aged 7–15 years give one injection of dTap-IPV or dTap; if aged over 15 years give one injection of Td. (See section 4.5.)
- Unimmunised children up to and including six years of age: follow the catch up schedules outlined in Appendix 2.
- Unimmunised individuals seven years of age and over: give two injections of Td followed by one dose of dTap-IPV if aged 7–15 years; give three doses of Td at monthly intervals for adults. Alternatively three doses of dTap-IPV may be given (see section 4.5). See also Appendix 2 for catch-up schedules for other vaccines.

All close contacts should:
- have pharyngeal cultures taken
- remain under observation for seven days
- receive immunisation as described above
- be treated with erythromycin 40 to 50 mg/kg per day (maximum 2 g/day) for seven days. If compliance is uncertain, a single intramuscular dose of benzathine penicillin 600,000 to 1,200,000 units may be used (600,000 units for children weighing <30 kg and 1,200,000 units for children weighing ≥30 kg and adults). Cotrimoxazole 960 mg bd (adult dose) has been recommended in cases of erythromycin intolerance
- have a repeat pharyngeal culture to document eradication of infection (this should be taken from contacts that have been proven to be carriers, two weeks after completion of their therapy).

Child contacts should be excluded from school, early childhood services and community gatherings until they are known to be culture negative. Adult contacts who are food handlers or work with children should be excluded from work until known to be culture negative. Cases should be excluded from school until recovery has taken place and two negative throat swabs have been collected one day apart and one day after cessation of antibiotics.

For more details on control measures, refer to *Control of Communicable Diseases Manual*.21
References

5 Tetanus

5.1 Introduction
Tetanus has long been known as the scourge of parturient women, newborn babies and wounded soldiers. In the 18th century one out of every six infants born at the Rotunda Hospital in Dublin died from neonatal tetanus. Hippocrates described tetanus, but the cause was not recognised until 1884 and the toxin not purified until 1890. The toxoid (chemically inactivated toxin) was first prepared in 1924.

5.2 The illness
Tetanus is a clinical diagnosis, and is characterised by muscular rigidity and very painful contraction spasms. When severe, it is associated with a characteristic facial grimace (risus sardonicus) and arching of the back (opisthotonus). The patient suffering from tetanus remains alert unless they become severely hypoxic. A toxin produced by Clostridium tetani (a gram positive, spore forming, motile, anaerobic bacillus) causes the disease. The toxin reaches the central nervous system via the axons and irreversibly binds to nerve terminals at the neuromuscular junction, blocking release of inhibitory neurotransmitters and leading to the tetanic muscle spasms.

The incubation period is between four and 21 days, commonly about 10 days, but has been reported to vary from one day to several months. The bacteria need an anaerobic environment to grow, and this is often found in damaged and necrotic tissue.

Initial symptoms include weakness, stiffness or cramps, and difficulty chewing or swallowing food. Reflex muscle spasms usually occur within one to four days of the initial symptoms. The interval between initial symptoms and reflex spasms is called the onset period. The shorter the incubation and onset periods, the more severe the disease. Even with modern intensive care tetanus mortality is about 10 percent overall, and much higher in older people.

Neonatal tetanus, from infection of the umbilical stump, is the commonest form of disease in non-industrialised countries.

5.3 Epidemiology
Tetanus spores are ubiquitous in the environment, and are particularly common in soil and the alimentary tracts of animals. They can easily be introduced into a wound at the time of injury, even when the injury is quite trivial. The incidence of tetanus varies inversely with immunisation coverage.

Tetanus is not infectious, and vaccination provides only individual protection and no herd immunity.
New Zealand epidemiology

During 1980–92, 86 cases of tetanus occurred in New Zealand and there were eight deaths, a case fatality rate of 9.3 percent.\(^1\) Of all cases of tetanus, 79 percent were over 40 years of age. Of those who died, seven were over 70 years of age and one was 58 years; seven of the eight were female. The average incidence in New Zealand of 0.20 per 100,000 for the 13-year period compares with a 1992 rate of 0.08 in Australia, 0.01 in Canada, 0.02 in England, 0.04 in Scotland and 0.02 in the United States (US).

From 1993 to 2000 there were 18 cases of tetanus notified to the medical officers of health, a range of zero to six cases a year. Six cases were reported in 1999; two were in the age group 40–49 years and four were over 70 years of age. Four of the cases were unimmunised, and there was no information on the immunisation history of the other two cases. A total of eight cases were notified from 2001 to 2004, and among these was an unimmunised child aged one year diagnosed with tetanus in 2001. The single case notified in 2004 was a female aged 60–65 years with an unknown immunisation history, although there were five cases hospitalised with tetanus. Not all cases of tetanus are notified, as illustrated in the hospitalisations data shown in Figure 5.1.

Figure 5.1: Tetanus hospitalisations, by year, 1970–2004

![Tetanus hospitalisations, by year, 1970–2004](chart.png)
History of the New Zealand Immunisation Schedule

The history of tetanus vaccine use prior to the introduction of diphtheria, tetanus and whole cell pertussis (DTwP) vaccine in 1960 is not well recorded, but tetanus vaccine was widely used, in World War II and subsequently, by the armed forces.

In New Zealand, universal infant immunisation with tetanus toxoid started in 1960 with the use of three doses of triple vaccine. Anyone born before 1960 is less likely to have received a primary series, unless they were in the armed forces. Older women appear to be at particular risk. The first scheduled vaccine used for infants (from 1960) was the DTwP vaccine, with three doses at monthly intervals at three, four and five months of age; and a diphtheria tetanus (DT) booster before school entry (at five years of age). A DT booster at 18 months of age was added in 1964, primarily to enhance protection against tetanus. There was a change to a more immunogenic adsorbed vaccine in 1971 and the dose given at four months of age was dropped.

In 1980 the dose of DT given at five years of age was replaced by the monovalent tetanus toxoid (TT) given at 15 years of age, as part of a move from 10-yearly to 20-yearly boosters for tetanus. It was considered that more frequent boosters were unnecessary and the cause of significant local reactions. There was a return to a three dose primary series of DTwP (by the addition of a six weeks of age vaccination) in 1984, because two doses had been inadequate to control pertussis. In 1996 the booster of adult tetanus diphtheria vaccine (Td), previously given at age 15 years, was changed to age 11 years.

In 2002 the primary schedule for tetanus, given in combination vaccines at age six weeks, three months and five months followed by a dose at 15 months, was changed when a further dose was introduced at age four years before school entry. The Td given at age 11 years continued.

The adult tetanus diphtheria vaccine (Td) replaced the tetanus toxoid (TT) vaccine in 1994 and 10 yearly boosters were recommended. The change was recommended to maintain the adult population’s immunity to diphtheria, in response to outbreaks overseas affecting adults and the absence of natural boosting because the disease had become rare. From 2002 adult boosters have been recommended at 45 and 65 years of age (instead of 10 yearly) as a pragmatic attempt to increase coverage in the adult population.

Whether routine booster doses of tetanus vaccine, unrelated to the treatment of an injury, are necessary following the primary series in childhood is debated. As discussed above, the policy recommending boosters has changed over time. The population coverage for adult Td immunisation in New Zealand is unknown but is thought to be low. The change in 2002 to Td immunisation at 45 and 65 years of age aimed to increase the proportion of the population who receive boosters. The age specific recommendations may facilitate the linkage of adult immunisation with the delivery of other preventive health measures.
5.4 Vaccines

Tetanus immunisation protects by stimulating the production of antitoxin, providing immunity against the effects of the toxin. It does not prevent organisms growing in a contaminated wound. The tetanus vaccine is prepared from cell free toxin treated with formaldehyde to produce a toxoid. The toxoid is adsorbed onto an aluminium salt adjuvant to improve immunogenicity.

Tetanus vaccine is available as a single antigen or in combination with other vaccines. A primary immunisation course consists of three doses of vaccine. The adult Td vaccine, which has a reduced dose of diphtheria toxoid, is used in individuals seven years of age and older. (See also sections 4.4, 6.4 and 8.4.)

Efficacy

The tetanus vaccine was 100 percent effective when given to pregnant women to protect against neonatal tetanus in a randomised controlled trial (RCT). Tetanus in adults is too rare for vaccine efficacy to be tested in an RCT, but the vaccine was shown to be efficacious before RCTs became the standard. The efficacy of tetanus vaccine was clearly demonstrated in World War II, when only 12 cases of tetanus occurred among the 2.7 million wounded US army personnel (0.44 per 100,000), compared to 70 cases out of 520,000 wounded in World War I (13.4 per 100,000). Of the 12 cases, only four had completed primary immunisation. Immunised cases have less severe disease and a lower case fatality.

In most studies, 100 percent of infants have protective levels of tetanus antibody after three doses of vaccine given at intervals of one month or longer. The duration of antibody persistence depends on the initial antibody level. Calculations of tetanus antibody decay have shown that a three dose primary schedule in infancy will provide protection for at least five years, and a booster at five years will provide protection for at least another 21 years. Additional doses increase the duration of protection, but the immune response gets slower and lower in older people.

Dosage

The dose of DTaP-IPV, dTap-IPV, DT, Td and TT is 0.5 mL given by intramuscular injection. (See section 2.3 for needle sites and sizes.)

5.5 Recommended immunisation schedule

Usual childhood schedule

From 2006 a primary course of tetanus is given as DTaP-IPV at six weeks, three months and five months of age followed by a dose of DTaP-IPV at four years of age, before school entry. From 2006 the booster given at age 11 years (school year 7) includes a pertussis component given as the vaccine diphtheria, tetanus, acellular pertussis and inactivated polio vaccine (dTap-IPV, BOOSTRIX®-IPV, GSK). If pertussis vaccine is contraindicated (see sections 6.6 and 6.7), DT, or adult tetanus diphtheria
vaccine (Td) in older children and IPV should be substituted (see section 4.5). Note that the dTap-IPV vaccine given at age 11 years contains the smaller adult doses of diphtheria and pertussis antigens compared with the vaccines given to infants and children up to age seven years. The dTap-IPV vaccine will be given to children aged 11 years in 2006/07, as these children have not received four doses of polio vaccine. After this it is expected dTap will be given.

**Maximum number of doses for children**

Children who did not receive the pertussis vaccine as infants, but subsequently request to have pertussis vaccine, will receive additional doses of diphtheria and tetanus vaccine, because pertussis vaccine is only available as diphtheria, tetanus, acellular pertussis and inactivated polio (DTaP-IPV). In general, children should not have more than six doses of tetanus and diphtheria vaccine by their fourth birthday. For an individual child, the vaccinator may be guided by the extent of any local reaction when determining whether to give further doses. The only danger from the additional doses is a local reaction, and this needs to be balanced against the need to protect against pertussis.

**Adults and children from seven years of age**

For adults and children who present with a tetanus prone wound, boosters should be offered according to the guidelines in section 5.7 and Table 5.1.

For previously unimmunised adults and children from seven years of age, a primary immunisation course consists of three doses of 0.5 mL of Td at intervals of not less than one month. This is shorter than the manufacturer’s recommended schedule of zero, one and six months but is likely to increase compliance. A booster dose should be given 10 years later. Alternatively three doses of dTap-IPV may be given, plus the booster in 10 years (see section 4.5).

For children given a primary course as infants and a booster at age four years, a further booster of tetanus toxoid containing vaccine is given at age 11 years as dTap-IPV vaccine.

Adults are recommended to have booster doses of adult tetanus diphtheria (Td) vaccine at 45 and 65 years of age. Protection against tetanus is expected to last at least 20 years following a booster dose after the primary series. The recommendation for a booster dose at 45 and 65 years of age is intended to ensure ongoing protection, and to facilitate delivery by recommending the booster at a time when routine preventive care for adults may be taking place.

Note that the recommendations for diphtheria vaccine include: if someone is travelling to an endemic area, or there is another reason to ensure immunity, a booster dose of Td should be given if it is more than 10 years since the last dose (see section 4.5).
People born before 1960 are less likely to have had a primary series of tetanus vaccine. General practitioner visits at or around 45 and 65 years of age should be used to check on the immunisation history. If there is no reliable history of the patient having received a primary series, the vaccine at that episode should be considered the first of a primary series. The next two injections should be given at monthly intervals or at zero, one and six months. A booster dose should be scheduled in 10 years’ time.

Prior clinical tetanus does not usually confer immunity, and immunisation is required. In 1995 a 40-year-old man developed tetanus for a second time because he failed to complete the recommended course of immunisation after the first episode of tetanus.³

**Dose intervals between Td and dTap-IPV**

It is recommended that for students who have recently received a tetanus diphtheria (Td) vaccine booster, eg, at the time of an injury, the age 11 (year 7), dTap-IPV immunisation should be delayed until two years after the dose of Td, and offered before the student reaches the age of 16 years. Students who would normally receive the year 7 event at school should be referred to their general practitioner for follow up and recall.

**Prevention of tetanus following injury**

Following injury it is essential that all wounds receive adequate surgical toilet. Tetanus bacteria can only grow in anaerobic conditions. Further treatment must depend on the circumstances of each case. Tetanus prone injuries include those that are contaminated with dirt, saliva or faeces, puncture wounds (including unsterile injections), missile injuries, burns, frostbite, avulsions and crush injuries. Guidelines for management are shown in Table 5.1.
Table 5.1: Prevention of tetanus following injury

The following are offered as guidelines.

(i) Recipients should be divided into four categories.

Category 1: completed a course of tetanus toxoid (TT or Td), with the most recent
dose within the last five years

Category 2: completed a course of tetanus toxoid (TT or Td), with the most recent
dose between five and 10 years ago

Category 3: completed a course of tetanus toxoid (TT or Td) with the most recent
dose more than 10 years ago.

Category 4: never had a complete course of tetanus toxoid or immune status is
unknown.

(ii) Wounds should then be classified as ‘clean’ or ‘dirty’.

(a) ‘clean’ wounds – wounds less than six hours old, non-penetrating with
negligible tissue damage

(b) ‘dirty’ wounds – wounds not classified as clean, which may be contaminated,
infected, penetrating, more than six hours old and with tissue damage.

Recommendations based on the category of patient and the kind of wound are
summarised below.

From the person’s tetanus immunisation history, put them into one of the four
categories as stated above, and identify the time since a previous booster. Classify
the wound as clean or dirty and use the table to identify the need for Td or tetanus
immunoglobulin (TIG).

<table>
<thead>
<tr>
<th>Category based on history of tetanus course and/or booster</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of years since completing tetanus toxoid course or booster</td>
<td>&lt; 5</td>
<td>5–10</td>
<td>&gt; 10</td>
<td>Never or unknown</td>
</tr>
<tr>
<td>(a) Clean wound</td>
<td>Nil</td>
<td>Nil</td>
<td>Booster Td*</td>
<td>Course Td*</td>
</tr>
<tr>
<td>(b) Dirty wound</td>
<td>Nil</td>
<td>Booster Td**</td>
<td>Booster Td*</td>
<td>TIG plus course Td*</td>
</tr>
</tbody>
</table>

* A tetanus immunisation course consists of three doses at not less than monthly intervals.
** For children age 7–15 years, dTap-IPV may be used, if a booster is indicated and they have not
received a fifth pertussis dose and fourth IPV dose.

Immunised individuals respond rapidly to a booster injection of adsorbed tetanus or
tetanus diphtheria vaccine, even after a prolonged interval. Toxoid and TIG should be
given at the same time but into different limbs and using separate syringes.
**Tetanus immunoglobulin (TIG) availability and storage**

TIG is issued in ampoules, each containing 250 IU. (Ampoules of 2000 IU are used for treatment and not for prophylaxis.) These should be protected from light and stored in a refrigerator at +2° to +8°C. They must never be frozen. TIG is given intramuscularly.

**TIG dose**

The recommended dose to prevent tetanus is 250 IU of TIG for recent injuries, but this should be increased to 500 IU if more than 24 hours have elapsed since injury, or if there is a risk of heavy contamination or following burns.

There is no need to test the patient’s sensitivity before administering TIG, but caution is necessary if the patient is known to suffer IgA deficiency. In this situation, specialist help should be sought (see section 1.8).

Patients with impaired immunity who suffer a tetanus-prone wound may have failed to respond to prior vaccination and may therefore require TIG.

### 5.6 Expected responses and adverse events following immunisation (AEFI)

**Expected responses**

Local reactions such as pain, redness and swelling around the injection site have been reported in 0–95 percent of recipients. Local reactions generally increase with the number of doses given. The local reactions are usually minor and only last a day or so. In a small percentage of vaccine recipients the reactions will be severe enough to limit movement of the arm and may last for about a week.

High levels of antibody before immunisation (usually from an excessive number of immunisations) are associated with more severe local reactions. The reaction may be due to some of the other vaccine constituents (eg, aluminium).

See chapter 6: Pertussis for information on reactions following the fourth and fifth dose of a diphtheria, tetanus, pertussis antigen containing vaccine.

Sterile abscesses and persistent nodules at the injection site may develop if the injection is not given deeply enough into the muscle. The deeper the injection, the less the risk of reaction.4

The change from TT to Td was associated with the reporting of more local as well as other reactions. Generalised reactions after Td are uncommon, but may include headache, lethargy, malaise, myalgia and pyrexia.

**Adverse events following immunisation**

Anaphylaxis was reported at a rate of 1.6 per million doses of Td in the US from 1991 to 1995. There have been no reports of anaphylaxis after Td was introduced.
in New Zealand. The 1994 US Institute of Medicine\(^5\) review of adverse events from tetanus vaccine concluded that the evidence supported a link with brachial plexus neuropathy at a rate of 0.5 to 1 per 100,000 doses within one month of immunisation. No evidence has been found for a connection between receipt of tetanus vaccine and the Guillain-Barré syndrome in a large population based study. The study found no link in an estimated 730,000 children who were of eligible age to receive DTwP in a population of 2.2 million children under 15 years of age, or in adults who received tetanus containing vaccines.\(^6\)

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 http://carm.otago.ac.nz. If the patient or parent/caregiver does not consent to being identified, the report should be made without personal identification. When reporting local reactions, state the size of the redness and/or swelling, as well as the number of previous doses of vaccine.

### 5.7 Contraindications

See section 1.9 for general contraindications for all vaccines.

Although there is the general contraindication to administering a vaccine when a patient has a febrile illness, protection against the risk of tetanus is paramount if the wound is thought to be tetanus prone. Immunisation should not be postponed because the patient has a minor infection.

Immunisation with Td (or tetanus toxoid) should not be repeated in individuals who have had previous severe hypersensitivity reactions. Most cases of hypersensitivity have been reported in individuals who have had excessive numbers of booster injections outside the guidelines noted above. (See also sections 4.7 and 6.7.)

### 5.8 Control measures

All cases of tetanus, together with an accurate immunisation history, should be notified to the local medical officer of health.

**References**

6 Pertussis (Whooping Cough)

6.1 Introduction
Descriptions of pertussis appeared relatively recently (in the 16th century) in comparison with other common infectious illnesses, such as mumps and measles. As the disease became widely known it was given different names. The Italians spoke of the ‘dog bark’, while in England it became known as the ‘chin cough’ or ‘kin cough’, later to be called whooping cough. The Chinese called it the ‘100 day cough’ because of the protracted course of the disease. Thomas Sydenham first used the term ‘infantum pertussis’ in 1670, ‘pertussis’ meaning a violent cough of any kind.

Bordet and Gengou identified the causative organism in 1906 (hence the name *Bordetella pertussis*), and the first crude vaccine was developed soon after from killed bacteria. An improved understanding of the organism resulted in a standardised whole cell vaccine. During the 1980s and 1990s knowledge of the components of *B. pertussis* and their biological roles led to the development of acellular pertussis vaccines.

Pertussis is unusual for an infection in that it produces higher morbidity and mortality in females than in males, which is more apparent with increasing age. The reason for this is unknown.

6.2 The illness
Pertussis is a highly infectious bacterial disease spread by droplets, with an incubation period of 7–10 days (range 6–20 days). A case is most infectious from seven days after exposure until three weeks after the onset of the typical paroxysms. As many as 90 percent of non-immune household contacts will acquire the disease. *B. pertussis* is a small, gram negative, pleomorphic bacillus. The bacillus is fastidious, hard to culture, and will often have cleared or decreased in numbers by the time the typical cough develops, making laboratory confirmation difficult.

The initial catarrhal stage, which is the most infectious period, is of insidious onset with rhinorrhoea and an irritating cough that can progress to severe paroxysms of coughing. In the catarrhal stage, which usually lasts one to two weeks, the only clue to diagnosis may be contact with a known case. This stage is followed by the paroxysmal stage, with paroxysms characterised by a series of short expiratory bursts, followed by an inspiratory gasp or typical whoop and/or vomiting. Not all children whoop. Whooping is unusual in adults and relatively uncommon in infants. Infants may develop apnoea between paroxysms. Patients appear relatively well between paroxysms and are commonly afebrile.

The most common complications of pertussis are secondary infections, such as otitis media and pneumonia, and the physical sequelae of paroxysmal coughing (eg, subconjunctival haemorrhages, petechiae, epistaxes, central nervous system...
haemorrhages, pneumothoraces and herniae). At the peak of the paroxysmal phase vomiting can lead to weight loss, especially in infants and young children. Infection may be particularly severe in young infants, in whom prolonged periods of apnoea may result in cyanosis, anoxic encephalopathy, convulsions and death.

Only limited data is available on the risk of encephalopathy from pertussis, with estimates from early population based studies ranging from 0.008 to 0.08 percent of cases.¹ A review of notified cases of pertussis in the United States (US) between 1980 and 1989² found that 0.7 percent developed encephalopathy and 2.2 percent seizures. In contrast, 0.1 percent of cases reported in the US between 1992 and 1995 were complicated by encephalopathy. The lower rate may reflect an increased recognition of pertussis in adolescents and adults, who are less likely to have severe complications, or the more comprehensive reporting of milder, non-hospitalised cases.

Studies performed in Australia, Canada, France, Germany and the US during both epidemic and non-epidemic periods have shown that between 12 and 32 percent of adolescents and adults with persistent cough have evidence of recent *B. pertussis* infection.³⁴⁵⁶⁷ Infection frequently occurs in adults in households where there are other people with pertussis.⁸ Serological surveys also suggest that pertussis infection is a common occurrence during adult life.⁹¹⁰

### 6.3 Epidemiology

#### Pertussis mortality

Historically, pertussis mortality rates have always been higher in the first year of life than at any other age.¹¹ Beyond three years of age mortality rates have always been relatively low. The concentration of deaths in the first year of life, with markedly lower death rates in toddlers and preschool aged children, is different from the pattern seen with other acute childhood infectious diseases, where a larger proportion of deaths occur in children between one and five years of age. Mortality rates were and remain highest in the first few months of life. Young age, lack of immunisation, low socioeconomic status and premature delivery are associated with an increased risk of fatal pertussis.¹²¹³¹⁴¹⁵

Pertussis case fatality rates have decreased substantially over the past 100 years. For example, in the US the case fatality rate was 3.4 percent in 1930 compared with 0.2 percent in 1993.¹⁶¹⁷ The case fatality rates in the US from 1992 to 1994 were 0.6 percent for children under six months of age, 0.3 percent for children between six and 11 months of age, less than 0.1 percent for children between one and four years and 0.2 percent for those five to nine years of age.¹⁸

Mortality due to pertussis, diphtheria and measles started to decline in industrialised countries prior to the introduction of mass immunisation, indicating that the initial decline in mortality was due to a reduction in the case fatality rate. In 1951 Gordon argued that the principal reason for the decline in the case fatality rate
was ‘an absolute and proportional reduction in physically substandard children’\textsuperscript{19}.
This improvement in the general standard of health of children was due to a number of factors, including better nutrition, decreasing size of families and a decrease in birth rates during the Great Depression.

That immunisation made some contribution to the reduction in pertussis mortality was demonstrated in a review of the infant pertussis death rate in the US from 1900 to 1974. Had the decline in mortality from pertussis continued at the same rate as it was from 1900 to 1939, there would have been 8000 deaths from pertussis in the US between 1970 and 1974 rather than the 52 deaths that occurred\textsuperscript{20}.

However, pertussis deaths are under reported. It has been estimated that during the 1980s and 1990s the actual number of deaths from pertussis in the US and the United Kingdom (UK) was three to five times greater than the reported number of deaths\textsuperscript{21,22,23}.

Infants continue to die from pertussis. Death occurs despite state of the art intensive care\textsuperscript{24,25,26,27}. In the US the number of infant deaths from pertussis increased in the 1990s compared with the 1980s, mainly due to an increase in the number of deaths of infants less than four months old\textsuperscript{28}.

**Pertussis morbidity**

The majority of national epidemiological data on pertussis is collected via passive notification systems. Estimates of the proportion of pertussis cases that are notified vary between 6 percent and 25 percent. As well as underestimating disease incidence, passive notification systems are biased: a larger proportion of more clinically severe cases are notified and the proportion of cases that are notified decreases with increasing age\textsuperscript{29}. The proportion of those hospitalised with pertussis who are notified has been estimated to be 23 percent\textsuperscript{30}.

Prior to mass immunisation, pertussis incidence was not decreasing. The introduction of mass immunisation was associated with a 5-to-100-fold reduction in pertussis incidence in Canada, England and Wales and the US between 1930 and 1980\textsuperscript{31,32,33}. Countries with consistently low pertussis incidence rates have had consistently high immunisation coverage rates (eg, Hungary and the former East Germany)\textsuperscript{34,35}.

The higher incidence of pertussis in Canada compared with the US during the 1980s and 1990s was associated with the lower efficacy of the pertussis vaccine used in Canada\textsuperscript{36}. Countries that have experienced large increases in pertussis incidence in association with reductions in vaccine coverage include the UK, Sweden and Japan\textsuperscript{37,38,39,40,41}.

The decrease in incidence following the introduction of mass immunisation has been most pronounced in those aged under 10 years. Despite this, the reported pertussis disease rates have remained highest in infants and young children\textsuperscript{42,43,44}. In the birth
to four years age group the majority of disease occurs in those under one year of age, and a large proportion of cases in these infants now occurs in the first three months of life.\textsuperscript{45,46}

The epidemiology of pertussis varies with age. Epidemic disease in young children occurs every three to four years, and the periodicity of these epidemics is unchanged by mass immunisation. Fully vaccinated individuals suffer less severe disease. Pertussis remains an endemic disease in adolescents and adults, with studies showing between 12 and 32 percent of adolescents and adults with persistent cough have evidence of recent \textit{B. pertussis} infection (see section 6.2). This suggests that an adolescent and adult immunisation programme may decrease the circulation of \textit{B. pertussis} in these age groups.\textsuperscript{47}

\textbf{New Zealand epidemiology}

\textit{Pertussis mortality in New Zealand}

The estimated pertussis case fatality rate in New Zealand for the period 1970 to 1992 was 0.4 percent.\textsuperscript{48} This is comparable to reported case fatality rates from the UK and the US over a similar period.\textsuperscript{49,50,51,52,53} There were no deaths from pertussis in New Zealand between 1988 and 1995, one death in 1996, and since 1999 there has been one death each year up to 2004.

\textit{Pertussis morbidity in New Zealand}

Pertussis morbidity in New Zealand has been described primarily using hospital discharge data. National passive surveillance data has been available since 1996, when pertussis became a notifiable disease. Comparison of notification and hospitalisation data from 1996 and 1997 demonstrates that fewer than 50 percent of hospitalised cases are notified.\textsuperscript{54}

The three to four year periodicity of pertussis epidemics in New Zealand is similar to that seen in many other countries.\textsuperscript{55} The pertussis hospital discharge and notification data are shown in Figure 6.1. It is apparent from this figure that the decrease in the pertussis hospitalisation rate that occurred following the introduction of mass immunisation has not been sustained.
National notification data was used to describe the epidemics in 1995–97, 1999–2001 and 2004/05. The rate of notified pertussis in 1996/97 was 19.8 per 100,000, and 82 percent of the cases notified were 15 months of age or older. In these epidemics the notification rate was highest in those less than one year of age.

During the epidemic of pertussis from 1999 to 2001 there were 6523 cases notified to medical officers of health: 1046 cases notified in 1999, 4140 in 2000 and 1334 in 2001. The number of notified cases remained high in 2002, when 1068 cases were notified. In 2000, of the 4140 cases notified, 1979 (48 percent) were laboratory confirmed. The population rates for notified cases were 28.9 per 100,000 in 1999 and 114.6 per 100,000 in 2000. The rate was highest in infants under one year of age (773 per 100,000) in 2000, followed by children five to nine years of age (430 per 100,000) and children one to four years of age (398 per 100,000).56

The most recent epidemic of pertussis started in April/May 2004 and continued into 2005. In 200457 there were 3489 cases of pertussis notified, a population rate of 93.4 cases per 100,000, and of these 1085 (31 percent) were laboratory confirmed. The highest rates of disease were reported from the South Island, except on the West Coast, and the rate was especially high in Southland, with a rate of 592 per 100,000. In the North Island, Waikato had high rates of disease. From the notification data in 2004, a total of 159 cases were hospitalised (3.4 percent).
The highest rates of disease were in infants less than one year of age, with a rate of 327.5 per 100,000, although rates were high up to age 19 years. There were also many cases reported in adults (see Figure 6.2 below). Among the notified cases, the population rates were higher in those of European ethnicity with a rate of 105 per 100,000, compared with 64 per 100,000 in Māori, 33 per 100,000 in Pacific peoples and 48 per 100,000 in those of ‘Other’ ethnicity. However, the highest rate of all groups was in Pacific infants under the age of one year, with a rate of 428 per 100,000. The hospitalisation rates were higher in Māori and Pacific infants during 2004.58

An Auckland study of infants found that delayed immunisation in infancy is a risk factor for infants being hospitalised with pertussis.59

Figure 6.2: Age specific rates of pertussis notifications during epidemics in 2000 and 2004

![Chart showing age specific rates of pertussis notifications during epidemics in 2000 and 2004.](chart)

From Figure 6.2, although it is still too early to be sure, it does seem that the change of immunisation schedule in 2002 to include a dose at age four years has improved protection, and decreased disease in children age five to nine years in the current epidemic.

History of the New Zealand Immunisation Schedule

The monovalent pertussis vaccine was introduced by the Department of Health in 1945, and from 1953 was also available combined with the diphtheria vaccine. Routine childhood immunisation started in 1960, using the plain (ie, no adjuvant, not adsorbed) diphtheria tetanus and pertussis (DTwP) triple vaccine. Three doses were given at three, four and five months of age.
In 1971 the policy was altered to two doses of adsorbed triple vaccine given at three and five months of age. It was believed efficacy would be unaltered and the risk of serious reactions would be reduced. Following this schedule change there was a progressive increase in hospitalisations in 1974, 1978 and 1982. Review of the increase in hospitalisations led to the addition, in 1984, of a third dose of DTwP, given at six weeks of age, to provide earlier protection. The pertussis component used in New Zealand was a whole cell vaccine. From 1994 this was administered as a quadrivalent vaccine with diphtheria and tetanus toxoids and conjugate Haemophilus influenzae type b (DTwPH).

A fourth dose of pertussis vaccine was added in 1996 (as DTwPH vaccine) given at 15 months of age, with the goals of increasing protection in young children and reducing risk of transmission to younger siblings.\(^\text{60}\)

Acellular pertussis vaccine was introduced in August 2000, and diphtheria, tetanus and acellular pertussis (DTaP) and DTaP/Hib replaced the whole cell pertussis vaccines. In February 2002 the vaccine given at age six weeks, and at three and five months, was changed to DTaP with inactivated polio vaccine (DTaP-IPV), and a booster dose of DTaP-IPV was introduced and given at four years of age to protect children during the early school years and to decrease transmission of the infection to younger children.

In 2006 the timing of the pertussis schedule was changed so that, following the three doses of a pertussis containing vaccine in the first year of life, boosters will be given at ages four years and 11 years. The vaccine to be given at age 11 years is formulated with an adult dose of pertussis vaccine combined with tetanus, diphtheria and inactivated polio vaccine. This dose will improve protection in young adults. Note: A diphtheria, tetanus and pertussis vaccine is no longer administered at 15 months. Monovalent Hib and MMR vaccines are now given at age 15 months.

**Immunisation coverage in New Zealand**

The information available on immunisation coverage indicates that from the 1970s to the 1990s between 70 and 90 percent of children have received the complete series of the pertussis vaccine as prescribed by the National Immunisation Schedule. The 1991/92 national and the 1996 northern regional immunisation surveys indicated that 80–90 percent of children received the three dose primary series, but that only 50–60 percent of children completed the series within one month of the due date.\(^\text{61,62}\) A case control study performed in Auckland during the 1995–97 epidemic found that delay in receipt of any of the three infant doses of pertussis vaccine was associated with a five-fold increase in risk of hospitalisation with pertussis.\(^\text{63}\) The analysis of the 2005 National Immunisation Coverage Survey shows that the overall immunisation coverage for the first three doses of pertussis vaccine during the first year of life is 89 percent, and that of these, only 52 percent received the third dose of DTaP-IPV on time, within four weeks of the due date (see also the Introduction). There has been only a small increase in immunisation coverage rates over the past 25 years.
Comparison of pertussis incidence rates and immunisation coverage rates from a number of countries demonstrates that immunisation coverage rates of 80–90 percent reduce pertussis notifications to a level approximately one tenth of that before pertussis immunisation was introduced. Immunisation coverage rates of approximately 95 percent reduce pertussis notifications to a level approximately one hundredth of that before pertussis immunisation was introduced. For the burden of disease caused by *B. pertussis* infection in New Zealand to be decreased, immunisation coverage and on time immunisation need to increase significantly.

**Reducing the size of future pertussis epidemics**

The strategies to reduce the size of future pertussis epidemics include ensuring high immunisation coverage and on time immunisation, extending the duration of protection through either improved vaccines or a change in schedule, and offering pertussis vaccine to other population groups (eg, adolescents or adults). The current acellular pertussis vaccine used in New Zealand is around 84 percent effective (95 percent confidence interval [CI] 76–90 percent) in the first two years of life. Subsequent surveillance of the original study population demonstrated sustained efficacy through to six years.

The goal of the current pertussis immunisation schedule is to reduce disease in those most vulnerable to severe disease; that is, infants in the first year of life. Even in countries with high immunisation coverage with pertussis vaccines, cases of pertussis continue to occur and the number and proportion of cases in young children appears to be increasing. As a result, there is growing interest in investigating how early effective immunisation may be started after birth, and whether, with the development and licensure of pertussis vaccines for adolescents and adults, pertussis disease can be reduced in adolescents and adults and thus reduce spread to vulnerable infants.

Early studies in neonates with whole cell pertussis vaccines had not shown benefit when given before one month of age. However, a recent Italian study using acellular pertussis vaccine given at age four days, followed by three, five and 11 months of age, found at age five months significantly higher proportions of the early vaccine recipients had a four-fold increase or more from baseline of anti-PT, anti-FHA (anti-filamentous haemagglutinin) and anti-PRN (anti-pertactin) antibody levels compared with control infants. These findings need confirmation from larger studies before recommendations for earlier immunisation can be made.

In 2001 an International Consensus Group on Pertussis Immunisation looked at the role for the adult type acellular pertussis vaccine in preventing pertussis in adolescents and adults. The group reviewed studies on the disease burden of pertussis in all age groups and likely sources of infection. Adults in the household, unimmunised children, older children and health care workers were reported as sources of infection for young infants. There is limited information on the economic
benefits of adult pertussis booster vaccination. The group considered the aims of the vaccination programme to be to prevent clinical disease and to indirectly protect susceptible groups in the community. Although the ideal strategy was thought to be a booster programme for all adolescents and adults, it was considered unrealistic and a targeted approach was discussed.

Groups identified for targeted programmes included:

- adolescents in schools
- adults likely to come into contact with young infants, including parents, older children and health care workers
- new mothers after giving birth
- vulnerable adults and their close contacts whose health or age predisposes them to severe pertussis disease.

However, it was concluded that more research was needed on the incidence and natural history of pertussis in the population and on the immune response in women in the postpartum period, and that individual country decisions should be based on their own epidemiology.

If pertussis epidemiology is modelled mathematically, it shows that even with three doses of pertussis vaccine in the first year, a dose in the second year of life and a booster at age four years, epidemics will continue to occur. The model shows that when pertussis vaccine is given at age 15 months and four years, the dose at 15 months adds little protection. This is because protection is expected to last six years, and is followed by gradual waning immunity. If the immunity is not boosted, either with vaccine or natural infection, the population gradually becomes increasingly susceptible to pertussis infection, and eventually an epidemic may be triggered. As can be seen from the cases reported in 2004, older children, many adolescents and adults developed pertussis, and they are known to pass the pertussis infection on to babies and infants.

A combination pertussis vaccine (see 6.4 below) has been registered for use in adolescents and adults in New Zealand. Pertussis vaccine given at age 11 years is expected to prevent outbreaks of pertussis in young adults.

The mathematical model for pertussis epidemics was run incorporating a dose of pertussis vaccine at age 11 years and dropping the dose at age 15 months. Overall population protection was somewhat improved. The mathematical model was also run simulating giving doses of pertussis vaccine to adults at age 45 and 65 years, when boosters of Td are due on the National Immunisation Schedule. The levels of protection expected in the community were improved, but because of waning immunity and gradually increasing numbers of susceptible children and adults, it was predicted that epidemics would continue to occur.
Modelling suggests that epidemics of pertussis would occur with the current vaccines even if boosters were given to adults at intervals of 10 years and coverage for all doses of pertussis vaccine was high. However, adult pertussis vaccine doses would reduce the potential reservoir of infection in the adult population. The effects of giving a birth dose of vaccine were modelled, but had little effect on the transmission of pertussis in the population. The focus for prevention and protection from pertussis must therefore continue to be on time immunisation and high coverage to all children, to protect infants as early as possible.

6.4 Vaccines

From 2006 the publicly funded acellular pertussis vaccine for the schedule is DTaP-IPV (INFANRIX™-IPV, GSK), a combination vaccine given at six weeks, three months and five months of age, and a fourth dose of DTaP-IPV at four years of age, prior to school entry. In addition, from 2006 a publicly funded combination vaccine of adult pertussis, diphtheria and tetanus, together with IPV, dTap-IPV (BOOSTRIX®-IPV, GSK), will be given at age 11 years (school year 7).

The INFANRIX™ contains diphtheria and tetanus toxoids and three purified *B. pertussis* antigens (pertussis toxoid – PT, filamentous haemagglutinin – FHA, and the 69 kilodalton outer membrane protein pertactin) adsorbed onto aluminium salts. The IPV content contains three poliovirus strains (see chapter 8: Poliomyelitis). The vaccine is formulated in saline and contains 2-phenoxyethanol as a preservative. INFANRIX™-IPV is presented as a turbid white suspension in a glass pre-filled syringe. On storage, a white deposit and clear supernatant are observed. The 0.5 mL dose contains not less than 30 IU of diphtheria toxoid, 40 IU of tetanus toxoid, 25 µg of PT, 25 µg of FHA and 8 µg of pertactin.

BOOSTRIX®-IPV contains not less than 2 IU of diphtheria toxoid, not less than 20 IU of tetanus toxoid, 8 µg of PT, 8 µg of FHA and 2.5 µg of pertactin, adsorbed into aluminium salts. The IPV content contains three poliovirus strains (see chapter 8: Poliomyelitis).

Other vaccines

Adult diphtheria, tetanus and acellular pertussis vaccine, dTap (BOOSTRIX™, GSK), is available for adult boosters but is not currently funded. Other acellular pertussis vaccines licensed for children in New Zealand include DTaP (TRIPACEL®, Aventis) and other combination vaccines, which include IPV, hepatitis B or Hib.

Efficacy of the acellular pertussis vaccine

The acellular pertussis vaccines licensed for use in New Zealand have been shown to provide 84 percent efficacy (95 percent CI 76–90), after three infant doses, with subsequent studies showing similar efficacy persisting to six years of age.\(^74,75\)

The reported efficacy in a trial of a monovalent acellular pertussis vaccine among adolescents and adults, aged 15 to 65 years, after a median of 22 months of follow
up, was reported as 92 percent (95 percent CI 32–99).\textsuperscript{26} The case definition for primary pertussis in this trial was a laboratory confirmed case of pertussis with a history of cough illness of five or more days.

**Dosage**

The dose of DTaP-IPV and dTap-IPV is 0.5 mL, given by deep intramuscular injection. (See section 2.3 for needle sites and sizes.)

### 6.5 Recommended immunisation schedule

From February 2006 the recommended immunisation schedule is for the primary course of DTaP-IPV at six weeks, three months and five months of age. A booster dose is recommended at four years of age in the combination DTaP-IPV prior to school entry, to extend the duration of protection during the school years.

A further booster is given at age 11 years (school year 7) as dTap-IPV. The dTap-IPV vaccine will be given to children aged 11 years in 2006/07 because these children have not received four doses of polio vaccine. After this it is expected dTap will be given. The addition of pertussis antigen to the tetanus-diphtheria schedule at age 11 is expected to protect adolescents and young adults. If coverage is sufficient, this will reduce pertussis disease in this age group. IPV will continue to be given until the end of 2007, when all children would be expected to have received four doses of polio vaccine (see chapter 8).

*Dose intervals for the primary series:* the minimum interval between doses is four weeks, and the first dose should not be given before four weeks of age.

As at 2006, dTap and dTap-IPV are licensed for distribution for booster doses only. However, there are expected to be no safety concerns to giving three doses of dTap-IPV to previously unimmunised older children and adults. Therefore, using dTap should be considered for all catch up and adult schedules for primary and booster immunisation.

**Dose intervals between Td and dTap-IPV**

It is recommended that for students who have recently received a tetanus diphtheria (Td) vaccine booster, eg, at the time of an injury, the age 11 (year 7), dTap-IPV immunisation should be delayed until two years after the dose of Td, and offered before the student reaches the age of 16 years. Students who would normally receive the year 7 event at school should be referred to their general practitioner for follow up and recall.

**Other recommendations**

A booster of acellular pertussis containing vaccine is recommended, but not funded, for adults in the following occupations:

- health care workers working on paediatric wards, and in neonatal units
- adults in any occupation involving the care or education of infants and young children.
Recommendations for subsequent boosters will be made when further information is available.

6.6 Expected responses and adverse events following immunisation (AEFI)

Unless the specific contraindications and precautions outlined in section 6.7 are present, practitioners should have no hesitation in advising the administration of acellular pertussis vaccine. There is no convincing evidence that the pertussis vaccine can cause permanent neurological damage or disease (see section 20.2: f ii). Disorders for which any causal association with pertussis vaccine have been disproved include infantile spasms, hypsarrhythmia, Reye’s syndrome and sudden infant death syndrome (SIDS). The New Zealand Cot Death Study also found a lower rate of SIDS in immunised children.

Expected responses associated with pertussis vaccines

The acellular pertussis vaccines cause significantly fewer reactions than the previously used whole cell vaccines. Up to one third of infants will have redness at the site of the injection and 20 percent will develop a mild fever after a dose of acellular pertussis vaccine (see Table 6.1). As with the whole cell vaccine, the frequency of local reactions tends to increase with the number of doses administered.

Table 6.1: Percentage of mild to moderate reactions within 24 hours following a dose of acellular DTaP

<table>
<thead>
<tr>
<th>Adverse reactions</th>
<th>Acellular vaccines*</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Range</td>
</tr>
<tr>
<td>Redness 1–20 mm</td>
<td>15.1–44.0</td>
</tr>
<tr>
<td>Redness &gt; 20 mm</td>
<td>1.4–5.9</td>
</tr>
<tr>
<td>Oedema 1–20 mm</td>
<td>7.5–28.6</td>
</tr>
<tr>
<td>Oedema &gt; 20 mm</td>
<td>0.8–8.0</td>
</tr>
<tr>
<td>Pain</td>
<td>1.6–13.2</td>
</tr>
<tr>
<td>Temperature 37.8°C–38.3°C</td>
<td>16.0–29.2</td>
</tr>
<tr>
<td>Temperature &gt; 38.3°C</td>
<td>1.6–5.9</td>
</tr>
<tr>
<td>Irritation</td>
<td>12.0–24.4</td>
</tr>
<tr>
<td>Drowsiness</td>
<td>29.4–52.2</td>
</tr>
<tr>
<td>Loss of appetite</td>
<td>17.7–27.2</td>
</tr>
<tr>
<td>Vomiting</td>
<td>7.4–21.6</td>
</tr>
</tbody>
</table>

* There are 13 different acellular pertussis vaccines.

Update on expected responses following four or five doses of a DTaP containing vaccine

There is an increase in frequency of local reactions with increasing doses of a DTaP containing vaccine, although the number of reactions overall is not increased compared with a whole cell vaccine. Extensive limb swelling has been reported in some children following a fourth dose and/or a fifth dose of DTaP vaccine. The cause of this reaction is unknown but may be due to either or both the diphtheria or pertussis components of the vaccine. Pain is not usually prominent with this reaction and no treatment is necessary. Extensive limb swelling is defined as swelling extending from the injection site beyond one or both joints, or swelling of the entire proximal limb from joint to joint.

Children who suffer large swelling (over 50 mm) after a fourth dose of DTaP vaccine are more likely to have a reaction after the fifth dose, but neither the large reaction nor extensive limb swelling is considered to be a contraindication to a subsequent dose. No treatment is necessary, but parents should be advised of the risk.

Studies on reactions after four or five doses of acellular pertussis vaccine

The rates of large swelling, defined as > 50 mm, following DTaP vaccine have been reported as varying between 1.6 and 10 percent after the fourth dose, and between 8.3 and 27.3 percent after the fifth dose of the same vaccine. Of the children with entire thigh swelling, 60 percent had local pain and 60 percent had erythema. There were no differences in the proportion with fever when those children with entire limb swelling were compared with those without such swelling. In this study of 12 acellular vaccines and one whole cell vaccine, the rate of entire thigh swelling seemed to be correlated with the diphtheria toxoid content of the vaccine.

In a study from South Australia, the rate of local reactions reported to the South Australia Immunisation Coordination Unit was 171 per 100,000 administered doses of DTaP vaccine after the fourth dose, compared with 12 per 100,000 reactions after the third dose. Practitioners were asked to report all severe and unexpected reactions, and details were collected on 45 of 71 infants reported with a reaction after the fourth dose of DTaP vaccine. After the fourth dose, swelling and redness occurred 0–72 hours post-injection (median 19.3 hours), and the swelling lasted for a median duration of 77 hours (range 24 to more than 168 hours), with complete recovery in all children reported by the author. Eight (18 percent) of the 45 children followed up had extensive limb swelling, a rate of 19.3 per 100,000 administered doses.

Large limb swelling after immunisation was reported from the US Vaccine Adverse Event Reporting System in 2003. Reports to the system of whole limb swelling after immunisation from 1990 to 16 January 2003 were examined, over which time approximately two billion vaccine doses were distributed; 497 cases were identified, with 418 of these involving a single vaccine administered in the affected limb. Swelling involved the proximal limb, that is the area around the injection site in
67 percent, more than proximal limb in 16 percent and the whole limb in 17 percent. These reactions were reported in association with 23 different vaccine types in people ranging in age from 0.1 to 91 years. The most common vaccines with which limb swelling was reported were polyvalent pneumococcal vaccine, DTaP, Td, DTwP and influenza vaccine. Among patients seven years of age and under, entire limb swelling was more likely to occur after a higher number of doses of DTwP and DTaP. It was reported more commonly after the fourth (33 percent of 67 reports) and fifth (31 percent) doses of DTaP than after the first (10 percent), second (12 percent) or third (3 percent).\textsuperscript{90}

**Adverse events associated with pertussis vaccines**

The incidence of major adverse events following acellular pertussis vaccine (INFANRIX\textsuperscript{TM}) is summarised in Table 6.2 below.

**Table 6.2: Incidence (per 100,000 doses) of major adverse reaction following acellular pertussis vaccine**

<table>
<thead>
<tr>
<th>Event following immunisation</th>
<th>Timing</th>
<th>Incidence per 100,000 doses</th>
</tr>
</thead>
<tbody>
<tr>
<td>Persistent (&gt; 3 hours)</td>
<td>0–24 hours</td>
<td>44</td>
</tr>
<tr>
<td>inconsolable screaming</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Seizures</td>
<td>0–2 days</td>
<td>7</td>
</tr>
<tr>
<td>Hypotonic, hyporesponsive</td>
<td>0–24 hours</td>
<td>Nil in trial (7 to 26 per 100,000 in trials of other acellular vaccines)</td>
</tr>
<tr>
<td>episode (HHE)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Anaphylaxis</td>
<td>0–1 hour</td>
<td>Very rare</td>
</tr>
</tbody>
</table>


**Expected responses and adverse events after adult pertussis vaccine**

An enhanced surveillance programme for vaccine associated adverse events was reported following a catch up dTap programme in 417 high school students in Yukon, Canada.\textsuperscript{91} The grade 12 students who took part in the study had received a dose of tetanus, diphtheria and inactivated polio vaccine in grade 9. It has been suggested that rates of local reactions increase with increasing number of doses of tetanus vaccine. In this study, the rate of reactions in students who had received their last dose of tetanus toxoid three to less than five years previously were compared with those in students who received the tetanus toxoid five or more years previously. Students who received the tetanus toxoid three to less than five years previously were more likely to report pain at the injection site than those who had received a dose five or more years before: 69 percent compared with 57 percent (Odds Ratio 1.72, 95 percent CI 0.96–3.1). Students who received tetanus toxoid three to five years before were less likely to report swelling at the injection site (3 percent compared with 13 percent), limitation of movement (27 percent compared with 47 percent), headaches (3 percent and 11 percent), body ache (1 percent and 9 percent), or sore joints (3 percent and 14 percent).
Severe events were defined as absence from school with symptoms related to vaccination, and one or more of the following: erythema or swelling $> 46$ mm, fever over 38.3°C and/or medical attention sought. Only 1 percent of those receiving toxoid three to less than five years ago had such a reaction, compared with 6 percent of those whose toxoid vaccination had been more than five years previously. The difference in rate of severe reactions between the two groups was not significant.

**Evaluation of serious adverse events temporally associated with pertussis immunisation**

All children who have a serious adverse event should be investigated with appropriate diagnostic tests to establish the cause. The adverse event may be unrelated to the vaccine. 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 http://carm.otago.ac.nz. If the patient or parent/caregiver does not consent to being identified, the report should be made without personal identification.

### 6.7 Contraindications and precautions

See section 1.9 for general contraindications for all vaccines.

Contraindications to pertussis vaccine have been overstated in the past. The only contraindication now accepted is severe reaction following a previous dose of pertussis vaccine (ie, immediate severe anaphylactic reaction to the vaccine, or any component of the vaccine), or an encephalopathy within seven days. Those with an evolving neurological disorder should not be immunised until stabilised (eg, uncontrolled epilepsy or deteriorating neurological state).

Before administering each dose of pertussis vaccine, the child’s parent/caregiver should be asked about possible adverse events following the previous dose. Unless the child suffered a contraindication as above, the pertussis vaccine may be given.

**Studies of reactions following pertussis vaccine**

A small follow up study found that neither convulsions nor hypotonic, hyporesponsive episodes (HHE) were associated with long term consequences.92 Other follow up studies of children with HHE,93 or convulsions following vaccination,94,95 have not identified any long term problems in these children when compared with children with febrile seizures not associated with vaccination. Children who have febrile seizures after pertussis immunisation do not have an increased risk of subsequent seizures or neurodevelopmental disability.96 A Dutch study of 101 children with HHE after pertussis vaccination found that the 84 children who completed the course of pertussis vaccination did not have another HHE or other adverse event.97 However, in another study, a child did have a second episode of HHE when given another dose of vaccine.98 The safety of further pertussis immunisations after an HHE has also been shown in Australia.99
When pertussis vaccine is genuinely contraindicated, DT, monovalent Hib and IPV vaccines should be offered instead.

### 6.8 Control measures

All cases of pertussis should be notified immediately on suspicion to the local medical officer of health. When the diagnosis of pertussis is suspected, all cases should have a laboratory test for confirmation of the diagnosis, as described below.

Consider the diagnosis of pertussis and the need for a nasopharyngeal swab in adults who present with a cough illness when there is a child under the age of one year living in the same household, particularly if the child is unimmunised.

**Laboratory diagnosis of *Bordetella pertussis* infection**

Pertussis can be diagnosed by direct detection of the *B. pertussis* in nasopharyngeal samples (a throat swab may be acceptable for testing although nasopharyngeal swab is preferable) by culture or PCR (polymerase chain reaction), or by serological methods. PCR is more sensitive than culture and is the preferred method for diagnosing pertussis early in the course of the illness.

Serology is particularly useful when symptoms have been present for several weeks, at a time when PCR and culture are likely to be negative. A variety of *B. pertussis* antibody tests are available, but only the detection of antibodies to pertussis toxin is specific for *B. pertussis* infection. Assays that detect antibodies to other antigens (eg, whole cell lysates) may be positive for infections due to other bacteria, such as *H. influenzae*.

Immunisation cannot be used to control an outbreak because a course of at least three doses of pertussis antigen (DTaP) may be required to induce protective immunity. However, individual immunisation status should be checked and immunisation completed. Infants as young as four weeks of age can commence immunisation.

A number of antibiotics are available for treatment and prophylaxis of pertussis. There are clinical trials to support the use of erythromycin, clarithromycin and azithromycin. Only erythromycin is fully funded in New Zealand, but it is associated with a wide range of side effects. Two weeks’ therapy with erythromycin was originally recommended, but recent data suggests that one week of erythromycin estolate is as effective, and much better tolerated.\(^{100}\) The newer macrolides probably have fewer gastrointestinal side effects. All antibiotics need to be started early, within 21 days of onset of cough, to have any appreciable impact on the duration of illness. Alternative antibiotics with *in vitro* or limited *in vivo* data to support their use include cotrimoxazole (960 mg bd for adults), roxithromycin, doxycycline and fluoroquinolones.\(^{101}\)

Erythromycin has been shown to reduce the duration of time a person with pertussis is culture positive, but has not been shown to significantly alter the course of the
illness. There is some evidence that 14 days of oral erythromycin (40 to 50 mg/kg per day in divided doses, with a maximum of 2 g per day) may prevent pertussis from developing in close contacts (a seven-day course of erythromycin estolate may be used). Estolate may be more effective at eliminating carriage. There have been no studies of the effectiveness of seven days of erythromycin succinate therapy. In order to prevent the spread of pertussis in households, chemoprophylaxis with erythromycin must be started before a second person has started coughing and no later than 21 days after the first person with pertussis started coughing.  

The antibiotic with the greatest clinical evidence is erythromycin in full dose for two weeks, although there is data supporting the use of azithromycin. An association has been reported between orally administered erythromycin and infantile hypertrophic pyloric stenosis (IHPS) in infants younger than two weeks of age. The risk of IHPS with other macrolides is unknown. Because the risk of severe illness in neonates is high, it is recommended that erythromycin continue to be used in neonates for the prophylaxis and treatment of pertussis. Parents should be warned of the risk and signs of IHPS, and to report any concerns.

Those most at risk from pertussis are infants under one year of age. In households where a patient has pertussis and an infant less than one year of age resides, chemoprophylaxis should be offered to everyone in the household, especially if the infant has not received three doses of pertussis vaccine. This does not apply if the only infant in the household is the index case. Individuals in a household with a woman in the late stages of pregnancy should also be offered prophylaxis because of the risk of severe pertussis in the neonate. In early childhood services with infants under one year of age, prophylaxis may be considered for children who are in close contact, such as while sleeping at the centre.

Cases should be excluded from early childhood services, school, or community gatherings until:

- they are well enough to attend, and

- either they have received five days of antibiotics, or three weeks have elapsed since the onset of the coughing paroxysms (at which point they are unlikely to be infectious).

Children who have culture proven pertussis disease should complete their immunisation series with all of the scheduled doses recommended for their age. Inadequately immunised household contacts may be infectious during the prodromal stage of the illness and therefore should avoid contact with young children for up to two weeks following exposure. If household contacts receive a course of erythromycin, as described above, this period may be reduced to five days.

For more details on control measures, refer to Control of Communicable Diseases Manual.
References


7  **Haemophilus influenzae** type b (Hib)

7.1 Introduction

*Haemophilus influenzae*, first described by Pfeiffer in 1889, is a gram negative coccobacillus, which occurs in encapsulated (typeable) and non-encapsulated (untypeable) forms. There are six antigenically distinct capsular types (a–f), type b being the most important.

7.2 The illness

Before the introduction of the vaccine, *H. influenzae* type b (Hib) caused 95 percent of *H. influenzae* invasive disease in infants and children. Hib causes meningitis, pneumonia, epiglottitis, septic arthritis, bacteraemia, cellulitis, and empyema in infants and young children, particularly under the age of two years but up to four years. The incubation period of the disease is unknown, probably from two to four days.

Prior to immunisation, the two most common presentations of Hib invasive disease in New Zealand were meningitis and epiglottitis. Meningitis tends to occur in younger children between three months and three years of age, while epiglottitis usually occurs in children between two and four years of age. The common signs of meningitis include fever, irritability or lethargy, refusing feeds and neck stiffness, although in the young child the signs can be very vague and non-specific. The strongest lead to the diagnosis of Hib invasive disease may be an ominous deterioration in a child who has been a little unwell with a respiratory tract infection for a day or two.

The onset of epiglottitis is rapid, with initial features of fever and dyspnoea, progressing to dysphagia, pooling of oral secretions and drooling of saliva. The child characteristically adopts a sitting posture with the neck extended and the tongue protruding to reduce airway obstruction.

Non-encapsulated *H. influenzae* organisms usually cause mucosal non-invasive infections, such as otitis media, sinusitis and bronchitis, and occasionally are the cause of neonatal infections. Non-encapsulated strains are frequently present (60–90 percent) in the normal upper respiratory tract flora. In contrast, Hib was found in 2–5 percent of asymptomatic children in the pre-vaccine era. Immunisation against Hib will not protect against infections due to other *H. influenzae* types or untypeable strains.

Young infants (under two years of age) with Hib invasive disease do not produce an antibody response and are therefore still susceptible. They should be given a course of Hib vaccine when recovered (see section 7.5).

*H. influenzae* type b and untypeable strains also cause diseases, including pneumonia and sepsicaemia, in the elderly.
7.3 Epidemiology

The source of the organism is the upper respiratory tract, and transmission is by direct contact and by respiratory spread from secretions containing the Hib organism. Immunisation with a protein conjugate vaccine reduces the frequency of asymptomatic colonisation by Hib. Before the introduction of the vaccine, Hib was the most common cause of bacterial meningitis in children.

Hib vaccine is now on the schedule in most developed countries, but is not yet routinely on the World Health Organization (WHO) Expanded Programme of Immunization. Hib vaccine is not on the immunisation schedule in most Pacific Islands, but Tokelau started Hib immunisation in 2005.

In the United Kingdom (UK), Hib immunisation started in 1992 for infants, plus a catch-up for older children. Hib vaccine was given at two, three and four months of age, with no booster in the second year. In 2002 there was an increase in Hib cases reported in children born in 2000 to 2001 compared with children born during 1992–1999. Investigation showed that cases were more frequent, and the risk increased after each dose, in infants who had received DTaP-Hib vaccine (diphtheria, tetanus, acellular pertussis and Hib) instead of the usual DTwP-Hib vaccine (diphtheria, tetanus, whole cell pertussis, and Hib) following a vaccine shortage.¹

A national catch-up of a fourth dose of Hib was given to all UK children aged six months to four years in 2003. Results of Hib surveillance following the catch-up showed there were six reported cases of Hib disease in 2004 in children aged one to four years, compared with 46 cases in 2003.² Surveillance will continue and further consideration will be given to a booster dose. It was thought the increase in cases was the result of giving the Hib vaccine schedule at two, three and four months without a booster, and the change of vaccine to DTaP-Hib, which induces lower antibody titres than the whole cell DTwP-Hib.

New Zealand epidemiology

In 1993, 101 isolates of Hib from children under five years of age with invasive disease were referred to the Institute of Environmental Science and Research (ESR). This equates to an age specific rate of 36.4 per 100,000, which can be compared with five isolates referred in 1999 for a rate of 1.7 per 100,000 (see Figure 7.1). Since the introduction of Hib vaccine in January 1994 there has been a greater than 90 percent reduction in the incidence of Hib disease in children less than five years of age. However, the reduction of Hib incidence in New Zealand has not been as great as in those countries where immunisation coverage is higher.
Before immunisation was available in New Zealand, Hib was the commonest cause of life threatening bacterial infection, usually meningitis, in children under five years of age.\(^3\) Approximately one in every 350 New Zealand children developed an invasive Hib infection by that age. The peak occurrence of invasive disease in New Zealand was between six and 11 months of age. Despite the availability of antibiotics and medical care, the case fatality rate remains up to 5 percent, and survivors of Hib meningitis have a 30–40 percent risk of long term neurological developmental impairment. In the pre-vaccine era, Māori and Pacific children had higher rates of Hib infection, especially meningitis, and presented at a younger age. More than 25 percent of Hib meningitis in Māori and Pacific children occurred before the age of six months, and 80 percent by 18 months. Overcrowding and early exposure to the disease were seen as contributing factors. European children were more likely to be affected at an older age and to suffer from epiglottitis.

The conjugate Hib vaccine protects against disease and reduces nasopharyngeal carriage. Vaccinating around 80 percent of children under five years of age results in the virtual disappearance of the disease. Analysis of the cases of invasive Hib disease from 1995 to 1999 showed that 43 cases were in children less than five years of age, and that of these, 12 cases were babies under five and a half months of age; 14 children were not fully vaccinated for their age, and nine cases occurred in children who were fully immunised.\(^4\) The New Zealand epidemiology suggested that early protection was important and supported the change to a Hib-OMP (outer
membrane protein) vaccine, which provides protection after one dose (see also the discussion in section 7.4).

In 2000 there were seven laboratory confirmed cases of Hib reported in children under the age of five years, followed by six cases in 2001 and zero cases in 2002. Of the cases in 2000 and 2001, 11 out of 13 children had either received no Hib immunisation or were incompletely immunised for their age. The other two children, aged four months and four years, had both received Hib immunisation appropriate for their age.

In 2003 there were seven laboratory confirmed cases of Hib in children under the age of five years. The children’s ages ranged from two to 14 months. Four infants were of European ethnicity, one was Māori, one Pacific and the ethnicity of one child was not reported. Three of the four infants with Hib infection under the age of one year were not up to date with their immunisations, one baby of two months had not received Hib vaccine, and two infants aged five to 11 months had both received only one dose of Hib vaccine. The immunisation history on the fourth infant under one year of age was not known. There were two infants aged 12 months who had both received the scheduled two doses of vaccine, and one child aged 14 months whose immunisation history was uncertain. In 2004 there were two laboratory confirmed cases of Hib in children, both over the age of one year. One child had received no Hib vaccine and the other the first two doses.

Of the small numbers of children who have developed Hib infection in New Zealand since the change in schedule in 2000, most were incompletely vaccinated for their age.

It is important to continue to monitor the epidemiology of Hib to provide the optimum schedule for protecting children. However, at the present time improving coverage and providing immunisation on time are the most important factors.

History of the New Zealand Immunisation Schedule

Hib vaccine was added to the National Immunisation Schedule in January 1994, with diphtheria, tetanus, whole cell pertussis and Hib (DTwPH) vaccine replacing the diphtheria, tetanus and whole cell pertussis (DTwP) vaccine given at six weeks, three months and five months of age. A monovalent Hib vaccine was given at 18 months of age, and a catch-up programme of a single dose of monovalent Hib vaccine was recommended for all children under the age of five years (ie, those born from January 1989).

From February 1996 the fourth dose was changed to 15 months of age and given as DTwPH to reduce the two immunisation events in the second year to one at 15 months of age.

In August 2000, because of the unavailability of DTwPH, the planned change to acellular pertussis vaccine was brought forward. The vaccines introduced were
diphtheria, tetanus, and acellular pertussis vaccine (DTaP) at six weeks, three months and five months, plus the combination vaccine Hib and hepatitis B (Hib-Hepatitis B) at six weeks and three months and the monovalent hepatitis B vaccine at five months. DTaP/Hib vaccine replaced the DTwPH at 15 months. The PRP-OMP (polyribosylribitol phosphate outer membrane protein) component of the Hib-Hepatitis B combined vaccine requires only two doses in the first six months of life followed by a booster in the second year. PRP-OMP induces a significant immune response and protection after a single dose as early as six weeks.4

In 2006 the Hib schedule continues as two doses of Hib-Hepatitis B at the age of six weeks and three months, and a booster of Hib vaccine at age 15 months. There is no longer a dose of DTaP given at age 15 months, and therefore the Hib vaccine given at age 15 months is a single antigen Hib-PRP-T vaccine (see below).

7.4 Vaccines

The best way to control Hib disease, with the aim of elimination, is immunisation because of the increasing resistance to antimicrobial agents and continuing morbidity and mortality despite treatment.

Antibodies to PRP (polyribosylribitol phosphate), a component of the polysaccharide cell capsule of Hib, are protective against invasive Hib disease. The first generation Hib vaccine was an unconjugated vaccine and was not used in New Zealand. This polysaccharide Hib-PRP vaccine was poorly immunogenic in children under two years of age, who do not mount a T-cell dependent immune response to polysaccharides. The T-cell dependent antibody response is poor until about two years of age and does not induce immunological memory. To induce a T-cell dependent immune response, the PRP polysaccharide has been linked to a variety of protein carriers. These conjugate Hib vaccines are more immunogenic and effective in young infants. The protein carriers used are either a mutant diphtheria toxin (Hb-OC Hib vaccine), or an outer membrane protein of Neisseria meningitidis (PRP-OMP Hib vaccine) or tetanus toxoid (PRP-T Hib vaccine). It should be noted that the protein conjugates used in Hib vaccines are not themselves immunogenic and do not give protection against diphtheria, tetanus or N. meningitidis.

The current vaccines available for use in New Zealand are as follows.

1 PRP-OMP (given as the combination vaccine Hib-Hepatitis B, COMVAX®, MSD) – two doses are given, at six weeks and three months of age. This vaccine has been found to be protective, with good immunogenicity when two doses are given to infants from two months of age with a booster at 12 months. One dose of this vaccine offers protection to a substantial percentage of infants at risk of Hib invasive disease.

2 PRP-T – one booster dose is given at 15 months. The vaccine is the monovalent Hib vaccine (Hib-PRP-T, Hiberix™, GSK).
The other protein conjugate Hib vaccine licensed for distribution, but not marketed, in New Zealand is Hb-OC (HibTITER, Wyeth). HbOC has been found to be protective with good immunogenicity when three doses are given in the first six months of life and a booster at 15 months of age. This vaccine had an efficacy of 100 percent in one study, with no Hib disease in those who had received at least two doses.\(^6\) The vaccine was mostly given as the combination vaccine DTwPH (TETRAMUNE\(^\circledR\)), which is no longer available.

With all of these vaccines, it is recommended that a booster dose be given in the second year of life. All these vaccines can be given as a single dose for children 15 months of age and over.

**Efficacy**

A primary course of Hib-OMP at two and four months of age and a booster dose at 12 months, had an efficacy of 100 percent in 2588 Navajo children less than 15 months of age, who had received either one or two doses.\(^7\) The trial had a single failure, with a case at 15.5 months, but this was in the context of continuous exposure to the organism, as only a minority of infants were enrolled in the trial and received vaccine.\(^8\)

A study of three doses of Hib PRP-T given in the first 12 months of life to Gambian children found an efficacy of 95 percent protection against invasive Hib disease.\(^9\) Disease following a full course of Hib vaccine is rare. In the United States (US), 15 cases per year are expected in children who have completed their Hib immunisation.\(^10\)

**Dosage**

The dose of either Hib-Hepatitis B (COMVAX\(^\circledR\), MSD) or Hib (Hiberix\(^\text{TM}\), GSK) is 0.5 mL, given by intramuscular injection. (See section 2.3 for needle sites and sizes.)

### 7.5 Recommended immunisation schedule

Hib vaccine is publicly funded, as part of the National Immunisation Schedule, to all children under five years of age. Hib-OMP as Hib-Hepatitis B (COMVAX\(^\circledR\), MSD) is given at six weeks and three months of age, and a booster of Hib (Hiberix\(^\text{TM}\), GSK) is given at 15 months of age. The number of doses of Hib vaccine needed is age dependent, as described above.

For children up to the age of five years who, for whatever reason, have missed out on Hib vaccine alone in infancy, a catch-up schedule should be instituted (see Appendix 2: Immunisation Catch-up Schedules). The total number of doses of Hib vaccine required is determined by the age at which Hib immunisation commences. Where possible, the combined available vaccines should be used, but individual immunisation schedules based on the recommended national schedule may be required for children who have missed some immunisations. (See Appendix 2 for details.)
Preterm babies
All preterm babies should be given immunisation at the usual chronological age. Because it is uncertain whether very low birthweight preterm babies are able to mount an adequate response to the Hib vaccine, it is recommended that babies whose birthweight is under 1000 g or gestation is less than 29 weeks should be given Hib-Hepatitis B instead of hepatitis B vaccine, at five months of age, as well as routinely at six weeks and three months. The usual booster of Hib vaccine is given at 15 months of age. (See also section 1.8 for general recommendations, and section 3.5 on hepatitis B.)

Special groups
Because of an increased risk of infection, it is particularly important that the following groups of children, whatever their age, receive the Hib vaccine schedule as per the National Immunisation Schedule:

- children with anatomic or functional asplenia, or who are suffering from sickle cell disease (if possible, children should be immunised prior to splenectomy, see section 1.8)
- children with partial immunoglobulin deficiency, Hodgkin’s disease or following chemotherapy (note, however, that responsiveness to the vaccine in these children has not been confirmed and is likely to be sub-optimal)
- children with nephrotic syndrome
- HIV (human immunodeficiency virus) positive children.

Recommendations for Hib vaccine for older children and adults with asplenia
Although there is no strong evidence to support immunisation with Hib vaccine for asplenic older children and adults, and the vaccine dosage is not defined, some authorities recommend Hib immunisation for these individuals. The Hib PRP-T vaccine has been shown to be immunogenic in adults.

From 2006, Hib vaccine (Hiberix™) and administration is funded for older children and adults pre- or post-splenectomy; one dose of vaccine is recommended. (See also the vaccine recommendations in sections 15.5 A and C, and 16.5 A and B for information on pre- and post-splenectomy recommendations).

Children who have suffered invasive Hib disease
As described above, children under two years of age with Hib disease do not reliably produce antibodies, so these children need to receive a complete course of Hib vaccine. The number of doses required will depend on the age at which the first dose after the illness is given, ignoring any doses given before the illness (see Appendix 2). Reimmunisation should be initiated approximately one month after the onset of disease.
Any immunised child who develops Hib disease or who experiences recurrent episodes of Hib invasive disease requires consideration for immunological investigation by a paediatrician.

### 7.6 Expected responses and adverse events following immunisation (AEFI)

#### Expected responses following Hib-Hepatitis B (COMVAX®)

Clinical trials involving the administration of COMVAX® to healthy infants between six weeks and 15 months of age have shown that adverse experiences observed within a five-day period following each dose of COMVAX® were generally similar in type and frequency to those observed in infants who received concurrent injections of PRP-OMP (Hib vaccine) and H-B-Vax II® (hepatitis B vaccine) at separate sites. Other studies have also shown that rates of local injection site reactions and systemic adverse experiences in vaccinees given COMVAX® were similar to those in vaccinees given separate but concurrent injections of PRP-OMP and H-B-Vax II®. The most frequently cited events were mild, transient signs and symptoms of inflammation at the injection site, sleepiness and irritability (see manufacturer’s data sheet).

#### Expected responses following Hib (Hiberix™)

The most frequently reported reactions following Hib vaccine are local reactions in up to 32 percent of children, and a fever higher than 38°C in 5 to 10 percent.

#### Adverse events following immunisation with Hib-Hepatitis B or Hib vaccine

No serious vaccine related adverse experiences were observed during clinical trials of Hib-Hepatitis B vaccine or Hib vaccine alone. There have been rare reports, not proven to be causally related to Hib vaccine, of erythema multiforme, urticaria, seizures, and Guillain-Barré Syndrome following Hib vaccine.

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 [http://carm.otago.ac.nz](http://carm.otago.ac.nz). If the patient or parent/caregiver does not consent to being identified, the report should be made without personal identification.

### 7.7 Contraindications

In any child with a suspected contraindication to the Hib vaccine, the circumstances should be discussed with a paediatrician. (See also section 1.9 for general contraindications for all vaccines, and section 3.7 for contraindications to hepatitis B.)

Hib-Hepatitis B (COMVAX®) or Hib (Hiberix™) should not be administered to individuals:

- with known hypersensitivity or anaphylaxis to any component of the vaccine
- who develop symptoms of hypersensitivity after a previous Hib injection.
Significant hypersensitivity reactions to Hib vaccines appear to be extremely rare.

These vaccines will not protect against infection with non-encapsulated strains of *H. influenzae*, and therefore do not prevent otitis media, recurrent upper respiratory tract infections, sinusitis or bronchitis.

### 7.8 Control measures

All cases of Hib disease should be notified immediately to the local medical officer of health, who will arrange for contact tracing, immunisation and administration of prophylactic rifampicin where appropriate. All contacts should have their immunisation status assessed and updated as appropriate. Note that the prophylaxis for Hib is different from that for meningococcal disease (see chapter 15).

Immunisation reduces – but does not necessarily prevent – the acquisition and carriage of Hib. Therefore, immunised children still need rifampicin prophylaxis, when indicated, to prevent them transmitting infection to their contacts.

Careful observation of exposed household and early childhood service contacts is essential. Exposed children who develop a febrile illness should receive prompt medical evaluation.

**Rifampicin chemoprophylaxis**

The risk of invasive Hib disease among household contacts increases in those under four years of age. Asymptomatic colonisation with Hib is more frequent in household contacts of all ages than in the general population. Secondary cases are more common in the first week after diagnosis of the index case, although prophylaxis started after seven days may still be of benefit. Family members should receive prophylaxis as soon as possible, because 54 percent of secondary cases occur within one week of the index case.

Rifampicin is thought to be 95 percent efficient in clearing the carrier state. Reinfection can occur, and secondary cases have been reported in spite of prophylaxis.

*Household contacts*

Chemoprophylaxis with rifampicin is recommended for the following contacts of an index case of Hib:

- all household contacts, regardless of age, who live in a home where there is one or more children below four years of age who are either unimmunised or partially immunised
- all members of a household where there is a child younger than 12 months of age, even if the child has had two doses (primary series) of the Hib vaccine
- all members of a household where there is a child with immune suppression, regardless of whether the child is fully immunised against Hib or not.
The index case should also receive rifampicin unless treated with cefotaxime or ceftriaxone.

**Early childhood services**

The administration of rifampicin to children in early childhood services is controversial. The risk of infection is greatest if the facility caters for children less than two years of age. It is therefore recommended that chemoprophylaxis should be offered to all early childhood service people (children and teachers), regardless of the age of the children, when two or more cases of Hib invasive disease have occurred within 60 days. When a single case has occurred in an early childhood service, chemoprophylaxis is no longer recommended to attendees.

Parents of children attending an early childhood service should be advised the child should see their family doctor in the event of any febrile illness occurring within 60 days of the onset of the index case of Hib. Unimmunised or incompletely immunised children should receive Hib vaccine and have arrangements made for them to complete the course of vaccine. When rifampicin prophylaxis is given (after two cases in 60 days), children and staff should be excluded from the early childhood service until rifampicin therapy has been initiated. Children entering the group while prophylaxis is being given should also receive it.

The efficiency of rifampicin prophylaxis in early childhood services is dependent on prompt initiation of treatment and strict compliance by the children and parents/caregivers. This is best achieved through the medical officer of health, who should be notified on suspicion of any case of invasive Hib disease. It is the responsibility of the treating doctor to initiate prophylaxis in the primary case, although in practical terms the household contacts of the index case may also be treated.

**Recommendations for other groups**

Chemoprophylaxis is not recommended for:

- pregnant women
- occupants of households where there are no children under four years of age other than the index case
- occupants of households where all contacts younger than four years have completed their immunisation series.

**Dosage**

Rifampicin prophylaxis for Hib disease is given orally once daily in a dose of 20 mg/kg per day to a maximum of 600 mg per day for four days. The dose for infants less than one month old has not been established, but a dose of 10 mg/kg per day is recommended. This is a different regimen to that recommended for prophylaxis from meningococcal disease (see chapter 15). The medical officer of health will advise on the availability of rifampicin supplies.
Side effects

Rifampicin causes orange discoloration of urine, sputum and tears, and staining of soft contact lenses. The colour change in body secretions is harmless, but patients should be warned and advised not to wear soft contact lenses. Rifampicin increases the hepatic metabolism of oral contraceptives, and women on these should be reminded of the seven-day rule: to use extra contraceptive precautions during antibiotic therapy and following completion of the course of antibiotics use extra contraceptive precautions until after seven consecutive days on the active pills (hormone containing, not sugar pills) of oral contraceptive.

For more details on control measures, refer to Control of Communicable Diseases Manual.11

References

Chapter 8: Poliomyelitis

8.1 Introduction

Although a 3500-year-old Egyptian stele depicts a man with the characteristic features of poliomyelitis (polio), the first written description of polio as a distinct disease was by Michael Underwood in 1789. The epidemiology of polio changed from endemic to periodic epidemics, starting in Sweden and Norway in the late 19th century and then affecting other industrialised countries. These changes were presumably due to improvements in hygiene increasing the average age of infection, which is more likely to be symptomatic in older children and adults.

In 1908 the association of polio with a specific infectious agent was recognised by Landsteiner and Popper. Salk introduced his inactivated vaccine in 1955 and Sabin the attenuated live virus vaccine in 1960. With the introduction of effective vaccines, the devastating epidemics that had swept through Western Europe, the United States (US), Australia and New Zealand every two to three years disappeared.

Global poliomyelitis eradication

In 1988 the World Health Organization (WHO) estimated an annual world toll of about 350,000 cases of paralytic polio, and the World Health Assembly set the target of global polio eradication by the year 2000. In 2000, 722 cases were confirmed worldwide and the new target set for eradication was 2005. Polio continued to occur in the six countries where it remained endemic: Nigeria, India, Pakistan, Afghanistan, Niger and Egypt. Then in October 2005 WHO reported not only that there had been cases in the six endemic countries, but also outbreaks in 10 countries that had been polio free. These countries, which were reinfected in late 2004/05, were Somalia, Indonesia, Yemen, Angola, Ethiopia, Chad, Sudan, Mali, Eritrea and Cameroon. Yemen and Indonesia were reinfected after there had been no cases of wild polio since 1995 and 1996.

The spread across Africa through to Indonesia is thought to be a result of the failure of immunisation programmes in Nigeria, where immunisation against polio ceased in parts of the country for 12 months in 2003/04, as well as the failure to maintain high immunisation coverage in other countries. The Advisory Committee on Polio Eradication to WHO met in 2005 and estimated that polio could be eliminated within the next six months everywhere except Nigeria, where elimination will not be achieved for at least 12 months. A monovalent oral polio vaccine (mOPV1) will be used instead of the usual trivalent oral polio vaccine. The monovalent vaccine builds immunity faster, and its use in Egypt and some areas of India successfully stopped polio transmission. Poliovirus 2 has been eliminated since 1999, and type 3 is limited to three areas of focal transmission.

Until eradication throughout the world is confirmed there is a risk of polio returning to New Zealand. Polio vaccination will continue worldwide until the WHO authorises cessation. This is unlikely to occur in the foreseeable future.
The Americas were certified polio free in 1994. The Western Pacific, which includes New Zealand, was the second region to be certified polio free in October 2000, with no indigenous polio cases since March 1997. This is an impressive achievement given that there were over 6000 cases notified in the Western Pacific region in 1990 at the beginning of the programme. For a region to gain certification as polio free, all countries must provide details of their immunisation programmes, the disease surveillance programmes, information on immunisation delivery and coverage, and reports on the country’s systems for identification, laboratory testing and diagnosis of cases of acute flaccid paralysis (AFP) over at least three years.

In New Zealand, poliomyelitis is a notifiable disease. Institute of Environmental Science and Research (ESR) laboratories perform reference testing for the poliovirus, and AFP is investigated and reported by paediatricians to the New Zealand Paediatric Surveillance Unit at the University of Otago.

For information on outbreaks caused by the vaccine virus, see section 8.3.

8.2 The illness

Humans are the only reservoir of the poliovirus and infection is more common in young children. The virus is transmitted by the faecal–oral route or by pharyngeal secretions.

Poliomyelitis is the acute illness following infection of the gastrointestinal tract with one of three types of poliovirus: types 1, 2 and 3. The virus is highly neurotropic and its primary effect occurs in the neurones of the spinal anterior horn or the motor ganglia of the brain stem. Infection may be clinically inapparent in up to 95 percent of infections, or range in severity from a non-paralytic fever to viral meningitis and flaccid paralysis.

Symptoms include fever, headache, gastrointestinal disturbances, malaise, stiffness of the neck and back, and pain in the limbs, back and neck, with or without paralysis. In children who develop paralysis, the illness may be biphasic, the initial phase of one to three days duration being indistinguishable from other viral infections. The patient appears to recover, only to be struck down abruptly two to five days later with meningism, followed by paralysis. In adults and adolescents the illness presents with a gradual onset of paralysis and pain without the early symptoms.

Asymptomatic people with the infection will shed the virus in their stool and through poor hygiene spread the infection to others. Infection rates may be as high as 100 percent in households where there are non-immune young children, although paralysis may occur in only 0.1–2 percent of infected individuals. Paralysis is more common in adults, occurring in up to 1 in 75 cases of infection. Case fatalities from paralytic polio vary from 2–10 percent and increase markedly with age.

The incubation period for poliomyelitis is commonly 7–14 days for paralytic disease, with a reported range of 3–21 days. The risk of transmission of infection is greater
for 7–10 days prior to and following the onset of symptoms. The virus persists in the pharynx for approximately one week and in the faeces for three to six weeks or longer, particularly in the immune suppressed. The diagnosis may be confirmed by isolation of the virus from two faecal specimens taken at least 24 hours apart in the first 14 days after the onset of paralysis. Serological tests are available, although virus isolation is required to confirm the diagnosis.

The post-polio syndrome occurs some 30–40 years after poliomyelitis. The cause is not known but is probably related to the ageing or death of nerves and muscles that were compensating for the original damage. Patients experience muscle pain and exacerbation of existing muscle weakness. The risk of developing post-polio syndrome is greater in women than in men, and the risk increases with time since the episode of acute polio.2

**Vaccine associated paralytic poliomyelitis (VAPP)**

After receiving the OPV most infants excrete the polio vaccine virus for about six weeks. Their family and other contacts are exposed to the vaccine virus and the contacts may then excrete the virus in faeces. There is a small risk that the vaccine virus causes VAPP (see sections 8.1, 8.3 and 8.6) in a vaccine recipient or non-immune contact. VAPP presents with AFP from 7 to 30 days after vaccination in the recipient and from 7 to 60 days in the contact of a vaccine recipient. The immune suppressed are more likely to suffer VAPP, whether they acquire infection directly or as a contact.

### 8.3 Epidemiology

Before poliovirus vaccines were available, cases of poliomyelitis occurred sporadically and in epidemics in industrialised countries of temperate zones. Cases were more common in the summer and autumn but with some variation from year to year. In tropical countries, where the virus still circulates, there is no seasonal pattern.

Characteristically, poliomyelitis is a disease of young children and adolescents. However, with improvements in living standards a greater number of cases have occurred in older individuals, with an associated higher frequency of paralytic disease. Paralytic disease is a particular risk in early adult life. In countries where polio was endemic, most children acquired antibodies to all three subtypes by five years of age and most paralytic disease occurred in children under three years of age. As the disease became rare because of the effective vaccines and immunisation programmes, only sporadic outbreaks occurred in those groups not reached by the programmes, whether because of socioeconomic circumstance or because of specific religious beliefs. This has been shown by outbreaks of poliomyelitis in unimmunised groups in the Netherlands in 1993, and in Israel.3,4 More recently there have been outbreaks of acute paralysis in Egypt, the Dominican Republic, Haiti, the Philippines and Madagascar associated with the sustained circulation of vaccine derived fully neurovirulent strains of poliovirus when population immunity was low.5,6,7,8
In 2005 the US reported poliovirus infections with a vaccine derived poliovirus (VDPV) of type 1 in four unvaccinated children of an Amish community, whose members were mostly unvaccinated. These were the first identified infections since 2000, when the US switched from OPV to IPV. The VDPV was identified in an immune deficient infant, and subsequent screening of community members found the virus in three asymptomatic unvaccinated siblings of another household. Analysis of the VDPV suggested that because of differences between the virus found in the children and the usual oral vaccine derived strain, this VDPV had been replicating and circulating for up to two years, and was likely to have originated from a visitor from a country where OPV is still used.

Intensive polio immunisation campaigns throughout the world have been successful in reducing cases of paralytic poliomyelitis. The global eradication programme uses OPV. As indigenous polio is eliminated from a country the risk remains that paralytic disease may be imported from a country where the wild virus still circulates. However, with the success of the global immunisation programmes, infection with the wild virus is now uncommon and localised to specific countries, so that the risk of VAPP is now higher than the risk of imported wild virus disease. This has led countries such as the US and New Zealand, and Australia from 1 November 2005, to change from OPV to IPV to eliminate the risk of VAPP. The risk of importing wild type or neurovirulent oral vaccine derived strains means that maintaining high vaccine coverage is essential.

New Zealand epidemiology
Deaths from polio were reported in official statistics from 1908, and notifications show large epidemics (about 1000 cases) in 1916, 1925 and 1937. Polio epidemics became more frequent and prolonged during 1948/49, 1952/53 and 1955/56. The use of the Salk (inactivated) vaccine delayed the next epidemic until 1961; this epidemic was halted by the use of the Sabin (oral) vaccine.

Following mass immunisation campaigns with OPV in 1961 and 1962 there have been no cases of poliomyelitis from indigenously acquired wild type poliovirus in New Zealand. It appears likely that poliovirus circulation was effectively stopped by these campaigns because of the high population coverage achieved (see Figure 8.1).
Since 1962 there have been four definite laboratory confirmed cases of VAPP and two probable cases of VAPP identified in New Zealand (see Table 8.1). Two cases were notified in 1970, one in a vaccinee and the other in an unimmunised contact. A probable case notified in 1977 may not have been polio as no virus was isolated and the child was reported to have made a ‘good recovery’. There were two notifications in 1990, one of a child notified on suspicion who was subsequently diagnosed as having Guillain-Barré syndrome. The 1990 case reported as VAPP was an unimmunised adult contact with a high titre on serological testing, although no stool specimens were taken to support this diagnosis. The two most recent cases in 1998 were a child who had received their second dose of OPV, and an unimmunised mother following her infant’s first dose of the vaccine. The number of cases in New Zealand was higher than would be expected from the estimated risk of VAPP in the US.
Table 8.1: Cases of VAPP in New Zealand, 1962–2000, confirmed and probable cases

<table>
<thead>
<tr>
<th>Year</th>
<th>Number of notified cases of VAPP in vaccine recipient</th>
<th>Number of notified cases of VAPP in contacts of a vaccine recipient</th>
<th>Number notified but not VAPP</th>
<th>Total probable VAPP*</th>
<th>Total number of laboratory confirmed cases of VAPP</th>
</tr>
</thead>
<tbody>
<tr>
<td>1970</td>
<td>1</td>
<td>1</td>
<td></td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>1977</td>
<td>1</td>
<td></td>
<td></td>
<td>1**</td>
<td></td>
</tr>
<tr>
<td>1990</td>
<td>1</td>
<td>1</td>
<td>1***</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>1998</td>
<td>1</td>
<td>1</td>
<td></td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>Total 1962–2000</td>
<td></td>
<td></td>
<td></td>
<td>2</td>
<td>4</td>
</tr>
</tbody>
</table>

* No laboratory confirmation but clinical course consistent.

** Child made a good recovery.

*** Final diagnosis Guillain-Barré syndrome.

In 1976 there was one case of imported poliomyelitis. An infant who arrived in New Zealand, having become ill in Tonga, had wild poliovirus. This case is not included in Table 8.1 above because the child had become ill outside New Zealand.

There has been no case of VAPP detected since the change in the National Immunisation Schedule (Schedule) to IPV in 2002.

History of the New Zealand Immunisation Schedule

Limited supplies of the Salk vaccine (IPV) became available in 1956 and immunisation initially targeted eight and nine year old children. As supplies improved, immunisation was extended to include all 5 to 10 year olds, then children 11 to 15 years of age, with approximately 80 percent coverage. By 1960 immunisation was offered to everyone between six months and 21 years of age (with three doses of vaccine).

The Sabin vaccine (OPV) was introduced in August 1961, initially for children up to 12 months of age; eight months later it was made available to all school children. On completion of this programme in September 1962 the vaccine was offered to adolescents and adults.

In 1967 OPV was given with diphtheria, tetanus and whole cell pertussis (DTwP) vaccine at three, four, five and 18 months of age. The four-month dose was dropped in 1971 when the DTwP dose was dropped from the Schedule. An extra dose of polio vaccine was added at five years of age in 1980, based on serological data, which showed decreased immunity to poliovirus types 1 and 3 in school entrants.

In 1996, as part of the National Immunisation Schedule changes, the three dose primary series was moved to the first year of life, with OPV given at six weeks, three
months and five months of age. The booster dose was moved to 11 years of age to be given at the same time as the measles, mumps and rubella (MMR) and adult tetanus diphtheria (Td) vaccines. In 2001 the Schedule was changed to give the fourth dose of OPV at four years of age at the same time as the second dose of MMR. Students aged between 5 and 10 years in 2001, who did not receive the fourth dose of polio vaccine at four years of age, are offered a dose at 11 years; this will continue until the end of 2007. From 2002 IPV replaced OPV for all doses (see section 8.4).

**Change to inactivated polio vaccine on the National Immunisation Schedule in 2002**

The Sabin live attenuated vaccine is given orally as oral polio vaccine (OPV). Because of the advantages of oral administration, OPV has been used in most countries of the world to control poliomyelitis. However, as the wild poliovirus infection becomes uncommon in a population through high immunisation coverage and low exposure, the risk of adverse events following the vaccine must be weighed against the decreased risk of the disease. Following OPV there is a small risk of vaccine associated paralytic poliomyelitis (VAPP) in the vaccine recipient or a non-immune contact. It has been estimated in the US that the risk is one case of VAPP per 2.4 million doses of OPV distributed. The risk is higher after the first dose of vaccine and estimated to be one case of VAPP for every 750,000 children vaccinated16 (see section 8.2). VAPP presents with acute flaccid paralysis typical of poliomyelitis, and the vaccine virus may be isolated from faecal specimens from cases.

In 2006 the Schedule will continue to be three doses of DTaP-IPV in the first year of life, and a booster at age four years. Those children who have not received four doses of polio vaccine will be offered IPV with the dTap, as dTap-IPV (BOOSTRIX®-IPV) at 11 years of age in 2006/07. Beyond 2007 it is expected that dTap will be offered at age 11 years (as all children should then have received four doses of polio vaccine by age four years). Note that if the dose of IPV at 11 years is the fifth dose, this is not expected to increase reactivity and may be safely given.

### 8.4 Vaccines

Since February 2002 IPV has been the publicly funded poliovirus vaccine on the National Immunisation Schedule. Vaccines available are as follows.

1. **Inactivated polio vaccine (IPOL, Sanofi Pasteur/MSD)**

IPV contains three strains of poliovirus (40D antigen units of the Mahoney, 8D units of the MEFI, and 32D antigen units of the Saukett strains), inactivated by formaldehyde and containing phenoxyethanol as a preservative. The viruses are highly purified and grown in cultures of VERO cells, a continuous line of monkey kidney cells. Trace amounts of neomycin, streptomycin, polymyxin B and bovine serum albumin may be present. This IPV vaccine is an ‘enhanced potency’ form of IPV. It is a different formulation with a greater antigenic content than the IPV introduced by Jonas Salk.
2  Diphtheria, tetanus, acellular pertussis and inactivated polio vaccine
   (DTaP-IPV, INFANRIX™-IPV, GSK)

DTaP-IPV is the Schedule vaccine for infants and children. The IPV in this combined vaccine is expected to provide protection equivalent to IPV alone. The IPV in INFANRIX™-IPV is also produced from a VERO cell line. (See section 6.4.)

3  Adult diphtheria, tetanus, acellular pertussis and inactivated polio vaccine
   (dTap-IPV, BOOSTRIX®-IPV, GSK)

This vaccine is available as a booster against diphtheria, tetanus, pertussis, and polio for individuals from the age of seven years. The dTap-IPV will be the Schedule vaccine offered to children at age 11 years (school year 7). (See section 6.4.)

Efficacy of IPV

Virtually all infants will seroconvert after three doses of IPV, and more than 85 percent will seroconvert after two doses. The efficacy of IPV is more than 90 percent.17 Follow up studies show that following two or three doses in the first year of life and a booster in the second year, close to 100 percent show seropositivity four years later.

The need for any further boosters is not clear. Some experts believe immunological memory is established and no further doses are necessary because the vaccinated individuals develop an anamnestic response if further challenged. The response to future infection is likely to be the same.18

Efficacy of DTaP-IPV and dTap-IPV

One month after receipt of the three dose primary vaccination series with DTaP-IPV, the overall seropositivity for poliovirus serotypes 1, 2 and 3 was 99.5 percent. The immune response to the diphtheria, tetanus, acellular pertussis and IPV components of DTaP-IPV is similar to that for DTaP and IPV administered separately and it is therefore expected that the clinical protection of the DTaP component is comparable.

One month after dTap-IPV the immune responses to poliovirus were similar to the responses to IPV alone.

Dosage

Follow the manufacturer’s directions. IPV is given by subcutaneous injection (0.5 mL). DTaP-IPV is given by intramuscular injection (0.5 mL). The dTap-IPV is also given by intramuscular injection (0.5 mL), preferably in the deltoid region. (See section 2.3 for needle sites and sizes.)

Oral poliomyelitis vaccine

OPV is no longer used in New Zealand. However, OPV will continue to be used in many countries because it remains the vaccine for the WHO Expanded Programme of Immunization. OPV contains poliovirus types 1, 2 and 3 grown either on monkey kidney or human diploid cells.
8.5 Recommended immunisation schedule

The recommended immunisation schedule is four doses of polio vaccine given at six weeks, three months, five months and four years of age, before school entry, as DTaP-IPV.

IPV is given as the vaccine dTap-IPV at age 11 years (school year 7). This will continue until 2007, when the children who were between 5 and 10 years of age in 2001 will have already received four doses of polio vaccine.

Preterm infants

Preterm infants who are still in hospital at six weeks of age should receive IPV as part of the usual childhood schedule.

Adults and children

Previously unimmunised individuals are given a primary course of three doses of IPV. The recommended interval is eight weeks between the first two doses, followed by the third dose approximately 12 months later. However, if necessary they may be given with a minimum of four weeks between doses.

If a course of vaccine is interrupted, it may be resumed without repeating prior doses. A booster may be given if 10 years has elapsed since the last dose and exposure is possible (eg, a traveller to an area where the virus circulates).

A combination of OPV and IPV is acceptable. Four doses, in any combination of OPV and IPV (given at least four weeks apart) by the time of school entry, is considered a complete vaccination series. This is particularly relevant when a child who was begun on a course of OPV in another country moves to New Zealand. It is not necessary in that situation to start the full IPV series, and it is acceptable to continue the series using IPV for the final doses.

Recommendations for other groups

Booster doses of IPV are recommended for:

- travellers to areas or countries where poliomyelitis remains endemic – a booster of IPV should be offered to these individuals if more than 10 years has elapsed since their last dose; where there is uncertainty about previous immunisation, a full course of IPV should be started (see Health Advice for Overseas Travellers, Ministry of Health, 1996)

- health care workers in direct contact with a case of poliomyelitis

- individuals at particular risk of exposure (eg, laboratory workers handling specimens, which may contain wild or vaccine derived polioviruses); a booster dose of IPV vaccine should be considered every 10 years in these individuals.

There is no evidence of the need for boosters, but they are recommended to reduce any possible risk from waning immunity in situations of increased risk of exposure.
Note: all immune suppressed individuals and their household contacts may receive IPV. OPV was contraindicated in the immune suppressed because of the risk of VAPP. There is no risk of VAPP with IPV.

8.6 Expected responses and adverse events following immunisation (AEFI)

IPV

Expected responses
A small proportion of individuals experience mild local symptoms following IPV. Erythema, induration and pain occur in 33, 1 and 13 percent of all vaccines, respectively, and symptoms of sleepiness, fussiness, crying and change in feeding have been noted in more than 5 percent of infants (manufacturer’s data sheet for IPOL). There is no poliovirus excretion following IPV.

Adverse events following immunisation
Serious adverse events are very rare following administration of the IPV currently manufactured. More than 90 million doses have been used with no association with subsequent polio, Guillain-Barré Syndrome, anaphylaxis or other serious reaction. IPV contains streptomycin and neomycin, and hypersensitivity reactions to these are possible.

For adverse events after DTaP-IPV and dTap-IPV, see Pertussis chapter, section 6.6.

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 http://carm.otago.ac.nz. If the patient or parent/caregiver does not consent to being identified, the report should be made without personal identification.

OPV

OPV is no longer used on the National Immunisation Schedule in New Zealand. VAPP following OPV is discussed above. There was concern after some batches of OPV produced before 1962 were found to be contaminated with SV40, a simian (monkey) virus, which causes cancer in rodents. Production was changed, and after 1963 SV40 was excluded from all vaccines. Long term studies of vaccine recipients and their offspring do not support any association of exposure to SV40 contaminated vaccine with human cancer.

8.7 Contraindications
See section 1.9 for general contraindications for all vaccines. IPV is contraindicated if there is a history of an anaphylactic reaction to a previous dose of IPV or to the antibiotics streptomycin, neomycin or polymyxin.
During pregnancy

No adverse effects on the fetus have been reported following administration of polio vaccine during pregnancy, but immunisation should not be carried out during the first or second trimester unless there are compelling reasons to do so, such as planned travel to an endemic area. However, pregnant women are particularly susceptible to paralytic polio. If a pregnant woman plans to travel to an endemic area, then two doses should be administered four weeks apart prior to departure. If departure cannot be delayed to allow a four week gap then two doses should be given at the maximum possible interval, though protection cannot be guaranteed. If the available interval is less than two weeks, a single dose should be administered.

Use with other vaccines

IPV may be given at the same time as inactivated or attenuated virus vaccines.

8.8 Control measures

All cases of poliomyelitis should be notified immediately on suspicion to the local medical officer of health. Case investigation and surveillance for AFP will continue in New Zealand to monitor the successful eradication of polio. All cases of AFP should be immediately notified to the local medical officer of health and investigated as suspected poliomyelitis.

A stool sample needs to be taken within 14 days of onset to search for poliovirus. Serology should also be done. All paediatricians or physicians caring for any person less than 15 years of age with AFP should report the case to the New Zealand Paediatric Surveillance Unit (NZPSU) based at the University of Otago. The NZPSU is responsible for sending case investigation and follow up forms to clinicians to continue to monitor that New Zealand has eradicated polio and to provide information to the WHO.

There are no outbreak control measures recommended if the case is VAPP.

A single case of paralytic wild poliomyelitis would be a major public health emergency. Control measures would involve mass vaccination of all people in the immediate neighbourhood, regardless of a previous history of immunisation, except where there are genuine contraindications. In those who have not previously received vaccine, a full course of three doses should be given at monthly intervals. There would need to be a careful search for the source of the virus and for other potential cases.

Although polio has been eradicated in the WHO Western Pacific Region, New Zealand will need to continue with high levels of IPV coverage. This is because of the small risk that polio may be imported from another region where polio remains endemic.

For more details on control measures, refer to Control of Communicable Diseases Manual.²⁰
References


9 Measles

9.1 Introduction
The earliest written description of measles is classically attributed to the Persian born physician Abu Becr (Rhazes) in the 10th century. Rhazes was the first to differentiate measles from smallpox and considered the former to be more dreaded. Although he recognised both the cyclical and seasonal nature of the disease, it was not until the 17th century that Thomas Sydenham of London identified the infectious nature of measles. The studies of Peter Panum in the Faroe Islands in 1846 showed that the disease was acquired solely by direct transmission. Outbreaks of measles occurred for the first time in the South Pacific during the mid- and late 19th century, with devastating results among the Fijians and New Zealand Māori. In 1954 Enders and Peebles in the United States (US) reported the first successful isolation and propagation of the measles virus in human and monkey kidney cells. This led to the production of a live attenuated measles vaccine, which was first licensed for use in the US in 1963.

9.2 The illness
Measles is an acute, highly communicable viral illness, usually transmitted via exposure to infected respiratory secretions. There is a prodromal phase of two to four days with fever, conjunctivitis, coryza and Koplik spots on the buccal mucosa. The characteristic maculopapular rash appears on the third to seventh day, spreads over three to four days from the head over the trunk to the extremities, and lasts for up to one week. The patient is most unwell during the first day or two after the appearance of the rash.

The incubation period is usually 10 to 12 days, but may range up to 21 days, and is prolonged in the immune suppressed. Measles is highly infectious from the beginning of the prodromal phase until four days after the appearance of the rash. Complications are common in 10 percent of cases (see Table 9.1), and include otitis media, pneumonia, croup or diarrhoea. Encephalitis has been reported in 1 in every 1000 cases, of whom some 15 percent die and a further 25 to 35 percent are left with permanent neurological damage. Other complications of measles include bronchiolitis, sinusitis, myocarditis, corneal ulceration, mesenteric adenitis, hepatitis and thrombocytopenic purpura.

Subacute sclerosing panencephalitis (SSPE), a rare degenerative central nervous system disease resulting from persistent measles virus infection, is fatal. In the US, where there is widespread measles immunisation, this complication has virtually disappeared. The case fatality rate for reported cases of measles in the US is 1 in 1000. Measles is particularly severe in the malnourished and in patients with defective cell-mediated immunity, who may develop giant cell pneumonia or encephalitis without evidence of rash, and have a much higher case fatality rate.
Measles is also serious in healthy children: over half of all the children who died from measles in the United Kingdom (UK) between 1970 and 1983 were previously healthy.¹ No other conditions were reported as contributing to the death of seven people who died from measles in the 1991 New Zealand epidemic.

In general, vitamin A is not necessary for children with measles in industrialised countries. However, it is recommended for children under two years of age who are hospitalised with complications of measles, and other children with risk factors such as immune deficiency or malabsorption (see section 9.8).

### 9.3 Epidemiology

Measles is the most common vaccine preventable cause of death among children throughout the world. The Global Burden of Disease Study ranked measles eighth, both as a cause of death and as a cause of disability adjusted life years (DALYs) lost, in the global population (all ages combined) in 1990.² Among children aged between zero and four years in non-industrialised countries, measles ranked fourth as a cause of DALYs lost, and was the infectious agent with the highest burden of disease. In 1989 the World Health Organization (WHO) Expanded Programme on Immunization estimated that 1.5 million children died annually from measles or its complications. The disease is highly infectious in non-immune communities, with epidemics occurring approximately every second year. A 1951 outbreak of infection in southern Greenland, a country which had not previously experienced measles, resulted in an almost 100 percent infection rate of adults and children. Indigenous cases of measles, mumps and rubella have been eliminated from Finland over a 12-year period using a two-dose measles, mumps and rubella vaccine (MMR) schedule given between 14 and 16 months and at six years of age.³

The US reported⁴ that of the 251 cases of measles reported in the US from 2001 to 2004, 177 (71 percent) were in US residents, and of these 100 were preventable. Forty-three percent of these preventable cases were associated with international travel; the rest were acquired in the US. Preventable cases are those that would not occur had the person received the recommended immunisation schedule, including MMR vaccination at six to 11 months if the infant is travelling outside the US. The 77 non-preventable cases had received a measles containing vaccine, or were expected to be protected because of their age, and of these 16 percent were associated with travel. International travel is an important factor in reintroducing measles into a country.

In October 2005 the Regional Health Assembly of the Western Pacific Region of WHO endorsed a target that by 2012 measles would be eliminated from the Western Pacific Region. To reach this target, all countries in the region will need to have ongoing high levels of measles immunisation coverage with two doses of vaccine, including at least one dose after the age of one year. All countries will also need to have surveillance systems for measles, and in order to monitor progress every
suspected case of measles will need laboratory confirmation at a national measles reference laboratory. Positive viral cultures will be sent to the regional laboratory in Melbourne, Australia, for detailed analysis of the virus. The New Zealand National Measles Laboratory, set up in 2005, is at Canterbury Health Laboratories. (See section 9.8.)

**New Zealand epidemiology**

Despite the introduction of the measles vaccine in 1969, measles occurred every year until 1980, with a pattern of 'low' years (an average of approximately 100 hospitalisations per year) alternating with 'high' or 'epidemic' years (an average of approximately 300 hospitalisations per year). Increased uptake of the measles vaccine, which is thought to have reached 70 percent or more by 1980, resulted in this epidemic cycle becoming more accentuated. Measles virtually disappeared between epidemic years, which occurred less frequently (1984/85, 1991 and 1997) but were of increased size, with 400 hospitalisations in 1984/85 (see Figure 9.1 for hospital discharges, notifications of measles, and laboratory confirmed cases). A shift in the age distribution of cases towards older ages was also noted. This effect was most evident in the 1991 epidemic, and was seen more in European than in Māori or Pacific children.

**Figure 9.1:** Hospital discharges from measles, 1970–2004, notifications, 1996–2004, and laboratory confirmed cases, 1984–2004.
The 1991 epidemic involved increased hospitalisations from May 1991 to January 1992. During this period a total of 629 people were hospitalised with a principal or secondary diagnosis of measles; for 568, measles was the primary diagnosis. During the epidemic the deaths of four unimmunised children were reported, but mortality records revealed a total of seven deaths during the epidemic. Excluding the cases that died, there were 10 hospitalised cases of measles encephalitis, 94 of pneumonia and 61 of otitis media. In the second half of the epidemic, reports of measles were requested and 10,000 were received; on this basis it was estimated that the epidemic involved 40,000 to 60,000 cases.

An epidemic was predicted in 1997, and an immunisation campaign was planned to prevent it. However, the epidemic began in April 1997, three months before the planned start of the campaign. The campaign was then brought forward so that 90–95 percent of cases were prevented (see Figure 9.2). There were 2169 cases identified via notification, laboratory and hospitalisation data, including 314 hospitalisations. There was one case of disease related measles encephalitis and no deaths. The total number of cases in this epidemic is unknown as under reporting was likely. Figure 9.2 shows the effect of the immunisation campaign in limiting the extent of the epidemic.

Figure 9.2: Actual number of notified cases of measles compared with predicted cases during the 1997 measles epidemic
Large scale measles epidemics occur when the number in the susceptible population increases and the immunisation coverage is low. It has been estimated that to prevent recurrent outbreaks of measles, 95 percent of the population must be immune. Since measles vaccine efficacy is 90–95 percent and not all children receive the first scheduled dose, the only way to achieve this level of immunity is by implementing a two dose immunisation strategy, as is now recommended.

In 2000 a mathematical model was developed to estimate the future timing of measles epidemics in New Zealand. The model included MMR immunisation coverage, the numbers of notified cases of measles, and the MMR coverage in the 1997 MMR campaign. The results suggested that if no changes were made to the MMR schedule of 15 months and 11 years, the next measles epidemic would be between 2002 and 2004. However, if the schedule was changed to give MMR at 15 months and at four years, before school entry, the length of time between epidemics would increase and eventually measles may be eradicated, if coverage was high. Therefore from January 2001 the National Immunisation Schedule was changed to give the first dose of MMR at 15 months and the second dose at four years of age, prior to school entry. During 2001 there was an MMR school catch-up programme throughout the country for all children between 5 and 10 years of age who would not receive MMR in year 7 (form 1) because of the 2001 schedule change.

During the 2001 MMR school catch-up programme it is estimated that 71 percent of all children received a first or second dose of MMR, or reported they had already received two doses of a measles containing vaccine. An additional 10 percent of children reported they would be going to their general practitioner for an MMR vaccine, so that an estimated total of about 81 percent of children were immunised.

There have been no further measles epidemics since 1997. Figure 9.1 shows the numbers of notified cases and those that are laboratory confirmed. Small numbers of cases of measles are notified each year: in 2003 there were 67 cases of measles notified, of which 11 were laboratory confirmed; and in 2004, 33 cases were notified, of which nine were laboratory confirmed. As the number of cases reported decreases it is important that all cases of suspected measles are laboratory investigated.

In 2005 the measles mathematical model was updated to calculate the effect of the measles catch-up in 2001 and to estimate the effect of changing the National Immunisation Schedule to give MMR at age 15 months and at age four years before school entry. Because there is no accurate immunisation coverage data until the National Immunisation Register (NIR) is fully operational, the model relies on estimates of coverage. The model shows that if the MMR immunisation coverage at 15 months is 85 percent, and at age four years is 80 percent, then New Zealand would not expect an epidemic of measles for another 10–20 years. If immunisation
coverage were higher, a longer time interval between epidemics would be likely. Although MMR coverage of 85 percent of both doses is likely to prevent further epidemics, because areas of low coverage may exist within any population, the model suggests that New Zealand needs to achieve a coverage level of 90 percent for both doses of MMR at 15 months and four years to eliminate epidemics. If MMR coverage of 90 percent or higher for both doses of MMR is achieved and maintained, the length of time between epidemics will increase and may lead to the eradication of measles.

As the incidence of measles decreases in New Zealand, it is important to continue high MMR immunisation coverage to lower the risk of imported measles causing outbreaks. Every suspected case of measles will need laboratory confirmation and characterisation to inform the local medical officer of health, so that public health control measures can be put in place.

**History of the New Zealand Immunisation Schedule**

The measles vaccine was introduced in 1969 for children between 10 months and five years of age who had not had measles, and for those under 10 years at special risk. In 1974 the recommended age for the measles vaccine was changed from 10 months to 12 months, and in 1981 was changed to 12–15 months of age. These changes attempted to find a balance between too early immunisation, where the vaccine is neutralised by maternally acquired antibody, and the requirement to protect the very young during an epidemic.

MMR vaccine was introduced in 1990 to be given at 12–15 months of age in place of the measles vaccine. The dose at age 11 years was introduced in 1992. In 1996 the timing of the first dose of MMR was changed to 15 months of age to be given at the same time as the booster dose of diphtheria, tetanus, whole cell pertussis and *Haemophilus influenzae* type b (DTwPH) vaccine.

At the start of the 1997 epidemic, the measles immunisation campaign, using MMR, targeted all children under 10 years of age. During the campaign the recommended time for the first dose was brought forward to 12 months of age, and in Auckland a dose was recommended for children six to 11 months of age repeated at 15 months of age. The national coverage achieved in the campaign is not known, but estimates for the school aged population range from 55 percent for Auckland to 85 percent for the Wellington region.

In 2001 the schedule was changed to give the first dose of MMR at 15 months of age and the second dose at four years. There was a school catch-up programme for the second MMR dose for children between five and 10 years of age. This schedule of two doses of MMR at the age of 15 months and four years continues.
9.4 Vaccines

The measles vaccine is only available as one of the constituents of MMR vaccine. (See below for administration in infants under 12 months of age.) The M-M-R® II (MSD) vaccine used and publicly funded is a freeze dried preparation containing live attenuated measles, mumps and rubella viruses. It must be stored in the dried state at +2°C to +8°C and protected from light. It must be reconstituted only with the diluent supplied by the manufacturer, refrigerated at +2°C to +8°C and used within eight hours or discarded.

The MMR vaccine viruses have been regarded as being non-transmissible from vaccinees. There are two poorly documented case reports of transmission: one of rubella and one of a mumps vaccine strain from a vaccine that is no longer in production.10 Following immunisation with both measles and rubella vaccines, live virus has been isolated rarely from pharyngeal secretions.11,12 There have been no confirmed cases of disease transmission from vaccine virus. The measles and mumps vaccines are grown in chick embryo cell cultures and rubella vaccine in human diploid cell culture.

MMR vaccines licensed in New Zealand are:

- M-M-R® II (MSD), which contains further attenuated Enders’ Edmonston (Moraten) strain measles, RA 27/3 rubella, and Jeryl Lynn mumps
- PRIORIX™ (GSK), which is now available and contains Schwartz strain measles, RA 27/3 rubella, and RIT 4385 mumps strain derived from the Jeryl Lynn strain
- Triviraten Berna (Swiss Serum and Vaccine Institute), which contains the measles Edmonston-Zagreb strain, the mumps high titre Rubini strain and the rubella Wistar RA 27/3 strain. This vaccine is not recommended in New Zealand because it has been shown to be less effective against mumps compared with other MMR vaccines.13

Quadrivalent measles, mumps, rubella and varicella vaccine (MMRV)

Successful clinical trials of an MMRV vaccine have led to regulatory approval in the US.14 The antibody response rates in children aged 12 to 23 months given a dose of MMRV vaccine were comparable with children given MMR and varicella vaccines at different sites. Children given MMRV showed higher geometric mean titres to measles and mumps than children receiving MMR and varicella vaccines separately. A second dose of MMRV given 90 days later elicited a further rise in titres to MMR and a greater rise in response to varicella. The vaccine studied had a higher dose of varicella vaccine virus than the varicella vaccine alone, because previous studies with a lower dose of varicella had been unsuccessful.

An MMRV vaccine is expected to be available in New Zealand soon (in the next one to three years). (See section 17.4.)
Efficacy
‘Primary vaccine failure’ refers to the lack of protective immunity despite vaccination. It is due to failure of the vaccine to stimulate an immune response. This occurs in 5–10 percent of recipients after the first dose and is rare after a second dose.

Seroconversion to all three viruses of MMR vaccine occurs in 85–100 percent of recipients. Most studies show 90–95 percent efficacy against measles. Those who do not seroconvert after the initial MMR dose almost always seroconvert after the second.

Even though antibody levels decline over time, secondary vaccine failure (ie, vaccine failure due to waning of protective immunity) has only rarely been documented for any of the three components of the vaccine. A meta-analysis of the measles vaccine found no evidence of secondary vaccine failure in the US manufactured vaccine currently used in New Zealand.15

Dosage
The correct dose is all of the reconstituted vaccine (about 0.5 mL) given by subcutaneous injection in the deltoid area to all age groups. (See section 2.3 for needle sites and sizes.)

9.5 Recommended immunisation schedule

Children
Measles vaccine is recommended as MMR at 15 months and four years of age, before school entry. Two doses of measles vaccine are recommended because the 5–10 percent who fail to be protected by the first dose will nearly all be protected by the second. The second dose of measles vaccine can be given as soon as four weeks after the first dose. The MMR vaccine may be given to children of any age whose parents/caregivers request it and no opportunity should be missed to achieve immunity.

The MMR vaccine should be given irrespective of a history of measles, mumps or rubella infection or measles immunisation. A clinical history does not reliably indicate immunity unless confirmed by serology. Furthermore, there are no known ill effects from vaccinating children, even if they have had serologically confirmed measles.

After reimmunisation, reactions are expected to be clinically similar but much less frequent since most vaccine recipients are already immune. No unusual reactions have been associated with measles or MMR reimmunisation.16

Adolescents and young adults born in 1989 or earlier
Adolescents and young adults born in 1989 or earlier may have received the measles vaccine at 12 to 15 months of age, and MMR during the 1997 campaign. They will
have therefore received the recommended two doses of measles, but only one of mumps and rubella. While the main reason for a two-dose MMR schedule is to protect against measles, two doses of all three antigens is recommended. These individuals should receive a second dose of MMR (ie, a third dose of measles vaccine).

**Adults**

MMR should be given to any adult who is known to be susceptible to one or more of the three diseases. 

*Adults born before 1969* should be considered to be immune to measles.

*Adults born after 1969*, who do not have a documented history of two doses of measles / MMR immunisation – administer one dose of MMR to those who fulfil one of the following conditions:

- born after 1969
- a student in post-secondary education
- a health care worker with patient contact – all should be immune to measles, mumps and rubella, but if a health care worker does not have a documented history of two doses of a measles containing vaccine they should receive a single dose of MMR
- a susceptible international traveller visiting a country in which measles is endemic.

The reactions to reimmunisation are expected to be less frequent than with primary immunisation, as most vaccinees will be immune.

**Administration**

MMR vaccine can be given concurrently with other vaccines, as long as separate syringes are used and the injections are given at different sites. If not given concurrently, live vaccines should be given one month apart. MMR can be given to non-immune adults and should be considered for those in institutional care or whose occupation may expose them to a higher risk (eg, health professionals or those training as health professionals).

**Immune suppression**

MMR is contraindicated in children who are immune suppressed (eg, those suffering from leukaemia), but they may be partially protected from exposure to infection by ensuring that all contacts are fully immunised, including hospital staff and family members.

MMR vaccination is recommended for children with HIV (human immunodeficiency virus) infection at 12 months of age who are asymptomatic and children who are
not severely immune compromised. MMR is contraindicated in children with severe immune suppression from HIV because vaccine related pneumonitis (from the measles component) has been reported.\textsuperscript{17} Discuss vaccination of children with HIV infection with their specialist.

**MMR vaccine under 12 months of age**

MMR may be recommended to infants between 6 and 12 months of age during measles outbreaks if cases are occurring in the very young (see section 9.8). These children still require MMR at 15 months and four years of age because their chance of protection from measles is lower when the vaccine is given at less than 12 months of age. Any recommendations will be made by the medical officer of health and Ministry of Health based on the local epidemiology.

**9.6 Expected responses and adverse events following immunisation (AEFI)**

**Expected responses**

It is commonly reported that 5–15 percent of children experience a fever of 39.5°C or over and 5 percent a rash 6–12 days post-immunisation. A placebo controlled study has shown that fever and/or rash in most cases are unrelated to immunisation, and only rash in 1.6 percent and high fever in 1.4 percent of cases could be attributed to MMR; these fevers were most likely nine or 10 days after immunisation and the rash occurred in the second week.\textsuperscript{18} The mumps vaccine may produce parotid and/or submaxillary swelling in about 1 percent of vaccinees, most often 10–14 days after immunisation. The rubella vaccine can cause a mild rash, fever and lymphadenopathy between two and four weeks after immunisation. There were no persisting sequelae associated with the administration of three million doses of MMR to 1.5 million children in Finland.\textsuperscript{19,20}

Febrile convulsions occur in 1 in 3000 children, six to 12 days after immunisation. Parents/caregivers should be advised to give the child paracetamol 15 mg/kg four hourly (up to a maximum of four doses in 24 hours) if a fever develops. Children with a history of convulsions should be given MMR, but the parents/caregivers should be warned that there may be a febrile response.

Arthritis or arthralgia occurs after both the rubella disease and vaccine, especially in adults. About 15 percent of adult women and less than 1 percent of children get joint symptoms about two to four weeks after immunisation. There is no evidence to suggest that rubella vaccine leads to long term arthritis: two large controlled studies found no evidence,\textsuperscript{21,22} while another study did find a slight increase in arthritis risk from rubella vaccine, but this was of borderline statistical significance.\textsuperscript{23} A review of the available evidence concluded that rubella vaccine does not cause chronic arthritis.\textsuperscript{24}
Adverse events following immunisation

Thrombocytopenia occurs in approximately 1 in 30,000 doses, 15 to 35 days after immunisation. The clinical course of these cases is usually transient and benign. The risk may be increased in those with a previous diagnosis of immune thrombocytopenic purpura (ITP), especially if it occurred after an earlier dose of MMR vaccine. Therefore it is recommended that any child who develops ITP within six weeks of receiving the first dose of measles vaccine or MMR undergo serological evaluation before receiving a second dose. The second dose is recommended for children who are not fully immune against measles, mumps and rubella.

Central nervous system symptoms following measles vaccine are reported to occur in one in one million children. In most cases this seems to be a chance occurrence that is not caused by the vaccine. An analysis of claims for encephalitis following measles vaccine in the US found clustering of events at eight to nine days after immunisation. This clustering supports, but does not prove, the claim that the vaccine causes encephalitis, albeit rarely and at a lower rate than the wild virus illness.

The MMR vaccine containing the Urabe strain of mumps was withdrawn in 1992 following a UK study that found a 1 in 11,000 risk of mumps vaccine meningitis. MMR containing the Urabe strain was used from 1991 until it was withdrawn in 1992 in New Zealand. Aseptic meningitis occurs in 1 in 800,000 doses following administration of the Jeryl Lynn strain of mumps vaccine, which is used in New Zealand.

Adverse outcomes not linked to MMR

There have been several epidemiological studies published from the UK, Finland and elsewhere confirming there is no link between MMR vaccine and the development of autism in young children.

The concern arose because in 1995 a group of researchers from the Royal Free Hospital in London published a study comparing children who took part in the 1964 UK Medical Research Council measles vaccine trial and received the measles vaccine at 10 to 24 months of age, with a cohort of their unvaccinated partners and with a longitudinal birth cohort from the National Child Development study born in 1958. The researchers looked at the history of inflammatory bowel disease (IBD) – that is, Crohn’s disease and ulcerative colitis – in all three groups and found that the group receiving the measles vaccine had an increased risk of Crohn’s disease (with a relative risk [RR] of 3.01, and 95 percent confidence interval [CI] 1.45–6.23) and of ulcerative colitis (RR 2.53, 95 percent CI 1.15–5.58) compared with the birth cohort. The researchers suggested this indicated that the measles virus might play a part in the development of Crohn’s disease and ulcerative colitis.

In 1998 the researchers found that in a series of 12 children with chronic bowel disease and a regressive developmental disorder, parents thought the onset of
neurological symptoms was associated with MMR in eight of the 12 children, measles infection in one child and otitis media in one child. In nine of the children the neurological syndrome was classified as autism. All the children had intestinal abnormalities of chronic colitis and 11 children had lymphoid nodular hyperplasia. It was suggested by the researchers that there was an association between IBD, autism and the MMR vaccine.

The methodology used in this study was criticised\(^3^6\) because of the small number of cases in the series, and selection bias. There was concern that the report was based on cases referred to a group known to be interested in the relationship between MMR vaccine and IBD rather than based on a population based study. There were no controls to compare events following immunisation, and there was no clear case definition for cases. There are no other reports suggesting an association between IBD and behavioural syndromes or autism following MMR or measles vaccine in the millions of doses of vaccine used worldwide since the 1960s.\(^3^7\),\(^3^8\),\(^3^9\),\(^4^0\)

Members of the original study group proposing the association have now withdrawn their claims.\(^4^1\)

The hypothesis was also examined in studies by other researchers and in other countries. A study from Finland\(^4^2\) followed up those children who developed gastrointestinal disease after MMR. At the end of 1996 three million doses of MMR vaccine had been delivered with 31 children reported with gastrointestinal symptoms, none of whom developed either IBD or autism. A population based study from the UK, which examined the incidence of autism after the introduction of MMR,\(^4^3\) also failed to find any association or increase in the incidence of autism. In this study a community child health system was used to identify children diagnosed with autism born since 1979. The records showed no increase in incidence following the introduction of MMR and no difference in the age at diagnosis of cases who had received MMR before or after 18 months, compared with those never vaccinated with MMR.

The Institute of Medicine in the US reviewed this issue\(^4^4\) and concluded in their report that the evidence does not support, at the population level, a link between MMR vaccine and autistic spectrum disorder (ASD). The Immunisation Safety Review Committee did not exclude the possibility that MMR could contribute to ASD in a small number of children, because it is difficult to assess a rare occurrence and biological models have not been disproved. The Committee recommended no change or review of MMR licensure, or change in the US MMR programme.

Table 9.1 shows the complications associated with contracting measles, mumps and rubella, and from receiving the MMR vaccine.
Table 9.1: Risks from contracting measles, mumps and rubella, and from receiving the MMR vaccine

<table>
<thead>
<tr>
<th>Measles complications</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Otitis media, pneumonia, diarrhoea</td>
<td>1/10–100</td>
</tr>
<tr>
<td>Encephalitis, probably resulting in brain damage</td>
<td>1/1000</td>
</tr>
<tr>
<td>Death</td>
<td>1/1000</td>
</tr>
</tbody>
</table>

Rubella complications
Congenital rubella: cataracts, deafness, cardiac malformations, and brain damage. Some abnormality of the fetus will be detectable in 85 percent of women infected in the first eight weeks of pregnancy. (See Table 11.1.)

<table>
<thead>
<tr>
<th>Mumps complications</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Meningitis</td>
<td>1/7</td>
</tr>
<tr>
<td>Orchitis</td>
<td>1/5 post-pubertal males</td>
</tr>
<tr>
<td>Nerve deafness</td>
<td>1/15,000</td>
</tr>
<tr>
<td>Death</td>
<td>1.8/10,000</td>
</tr>
</tbody>
</table>

Vaccine complications
Rashes, fever, local reactions, parotid swelling | 1/7 |
Febrile convulsions | 400/1,000,000 |
Transient joint symptoms – children | 1/35 |
Thrombocytopenia | 33.3/1,000,000 |
Encephalitis | 1/1,000,000 |
Aseptic meningitis | <1/100,000 |

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 http://carm.otago.ac.nz. If the patient or parent/caregiver does not consent to being identified, the report should be made without personal identification.

9.7 Contraindications
The general contraindications that apply to all immunisations are relevant to the MMR and single antigen measles vaccines (eg, children with an acute febrile illness should have their immunisation deferred) (see section 1.9).

Anaphylaxis following a previous dose of measles vaccine or MMR is a contraindication to a further dose of MMR. Children who have anaphylaxis after MMR should be serologically tested, and referred to or discussed with a paediatrician if non-immune to rubella or measles.
Children who have a hypersensitivity reaction after MMR should be serologically tested for immunity, and if non-immune referred to a paediatrician for evaluation and consideration of skin testing before receiving a second dose of MMR.

Other specific contraindications include:

- individuals with proven anaphylaxis (but not contact dermatitis) to neomycin
- children with immune suppression (ie, children with significantly impaired cell mediated immunity, including those with untreated malignancy, altered immunity as a result of drug therapy – including high dose steroids – or receiving high dose radiotherapy) (see section 1.8)
- children who have received another live vaccine, including Bacillus Calmette-Guérin (BCG), within the previous month (See Chapter 12: Tuberculosis)
- pregnant women
- women of childbearing age, who should be advised to avoid pregnancy for the next 28 days after the MMR or measles vaccines
- individuals who have received immunoglobulin or a blood transfusion during the preceding 11 months (see Table 1.11 for the length of time to defer measles vaccine after specific blood products)
- children with HIV infection who are severely immune compromised.45

**Egg allergy**

Egg allergy is no longer considered a contraindication to the measles or MMR vaccines. Various studies have confirmed these children can be vaccinated safely.46,47,48 Other components of the vaccine (eg, gelatin)49 may be responsible for allergic reactions. It is, however, recommended that any child who has a history of anaphylaxis with cardiorespiratory symptoms for reasons other than a reaction to MMR (see above) should be vaccinated under close supervision, with adrenaline and age appropriate resuscitation equipment immediately available.

Vaccinators should be aware of the possibility that allergic reactions including anaphylaxis may occur. (See also section 1.8 for information on immunising a child on steroids.)

**9.8 Control measures**

Notify all cases of measles on suspicion to the local medical officer of health. A single case of measles should be considered an outbreak and result in a suitable outbreak response. Practitioners are reminded that a diagnostic measles serology test (IgM) should be done on every child when measles is suspected, to confirm the diagnosis.

There are other causes of rash, respiratory symptoms, conjunctivitis and fever in children, and a laboratory confirmed diagnosis is needed to guide control measures.
and predict disease spread. When measles is suspected, do an IgM test on the patient for rapid diagnosis and send a sample for viral isolation.

The recommended laboratory test for measles diagnosis is measles specific IgM (see Table 1.5). Although measles virus may be isolated very early in the illness or prodrome, the virus is quite delicate and often may not be cultured. The diagnosis is usually made serologically, with a rise in serum immunoglobulin G (IgG) antibodies demonstrated on paired sera. A rapid diagnosis may be made if IgM can be demonstrated in the initial serum sample.

The sensitivity of the measles IgM assay varies, and may be diminished if the specimen is taken during the first 72 hours after rash onset. If the test is negative and the generalised rash persists, the IgM test should be repeated. Measles IgM is detectable for at least one month after rash onset.

Serological or virological diagnosis of the early cases is essential, and outbreak control planning and response should not be delayed. All children who could be infected during the outbreak and have not received two doses of measles vaccine should be offered MMR, ideally within three days of diagnosing the index case. The live measles vaccine, if given within 72 hours of measles exposure, will provide protection in some cases, so prompt immunisation may protect those susceptible.

If there is doubt about the state of immunity, the vaccine should be given because there are no ill effects from vaccinating an individual who is already immune. Particular attention should be paid to individuals born during 1969–75. At that time the measles vaccine was given at 10 months of age. There is now good evidence that the vaccine is less effective at that age because of residual maternally acquired passive immunity, and so these people are less likely to be protected.

In an outbreak affecting infants, the use of MMR vaccine for infants between six and 14 months of age should be considered. If the MMR vaccine is given before the first birthday, MMR should still be given at 15 months and four years of age because of the lower seroconversion rate for those receiving the vaccine under 12 months.

Immunoglobulin should be administered to protect measles exposed individuals in whom the vaccine is contraindicated (see section 9.7). Children with compromised immunity (eg, those with leukaemia) who come into contact with measles should be given normal human immunoglobulin (IG) (0.5 mL/kg to a maximum of 15 mL) as soon as possible after exposure. IG should also be considered for immune compromised adults who have no antibodies to measles. If immune competent individuals need IG prophylaxis, the dosage should be 0.25 mL/kg to a maximum of 15 mL. IG is most effective if given within 72 hours of exposure, but can be effective even if given within six days. If a large dose is needed, an intravenous preparation of IG (IVIG) may be used.
Parents/caregivers should be advised that cases should be excluded from early childhood services, school or community gatherings until at least four days after the appearance of the rash. Immunised contacts (ie, who have received two doses after their first birthday) need not be excluded from early childhood services, school or community gatherings. Non-immune contacts (those with no documentation of any immunisation or laboratory confirmed measles) should be excluded from school, early childhood services or community gatherings because of the risk of catching the disease themselves, and the risk of passing on the disease during the prodromal phase to other susceptible children.

The recommended period during which absence from an early childhood service or school is advised extends from diagnosis of the first case until 14 days after the appearance of the rash in the last case. Non-immune contacts may return to school immediately after receiving the measles vaccine, although there is a small risk that some may be incubating the disease.

**Recommendations for vitamin A for infants and children with measles infection**

In developing countries, the use of vitamin A has been associated with decreased morbidity and mortality. In Australasia, vitamin A supplementation is recommended for:

- infants hospitalised with measles and its complications, where there is pre-existing marginal nutrition or where community vitamin A deficiency is a recognised problem.
- older patients with acute measles, who are in a wider risk group including those with fat malabsorption (cystic fibrosis, short bowel syndrome and cholestasis), those with moderate to severe malnutrition (including adolescents with eating disorders), and those with immunodeficiency, including those on immunosuppressive therapy.

The recommended dosage is a single oral dose of 100,000 IU at the time of diagnosis, and for those cases who are malnourished or who have overt vitamin A deficiency a repeat dose on day 2 and day 28 following diagnosis.

The only form of vitamin A available in New Zealand is a tablet called Ro-A-Vit. Each Ro-A-Vit contains 50,000 IU of vitamin A. The replacement dose for a child who is vitamin A deficient is one tablet a day for two days for a child under one year of age, and two tablets a day for two days for a child aged one to two years. This tablet is dispersible in water. It is recommended that the family be advised to cut the tablet into four to eight pieces and dissolve them in milk. The tablet has a chocolate flavour.

For more details on control measures, refer to *Control of Communicable Diseases Manual.*
References


10 Mumps

10.1 Introduction
Mumps has been recognised as an acute disease since antiquity. In the fifth century BC Hippocrates described mumps as an illness accompanied by swelling of the ear and painful enlargement of the testes, either unilaterally or bilaterally. The infectious nature of the disease was recognised in the 19th century. By the early 20th century it was noted that mumps was particularly likely to occur in institutions and the armed forces. Large outbreaks occurred among the United States (US) armed forces in France during the First World War. In 1934 Johnson and Goodpasture demonstrated that a virus in human saliva could transmit the disease. The first safe and immunogenic attenuated mumps virus vaccine became available in 1967.

10.2 The illness
Classical mumps, an acute viral illness, is characterised by fever, headache, and swelling and tenderness of one or more salivary glands. At least 30 percent of mumps infections in children are asymptomatic. Patients may have no involvement of salivary glands, but still experience involvement of other organs (eg, orchitis or meningitis). The complications of symptomatic mumps include aseptic meningitis in 15 percent (almost always without sequelae), orchitis (usually unilateral) in up to 20 percent of post-pubertal males, and oophoritis in 5 percent of post-pubertal females. Sterility occurs rarely. Profound unilateral nerve deafness occurs in 1 in 15,000 cases. Encephalitis has been reported to occur at a frequency of between 1 in 400 and 1 in 6000, the latter being a more realistic estimate. The case fatality rate for mumps encephalitis is 1.4 percent, while the overall mumps case fatality rate is reported as 1.8 per 10,000 cases. Pancreatitis, neuritis, arthritis, mastitis, nephritis, thyroiditis and pericarditis may also occur. Mumps in the first trimester of pregnancy may increase the rate of spontaneous abortion, but there is no evidence that it causes fetal abnormalities.

The incubation period (until the appearance of the clinical illness) for mumps is usually 16 to 18 days but may range from 12 to 25 days. The period of communicability ranges from one week before to nine days after the onset of parotitis. Exposed non-immune individuals should be considered infectious from 12 to 25 days after exposure.

10.3 Epidemiology
Humans are the only known host of the mumps virus. Prior to the introduction of immunisation, approximately 85 percent of adults had evidence of past mumps infection. Most infections in those less than two years of age are subclinical, while those affected in adulthood are more likely to experience severe disease. The peak incidence is in late winter and spring.
In the under 15 age group mumps is the most commonly identified cause of viral meningitis in an unimmunised population. For example, prior to immunisation, mumps resulted in about 1200 hospital admissions per year in England and Wales. Before the introduction of immunisation in the US, mumps was the leading identified cause of viral encephalitis, responsible for up to 30 percent of cases. Since being licensed in 1967 the mumps vaccine has been in widespread use. The disease is now responsible for only 0.5 percent of cases of viral encephalitis and the overall incidence of reported mumps and its complications has reduced dramatically.

In the United Kingdom (UK) in 2004, the number of cases of mumps rose to more than 16,000, from 4204 cases in 2003. Most cases were in older teenagers and young adults born before 1987, and the mumps epidemic occurred because they had either not received a dose of measles, mumps and rubella vaccine (MMR) containing the mumps antigen, or had only received one dose of MMR. A two-dose schedule of MMR was not introduced in the UK until 1996, and MMR was first introduced as one dose in 1988.¹

**New Zealand epidemiology**

Between 1970 and 1991 there were 2002 hospital admissions for mumps,² with an increase in the number of cases every three to four years. The mumps epidemic expected in 1993 was delayed to 1994, presumably by the introduction of MMR immunisation in 1990, and there has not been an epidemic since then (see Figure 10.1).

**Figure 10.1: Mumps hospitalisations, 1970–2004 and notifications, 1996–2004**

![Figure 10.1: Mumps hospitalisations, 1970–2004 and notifications, 1996–2004](image-url)
History of the New Zealand Immunisation Schedule

Mumps vaccine (as MMR) was introduced to the National Immunisation Schedule in 1990 for children between 12 and 15 months of age. In 1992 a second dose of MMR was added, given at 11 years of age in year 7 (form 1). The timing of the first dose was changed in 1996 to 15 months of age to be given at the same time as the booster dose of diphtheria, tetanus, whole cell pertussis and *Haemophilus influenzae* type b vaccine (DTwPH). (This is discussed fully in section 9.3.) In 2001 the schedule for MMR vaccine was changed, maintaining the first dose at 15 months and changing the second dose to four years of age in order to prevent further epidemics of measles. There was an MMR school catch-up programme throughout the country in 2001 for all children between five and 10 years of age who would not receive MMR in school year 7 because of the schedule change.

10.4 Vaccines

Mumps vaccine is one of the components of the MMR vaccine (M-M-R® II, MSD), which is considered in section 9.4. M-M-R® II contains the Jeryl Lynn strain of mumps. The more reactive Urabe strain was used in New Zealand for a short time from 1991 until it was withdrawn in 1992. There is no single antigen mumps vaccine available in New Zealand. (See section 9.4 for information on other vaccines.)

Efficacy

The protective efficacy of the Jeryl Lynn strain of mumps vaccine is about 95–96 percent. In the US the introduction of a second dose has been associated with a further reduction in mumps cases. In Finland, a two-dose strategy and good immunisation coverage have led to the elimination of mumps.

Dosage

The correct dose is all of the reconstituted vaccine (about 0.5 mL) given by subcutaneous injection in the deltoid area to all age groups. (See section 2.3 for needle sites and sizes.)

10.5 Recommended immunisation schedule

Two doses of mumps vaccine (as MMR) are recommended for children at 15 months and four years of age, before school entry. Approximately 5 percent of children fail to be protected by the first dose; of these, nearly all will be protected by the second. The second dose can be given as soon as four weeks after the first dose.

10.6 Expected responses and adverse events following immunisation (AEFI)

See section 9.6 for adverse events after MMR.

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

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reporting at http://carm.otago.ac.nz. If the patient or parent/caregiver does
not consent to being identified, the report should be made without personal
identification.

10.7 Contraindications
See sections 1.9 and 9.7. Anaphylaxis to a previous dose of MMR is a
contraindication to a second dose of MMR.

Although the mumps vaccine is grown in chick embryo cell culture, mumps and MMR
vaccines may be safely given to those with anaphylactic allergy to egg. However,
allergy to gelatin may be associated with anaphylactic reaction to MMR. See section
9.7 for further information about egg allergy and immunisation of children with a
history of anaphylaxis.

10.8 Control measures
All cases of mumps should be notified to the local medical officer of health.

When an outbreak of mumps occurs, all susceptible people (ie, those who have
no previous history of mumps and have not received the mumps or MMR vaccine)
should be offered the MMR vaccine. The mumps vaccine given after exposure has
not been shown to be effective in preventing infection, but immunisation will provide
protection against future exposure. There is no increased risk of adverse events after
immunisation during the incubation period of mumps or if the recipient is already
immune.

Immunoglobulin is ineffective after exposure to mumps.

Parents/caregivers should be advised that cases should be excluded from early
childhood services or school until nine days after the appearance of parotitis, at
which time they cease to be infectious. Immunised contacts need not be excluded
from early childhood services or school.

Unimmunised contacts who have no previous history of mumps infection should be
advised not to attend early childhood services or school because of:
• the risk of catching the disease themselves
• the risk of passing on the disease, when asymptomatic or in the prodromal
  phase, to other susceptible children.

The recommended period during which absence from early childhood services or
school is advised for unimmunised contacts is from the date of exposure to a case
until 26 days after the appearance of parotitis in the last case in school or early
childhood service. The reason for the 26-day exclusion period is that cases may
occur up to 25 days after exposure. To quote from the Red Book:\textsuperscript{5}
When determining means to control outbreaks, exclusion of susceptible students from affected schools and schools judged by health authorities to be at risk of transmission should be considered. Such exclusion should be an effective means of terminating school outbreaks and rapidly increasing rates of immunisation. Excluded students can be readmitted to school immediately after immunisation.

For more details on control measures, refer to *Control of Communicable Diseases Manual*.6

References


11 Rubella

11.1 Introduction
Rubella has probably afflicted humans for centuries, but its often mild symptoms and the similarity of its rash to many other infections prevented recognition of the disease as a separate entity until the late 18th century. George Maton gave a clear description of the disease in 1814. Henry Veale named the illness ‘rubella’ half a century after he observed an outbreak in India. The viral nature of the infection was demonstrated by Hess in 1914 and confirmed by Hiro and Tasaka in 1938, when they inoculated children with the filtered nasal washings of infectious cases. In 1941 Gregg published his classic account of Congenital Cataract Following German Measles in the Mother. The virus was not isolated in tissue culture until 20 years later in 1962. The first effective live attenuated virus vaccine, based on the Cendehill strain, was released for use in 1969 following a major outbreak of rubella, starting in Europe in 1962/63 and spreading to the United States (US) in 1964/65, with many cases of the congenital rubella syndrome. A triple vaccine containing attenuated measles, mumps and rubella viruses has been in use in the US since the early 1970s. The RA27/3 strain has been used since 1979 because of its superior immunogenicity and lower rate of reactions.

11.2 The illness
Rubella is a common childhood disease that can affect adults and, like measles, often occurs in epidemics. It is most common in children of early school age. Clinical features include a transient erythematous rash, lymphadenopathy (particularly in the posterior auricular and suboccipital nodes), without respiratory symptoms. In adults, arthritis or arthralgia may occur. Rubella may also present as a more severe illness, clinically indistinguishable from measles. Encephalitis occurs more frequently than the previously estimated 1 in 6000 cases and may result in residual neurological damage or occasionally death. Thrombocytopenia rarely occurs.

Clinical diagnosis is unreliable because the symptoms are often fleeting and can be mimicked by other viruses. In particular, the rash is not diagnostic of rubella. A history of ‘rubella’ should never be accepted without confirmation by positive serology. The incubation period is 14–21 days, usually 16–18, and infectivity is from seven days before until seven days after the onset of the rash. Transmission is primarily via respiratory secretions.

Maternal rubella in the first eight weeks of pregnancy results in fetal damage in up to 85 percent of infants, and multiple defects are common. The risk of damage declines to 10–20 percent by about 16 weeks’ gestation, and after this stage of pregnancy fetal abnormalities are rare. Infants born with the congenital rubella syndrome (CRS) may have cataracts, nerve deafness, cardiac malformations, microcephaly, mental retardation and behavioural problems. Inflammatory changes may also be found in the liver, lungs and bone marrow. Some infected infants may appear normal at birth,
but have nerve deafness detected later. Infants with CRS may excrete the virus for a year or more after birth.

The risks from rubella are best described from the 1963/64 US outbreak, involving 12.5 million cases of rubella and 30,000 infants damaged by intrauterine rubella, an incidence rate of 100 per 100,000 pregnancies (see Table 11.1 below, and Table 9.1).

Table 11.1: Estimated morbidity/mortality associated with 1963/64 US rubella epidemic

<table>
<thead>
<tr>
<th>Total number of cases of rubella</th>
<th>12,500,000</th>
</tr>
</thead>
<tbody>
<tr>
<td>Complications of rubella</td>
<td>Risk per case</td>
</tr>
<tr>
<td>Arthritis or arthralgia</td>
<td>1.3%</td>
</tr>
<tr>
<td>Encephalitis</td>
<td>17 per 100,000</td>
</tr>
<tr>
<td>Neonatal deaths</td>
<td>17 per 100,000</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Complications caused by congenital rubella syndrome (CRS)</th>
<th>Numbers of cases (% of CRS cases)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total number CRS</td>
<td>20,000</td>
</tr>
<tr>
<td>Deaf children</td>
<td>8055 (40%)</td>
</tr>
<tr>
<td>Deaf-blind children</td>
<td>3580 (18%)</td>
</tr>
<tr>
<td>Intellectually handicapped children</td>
<td>1790 (9%)</td>
</tr>
</tbody>
</table>


The risk of rubella infection increases in later pregnancies because parous women with older children are more likely to be exposed to rubella from their children. Rubella infection can occur (very rarely) in individuals with either naturally acquired or vaccine induced antibody. Rare cases of CRS have been reported after reinfection during pregnancy.

11.3 Epidemiology

Humans are the only source of rubella infection. Asymptomatic infection is common. In the pre-vaccine era the highest incidence of clinical cases occurred in the spring among five to nine year old children, and 80–90 percent of adults were immune to rubella. Extensive outbreaks of rubella occurred every six to nine years, in which many children were affected by CRS. Immunisation against rubella, introduced to prevent the occurrence of CRS, has resulted in a significant reduction, especially where there is extensive use of the rubella vaccine.

New Zealand epidemiology

Outbreaks of rubella continue to occur in New Zealand. Although rubella immunisation was offered from 1979 to all girls in year 7 (form 1), it was not offered to boys until 1992, allowing spread in the community. There were 100 cases
reported between August 1989 and February 1990, some among pregnant women, and there were three cases of CRS reported. The outbreaks of rubella in 1993 and a larger one in 1995 have mostly involved young adult males, who would not have been offered immunisation. These outbreaks emphasise the need to immunise both boys and girls to reduce the risk of exposure in pregnant women, as well as to reduce illness in men.

Rubella has been a notifiable disease since 1996. In 2003 there were 26 cases of rubella notified, of which three cases were laboratory confirmed; and in 2004 there were 25 cases notified, of which three were laboratory confirmed. It is important that suspected cases are notified and are laboratory confirmed so that public health control programmes can limit spread (see section 11.8). (See Figure 11.1 for notifications and laboratory confirmed cases of rubella.)

There have been no cases of CRS in New Zealand newborns reported to the New Zealand Paediatric Surveillance Unit between 1998 and 2004.

**History of the New Zealand Immunisation Schedule**

Immunisation with an attenuated rubella vaccine (Cendehill strain) was first offered to all four year old New Zealand children in 1970, the rationale being to prevent transmission of the wild virus in five to nine year old children, who were the main sufferers from clinical disease. At the same time the Department of Health delivered a school based programme, which succeeded in immunising 95 percent of children five to nine years of age. The acceptance rate of the preschool entry dose of rubella was only about 40 percent, and many practitioners did not feel it was appropriate to immunise males.

In 1979 the immunisation policy for rubella was altered to offer the vaccine to girls of 11 years of age, in year 7 (form 1). The aim was to immunise females before they attained childbearing age. In 1990 MMR was introduced at 15 months for all children and rubella vaccine continued to be offered to girls in form 1. Since 1992 two doses of rubella vaccine – as measles, mumps and rubella (MMR) vaccine – have been offered to all children, the first dose in the second year of life and the second dose at 11 years of age. This was changed in 2001, maintaining the first dose of MMR at 15 months and changing the second to four years of age, before school entry. The aim of this strategy was to prevent rubella epidemics, reduce the background incidence of rubella and continue to protect women before childbearing, therefore eventually abolishing CRS (see Figure 11.1). In 2001 there was an MMR school catch-up programme throughout the country for all children between five and 10 years of age who would no longer receive an MMR dose in year 7.

In 2006 the rubella schedule will continue as two doses of MMR vaccine offered at age 15 months and four years. All young women should be screened to check their rubella immunity. The MMR vaccine is available and publicly funded for all susceptible adult women. All women are screened for rubella immunity during pregnancy, and susceptible women are offered MMR vaccine after delivery.
11.4 Vaccines

The rubella vaccine is one of the components of the MMR vaccine, which is considered in section 9.4. Single antigen rubella vaccine is no longer available in New Zealand.

Efficacy

The rubella vaccine has been shown to be 90–97 percent effective in an outbreak after a single dose, and this is likely to be higher with a two dose schedule.

One dose of rubella vaccine at 12 months or older induces an antibody response in at least 95 percent of recipients. A recent review found no evidence of waning in protection over decades of follow-up.\(^1\)\(^2\) In 90 percent of recipients antibodies persisted for 16 years, other studies have reported persistence up to 21 years.\(^3\) A few recipients fail to produce antibodies following immunisation, and a small number of individuals lose antibodies, whether derived from natural infection or the vaccine.

Serological testing

Women should be screened for the rubella antibody in their early reproductive years before pregnancy, in the antenatal period of every pregnancy, and at their request when pregnancy is planned (see sections 11.5 and 11.8).
Although it has been considered that a rubella antibody level of greater than 10 IU/mL indicates protection is likely, reinfection with rubella can occur even with antibody levels above 15 IU/mL and the risk is expected to be greater with rubella antibody levels of 10–15 IU/mL or lower. However, CRS is less likely after reinfection with rubella in pregnancy compared with a primary infection (see section 11.2). It is estimated that the incidence of CRS is 5 percent after reinfection with rubella in the first trimester, and negligible later in pregnancy.4

It is therefore recommended that pregnant women with a rubella antibody level below 15 IU/mL be counselled to avoid contact with cases of rubella. If the antibody level is below 25 IU/mL, the woman should be offered MMR after delivery if she has not already received two doses of a rubella containing vaccine.

A pregnant woman with low anti-rubella antibody levels should have her serology repeated if she comes into contact with someone with a rash. If a rise in titre is detected, the results should be discussed with an expert (see section 11.8). Women exposed to rubella during pregnancy should be tested as in section 11.8. Reinfection with rubella is associated with a rise in IgG but not a rise in IgM.5

Although the vaccine virus is excreted, mostly from the pharynx, extensive efforts to identify transmission to susceptible contacts have failed (see section 9.4). A recently immunised contact is not a risk to a pregnant woman.

If an individual has no documented history of immunisation with MMR vaccine they should be given a dose of MMR vaccine rather than performing serology. There are no undue adverse effects from vaccinating individuals who are already immune to measles, mumps and/or rubella, and no reliance can be placed on a prior clinical history of rubella. (See also section 9.5.)

Dosage
The correct dose is all of the reconstituted MMR vaccine (about 0.5 mL) given by subcutaneous injection in the deltoid area to all age groups. (See section 2.3 for needle sites and sizes.)

11.5 Recommended immunisation schedule
Two doses of rubella vaccine (as MMR) are recommended at 15 months and four years of age, before school entry. Two doses are recommended because the 2–5 percent who fail to be protected by the first dose will nearly all be protected by the second. The second dose of vaccine can be given as soon as four weeks after the first dose. (See below for the recommendations for other groups.)
It is important for vaccinators to be able to explain why boys need rubella vaccine, given that the primary aim is to prevent rubella in pregnancy. In New Zealand and the United Kingdom (UK) where a targeted approach was used and 11 year old girls were offered rubella immunisation, even with high coverage there were still women of child bearing age who were susceptible to rubella, either because of failure to be vaccinated or vaccine failure. Rubella continued to circulate in New Zealand because no one under age 11 and males were not vaccinated and CRS continued to occur, although at a reduced rate.

To prevent all cases of CRS, rubella must not circulate in the community and therefore males must be immunised. Achieving at least 95 percent coverage of two doses MMR should prevent the circulation of rubella, which is less infectious than measles, and therefore lead to the elimination of rubella and CRS.

At risk groups from rubella

1 Non-pregnant susceptible women

MMR should be offered (and is publicly funded) to all women to protect against all three diseases. If the woman is already immune, the vaccine virus will not replicate and any boosting of rubella antibodies will increase the duration of protection for any future babies.

**Figure 11.2: Guide to rubella immunisation for women with low levels of antibodies**
It is important to ensure that all women of childbearing age have been screened for rubella antibodies and, if not immune, vaccinated prior to pregnancy. Opportunities for screening arise at any health service encounter. Every effort must be made to identify and immunise seronegative women. All women should be informed of the result of their antibody test. Note that female immigrants may not have been immunised, and may be at risk (see below).

2 Women born between 1965 and 1967
These women are at risk of rubella because they were too young for the initial 1970 campaign targeted at children four to nine years of age, and too old to be immunised in year 7 (form 1) during 1979 (see section 11.3). This cohort is less likely to develop natural immunity in childhood because of high coverage in the proximate cohorts, and they may be at increased risk of susceptibility to rubella. It is important that these women have their rubella antibody status checked and, if not immune, be offered rubella immunisation.

3 Pregnant susceptible women
All women should be routinely tested for rubella antibodies during the antenatal period. Women found to be seronegative on antenatal screening should be immunised (publicly funded) after delivery (with MMR vaccine) before they leave the supervision of the lead maternity carer.

If MMR vaccine and anti-D immunoglobulin are required after delivery, both the vaccine and anti-D immunoglobulin may be given at the same time, in separate sites with separate syringes. The vaccine may be given at any time after the delivery. Anti-D immunoglobulin does not interfere with the antibody response to the vaccine, but whole blood transfusion does inhibit the response in up to 50 percent of vaccinees. Rubella serology should be checked six to eight weeks later to ensure that seroconversion has occurred, with immunisation repeated if it has not. MMR may be given to women who are breastfeeding.

4 Immigrants to New Zealand
The rubella status of immigrants should be checked as a priority group. While most industrialised countries have for many years included rubella vaccination on their immunisation schedules, rubella has not been a component of the immunisation schedules in most non-industrialised countries such as the Pacific Islands. Surveys of susceptibility to rubella in women of childbearing age have found rates greater than 25 percent in India, Israel, Malaysia, Nigeria, Singapore, Sri-Lanka and Thailand, and rates of 10–25 percent in many African, Middle Eastern and South American countries. Immigrants from non-industrialised countries should be offered two doses of MMR vaccine (four weeks apart).

5 Health care workers and students
Health care workers and students should all (both male and female) be screened for rubella antibodies and immunised with at least one dose of MMR if seronegative, to avoid risk to their patients. Health care workers without a documented history of two doses of MMR vaccine should be given one dose of MMR.
11.6 Expected responses and adverse events following immunisation (AEFI)

Expected responses
Mild reactions after immunisation with the rubella or MMR vaccines include fever, sore throat, lymphadenopathy, rash, arthralgia and arthritis (see section 9.6). The incidence of these side effects is age related. Joint symptoms may occur in 0–3 percent of infants and 12–20 percent of adult women. Symptoms begin one to three weeks after immunisation and are usually transient. The incidence of joint symptoms following rubella immunisation is at a lower rate than occurs with natural infection at a corresponding age.

It was previously thought that the rubella vaccine might lead to long term arthritis. However, two large controlled studies found no supporting evidence of this.7,8 Another study did find a slight increase in risk from rubella vaccine, but this was of borderline statistical significance.9 A review of the available evidence concluded that the rubella vaccine does not cause chronic arthritis.10

Thrombocytopenia and, rarely, neurological disturbances have been reported (see section 9.6 for information on adverse events and reimmunisation).

Adverse events following immunisation
Anaphylaxis to a previous dose of MMR is a contraindication to a further dose of MMR. (See also section 9.6 for further information on the MMR vaccine.)

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 http://carm.otago.ac.nz. If the patient or parent/caregiver does not consent to being identified, the report should be made without personal identification.

11.7 Contraindications
The general contraindications, which apply to all immunisations, are relevant to MMR (see sections 1.9 and 9.7).

Rubella vaccines contain traces of neomycin and/or polymyxin. Previous anaphylactic reactions to these substances contraindicate rubella vaccine.

The MMR vaccine should not be given to women who are pregnant, and pregnancy should be avoided for 28 days after immunisation.11 However, inadvertent immunisation with a rubella containing vaccine in early pregnancy is no longer considered an indication for abortion. There have been no cases of teratogenic damage from vaccine virus despite intensive surveillance in the US, UK and Germany.12
11.8 Control measures

It is recommended that when a diagnosis of rubella is suspected, the diagnosis should be confirmed by laboratory testing (IgM) and the case notified to the medical officer of health to enable control measures to be put in place to halt an outbreak. All cases of CRS should also be notified to the local medical officer of health.

Parents/caregivers should be advised that children with rubella should be excluded from early childhood services or school for seven days after the appearance of the rash. Children with congenital rubella should be considered infectious until they are one year of age.

Unimmunised contacts need not be excluded from early childhood services or school but should be given advice about MMR and the National Immunisation Schedule. Female staff of childbearing age should ensure they are immune to rubella. Pregnant women known to be susceptible to rubella must avoid contact with known or suspected cases.

Management of a pregnant woman who has been exposed to rubella

All women should have been routinely tested for the presence of rubella antibodies before pregnancy and early in every pregnancy. If this result is available and the woman is known to be immune, she may be reassured that her fetus is at little risk (see sections 11.2 and 11.5).

Pregnant women whose immunity to rubella has not been confirmed for the current pregnancy, and who may have been exposed to rubella, must be investigated serologically irrespective of immunisation history, clinical rubella or previous positive rubella antibody. The rash is not diagnostic and infection can occur without clinical symptoms.

Serological testing

The pregnant woman should be tested for rubella antibodies as soon as possible after exposure. Request the laboratory to store (frozen) an aliquot of serum for later testing in tandem with a follow-up sample.

If the first sample is antibody positive, then a full assessment of the serological status is needed. These results must be interpreted in conjunction with the time lapse since exposure to determine whether or not acute infection has occurred.

If the woman is rubella antibody negative and remains asymptomatic, a second blood specimen should be obtained 28 days after the exposure date. However, a second blood specimen should be obtained as soon as possible if the woman
develops clinical symptoms suggestive of rubella. A third blood specimen may be necessary seven days after the onset of symptoms.

It is essential that all requests to laboratories state the:
• duration of pregnancy and last menstrual period
• date of exposure to possible rubella
• date of blood specimen.

Ideally, a virologist or infectious disease specialist should be consulted when the diagnosis is first considered. The clinical picture and all test results should be discussed by the virologist and the specialist to enable accurate interpretation of serological results before advising the woman about the risk to her fetus.

Management
This is well covered in the 2003 Red Book, which includes the following advice.

The routine use of immune globulin (IG) for post exposure prophylaxis of rubella in early pregnancy is not recommended. Administration of IG should be considered only if termination of the pregnancy is not an option. Limited data indicate that IG in a dose of 0.55 mL/kg may decrease clinically apparent infection in an exposed susceptible person from 87 percent to 18 percent compared with placebo. However, the absence of clinical signs in a woman who has received intramuscular IG does not guarantee that fetal infection has been prevented. Infants with congenital rubella have been born to mothers who were given IG shortly after exposure.

Live rubella virus vaccine given after exposure has not been demonstrated to prevent illness but theoretically can prevent illness if administered within three days of exposure. Immunization of exposed, nonpregnant persons may be indicated because if the current exposure does not result in infection, the immunization will protect the individual in the future. Immunization of a person who is incubating natural rubella or who is already immune is not associated with increased risk of adverse effects (p. 538).

For more details on control measures, refer to Control of Communicable Diseases Manual.

References
12 Tuberculosis

12.1 Introduction
The history of tuberculosis (TB) in New Zealand has been well documented. The present control programme took shape with the introduction of the Tuberculosis Act 1948. Under this Act the medical officer of health is given wide powers to investigate and control all TB cases and their contacts, while district health boards are required to make provision for the treatment and supervision of patients and their contacts.

The TB control programme, including some aspects of Bacille Calmette-Guérin (BCG) immunisation, are outlined in the Ministry of Health publication Guidelines for Tuberculosis Control in New Zealand, 2003 (see www.moh.govt.nz). The local medical officer of health can advise on local TB control programmes, including BCG immunisation. Under the Tuberculosis Regulations 1951, BCG immunisation in New Zealand may legally be performed only by gazetted BCG vaccinators. A detailed technical description for the administration of the BCG vaccine is provided in the Ministry of Health publication Technical Guidelines for Tuberculin Testing and BCG Vaccination, 1996.

12.2 The illness
Human TB is caused by infection with Mycobacterium tuberculosis or Mycobacterium bovis. It most commonly causes disease in the lungs, but any part of the body may be affected. The initial infection with M. tuberculosis often goes unnoticed, and most of those infected enter a latent phase. The lifetime risk for infected people progressing from this latent phase to active TB disease is commonly stated to be 5–15 percent, but this risk is strongly affected by the size of the infecting dose and the strength of the infected person’s immunity. For example, the risk of disease in young children is up to 40 percent. A small proportion of those infected progress directly to pulmonary TB, or by lympho-haematogenous dissemination of bacilli to miliary, meningeal or other extrapulmonary involvement. Infants, young children, older people and the immune compromised are more likely to progress to severe generalised infection.

TB infection and BCG immunisation lead to the development of a cellular immune response, which can be detected by the injection of tuberculin purified protein derivative. A positive 5 international tuberculin unit (TU) Mantoux test may be an indication of current infection, previous natural infection, or prior BCG immunisation. However, the reaction may be depressed if the patient is seriously ill from TB, is suffering from certain infectious diseases (notably human immunodeficiency virus (HIV) or measles), or has recently been administered live virus vaccines, and in those in whom disease or drugs have led to immune suppression. The interpretation of a positive Mantoux test must take account of all the above factors and the disease risk of the person being tested. This interpretation and the consequent clinical advice are therefore complex, and are discussed fully in the Ministry of Health publications described above.
12.3 Epidemiology

TB remains an important cause of death in non-industrialised countries. However, there has been a resurgence of TB in the industrialised world. The frequency of TB in certain population groups is increasing worldwide, partly in association with the HIV/AIDS epidemic. At present in New Zealand TB is not common in patients with HIV infection.

New Zealand epidemiology
The overall incidence rate of TB in New Zealand is low compared with most countries, but has not declined over the last 20 years (see Figure 12.1). TB is still one of the most common notifiable infectious diseases. Reasons for the persistence of TB as a public health problem in New Zealand are complex, and include immigration from countries where there is a high incidence of TB, social conditions favouring transmission, and the fact that identification and prophylaxis for all infected people is not practicable. High rates of TB exist in New Zealand among population groups from Asia, Africa and the Pacific, particularly recent immigrants from these areas.

In 2000 the incidence rates in New Zealand were 1.7 per 100,000 for Europeans, 13.8 for Māori, 36.4 for Pacific, and 91.8 for other ethnic groups. The proportion of TB cases born in New Zealand was stable at about 40 percent between 1995 and 2000. In 2004 there were 372 (new and reactivated) cases of TB notified, a rate of 10.0 per 100,000. As in previous years, rates were low in Europeans (1.5 per 100,000) and higher in Māori (13.9 per 100,000) and Pacific peoples (32.9 per 100,000). Rates were highest in those of ‘other’ ethnicity, with a rate of 78.1 per 100,000.

In 2004 there were 27 cases of tuberculosis reported, a rate of 3.2 per 100,000, in children aged 0–14 years. The age groups with highest rates of disease were females aged 20–29 years (52 cases, or 20.8 per 100,000) and males over 70 years (21 cases, or 15.7 per 100,000), and a high rate was especially seen in Pacific males over 70 years. In general the rates of disease increased with age, although in people of ‘other’ ethnicity there was a bimodal peak, with a high rate in those from 20 to 49 years as well as in older people.

Extrapulmonary TB (particularly miliary and meningeal), which is vaccine preventable in children, continues to occur in New Zealand (see Figure 12.2). Pacific, African and Asian children are disproportionately affected (see Figure 12.3). Figure 12.4 shows the number of hospitalisations for tuberculosis in children age 0–14 years from 1989–2004.

Bovine infection with M. bovis has spread to feral opossums, placing dairy herds, other cattle and deer at risk from the contamination of pastures. At present, because of herd testing and the widespread pasteurisation of milk, this causes very few cases of human M. bovis disease.
History of the New Zealand Immunisation Schedule

BCG immunisation was first introduced to New Zealand in 1948 and later extended to all adolescents. BCG immunisation of neonates was introduced in 1976, initially in high risk districts, but has been variably implemented throughout New Zealand.

Universal screening and vaccination of 13 year olds was discontinued in the South Island in 1963, was phased out in regions of the North Island in the 1980s, and had ceased by 1990. It was stopped because TB had declined to a point at which the advantages of vaccination (limited efficacy) were outweighed by the disadvantages (cost, side effects and reduced diagnostic value of the Mantoux test). An increase in TB transmission in particular districts or subpopulations would warrant reconsideration of this policy. Routine immunisation of adolescents with BCG is not regarded as necessary at present, although BCG could be reconsidered if the population specific rate rises to over 10 per 100,000.7

There have been different approaches to using BCG in the control of TB in developed countries. The United States (US) has not had a programme of universal BCG for adolescents, whereas New Zealand until 1990 (see above) and the United Kingdom (UK) have had programmes. The UK programme was discontinued in autumn 20058 because the annual risk of infection had fallen to less than 1 in 1000, and of people reported with TB in 2003 two-thirds were born outside the UK. The adolescent programme has been replaced by a neonatal BCG programme, whereby BCG is offered to high risk infants, defined as infants from communities where the incidence of TB is at least 40 per 100,000 and individuals who come from or whose parents or grandparents come from a country where the rate of TB exceeds 40 per 100,000 population.
Figure 12.1: Number of notifications of TB, 1970–2004

Figure 12.2: New Zealand miliary and meningeal TB admissions, by age, 1970–98
Figure 12.3: New Zealand extrapulmonary TB, by ethnicity, 0–14 years, 1990–98

Figure 12.4: Hospitalisations of TB in children age 0–4, 5–9 and 10–14 years, from 1989–2004
12.4 Vaccines

The BCG vaccine was first derived in France from an attenuated strain of *M. bovis* in 1921. Originally the vaccine was given orally, but this was found to be ineffective and the intradermal route was introduced in Sweden in 1927. The current BCG vaccine contains a live attenuated strain of *M. bovis*. It is presented as freeze dried material with a diluent in a separate ampoule, and must be protected from heat and light. Reconstituted vaccine should be stored at 4°C and used within four hours.

**Efficacy**

The principal role of BCG is to protect individuals at high risk of intensive exposure, but it does not have a significant impact on the incidence of the disease. Efficacy has varied in different trials between 0 and 90 percent. This has been attributed to variations in methodology, differences in vaccines used, and the prevalence of environmental mycobacteria in the areas where trials have taken place. However, it is widely regarded as efficacious in preventing serious extrapulmonary disease in neonates.

Although it is reported there is no good evidence that BCG provides protection more than 10 years after vaccination, some evidence has since been found that in certain populations protection has lasted for up to 60 years after BCG immunisation. Although the evidence is limited, BCG revaccination does not appear to offer any additional protection so no more than one immunisation should be given in a lifetime.

A recent study from Turkey, where BCG is recommended at two to three months of age and at age six to seven years, looked at the incidence of TB infection in children aged 16 or under, living in households where an adult had been diagnosed with smear positive TB. This prospective community study used both a tuberculin skin test and a T-cell based blood test (ELISpot) to assess the exposed children, and found that the amount of TB exposure in the household and the age of the child were risk factors for TB infection. The ELISpot test also identified that absence of a BCG scar was an independent risk factor for TB infection in the TB-exposed children. BCG vaccinated children had a 24 percent reduction in their risk of having TB infection compared with unvaccinated children (odds ratio 0.6, 95 percent confidence interval 0.43–0.83). This suggests that BCG offered some protection against TB infection.

**BCG given with other vaccines**

BCG can be given simultaneously with any other vaccine. However, it must be administered into a separate site and not in the same syringe. Because of the risk of local lymphadenitis, no further immunisations should be given into the arm used for BCG for at least three months.

Hepatitis B immunoglobulin (given at birth to babies of hepatitis B carrier mothers) or normal immunoglobulin is thought not to reduce the effectiveness of BCG immunisation, which principally acts through cell-mediated immunity.
Tuberculosis

Administration

Only gazetted vaccinators may give BCG immunisations. The vaccine is given by intradermal injection over the point of insertion of the left deltoid muscle. This is not much higher than the mid-point of the upper arm. For full details about administration, please refer to the Technical Guidelines for Tuberculin Testing and BCG Vaccination.

A local reaction usually develops at the site of a BCG immunisation within two to six weeks. This begins as a small papule, which increases in size for a few weeks and may break down into a shallow ulcer approximately 10 mm in diameter. The lesion may be covered by a dry dressing until a scab forms. It is essential that air is not excluded. The site should not be squeezed, incised or treated with antibiotic or steroid ointment.

If an impermeable dressing is necessary to allow activities such as swimming, the dressing should be left in place for only a short time. Prolonged occlusive coverage gives rise to a large, unsightly scar. The lesion usually subsides over several months and will usually leave only a small scar.

There is no relationship between the presence or absence of a post-vaccination tuberculin reaction and protective immunity. Nor are there any data relating to the presence or absence of a scar and protective immunity. Therefore, follow up of vaccinees is not recommended.

The 2003 Guidelines for Tuberculosis Control in New Zealand, chapter 8, p.11, offer advice on determining whether an individual has been previously vaccinated:

> Often it is uncertain whether an individual has been previously vaccinated or not. Previous BCG vaccination is defined as documented evidence of a BCG vaccination (including date), or history of BCG vaccination supported by a compatible scar. A compatible scar is considered to be one of at least 4 mm diameter at a likely site. The scar is usually at the insertion of the deltoid, but it may be elsewhere, such as scapula, thigh or buttock. Persons not meeting these criteria may be offered a vaccination. Inadvertent repeat vaccination is not harmful.

12.5 Recommended immunisation schedule

Mantoux testing before BCG immunisation

Mantoux testing is done before immunisation to exclude prior infection. It is not needed if BCG is given before the age of three months unless a history of contact with a known or possible case of TB is obtained. Because the Mantoux test is usually positive following BCG vaccination it has lower utility for diagnosing TB infection in a vaccinated individual.
**BCG immunisation in New Zealand**

The incidence of TB in Māori has been declining for many years, although there was a temporary increase in 1999 largely because of one outbreak. If there is a sustained increase in rates in Māori, then the re-introduction of universal neonatal vaccination for Māori will be considered either nationally or in affected districts. BCG immunisation is generally not recommended for people five years of age or older unless they are expected to be at very high risk of TB infection. This is because the efficacy of the vaccination is highest against extrapulmonary forms of TB, which mostly affect those under five years of age.

**Neonatal BCG eligibility criteria**

TB is more common in non-Māori and non-European people in New Zealand. However, all pregnant women should be assessed by their lead maternity carer as to the risk of TB for their baby. Neonatal BCG should be offered to infants at increased risk of TB, defined as those who:

- will be living in a house or family/whānau with a person with either current TB or a past history of TB
- have one or both parents who identify as being Pacific people
- have parents or household members who within the last five years lived for a period of six months or longer in countries where there is a high incidence of TB.
- during their first five years will be living for three months or longer in a high-incidence country.

Neonates at risk should be identified antenatally by lead maternity care providers, including midwives, general practitioners, practice nurses and obstetricians. Immunisation is desirable before infants leave hospital. If this does not happen, immunisation should be arranged through the local medical officer of health.

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a This indication is not absolute. Vaccination is usually advisable if the adult is foreign born and has spent at least six months in a high incidence country within the past five years. The decision is not so clear cut when the adult is a New Zealand resident who has travelled to a high incidence country. The vaccinator must assess the adult’s actual risk of exposure to TB during the past five years. For example, it is reasonable not to vaccinate the baby of a businessperson who has spent a year in a Hong Kong bank with a low risk of TB exposure. On the other hand, a baby living with a person who has returned recently from six months’ volunteer work in a poor rural Indian community should be vaccinated. Vaccination may even be appropriate for a baby living with an adult who has travelled to a high risk setting (eg, patient care in a hospital in a high incidence country) for less than six months in the past five years. In cases where there is difficulty assessing the level of risk, advice should be sought from the medical officer of health.

b All countries except Australia, Austria, Belgium, Canada, Czech Republic, Denmark, Finland, France, Germany, Greece, Holland, Iceland, Ireland, Israel, Italy, Luxembourg, Malta, Monaco, New Zealand, Norway, Slovakia, Sweden, Switzerland, the UK and US.

c All countries except those listed above.
Children who have missed immunisation at birth should be immunised at any time up to five years of age. If the child is 12 weeks or older they should have a pre-vaccination Mantoux test to detect whether they have already been infected.

If an infant meeting the criteria is born prematurely, vaccination should not be delayed until discharge from hospital or he/she reaches ‘term’. The evidence on the effectiveness of BCG given to premature infants at birth is conflicting, and is based on studies of post-vaccination Mantoux reactivity, which is known to have no clear relationship to protective efficacy. Low birthweight in term infants is not a contraindication.

If the baby has not been vaccinated before leaving hospital, and if there is a history of current TB in a relative who has had contact with the baby, do not vaccinate immediately. Withhold vaccination, conduct Mantoux testing, seek paediatric advice and vaccinate only after the possibility of infection in the baby has been excluded. This is because the baby may have been infected. Vaccination may not protect the baby who is incubating disease, and will prevent the Mantoux test from assisting with the diagnosis of disease.

A parent’s/caregiver’s request in itself should not be accepted as an indication for immunisation. Parents/caregivers seeking vaccination of their children who do not meet the above criteria should be referred to the local medical officer of health to discuss the risks and benefits of immunisation before a final decision is made.

Following implementation of the National Immunisation Register birth cohort in district health boards, information will be collected on BCG immunisation (see section 2.3).

Other high risk individuals or groups
BCG should be offered to the following at risk persons if they have not had a previous BCG immunisation and if a pre-vaccination 5 TU Mantoux test is negative (less than 5 mm):

- contacts of active TB cases less than five years of age (note that a contact exposed to TB in the preceding three months will need two negative Mantoux tests, 8–12 weeks apart, before vaccination)
- immigrants less than five years of age from high incidence countries
- health care workers, depending on their risk of exposure (refer to the Guidelines for Tuberculosis Control in New Zealand) – a baseline two-step Mantoux test is essential before health care workers have contact with patients or infectious materials; vaccination is recommended only for those working regularly with known TB patients, or who may be seconded to care for TB patients in institutions with high rates of multi-drug resistant TB, or in institutions where local epidemiology demonstrates a high annual risk of occupationally acquired infection
- people exposed to animals that are likely to be infected.
The medical officer of health may recommend vaccination programmes for specific populations with a high risk of TB, depending on local epidemiology. Staff and residents of rest homes, prisons and other closed populations may be recommended for vaccination, from time to time, depending on local epidemiology and in consultation with the medical officer of health.

Vaccination for overseas travel (even prolonged travel in high incidence areas) should be discouraged. It is more useful to ensure that a pre- and post-travel Mantoux test is documented and to carry out investigations and treatment or chemoprophylaxis in the event of Mantoux conversion. An exception to this is a child under five years of age travelling for prolonged residence in high incidence areas. In this instance, vaccination should be considered.

**BCG immunisation in other countries**

BCG is one of the vaccines that are part of the World Health Organization (WHO) Expanded Programme on Immunization. It is given at birth in non-industrialised countries. Revaccination with BCG is not recommended by the WHO\(^\text{27}\) but is still practised in many countries.

**Tuberculosis and measles vaccine**

There has been some concern that the measles vaccine could exacerbate TB. This concern is effectively addressed in the 2003 *Red Book*,\(^\text{28}\) p. 428 (see chapter 9: Measles):

*\(\text{Tuberculin skin testing is not a prerequisite for measles immunization, and measles vaccine does not exacerbate tuberculosis. If tuberculin skin testing is otherwise indicated, it can be done on the day of immunization. Otherwise testing should be postponed for 4 to 6 weeks because measles immunization may temporarily suppress tuberculin skin test reactivity.}\)*

**12.6 Expected responses and adverse events following immunisation (AEFI)**

**Expected responses**

Ninety to 95 percent of people vaccinated with BCG develop a local reaction, followed by healing and scar formation within three months. A minor degree of adenitis developing in the weeks following immunisation should be regarded as normal, not a complication. It may take months to resolve. Suppurative adenitis should be regarded as a complication.

**Adverse events following immunisation**

Adverse events following immunisation with BCG vary with age and vaccine strain and are summarised in Table 12.1.
Table 12.1: Age specific estimated risks for complications after administration of Bacille Calmette-Guérin vaccine

<table>
<thead>
<tr>
<th>Complication</th>
<th>Incidence per 1 million vaccinations</th>
<th>Age &lt; 1 year</th>
<th>Age 1–20 years</th>
</tr>
</thead>
<tbody>
<tr>
<td>Local subcutaneous abscess; regional lymphadenopathy</td>
<td></td>
<td>387</td>
<td>25</td>
</tr>
<tr>
<td>Musculoskeletal lesions</td>
<td></td>
<td>0.39–0.89</td>
<td>0.06</td>
</tr>
<tr>
<td>Multiple lymphadenitis; non-fatal disseminated lesions</td>
<td></td>
<td>0.31–0.39</td>
<td>0.36</td>
</tr>
<tr>
<td>Fatal disseminated lesions</td>
<td></td>
<td>0.19–1.56</td>
<td>0.06–0.72</td>
</tr>
</tbody>
</table>


Severe injection site reactions, large ulcers and abscesses are most commonly caused by faulty injection technique, where part of or the entire dose is administered too deeply (i.e., subcutaneously instead of intradermally). Immunisation of individuals who are tuberculin positive may also give rise to such reactions. Special care is needed both in interpreting initial Mantoux results and in delivering the BCG vaccine.

Keloid scars at the injection site, although not uncommon, are largely avoidable. Some sites are more prone to keloid formation than others and vaccinators should adhere to the site recommended (mid-upper arm). Most experience has been with the upper arm site and it is known that the risk of keloid formation increases greatly if the injection is given higher than the insertion of the deltoid muscle into the humerus.

Rarely, osteitis and osteomyelitis, lupoid and other types of skin disorders, and neurological disorders have been reported following BCG immunisation. A few cases have been described of widespread dissemination of the vaccine organism in immune compromised people, such as children with primary immune deficiency.

Between 1965 and 2001 there were 91 cases reported to the Centre for Adverse Reactions Monitoring (CARM), with 124 adverse events following BCG vaccination, as follows: injection site reactions including abscess (53), lymphadenopathy (12), skin reactions (12), alimentary (10), anaphylaxis (4) and other reactions (33).

Every effort should be made to recover and identify the causative organism from any lesions constituting a serious complication.

Adverse BCG events will usually resolve spontaneously. Isoniazid, isoniazid/ rifampicin and erythromycin prescribed for lymphadenitis are little better than observation. If reactions persist for longer than one to two months, seek specialist opinion.
It is important that all complications are recorded and reported to a paediatrician or chest physician. Abscesses and more serious complications should be reported to the local medical officer of health in the interests of quality control of BCG immunisation technique, and to CARM, PO Box 913, Dunedin, using the prepaid postcard HP3442 (see section 2.4) or via online reporting at http://carm.otago.ac.nz. If the patient or parent/caregiver does not consent to being identified, the report should be made without personal identification.

### 12.7 Contraindications

See section 1.9 for general contraindications for all vaccines.

BCG vaccine should not be given to individuals:

- receiving corticosteroids or other immune suppressive treatment, including radiotherapy (see chapter 1: General Considerations)
- suffering from malignant conditions such as lymphoma, leukaemia, Hodgkin’s disease or other tumours of the reticulo-endothelial system
- in whom an immune compromising disease is known or suspected, such as individuals with hypogammaglobulinaemia – primary immune deficiencies in children are often not detected until after the first few weeks of life (ie, after BCG vaccine is given) so a family history of immune deficiency should be sought and, if present, discussed with a paediatrician before vaccination
- known to be infected with HIV, including neonates with suspected HIV infection
- with a positive Mantoux reaction (5 mm or more)
- with a significant fever
- with generalised septic skin conditions – in the case of eczema, an immunisation site should be chosen which is free of skin lesions
- who are pregnant (this is a counsel of caution, as no harmful effects to the fetus have been observed following immunisation of the mother during pregnancy).

### 12.8 Control measures

The principal control measures for TB are case finding, treatment (directly observed, if necessary) of active and latent infection, contact tracing and selective screening. All cases of TB should be notified to the local medical officer of health.

A consideration of the diagnosis, management and public health follow up of TB is outside the scope of this document. For further information, please refer to Guidelines for Tuberculosis Control in New Zealand, or the Control of Communicable Diseases Manual.31
References


13 Influenza

13.1 Introduction

Influenza continues to be a major threat to public health worldwide 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. 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. 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.

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.
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.
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. 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).
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. 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, and 10 for the United Kingdom (UK).

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
cauhed 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

<table>
<thead>
<tr>
<th>Age</th>
<th>Dose</th>
<th>Number of doses</th>
</tr>
</thead>
<tbody>
<tr>
<td>6–35 months</td>
<td>0.25 mL</td>
<td>1 or 2*</td>
</tr>
<tr>
<td>3–8 years</td>
<td>0.5 mL</td>
<td>1 or 2*</td>
</tr>
<tr>
<td>&gt; 9 years</td>
<td>0.5 mL</td>
<td>1</td>
</tr>
</tbody>
</table>

* 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. Immunity lasts about one year 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.
Although less effective in preventing clinical illness in older people, 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. 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.

Large case control studies in diabetics and in older people with chronic lung disease have found similar results. Randomised controlled trials have shown influenza immunisation to reduce illness and days of sick leave in health care workers and to be cost effective for the employer. There is some evidence that immunising health care workers not only reduces illness in the workers, but also reduces mortality in long stay patients. 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.

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

<table>
<thead>
<tr>
<th>A – all people 65 years of age and over</th>
</tr>
</thead>
<tbody>
<tr>
<td>B – people under 65 years of age, including children with:</td>
</tr>
<tr>
<td>– cardiovascular disease (ischaemic heart disease, congestive heart failure, rheumatic heart disease, congenital heart disease, cerebrovascular disease)</td>
</tr>
<tr>
<td>– chronic respiratory disease (asthma if on regular preventive therapy; other chronic respiratory disease with impaired lung function)</td>
</tr>
<tr>
<td>– diabetes</td>
</tr>
<tr>
<td>– chronic renal disease</td>
</tr>
<tr>
<td>– any cancer, excluding basal and squamous skin cancers if not invasive</td>
</tr>
<tr>
<td>– other conditions (autoimmune disease, immune suppression, human immunodeficiency virus (HIV), transplant recipients, neuromuscular and central nervous system diseases, haemoglobinopathies, children on long term aspirin).</td>
</tr>
</tbody>
</table>
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. 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 services 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. 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.\(^\text{32}\) 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.\(^\text{33}\) 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.\(^\text{34}\)

A review of interventions to improve influenza vaccine uptake found that provider and system oriented interventions were more effective than patient oriented interventions.\(^\text{35}\) 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 study\(^\text{36}\) 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.

\subsection*{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.\(^\text{37,38,39}\)
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

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

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
References


14  Hepatitis A

14.1 Introduction
Hepatitis A virus (HAV) is an RNA virus belonging to the Picornavirus group. Denhart and his colleagues first demonstrated the viral nature of the disease in the 1960s when they transmitted the infection to marmosets. Subsequently, HAV was adapted to grow in a clonal line of fetal rhesus monkey kidney cells, a development that opened the way for the preparation of vaccine strains.

14.2 The illness
HAV infection is characterised by an acute febrile illness with jaundice, anorexia, nausea, abdominal discomfort, malaise and dark urine. In infants and preschool children most infections are either asymptomatic or cause only mild non-specific symptoms without jaundice. Adults have higher rates of symptomatic disease: 70 percent of adults have symptoms of illness, and the severity of illness generally increases with age. The case fatality rate is 1.8 percent in adults over the age of 50 years.1 Fulminant infections with hepatitis A are rare, and chronic carrier states do not occur. Permanent liver damage is extremely unlikely. Signs and symptoms usually last less than two months, although 10–15 percent of symptomatic persons have prolonged or relapsing disease lasting up to six months. The illness may be more severe in those infected with hepatitis B or hepatitis C viruses.

The incubation period is 15 to 50 days, with an average of 28 to 30 days. Faecal viral shedding continues for one to three weeks in adults, but has been reported to last longer in young children. The highest titre of HAV in the stool has been demonstrated in the two weeks prior to the onset of clinical illness, which is the time that subjects are most likely to spread the infection. Virus excretion falls sharply in the week following the onset of jaundice.

Diagnostic tests
Commercial serological test kits are available for the detection of anti-HAV antibodies. The presence of immunoglobulin M (IgM) specific antibody indicates recent infection. This can be detected 5–10 days after exposure, before the onset of symptoms, and can persist for up to six months. Immunoglobulin G (IgG) antibody is detectable shortly after the appearance of IgM. The presence of HAV IgG indicates previous infection and immunity, or vaccination conferring immunity. Routine virus culture for HAV is not available.
14.3 Epidemiology

The virus is usually transmitted by the faecal–oral route, either from person to person contact or through contaminated food or drink. In areas of the world with low living standards, poor hygiene and high population density, the disease is virtually confined to early childhood and is not an important cause of morbidity. Almost all adults in these countries are immune. In industrialised countries the infection is less common in childhood and only 20–40 percent of adults are immune.

Viral spread occurs readily in households and in early childhood services, which, in the United States (US) and (probably) New Zealand, are important sources of outbreaks in the community. In the early childhood service, typically the adult caregiver develops symptomatic disease while the primary source, the infected young child, is asymptomatic. The risk of spread in an early childhood service is proportional to the number of children under two years of age who are still in napkins.

Epidemics have arisen from eating shellfish contaminated by human sewage. Nosocomial outbreaks in newborn nurseries have been reported. Transmission by blood transfusion has also been reported, but is very rare. There have been outbreaks among injecting drug users, and among men who have sex with men.

Universal and targeted programmes for childhood immunisation have been introduced in the US and Australia. In north Queensland hepatitis A vaccine was introduced in 1999 for indigenous children at the age of 18 months and a second dose at two years of age, and there was a catch up for children up to their sixth birthday. The average annual notification rate of hepatitis A during 1996–99 was 110 cases per 100,000 in the indigenous population and 25 cases per 100,000 in the non-indigenous population; whereas during 2000–2003 the notification rates in the indigenous and non-indigenous populations were 4 and 2.5 cases per 100,000 persons, respectively. The vaccination programme in the indigenous community reduced the incidence of disease in the broader community.

New Zealand epidemiology

The number of notified cases of acute hepatitis A infection in New Zealand decreased from 1970 to 1989, but since then the number has fluctuated (see Figure 14.1). It is likely that part of the sharp decrease in the number of cases notified as hepatitis A resulted from changes in diagnostic testing, including the introduction of testing for hepatitis B. In 2000 a total of 107 cases of acute hepatitis A were notified to medical officers of health, a rate of 3.0 per 100,000, compared with 119 cases and a rate of 3.3 per 100,000 in 1999. Since 2000 the number of cases of hepatitis A notified has decreased further (see Figure 14.1). In 2003 there were 70 cases (a rate of 1.9 per 100,000) of hepatitis A notified, and there were 49 cases in 2004 (a rate of 1.3 per 100,000 population). In 2004 rates were highest in Tairawhiti (2.3 per 100,000), followed by Lakes (2.1 per 100,000) and Auckland (1.9 per 100,000) District Health
Boards. In 2004 there was a single outbreak of three cases of hepatitis A associated with the consumption of contaminated blueberries. Nineteen (39 percent) of the 49 cases notified in 2004 had a history of overseas travel identified as a risk factor.

Figure 14.1: Hepatitis A notifications, 1970–2004

Over recent years outbreaks in New Zealand have been associated with contaminated food, person to person spread in community outbreaks, and sexual transmission in men.³

14.4 Vaccines

Four inactivated hepatitis A vaccines are currently licensed in New Zealand, as well as a combined hepatitis A and B vaccine, and two hepatitis A and typhoid combined vaccines. Three of the hepatitis A vaccines – AVAXIM™ (Pasteur Mérieux-Connaught), HAVRIX (GSK) and VAQTA® (MSD) – are manufactured from cell culture adapted hepatitis A propagated in human fibroblasts. The HAV preparation is formalin inactivated and adsorbed to an aluminium adjuvant.

The fourth hepatitis A vaccine, Epaxal Berna (Swiss Serum and Vaccine Institute), is manufactured from HAV purified from infected human diploid cell cultures and inactivated with formalin. The preparation is adsorbed to biodegradable phospholipid vesicles spiked with influenza haemagglutinin and neuramidase.

The four hepatitis A vaccines are similar in terms of efficacy and side effect profile. The immunisation schedule, ages for which the vaccine is licensed and whether
Table 14.1: Hepatitis A vaccines, by age, dose, and timing

<table>
<thead>
<tr>
<th>Age</th>
<th>Vaccine</th>
<th>Dose</th>
<th>Volume (mL)</th>
<th>Number of doses</th>
<th>Schedule*</th>
</tr>
</thead>
<tbody>
<tr>
<td>1–15 years</td>
<td>HAVRIX JUNIOR</td>
<td>720 EU</td>
<td>0.5</td>
<td>2</td>
<td>0 and 6–12 months</td>
</tr>
<tr>
<td>1–17 years</td>
<td>VAQTA®</td>
<td>25 U</td>
<td>0.5</td>
<td>2</td>
<td>0 and 6–18 months</td>
</tr>
<tr>
<td>2 years – adult</td>
<td>AVAXIM™</td>
<td>160 antigen units</td>
<td>0.5</td>
<td>2</td>
<td>0 and 6–12 months</td>
</tr>
<tr>
<td>1 year – adult</td>
<td>Epaxal Berna</td>
<td></td>
<td></td>
<td>0.5</td>
<td>2 and 0 and 1–6 months in immune suppressed, including those with splenectomy; others 0 and 12 months</td>
</tr>
<tr>
<td>Adults 16 years and over</td>
<td>HAVRIX 1440</td>
<td>1440 EU</td>
<td>1</td>
<td>2</td>
<td>0 and 6–12 months</td>
</tr>
<tr>
<td>Adults 18 years and over</td>
<td>VAQTA®</td>
<td>50 U</td>
<td>1</td>
<td>2</td>
<td>0 and 6–18 months</td>
</tr>
</tbody>
</table>

Key: EU = enzyme-linked immunosorbent assay (ELISA); U = units of hepatitis A virus protein.

* Even after a longer interval between the first and second doses there is no need to restart the series. A substantial anamnestic response occurs after a second dose given up to eight years after the initial dose.4,5

Hepatitis A and B combination vaccines (TWINRIX)

TWINRIX (GSK) is an inactivated hepatitis A virus and recombinant DNA hepatitis B surface antigen vaccine. A 1 mL dose of TWINRIX contains not less than 720 ELISA units of inactivated hepatitis A virus, and 20 micrograms of recombinant HBsAg protein. The 0.5 mL TWINRIX JUNIOR preparation contains half these quantities.

Dosage of TWINRIX

For adults 16 years of age and over, three 1 mL doses are given at zero, one and six months. For children 1–15 years of age (inclusive), the dose is 0.5 mL at zero, one and six months.
TWINRIX may be used for rapid protection, with doses given at zero, seven and 21 days and a booster at one year. Refer to the current data sheet. There is a two-dose schedule for children 1–15 years of age using the adult vaccine.

(See also section 3.4 for further information regarding the TWINRIX vaccine.)

**Hepatitis A and typhoid vaccines**

**HEPATYRIX™**

This combination vaccine with inactivated hepatitis A and purified Vi polysaccharide typhoid vaccine (HEPATYRIX™, GSK) is available for adults and adolescents older than 15 years of age. The vaccine is given as a single 1 mL dose of HEPATYRIX™ at least two weeks before departure overseas to a high risk country. A booster of hepatitis A vaccine (HAVRIX 1440) is recommended 6–12 months after the dose of HEPATYRIX™. If the individual remains at risk from typhoid fever, a single dose of the Vi vaccine, TYPHERIX®, is recommended every three years.

**VIVAXIM®**

VIVAXIM® (Aventis Pasteur) contains inactivated hepatitis A virus vaccine and *Salmonella typhi* Vi polysaccharide vaccine. It is available for use in adults from the age of 16 years and given as a single 1 mL dose at least 14 days before travel; a booster of hepatitis A vaccine is given 6–12 months after the dose of VIVAXIM®. Revaccination with typhoid vaccine is recommended every three years in subjects who remain at risk.

**Method of administration**

The hepatitis A and hepatitis A combination vaccines should be injected intramuscularly into the deltoid region of the upper arm in adults and older children, or the antero-lateral aspect of the thigh in infants. (See section 2.3 for needle sites and sizes.)

These vaccines should not be administered into the gluteal region because this may result in a less than optimal antibody response.

**Administration with other vaccines**

The Advisory Committee on Immunization Practices (ACIP) has reported that limited data from studies in adults indicates that simultaneous administration of hepatitis A vaccine with any one of the diphtheria, poliovirus (oral and inactivated), tetanus, typhoid (both oral and intramuscular), cholera, Japanese encephalitis, rabies or yellow fever vaccines does not decrease the immune response to either vaccine or increase the frequency of reported adverse events. Studies indicate that hepatitis B vaccine can be administered simultaneously with hepatitis A vaccine without affecting either vaccine’s immunogenicity or increasing the frequency of adverse events. Several studies are being conducted among infants and young children to
evaluate whether simultaneous administration of hepatitis A vaccine with DTaP, Hib, hepatitis B, measles-mumps-rubella, or oral and inactivated poliovirus vaccines affects the immunogenicity and reactogenicity of these vaccines. Those reported to date suggest that there is no interference.

When hepatitis A vaccine is administered concurrently with other vaccines, it should be given in a separate syringe and needle at a different injection site.

For individuals requiring post-exposure prophylaxis, the hepatitis A vaccine may be administered concomitantly with immunoglobulin (IG) using separate sites and syringes.

Efficacy
AVAXIM™, Epaxal Berna, HAVRIX and VAQTA® are highly immunogenic in both adults and children, with 94 to 100 percent of recipients developing protective antibody levels one month after the first dose.

Although there are minor differences between vaccines, the administration and efficacy of these vaccines are essentially the same. They all require a booster 6–18 months after the first dose (see Table 14.1, and check the manufacturer’s data sheet for more information).

Hepatitis A vaccine has not yet been approved for children less than one year old. The limited data on immunogenicity in infants indicates high levels of seroconversion, but those with passively acquired maternal anti-HAV have lower serum antibody.

Almost all recipients after a single dose of hepatitis A vaccine have short term protection, and a second dose is thought to be important for long term protection. After the primary course of hepatitis A vaccine, a booster is not recommended and follow-up studies have shown that protective antibodies last for 10 years in healthy individuals.

In subjects with an impaired immune system, adequate anti-HAV antibody titres may not be obtained after a single dose.

Duration of immunity
Protective levels of antibodies have been observed in almost all immunised children and adults who have received two doses of vaccine, five years after immunisation. Mathematical models suggest protective levels of anti-HAV could persist for 20 years or more, and there is speculation that the induction of immune memory may mean that protection may be lifelong, but ongoing studies are necessary to confirm this hypothesis.
14.5 Recommended immunisation schedule

Immunisation against hepatitis A is recommended, but not publicly funded, for the following groups.

Individuals with chronic liver disease in whom HAV infection is likely to be more severe

Immunisation with hepatitis A vaccine is recommended for chronic carriers of hepatitis B and C. Studies have shown that in these individuals super-infection with HAV leads to increased morbidity and mortality.

Susceptible people with chronic liver disease should receive hepatitis A vaccine before liver decompensation and as early as possible before liver transplant. Susceptible people who have not been vaccinated should receive hepatitis A vaccine while awaiting a liver transplant; they may receive vaccination after transplantation, although the response is unlikely to be as good as early in liver disease. 9,10

Travellers

Individuals travelling from New Zealand to areas of high (Africa, Asia, Central and South America and the Middle East) or intermediate (the Mediterranean, Eastern Europe including Russia, and parts of the Pacific) endemicity should be offered hepatitis A vaccine rather than IG. This is because of the high level of safety and efficacy of the vaccine and the anticipated duration of protection. After one dose, protective levels of antibody have been demonstrated by two weeks, and 95–100 percent of vaccinees seroconvert by four weeks. IG is no longer recommended or available for pre-travel use. Hepatitis A vaccine given at any time prior to the day of departure may provide some protection.

Certain occupational groups

Immunisation with hepatitis A vaccine should be recommended for people in occupational groups exposed to faeces, including:

- employees of early childhood services, particularly where there are children too young to be toilet trained
- those involved in the care and education of the intellectually disabled
- health care workers exposed to faeces
- sewerage and other workers exposed to faeces
- military personnel.

Food handlers are not at specific risk for contracting hepatitis A, nor are they at specific risk for transmitting the infection, but they are expected to use safe food handling practices. Hepatitis A immunisation of food handlers may be considered, particularly when there is a community outbreak.
Others at higher risk

Consider hepatitis A vaccine for the following groups:

- men who have sex with men, among whom outbreaks of HAV infection have been reported
- injecting drug users
- recipients of blood products such as factor VIII because of the very small risk of hepatitis A transmission from this source.

Pre-immunisation screening for anti-HAV antibodies is not routinely recommended but should be considered for those who may have already been infected, including:

- those who are likely to have been exposed as children (born in a country of high endemicity) or in the course of their employment
- those with a history of jaundice
- men who have sex with men
- injecting drug users
- individuals who have frequently visited areas of high endemicity.

Routine immunisation for children

Hepatitis A vaccine is not routinely recommended and is not on the National Immunisation Schedule for children in New Zealand. It should, however, be considered during community outbreaks.

In the US, hepatitis A vaccine is recommended for universal immunisation of children if the regional incidence reaches greater than 20 per 100,000 (twice the national average in the US). It is also considered for children in those areas where the rate of infection is above the US national average population rate of 10 per 100,000 but below 20 per 100,000. In one area of California, where the rate of hepatitis A infection was 48 per 100,000, immunisation of children aged two to 12 years followed by ongoing immunisation of two-year-old children decreased the rate of hepatitis A infection by 93 percent. A two-dose schedule was given. The decrease was in both immunised and non-immunised populations.11

In Australia, hepatitis A vaccine was offered to aboriginal children in Queensland, Northern Territory, Western Australia and South Australia from 1 November 2005. Eligible children were given two doses of vaccine, with the first given after 12 months of age and the second dose six months later. There was a catch-up programme for children under the age of five years.
14.6 Expected responses and adverse events following immunisation (AEFI)

Expected responses

Expected responses to the vaccine are usually mild and of short duration. Soreness, redness and swelling at the injection site, as well as fever, malaise, headache, nausea and loss of appetite, have been reported for the available vaccines.

Adverse events following immunisation

Reviews of data from multiple sources have not identified any serious adverse events among children and adults that could be attributed to the hepatitis A vaccine.

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 http://carm.otago.ac.nz. If the patient or parent/caregiver does not consent to being identified, the report should be made without personal identification.

14.7 Contraindications

The usual general contraindications to immunisation apply to hepatitis A vaccine (see section 1.9). Administration of hepatitis A vaccine should be delayed in individuals suffering from acute severe febrile illness. Hepatitis A vaccine should not be administered to people with a history of a severe reaction to a prior dose of hepatitis A vaccine or to a vaccine component. In individuals with an impaired immune system, adequate anti-HAV antibody titres may not be obtained after a single dose.

The safety of hepatitis A vaccine in pregnancy and during lactation has not been determined. However, because hepatitis A vaccine is produced from inactivated HAV, the risk to the developing fetus and infant is expected to be low. Therefore the risk associated with vaccination in pregnancy and during lactation should be weighed against the risk of hepatitis A. Hepatitis A vaccines should be used during pregnancy and during lactation only when clearly needed.

Hepatitis A vaccines should be administered with caution to individuals with thrombocytopenia or a bleeding disorder, since bleeding may occur following intramuscular administration. Firm pressure should be applied to the injection site (without rubbing) for at least two minutes.

14.8 Control measures and passive immunisation

All cases of hepatitis A should be notified to the local medical officer of health.

Human normal IG provides protection against clinical disease due to hepatitis A and may be offered to close short term contacts of all ages in order to control outbreaks of hepatitis A in households and institutions. IG should be administered as soon as
possible after exposure. The recommended dose is 0.03 mL/kg intramuscular human normal IG. Hepatitis A vaccine should also be offered (see ‘Control of outbreaks’ below). IG is not usually offered if more than two weeks have elapsed since the onset of exposure to the index case.

Human normal IG is no longer recommended as pre-exposure prophylaxis for travellers. Hepatitis A vaccine is advised instead. The hepatitis A vaccine may be considered as an alternative, or in addition, to IG for post-exposure prophylaxis although further studies are needed to confirm its efficacy in these circumstances.

**Newborn infants of infected mothers**

Perinatal transmission is rare. If the mother develops symptoms two weeks before to one week after delivery, the infant may be given IG (0.02 mL/kg), although its efficacy in these circumstances has not been established. The mother may breastfeed.

**Early childhood services workers, children and household contacts**

Prevention of spread in these circumstances requires educating people about the modes of spread. For example, HAV can survive on objects in the environment for up to several weeks. IG or immunisation should be considered for unimmunised adult workers and children in the same room as the index case. An outbreak involving children still in napkins usually requires that all children at the facility and adult workers be given IG and/or vaccine. In addition, new workers appointed or children admitted up to six weeks after the outbreak should be vaccinated prior to entry, or offered IG if younger than the recommended age for vaccine.

All household and intimate contacts should receive IG in the dosage noted above, or vaccine as soon as possible after exposure (see ‘Control of outbreaks’ below). Schoolroom exposure does not usually lead to a significant risk of infection, and prophylaxis is not regarded as necessary in these circumstances.

**Control of outbreaks**

*Community wide outbreaks of hepatitis A infection*

IG is of limited use when used as a single agent, but there is strong evidence that hepatitis A vaccine is effective in controlling community wide epidemics of hepatitis A infection. Before the vaccine is used for outbreak control, consideration should be given to the current epidemiology in the community, the population at risk should be defined, and the feasibility and cost of delivering a programme should be assessed.

*Common source outbreaks of hepatitis A infection*

IG is effective at limiting transmission in defined outbreaks. IG given as post-exposure prophylaxis is effective at limiting transmission to contacts that have recently been exposed to HAV, if the last contact occurred within the previous two weeks while the case was in the infectious period of the illness.
There is some evidence that hepatitis A vaccine is effective at controlling common source outbreaks. Before the vaccine is used for outbreak control, however, consideration should be given to the current epidemiology in the community, and the population at increased risk needs to be clearly defined.

In the future, consideration may be given to administering hepatitis A vaccine to specific populations in areas where there are high rates of hepatitis A over time.

References
15 Meningococcal Invasive Disease

15.1 Introduction
Meningococcal disease is caused by *Neisseria meningitidis*, a gram-negative intracellular diplococcus typically seen within leucocytes. It causes both endemic and epidemic disease. The first epidemic was probably reported by Willin in 1661, but Weiselbaum did not identify the organism until 1887. Vieusseux published the first definitive description of meningococcal meningitis in 1905.

At least 13 serogroups of meningococci can be differentiated based on the chemical and immunological properties of the capsular polysaccharides. Most human disease is caused by serogroups A, B, C, W135 and Y, and these strains are responsible for nearly all outbreaks of disease. Meningococci can be further subdivided on the basis of the class 2 or 3 outer membrane protein (serotype) and class 1 outer membrane protein subtype and lipopolysaccharide (immunotype). Standard nomenclature lists serogroup, serotype, serosubtype and immunotype (eg, B:4:P1.7-2,4). Meningococci have the capacity to exchange genes and switch serogroups.

Group A is the most common epidemic strain throughout the world and was responsible for the 1985/86 Auckland epidemic. Since 1991 there has been a New Zealand wide epidemic of serogroup B disease with the B:4:P1.7b,4 strain (see 'New Zealand epidemiology' below). This long lasting epidemic has led to New Zealand working with vaccine manufacturers to produce a strain specific group B meningococcal outer membrane vesicle (OMV) vaccine (MeNZB™, Chiron) specific to the New Zealand strain, in order to combat the epidemic. Following immunogenicity, safety and reactogenicity trials in 2003/04, the vaccine was progressively introduced through the country in a programme for children and young adults aged 0–19 years (see 15.4C).

15.2 The illness
Infection with the meningococcus results in a wide range of presentations, but most commonly meningitis and/or septicaemia (meningococcaemia). Meningococcal invasive disease usually has a sudden onset with fever, malaise, prostration and a variety of other possible symptoms including nausea, vomiting and headache. Approximately two-thirds of cases have a rash, which may be petechial, purpuric or (less commonly) maculopapular and urticarial. The presence of a petechial or purpuric (haemorrhagic) rash must be taken very seriously. Those particularly at risk of meningococcal disease are children under five years of age, although all age groups may be infected and there is a higher case fatality rate in adults. The presentation may be non-specific in young infants.

In fulminant cases, disseminated intravascular coagulation, shock, coma and death can occur in a few hours despite appropriate treatment. The signs and symptoms of meningococcal meningitis do not differ from those caused by *Haemophilus*
*influenzae* type b (Hib) or *Streptococcus pneumoniae*, although petechiae or purpura are rare with these aetiologies. Invasive meningococcal infection can also give rise to arthritis, myocarditis, pericarditis, endophthalmitis and pneumonia. Other presentations include primary pneumonia, occult bacteraemia, conjunctivitis and chronic meningococcaemia. Patients with a deficiency of terminal complement components (C5–9) are at special risk of invasive infection and recurrent meningococcal disease. Therefore, individuals with illness caused by an uncommon serogroup, a second episode of meningococcal disease or a vaccine failure should be investigated for an immune deficiency.

A definitive diagnosis depends on culture or positive PCR (polymerase chain reaction) test of the bacteria from blood, cerebrospinal fluid or another usually sterile site. Bacteria may be observed intracellularly after gram staining cerebrospinal fluid specimens or aspirates from purpuric lesions. In those who have received prior antibiotics, 3–5 mL of blood should be taken in an EDTA tube for meningococcal PCR studies, and a throat swab (including the posterior nasopharynx), which may allow isolation of the organism. Acute and convalescent sera should also be taken for serum bacteriocidal antibodies assay (see Appendix 9).

Because of the fulminant nature of this disease, antibiotics should be administered on suspicion of diagnosis and before transferring the patient to hospital. The patients for whom this recommendation particularly applies are those who are obviously ill and deteriorating quickly, and those with delirium, coma or a haemorrhagic rash. These patients may or may not have neck stiffness.

Patients should receive:
- adults: benzylpenicillin 1.2 g (2 megaunits) IV (or IM); or amoxycillin 1–2 g IV (or IM)
- children: benzylpenicillin 25–50 mg/kg IV (or IM); or amoxycillin 50–100 mg/kg IV (or IM)
- or any other available parenteral antibiotic.

For more detail, see Appendix 9.

### 15.3 Epidemiology

Asymptomatic *N. meningitidis* colonisation of the upper respiratory tract occurs in 5–15 percent of individuals. Smoking, passive smoking, crowding, and viral or mycoplasma infections increase carriage. Spread from person to person is by respiratory droplets and from contact with respiratory secretions (eg, kissing or sharing a glass). Infants and young children under five years of age are the most susceptible to the disease, with peak incidence occurring in the 6–12 months age group.
Close contacts of primary cases of meningococcal infection are at increased risk of developing disease, particularly within families, early childhood services, semi-closed communities, schools and military recruit camps. Students in their first year of tertiary education living in hostel accommodation are also at higher risk.\(^1\) Household contacts are estimated to have 500–800 times increased risk of contracting the disease compared with the risk for the general population.\(^3\)

It is not possible to calculate the incubation period for meningococcal disease for sporadic cases. Those contacts of cases of meningococcal disease who develop the disease usually do so within four days, but it can be up to 10 days. Patients may be considered to be no longer infectious after 24 hours of antibiotic therapy, although rifampicin, ceftriaxone or ciprofloxacin is necessary to reliably clear nasopharyngeal carriage (see ‘Chemoprophylaxis’, in section 15.8).

The annual incidence of meningococcal disease is about 1–3 per 100,000 in developed countries, and 10–25 per 100,000 in some developing countries. Serogroup A can cause massive outbreaks of disease, such as the regular epidemics in the sub-Saharan Africa meningitis belt, where attack rates may approach one to two cases per 100 people per year. The polysaccharide group A vaccine may be used to control these epidemics. There have been outbreaks of group A disease, and more recently group W135 disease, associated with the Haj pilgrimage, and meningococcal vaccination is required before participation.\(^4\),\(^5\) Meningococcal disease appears to have increased in developed countries over the past decade or so.

Notification rates in Australia increased from less than 1 per 100,000 in 1986 to 1.9 in 1991, and 2.7 (499 notifications) in 1997.\(^6\) An increase in group C disease led to meningococcal C conjugate vaccine being introduced into the Australian infant schedule in 2004, with a catch up programme for all children and young adults aged 6 weeks to 20 years. Before the programme began, there were 162 cases of group C disease in 2002 (from a total of 393 isolates), which decreased to 71 in 2004.\(^7\),\(^8\)

In the United States (US), there has been an increase in localised outbreaks, often in school aged children and young adults, particularly of group Y disease.\(^9\) In Canada an increased incidence of group C meningococcal disease led to several community based immunisation programmes\(^10\) with the group C polysaccharide vaccine. This has been followed by the introduction of meningococcal group C conjugate vaccine onto the routine infant immunisation schedule in Canada.

In the United Kingdom (UK), outbreaks of group C disease in young adults and an increased rate of disease in infants led in 1999 to the introduction of a group C conjugate vaccine into the infant immunisation schedule and a mass immunisation campaign for all children, adolescents and young adults up to 20 years of age. Four years after introduction the reported efficacy was at least 83 percent in children who had received the conjugate vaccine from five months of age to 18 years. However, in infants who were immunised in the first six months of life, the vaccine offered little protection one year after the last dose.\(^11\) A booster dose in the second year of life may help to address this waning immunity.
Epidemics of group A or group C meningococcal disease usually resolve in one to three years. Polysaccharide vaccines against these strains are effective in adults and to a variable degree in children. In contrast, strain specific group B disease epidemics start slowly and may persist for 5–10 years or longer, as seen in Norway and Chile.\(^{12,13}\) A higher proportion of group B disease cases occur in children under five years of age, and at the start of an epidemic there may be an age shift towards higher rates in older children and adolescents. The serogroup B polysaccharide is poorly immunogenic in humans. Instead, vaccines using other bacterial components – especially preparations of outer membrane proteins (OMP) – have been developed. The protection provided by these vaccines is expected to be serotype specific, especially in younger age groups.

**New Zealand epidemiology**

Since 1991 there has been a persistently elevated rate of meningococcal disease in New Zealand, increasing from 53 cases recorded in 1990 to a peak of 648 cases in 2001. Since 2001 there has been a gradual decline in the number of cases reported, with 344 cases reported in 2004. This annual rate in 2004 was 9.2 cases per 100,000, compared with the rate of 1.5 per 100,000 in the non-epidemic years 1989/90 and a rate of 17.4 per 100,000 in 2001 (see Figure 15.1).

A workshop to discuss meningococcal disease control was held in 1995, where it was recommended that a case control study to investigate risk factors for the disease be undertaken.\(^{14}\) The case control study found household crowding to be an important risk factor independent of ethnicity.\(^{15}\)

**Figure 15.1: Notified cases of meningococcal invasive disease, 1970–2004**
Historically, in New Zealand the dominant serogroup has been serogroup B, except for a large outbreak of serogroup A in Auckland in 1985/86, and small group C outbreaks in south Wellington and Taranaki during 1994, Otago in 2002 and 2003, and Huntly in 2005. A mass immunisation programme using a group A polysaccharide vaccine controlled the group A outbreak in Auckland. In response to the group C outbreaks, quadrivalent vaccine was given to geographically defined populations two to four years of age in Wellington, and two to nine years of age in Taranaki. In response to the Otago outbreaks, staff and school students were given quadrivalent polysaccharide vaccine in one outbreak, and students in hostel accommodation were offered the quadrivalent vaccine in the second outbreak. The meningococcal conjugate group C vaccine was offered to school students in the Huntly outbreak in 2005.

The proportion of isolates from *N. meningitidis* serogroup B disease rose from 47.8 percent in 1990 to 88.4 percent (282 out of 319 isolates) in 2001, and 87.3 percent (220 of 252 isolates) in 2004. The increase in disease rate in all years is mostly from the epidemic strain B:4:P1.7b,4. In 2001, 262 of the 319 isolates (88.4 percent) and in 2004, 184 of the 252 isolates (73 percent) were of this sero-subtype. During this epidemic, disease rates have been higher in the winter months and consistently higher in Auckland and the northern region of New Zealand. The rate of disease in 2004 was 11.6 per 100,000 total population in the northern region compared with 9.7 per 100,000 in the midland region, and 7.0 per 100,000 in both the central and southern regions. In 2004, 273 of the 342 total cases (79.8 percent) were laboratory confirmed cases, with the remainder diagnosed on clinical grounds. Rates of disease are highest in infants under one year of age, and in children between one to four years of age (see Table 15.1).

### Table 15.1: Numbers and age-specific rates of cases of meningococcal disease, under 20 years of age, 2001 and 2004

<table>
<thead>
<tr>
<th>Age group (years)</th>
<th>Number of cases</th>
<th>Age specific rate per 100,000</th>
</tr>
</thead>
<tbody>
<tr>
<td>0–1</td>
<td>110</td>
<td>201.3</td>
</tr>
<tr>
<td>1–4</td>
<td>176</td>
<td>81.4</td>
</tr>
<tr>
<td>5–9</td>
<td>76</td>
<td>26.6</td>
</tr>
<tr>
<td>10–14</td>
<td>69</td>
<td>23.7</td>
</tr>
<tr>
<td>15–19</td>
<td>96</td>
<td>36.2</td>
</tr>
<tr>
<td>Total all ages</td>
<td>648</td>
<td>17.3</td>
</tr>
</tbody>
</table>

Rates are consistently higher in Māori and Pacific children compared with the total population. The rate in 2004 for Māori children one to four years of age was 85.9 per 100,000 and in Pacific children 93.9 per 100,000, compared with the total population rate of 44.4 per 100,000 for children one to four years of age. Similar increases of a lesser magnitude of serogroup B disease have been reported by other comparable countries, including Norway, the Netherlands, Oregon (US) and the UK.
15.4 Vaccines

Please note that:

- sections 15.4A, 15.5A, 15.6A and 15.7A refer to meningococcal polysaccharide vaccines
- sections 15.4B, 15.5B, 15.6B and 15.7B refer to protein conjugate meningococcal vaccines
- sections 15.4C, 15.5C, 15.6C and 15.7C refer to group B vaccines.

Table 15.2: Indications for meningococcal vaccines

<table>
<thead>
<tr>
<th>Vaccine</th>
<th>Licensure</th>
<th>Funded for</th>
<th>Recommended for</th>
<th>See section(s)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Meningococcal A</td>
<td>Y, NA</td>
<td>Nil</td>
<td>Nil</td>
<td>15.4A–7A</td>
</tr>
</tbody>
</table>
| Meningococcal B Outer Membrane vesicle (MeNZB™) | Special programme | Current programme: all children aged 6 weeks to 19 years, plus other specified groups. Programme from July 1 2006:  
- infants aged 6 weeks, and 3, 5 and 10 months  
- adults and children pre- or post-splenectomy  
- microbiologists and laboratory workers exposed to N. meningitidis isolates  
- others as notified by the Ministry of Health. | NA     | 15.4C–7C   |
| Meningococcal C conjugate                | Y         | May be funded for a community programme to control an outbreak | 1. Young adults in their first year of residence in hostel accommodation  
2. Close contacts of cases of meningococcal C disease (as an alternative to meningococcal A, C, Y, W135 polysaccharide vaccine) | 15.4B–7B |
<p>| Meningococcal C polysaccharide           | Y, NA     | Nil        | Nil             | 15.4A          |</p>
<table>
<thead>
<tr>
<th>Vaccine</th>
<th>Licensure</th>
<th>Funded for</th>
<th>Recommended for</th>
<th>See section(s)</th>
</tr>
</thead>
</table>
| Meningococcal A, C, Y, W135 polysaccharide  | Y                    | 1. Adults and children pre- or post-splenectomy.  
2. May be funded for a community programme to control an outbreak. | 1. Young adults in their first year of residence in hostel accommodation.  
2. Close contacts of cases of meningococcal C disease (an alternative for those in 1 and 2 is meningococcal C conjugate vaccine).  
3. Individuals at high risk of invasive disease, including those with:  
   · sickle cell anaemia  
   · deficiencies of terminal complement components  
   · HIV infection.  
4. Other groups at higher risk are:  
   · military recruits  
   · microbiologists and laboratory workers exposed to *N. meningitidis* isolates  
   · travellers to sub-Saharan Africa and Haj pilgrims | 15.4A–7A          |

Key: Y: yes licensed in New Zealand, N: no, not licensed in New Zealand, NA: not available in New Zealand.
15.4A Meningococcal polysaccharide vaccines: group A, C, Y and W135 vaccines

There are four meningococcal polysaccharide vaccines with consent for distribution in New Zealand: a monovalent group A vaccine (Menomune-A, Aventis Pasteur, used during the Auckland epidemic and no longer available); a bivalent vaccine containing groups A and C (Mencevax AC, GSK, no longer available); and two quadrivalent vaccines containing groups A, C, Y, and W135 (MENCEVAX ACWY, GSK; Menomune™ACYW-135, Sanofi Pasteur), containing 50 µg of each antigen. Normally the quadrivalent vaccine is administered.

The meningococcal vaccines are a purified, heat stable, lyophilised extract from the polysaccharide outer capsule of *N. meningitidis*. Like other unconjugated polysaccharide vaccines, they are less effective in children under two years of age and are licensed for use only in children over this age. The exception is group A antigen, which is immunogenic and may be efficacious in infants three months of age and older if given in two doses, three months apart. Group C polysaccharide vaccine, as available in the group A, C, Y and W135 vaccines, should be avoided in children under two years of age because it is not immunogenic in this age group. 16,17,18,19 For a consideration of the role of conjugate group C vaccine which is immunogenic in children under two years see 15.4B.

**Efficacy of group A, C, Y and W135 vaccines**

The efficacy against groups A and C has been shown in outbreaks to be 85 to 100 percent in older children and adults.20 There is no similar data for groups Y and W135, but they are immunogenic in those who are two years of age and over. The antibody responses to each of the four polysaccharides in the quadrivalent vaccine are serogroup specific.

Protective levels of antibody are usually achieved within 7–10 days after vaccination. Immunity lasts approximately three years, although in younger children there may be a more rapid decline in antibody levels. The decline in efficacy of the group A vaccine is age dependent. In a three-year study, efficacy declined from more than 90 percent to less than 10 percent among children under four years of age when vaccinated, compared to a decline to 67 percent in children older than four years.21 In the 1985/86 outbreak in Auckland the estimated efficacy of group A vaccine was 100 percent after two doses of vaccine for children between three and 23 months of age, and after one dose for children from two years of age.22

About 1.6 million doses of the tetravalent polysaccharide vaccine were administered in Canada to people between six months and 20 years of age in response to an epidemic of meningococcus group C in the early 1990s. The overall field efficacy of the vaccine was 79 percent (higher in teenagers and lower in children under five years of age).23 The epidemic waned both in provinces that vaccinated and in those that did not.24 A subsequent case control study found a good level of protection...
(77 percent) was provided over a five-year period by a single dose of the polysaccharide vaccine in individuals aged six years and over, but in those aged two to five years only short term protection was achieved.²⁵

**Dosage of polysaccharide vaccines**
For those two years of age and over the vaccine is administered as a single dose of 0.5 mL, given by subcutaneous injection. (See section 2.3 for needle sites and sizes.) In an epidemic the group A antigen may be considered for those under two years of age, and two doses will be required. Specific recommendations will be made depending on the situation.

**Revaccination**
There is little information available to determine the need for revaccination. Revaccination may be indicated for people at high risk of infection (eg, who are remaining in areas in which the disease is epidemic), particularly children who were first vaccinated when they were under four years of age; such children should be considered for revaccination after two to three years if they remain at high risk. Although the need for revaccination of older children and adults has not been determined, antibody levels decline rapidly over two to three years, and if there are still indications for immunisation, revaccination should be considered. Reimmunisation of adults before five years after initial immunisation does not seem to be necessary. Serological studies have reported that multiple doses of serogroup A and C polysaccharide vaccines may cause immune hyporesponsiveness to the antigens, although the clinical relevance of the phenomenon is unknown.²⁶,²⁷

**15.4B Protein conjugate meningococcal group C vaccines**
The conjugation of the serogroup C oligosaccharide to a protein carrier, such as tetanus toxoid, facilitates T-cell help and converts the immune response from a T-cell independent to a T-cell dependent one. This allows an effective primary immune response following vaccination in all ages, including infancy, and rapid anamnestic antibody responses with an increased avidity index on subsequent antigen exposure consistent with the development of immunological memory. In addition, conjugate vaccines reduce nasopharyngeal colonisation of meningococcus serogroup C, thereby protecting unvaccinated individuals by a herd immunity effect.

The UK was the first country to introduce a national immunisation programme for conjugate meningococcal group C vaccines.²⁸ Protein conjugate meningococcal group C vaccine, using the same technology as conjugate Hib vaccines, was introduced to the UK immunisation schedule in 1999 as three doses for infants, and a single dose to children from the age of one year to young adults up to and including 20 years of age. Initial results show the disease has decreased and the vaccine is effective in the vaccinated group.²⁹ The vaccines were introduced in response to increasing rates of serogroup C disease (~3 per 100,000) that occurred during the 1990s, which were associated in particular with outbreaks in universities...
and accompanied by high fatality rates. Licensure was not based on efficacy trials, but instead on safety and immunogenicity data, including extrapolation of serological correlates of protection from older children and adults who had received group C polysaccharide vaccines.

Pre-licensure studies had shown that conjugate meningococcal group C vaccines were well tolerated and induced bactericidal antibodies and immunological memory in UK toddlers after one dose, justifying a single dose catch up schedule for children aged one to 18 years. Similarly, the conjugate vaccines were immunogenic following a primary two-, three- and four-month series during infancy, and immunological memory persisted four years later when subjects were rechallenged with meningococcus serogroup C polysaccharide. Consequently, no booster doses have been given following the primary accelerated immunisation series during infancy. Of importance, infants in both the UK and Africa who received a primary series with conjugate meningococcal group C vaccines may have subsequent anamnestic responses attenuated by repeated doses of meningococcal polysaccharide group C vaccine.

Protein conjugate meningococcal group C vaccine has also been introduced to the routine childhood schedule in Australia. The protein conjugate meningococcal group C vaccine Meningitec® (Wyeth) and protein conjugate meningococcal group A and C vaccine Menjugate are now licensed in New Zealand.

Combination protein conjugate meningococcal vaccines

Other conjugate meningococcal vaccines, such as a conjugate vaccine active against groups A and C, have been developed. The conjugate vaccine Menjugate is now licensed in New Zealand.

A conjugate quadrivalent meningococcal vaccine effective against groups A, C, Y and W135 meningococcal disease (Menactra®, Sanofi Pasteur) is licensed in the US, but not in New Zealand at the time of writing, for individuals 11 to 55 years. Immunisation against meningococcal disease with this quadrivalent conjugate vaccine is now recommended in the US at the age of 11 years, or if missed it is given at age 15 years. A quadrivalent vaccine is also recommended before college entry. Post-licensure reports of five cases of Guillain-Barré syndrome in young adults aged 17–18 years, 14 to 31 days after the Menactra® vaccine led to an investigation. The manufacturer has advised medical practitioners of the association of Guillain-Barré syndrome with the vaccine, and the Centers for Disease Control have advised that parents and students should be warned of the association. To date there is insufficient information to conclude there is a causal relationship, and there is continuing follow up.

Efficacy of protein conjugate meningococcal group C vaccines

Since the introduction of the national meningococcal group C immunisation programme in the UK, coverage has exceeded 80 percent in all targeted age groups
younger than 19 years. During the first two years of the campaign the cases of serogroup C disease decreased by 86.7 percent, with short term vaccine efficacy of 97 percent in teenagers and 92 percent among toddlers.\textsuperscript{38} There was a concomitant decrease in deaths due to serogroup C from 67 in 1999 to five in 2001. By the end of 2001 there were 26 vaccine failures. More recent estimates place overall vaccine efficacy at 90.4 percent after four years.\textsuperscript{39} The vaccines have been well tolerated without serious adverse effects. Low grade fever was detected in 5 percent and mild local reactions were reported in about 40 percent of recipients.\textsuperscript{40,41,42}

Protective efficacy against carriage of serogroup C by adolescents one year after the immunisation campaign was estimated at 69 percent, with the vaccines providing induced mucosal immunity in 63 percent of those who had been immunised.\textsuperscript{43} At the same time there was no increase in colonisation by the other meningococcal serogroups. Consistent with the reduction in meningococcal carriage rates there has been a 67 percent reduction in serogroup C disease among unvaccinated children within the target age groups and a reduction of 35 percent of cases in adults over the age of 25 years.\textsuperscript{44} At the same time there is no evidence of capsular switching or an increase in disease by serogroup B strains.\textsuperscript{45}

Although at four years of follow up the vaccine's effectiveness remained at 90 percent, a significant trend for waning effectiveness after one year was observed, particularly among infants.\textsuperscript{46} Similarly, measures of seroprotection are absent in the majority of infants and toddlers within two to three years of their last vaccination after either the single valent group C vaccine or the quadrivalent conjugate vaccine.\textsuperscript{47,48} Even though the conjugate vaccines induce an anamnestic response, it is not clear whether circulating protective antibodies are also required to prevent meningococcal disease. If invasive disease develops within hours or days of acquisition and colonisation of the nasopharynx, it is unlikely there will be sufficient time to mount a memory response and produce protective serum antibody levels. Current protection from meningococcal disease is likely to require a combination of reducing the likelihood of exposure to disease and reduced carriage, immunological memory and circulating antibodies.\textsuperscript{49}

Despite these considerations, the meningococcal C vaccine has had a major impact on the epidemiology of meningococcal C disease in the UK. Further work may provide information on the persistence of mucosal and serological protective antibody responses and the effects of further boosting.

**Dosage of protein conjugate meningococcal group C vaccines**

Each 0.5 mL dose of Meningitec\textsuperscript{®} (Wyeth) contains 10 µg *N. meningitidis* group C oligosaccharide (MnCO) conjugated to approximately 15 µg *Corynebacterium diphtheriae* CRM\textsubscript{197} protein, given by intramuscular injection. (See section 2.3 for needle sites and sizes.)
The recommended dose of Meningitec\textsuperscript{\textregistered} vaccine for infants is three doses of vaccine at six- to eight-week intervals. For children over the age of one year, along with adolescents and adults, one dose is recommended.

### 15.4C Group B meningococcal vaccines

Group B vaccines are not commercially available. Vaccines derived from group B polysaccharides are poorly immunogenic, and therefore research has concentrated on the outer membrane protein (OMP) and in particular the outer membrane vesicle (OMV). Vaccines based on the OMP/OMV induce serum bactericidal antibodies. Any estimation of their clinical efficacy is limited by the quality of the available data.

The two most evaluated OMP vaccines are those produced in Norway in response to an epidemic with the strain B:15:P1.7.16, and a vaccine produced in Cuba in response to a B:4:P1.19.15 strain epidemic. The Norwegian vaccine was given as two doses to 13 to 14 year old school children and showed an efficacy of 57 percent at 29 months in a randomised controlled trial.\textsuperscript{50} A later evaluation estimated that the vaccine efficacy at 10 months after the introduction of the vaccine was 87 percent.\textsuperscript{51} The vaccine was not introduced nationally because the epidemic declined and the efficacy of 57 percent was judged insufficient.

The Cuban vaccine, a combined group C polysaccharide vaccine with the group B OMP vaccine, had an efficacy of around 80 percent in a randomised trial among adolescents.\textsuperscript{52} Vaccination of all Cubans under 20 years of age, and ongoing routine vaccination of all infants with two doses of the vaccine, had contributed to the continuing control of the disease in Cuba.

The Cuban vaccine was also used in mass immunisation campaigns in some Latin American countries experiencing outbreaks of meningococcal group B disease caused by varying proportions of the same strain as Cuba. Studies showed that two doses of the Cuban vaccine were effective in older children, but in children under four years of age results varied from showing no effect to a moderate effect. However, it was observed that if vaccination led to a rise in serum bactericidal antibody levels this was suggestive of vaccine efficacy. Vaccine efficacy appeared to be higher when the vaccine strain was similar to the outbreak strain.

A study in Chile, using both the Norwegian and the Cuban vaccines, compared the antibody response in infants, children and adults. Following three doses, over 95 percent of infants sustained a four-fold rise in serum bactericidal antibody against the vaccine strains.\textsuperscript{53} This suggests that three doses of an OMV vaccine could provide clinical protection in this age group.

### New Zealand Meningococcal B Immunisation Programme

Development and manufacture of a vaccine specific to the New Zealand epidemic strain (MeNZB\textsuperscript{TM}) in sufficient quantities for the nationwide immunisation programme was possible because of a partnership between the Ministry of Health
and Chiron Vaccines, working in collaboration with the Norwegian Institute of Public Health. The MeNZB™ clinical trials to determine immunogenicity, safety and reactogenicity were led by a research team from the University of Auckland. Three doses of MeNZB™ were administered six weeks apart, in an adult study and in studies of children aged 8–12 years, 16–24 months and 6–8 months. In an infant study, the MeNZB™ was administered together with the usual childhood schedule vaccines to infants starting at 6–10 weeks old.

The benchmark used in the clinical trials to indicate protection was a four-fold increase in serum bactericidal assay titre from a baseline titre of two. This test is the most reliable available measure of functional antibodies following vaccination. International experience with other similar vaccines indicates that the percentage of those who achieve a four-fold rise by serum bactericidal assay following vaccination may underestimate the percentage that will be protected from disease. For some individuals an immune response is seen but it fails to reach the four-fold rise cut off. Further information for medical practitioners on the MeNZB™ vaccine is available in the Meningococcal B Immunisation Programme: Programme Guidelines for Health Professionals (see www.moh.govt.nz).

Results from the MeNZB™ clinical trials

Clinical trials, using a schedule of three doses of MeNZB™ given concurrently with the routine schedule for young infants and with an interval of six weeks for older age groups, demonstrated that 55 percent of infants (aged 6–10 weeks), 74 percent of older infants (aged 6–8 months), 75 percent of toddlers (aged 16–24 months), 76 percent of children (aged 8–12 years), and 93 percent of adults developed a four-fold rise (compared with pre-vaccination values) in serum bactericidal assay titres four to six weeks after the third dose.

The successful trials in those age six months to 19 years led to licensure with provisional consent to vaccinate children and young people aged from six months to 19 years of age from 8 July 2004 and infants from 6 weeks of age on from 3 February 2005.

Additional data showed an improvement in the response rate (to 69 percent) after a fourth dose of MeNZB™ was given to infants at the age of ten months (43 weeks) and licensure with provisional consent for a fourth (further) dose of MeNZB™ vaccine for all infants who started their MeNZB™ course under six months of age, was granted on 16 January 2006. For infants who received the third dose of MeNZB™ vaccine at five to six months of age (21–26 weeks), the fourth dose should be given at ten months (43 weeks) of age. For babies who received the third dose of MeNZB™ vaccine at six months (26 weeks) of age or older, the fourth dose is given four months (17 weeks) after the third dose of MeNZB™ vaccine.

For babies who received the third dose of MeNZB™ vaccine before the age of five months (21 weeks), the fourth dose is recommended to be given nine weeks after the third dose to improve protection.
The necessity for further doses in other age groups has not been established.

The Meningococcal B Immunisation Programme commenced in July 2004 in the Counties Manukau District Health Board (DHB) area, followed by the greater Auckland and Northland DHB areas in November 2004. From late January 2005 the programme was extended DHB by DHB across the North Island and from Southland through to Nelson–Marlborough in the South Island, the latter beginning their programme in July 2005.

Children under five years of age, children not attending school and young people who had left school were immunised by primary care and outreach immunisation services.

Children and young people who were attending primary, intermediate and secondary school, were immunised at school by Public Health Nurse services.

The Meningococcal B Immunisation Programme finishes on 30 June 2006, although immunisation of babies from the age of six weeks, and for certain groups (see 15.5C) will continue until it is clear that the epidemic is controlled. MeNZB™ will also be available until the end of December 2006 for children and young adults to complete their three dose vaccine course.

The epidemiology of the disease will continue to be monitored so that vaccine efficacy may be assessed and the bacteria studied to detect any capsular change or emergence of different subtypes. Post-licensure vaccine efficacy and safety evaluations will be assessed and be sent to Medsafe as part of a full licence application.

Comprehensive safety monitoring

A comprehensive system of post-licensure safety monitoring is a key component of the Meningococcal B Immunisation Programme, and is designed to:

- detect serious adverse events following vaccination
- assess whether such events have a causal or coincidental relationship to vaccination
- increase public confidence in the immunisation programme, thereby helping to maintain coverage by alleviating unsubstantiated fears of vaccine reactions.

Dosage of group B vaccines

Each 0.5 mL dose of the MeNZB™ vaccine contains 25 µg of \(N. meningitidis\) group B OMV, and is given by deep intramuscular injection, preferably in the anterolateral thigh in infants/toddlers and in the deltoid region of the non dominant arm in toddlers, older children, adolescents and adults. (See section 2.3 for needle sites and sizes.)
The vaccine can be administered concomitantly with routine immunisation vaccines, using separate injection sites.

15.5  Recommended immunisation schedule

15.5A  Recommended immunisation: group A, C, Y, W135 polysaccharide vaccines

Routine immunisation with meningococcal polysaccharide vaccine is not recommended because the usual risk of vaccine preventable meningococcal disease is very low. The vaccine is not recommended under two years of age because of the poor immune response, but may be used in outbreak situations in younger age groups (eg, a group A polysaccharide vaccine was used in Auckland and a group C vaccine was used in Canada).

Funded immunisation schedule for individuals pre- and post-splenectomy: meningococcal group A, C, Y, W135 vaccine (upon the recommendation of a secondary care specialist)

The quadrivalent polysaccharide meningococcal vaccine (Menomune™ ACYW-135, Sanofi Pasteur) is recommended, and from 2006 will be publicly funded, for the following individuals at high risk of invasive meningococcal disease:

- adults pre- and post-splenectomy, and children pre- and post-splenectomy or with functional asplenia – individuals scheduled for splenectomy should be immunised at least two weeks before the operation (see section 1.8).

A booster of the quadrivalent vaccine is also funded for individuals considered at special risk.

Note: From 2006, for individuals pre- and post-splenectomy the quadrivalent meningococcal vaccine (ACYW135), the meningococcal B vaccine MeNZB™ (while the vaccine is available in New Zealand), Hib vaccine and pneumococcal polysaccharide vaccine are publicly funded (both the vaccine and administration) (see section 1.8 and individual vaccine chapters).

Organisation and community based outbreaks

The quadrivalent meningococcal vaccine or the conjugate group C vaccine is recommended and publicly funded in an outbreak for the following groups:

- organisation and community based outbreaks, defined as three primary cases of invasive meningococcal disease caused by strains in the quadrivalent polysaccharide vaccine (A, C, Y and W135) within a three-month period, giving a primary attack rate of \( \geq 10 \) cases per 100,000 population (See section 15.8).
Recommended immunisation for other individuals at increased risk of invasive meningococcal disease (not currently funded)

Individuals with a high risk of invasive meningococcal infection should be offered the quadrivalent polysaccharide meningococcal vaccine. Neither the vaccine nor the administration of the vaccine is currently funded. For children, see the schedules for use of the conjugate group C meningococcal vaccine in section 15.5B.

The quadrivalent polysaccharide meningococcal vaccine is recommended but not publicly funded for those with:

- sickle cell anaemia
- deficiencies of the terminal complement components
- individuals with human immunodeficiency virus (HIV) infection, who may be safely immunised with meningococcal polysaccharide vaccines.

The vaccine has been shown to be immunogenic in these groups, but there is no data on clinical protection.

Close contacts

Close contacts of cases of meningococcal disease are at increased risk of developing the disease over subsequent months, despite appropriate chemoprophylaxis. Immediate family or close contacts of cases of proven invasive meningococcal disease (if the disease is due to a group included in the vaccine) should be offered meningococcal vaccine as well as chemoprophylaxis.

Other groups

The quadrivalent meningococcal vaccine or the conjugate group C vaccine is recommended, but not publicly funded, for the following groups:

- young adults entering hostel accommodation (see section 15.5B)
- military recruits
- microbiologists and laboratory workers routinely exposed to *N. meningitidis* isolates
- travellers to countries during meningococcal epidemics, as in the sub-Saharan ‘meningitis belt’ during the annual Haj (see below).

Before travel

There are areas of the world where the risk of acquiring meningococcal infection is increased. Nevertheless, the risk to travellers to the developing world as a whole has been estimated as being less than one in a million per month. Recurrent epidemics of meningococcal disease occur in the sub-Saharan ‘meningitis belt’, from Senegal in the west to Ethiopia in the east, usually during the dry season (December to June). Epidemics are occasionally identified in other parts of the world and occurred
recently in Saudi Arabia (during a Haj pilgrimage), Kenya, Tanzania, Burundi, Mongolia and Nepal. For website sources for information about meningococcal vaccines for travellers, see Appendix 11.

15.5B Recommended immunisation: group C meningococcal conjugate vaccine

The vaccine is not on the New Zealand National Immunisation Schedule. It is recommended, but not publicly funded, for the following groups.

- Protein conjugate meningococcal group C vaccine may be offered, as an alternative to the quadrivalent polysaccharide vaccine, to young adults who will be resident in hostel type accommodation, particularly in their first year.

- The group C conjugate vaccine may be used to control an outbreak of meningococcal disease caused by group C55 (see section 15.8).

15.5C Special programme for MeNZB™ vaccine: schedule recommendations and funding

Until 30 June 2006, MeNZB™ is offered to all children and young people aged 0–19 years as three doses of vaccine. For infants aged six weeks to five months the vaccine is given at the same time as the usual infant schedule at age six weeks, and at three and five months, plus a fourth dose (offered since January 2006) at age ten months. From the age of six months to 19 years three doses of the vaccine are given six weeks apart. The Meningococcal B Immunisation Programme will be completed at the end of June 2006, except for infants starting the usual childhood schedule. From 1 July 2006, providing the provisional licensure is extended, MeNZB™ will be available and funded for the following groups.

- Infants will continue to be offered four doses of MeNZB™ with the infant schedule vaccines at age six weeks, at three and five months, and a fourth dose at ten months.

- Other children under the age of five years (three doses of MeNZB™ vaccine at six-week intervals).

- Children and young people aged 5–19 years who started a course of MeNZB™ vaccine before 30 June 2006 have until 31 December 2006 to complete the course.

- Microbiologists and laboratory workers routinely exposed to \( N. meningitidis \) isolates (three doses of MeNZB™ vaccines at six-week intervals).
• Individuals of any age with a high risk of invasive meningococcal infection and specific conditions (three doses of MeNZB™ vaccines at six-week intervals)

These include:

i. Actual or functional asplenia – individuals scheduled for MeNZB™ vaccine pre-splenectomy, will need to have completed their MeNZB™ vaccine course (all three doses) at least four weeks prior to the scheduled operation date

ii. Sickle cell anaemia

iii. Deficiencies of the terminal complement components

iv. Individuals with HIV infection, who may be safely immunised with meningococcal polysaccharide vaccines.

Practitioners will be informed if there are other recommendations and funding for MeNZB™ vaccine.

**Premature babies**

Preterm infants and other infants with low birthweight should be immunised at the usual chronological age with the usual vaccine dosage, as for other routine childhood vaccines. For infants still in hospital at six weeks of age, provided the infant is well, MeNZB™ should be given concurrently with other routine childhood vaccines, whether given at six weeks or prior to discharge.

**Ongoing programme monitoring**

The effects of the programme will continue to be monitored. This will include ongoing analysis of the epidemiology of meningococcal disease, investigation of vaccine failures, and reporting of adverse events. These results will be reviewed at six-monthly intervals and practitioners will be informed of any changes to the programme and when MeNZB™ vaccination will cease.

### 15.6 Expected responses and adverse events following immunisation (AEFI)

#### 15.6A Meningococcal polysaccharide vaccines

**Expected responses**

Generalised reactions to meningococcal vaccine are rare, but are more common in children than in adults. Reactions include fever, malaise and chills. In the Auckland epidemic, 130,000 Auckland children were immunised with group A vaccine, and there were 546 reports of unusual clinical events by parents and practitioners. These events included 152 reports of fever; 85 of rash and local reactions; 63 of headache, stiff neck and myalgia; and 92 of apparent peripheral nerve involvement. None were permanent. An independent panel of experts examined the data and concluded that there was no evidence of permanent sequelae caused by the vaccine.
Up to 80 percent of recipients will have some local reaction, but most are minor. Approximately 10 percent will develop local reactions at the injection site within 24 hours of the injection.

**Adverse events following immunisation**

The Canadian campaign delivered over a million doses of tetravalent polysaccharide vaccine, with reported allergic reactions in 9.2 per 100,000 doses, anaphylaxis in 0.1 per 100,000 doses, and neurologic reactions in 0.5 per 100,000 doses; there were no reports of long term sequelae or of encephalopathy, meningitis or encephalitis.

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 http://carm.otago.ac.nz. If the patient or parent/caregiver does not consent to being identified, the report should be made without personal identification.

**15.6B Group C meningococcal conjugate vaccine**

**Expected responses**

The most frequent response to the meningococcal C vaccine in the UK school programme was transient headache in 12 percent of students in the first three days after vaccination. Mild to moderate local reactions at the injection site consisting of pain, tenderness and occasional redness were also reported. These were maximal on the third day after the vaccine and resolved within a day.

**Adverse events following immunisation**

Adverse events were rare. Anaphylaxis was reported at a rate of 1 per 500,000 doses distributed.

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 http://carm.otago.ac.nz. If the patient or parent/caregiver does not consent to being identified, the report should be made without personal identification.

**15.6C MeNZB™**

**Expected responses and adverse events following immunisation**

Clinical trial adverse reactions reported across all age groups are provided in Tables 15.3–15.5 below. The age groups are infants 6–10 weeks old (523 doses), infants/toddlers 6–24 months old (1472 doses), children 8–12 years old (1606 doses), and
adults over 18 years old (103 doses). Note that the following categories of frequency have been defined:

- very common ($\geq 10$ percent)
- common ($\geq 1$ percent and $< 10$ percent)
- uncommon ($\geq 0.1$ percent and $< 1$ percent)
- rare ($\geq 0.01$ percent and $< 0.1$ percent)
- very rare ($< 0.01$ percent).

Adverse reactions were collected on the day of vaccination and each day following for up to seven days. The majority of reactions were self limiting and resolved within the follow up period. The full MeNZB™ data sheet is available at www.medsafe.govt.nz.

In all age groups, injection site reactions (tenderness/pain, redness, swelling and induration) were very common, but mild or moderate in intensity, with tenderness/pain being the most common. Most injection site reactions settled within two to three days, with those persisting for more than seven days being uncommon.

Crying (infants), irritability, sleepiness, change in eating habits, diarrhoea and vomiting, and fever of at least 38.0°C (infants, toddlers) were very common after vaccination, and most of these occurred at a similar rate in the control vaccine groups, where studied. Pyrexia greater than 38.0°C, six hours after vaccination, was observed in up to 20 percent of all infants aged 6–10 weeks receiving MeNZB™. However, most were apyrexial within 48 hours of vaccination.

After the fourth dose of MeNZB™ vaccine, there was an increase in the local reactions of erythema, induration and swelling. There was no increase in severe local reactions or systemic reactions.

In children and adults, very commonly reported adverse reactions include headache, malaise, nausea and myalgia.

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 http://carm.otago.ac.nz. If the patient or parent/caregiver does not consent to being identified, the report should be made without personal identification.
Table 15.3: Adverse reactions to MeNZB™ reported within seven days, all age groups

<table>
<thead>
<tr>
<th>General disorders</th>
<th>Fever $\geq 38.0^\circ$C axillary</th>
<th>Fever $\geq 38.5^\circ$C sublingual</th>
</tr>
</thead>
<tbody>
<tr>
<td>Very common</td>
<td>Infants 20%</td>
<td>Infants/toddlers 13%</td>
</tr>
<tr>
<td></td>
<td>Common 3%</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Injection site reactions</th>
<th>Redness</th>
<th>Swelling</th>
<th>Induration</th>
<th>Tenderness/pain</th>
</tr>
</thead>
<tbody>
<tr>
<td>Very common</td>
<td>Infants</td>
<td>9%</td>
<td>4%</td>
<td>10%</td>
</tr>
<tr>
<td></td>
<td>Infants/toddlers</td>
<td>44%</td>
<td>25%</td>
<td>51%</td>
</tr>
<tr>
<td></td>
<td>Children 11%</td>
<td>7%</td>
<td>10%</td>
<td>78%</td>
</tr>
<tr>
<td></td>
<td>Adults 16%</td>
<td>9%</td>
<td>17%</td>
<td>95%</td>
</tr>
</tbody>
</table>

Table 15.4: Additional reactions to MeNZB™ reported in infants (first year of life) and toddlers (second year of life) over all doses given

<table>
<thead>
<tr>
<th>General disorders</th>
<th>Irritability</th>
<th>Change in eating habits</th>
<th>Impaired sleeping</th>
<th>Unusual crying</th>
</tr>
</thead>
<tbody>
<tr>
<td>Very common</td>
<td>Infants 80%</td>
<td>35%</td>
<td>54%</td>
<td>44%</td>
</tr>
<tr>
<td></td>
<td>Infants/toddlers 45%</td>
<td>21%</td>
<td>18%</td>
<td>1%</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Gastrointestinal disorders</th>
<th>Diarrhoea</th>
<th>Vomiting</th>
</tr>
</thead>
<tbody>
<tr>
<td>Very common</td>
<td>Infants 17%</td>
<td>13%</td>
</tr>
<tr>
<td></td>
<td>Infants/toddlers 11%</td>
<td>8%</td>
</tr>
</tbody>
</table>

Table 15.5: Additional reactions to MeNZB™ reported in older children and adults over all doses given

<table>
<thead>
<tr>
<th>General disorders</th>
<th>Malaise</th>
<th>Headache</th>
</tr>
</thead>
<tbody>
<tr>
<td>Very common</td>
<td>Children 18%</td>
<td>23%</td>
</tr>
<tr>
<td></td>
<td>Adults 21%</td>
<td>26%</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Musculoskeletal, connective and bone disorders</th>
<th>Myalgia</th>
<th>Arthralgia</th>
</tr>
</thead>
<tbody>
<tr>
<td>Common</td>
<td>Children</td>
<td>9%</td>
</tr>
<tr>
<td>Very common</td>
<td>Adults</td>
<td>19%</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Gastrointestinal disorders</th>
<th>Nausea</th>
</tr>
</thead>
<tbody>
<tr>
<td>Common</td>
<td>Children 9%</td>
</tr>
<tr>
<td>Very common</td>
<td>Adults 13%</td>
</tr>
</tbody>
</table>
15.7 Contraindications

15.7A Meningococcal polysaccharide vaccines contraindications

See section 1.9 for general contraindications for all vaccines.

The available data does not suggest that giving meningococcal vaccine to pregnant women causes any adverse effects. Nevertheless, as with any vaccine in pregnancy, careful consideration of the risks and benefits of immunisation to the mother and fetus is needed. Maternal antibodies will protect the newborn for the first few months, and the subsequent response to the vaccine is not altered.60

15.7B Group C meningococcal conjugate vaccine contraindications

Anaphylaxis to a previous dose of the vaccine or any of the components is a contraindication to a further dose.

15.7C MeNZB™ contraindications

Hypersensitivity to any component of the vaccine or persons having shown signs of hypersensitivity after previous administration of MeNZB™ vaccine.

As with other vaccines, administration of MeNZB™ vaccine should usually be postponed in persons with an acute febrile illness (fever > 38.0 °C).

15.8 Control measures

All cases of invasive meningococcal infection should be notified immediately on suspicion to the local medical officer of health.

Adults and children in close contact with primary cases of invasive meningococcal infection should receive antibiotic prophylaxis, preferably within 24 hours of the initial diagnosis, but prophylaxis is recommended up to 10 days after contact. Those at particular risk include:

- household contacts (ie, people who have eaten or slept in the same house during the seven days prior to the onset of disease in the index case)
- early childhood service contacts
- those living in close contact in semi-closed communities and institutions
- individuals who have had contact with the patient’s oral secretions through kissing or sharing food and beverages.
Prophylaxis is not routinely recommended for health care personnel unless there has been intimate contact with oral secretions (eg, as a result of performing mouth to mouth resuscitation or suctioning of the case, before antibiotic therapy has started).

**Chemoprophylaxis**

The drug of choice for chemoprophylaxis is rifampicin. The recommended dose is 10 mg/kg (maximum dose 600 mg) every 12 hours, for two days. Some experts recommend four doses of 5 mg/kg per day over two days for infants under one month of age. Rifampicin causes orange discoloration of urine, sputum and tears, and staining of soft contact lenses. The colour change in body secretions is harmless, but patients should be warned and advised not to wear soft contact lenses. Rifampicin increases the hepatic metabolism of oral contraceptives, and women on these should be reminded of the seven-day rule (ie, extra contraceptive precautions during the antibiotic course and for seven consecutive days while taking the active pills after completion of the antibiotic course).

A single dose of intramuscular ceftriaxone (125 mg for children under 12 years of age and 250 mg for older children and adults) has been found to have an efficacy equal to that of rifampicin in eradicating the meningococcal group A carrier state. Ceftriaxone is the drug of choice in a pregnant woman because rifampicin is contraindicated in pregnancy. Ceftriaxone may be reconstituted with lignocaine (according to the manufacturer’s instructions) to reduce the pain of injection. A New Zealand study demonstrated that ceftriaxone and rifampicin were equivalent in eliminating naso-pharyngeal carriage of *N. meningitidis* serogroup B.61

Ciprofloxacin given as a single oral dose of 500 mg is also effective at eradicating carriage. Ciprofloxacin is not generally recommended for individuals under 18 years of age or for pregnant and lactating women because the drug causes cartilage damage in immature laboratory animals. However, an international consensus report concluded that ciprofloxacin could be used for chemoprophylaxis of children when no other acceptable alternative therapy is available.62

*Use of group C meningococcal vaccines for close contacts*

Close contacts of cases of group C meningococcal disease should be offered a group C containing meningococcal vaccine (see recommendations for the polysaccharide A, C, Y, W135 vaccine and for the conjugate vaccine). (See below for the use of the vaccines in the control of outbreaks.)

*Other vaccine serogroups*

The group B meningococcal vaccine, MeNZB™, is not used in outbreak control. The requirement for multiple doses means the vaccine offers no benefit in preventing early disease. Group A vaccines have been used in control. (See section 15.3.)
Outbreak control

When there is an outbreak of meningococcal disease of a vaccine serogroup, the medical officer of health and Ministry of Health assess the epidemiology of the cases. When there are three or more confirmed or probable cases of meningococcal disease of the same serogroup in a community or institution within a three-month period, and the overall rate reaches or exceeds 10 cases per 100,000, then an immunisation programme may be recommended to a defined population. The population in a community outbreak is the smallest geographically defined region in which the cases live, and the size of the population is determined from census data. The cases should not be close contacts or linked by common affiliation; that is, they should all be primary cases. In an institutional outbreak, a vaccine programme may be considered if two cases are identified in a three-month period.

For more details on control measures, refer to the *Control of Communicable Diseases Manual*.64

References


16  Pneumococcal Disease

16.1 Introduction

*Streptococcus pneumoniae* (pneumococcus) is a lance shaped gram-positive diplococcus. It is ubiquitous, with many asymptomatic individuals carrying the organism in the upper respiratory tract. There are some 90 identifiable serotypes of *S. pneumoniae*. Some more commonly affect children, while others are of greater significance in adults.

16.2 The illness

Transmission of the pneumococcus is from person to person, usually by droplet contact. The pneumococcus is the most common bacterial cause of otitis media in children and a frequent cause of sinusitis and pneumonia in all age groups. It also gives rise to meningitis and bacteraemia, especially in the very young, and is often the cause of bacteraemia with no obvious primary site of infection. The pneumococcus may also cause endocarditis, and, less commonly, sites such as joints, the peritoneal cavity and the fallopian tubes are affected. The incubation period of *S. pneumoniae* infection is variable but may be as short as one to three days. Illness usually occurs within one month of acquiring a new serotype in the upper respiratory tract. Illness does not usually result in prolonged carriage of the organism.

16.3 Epidemiology

Pneumococcal disease occurs throughout the year, but is more common in the autumn and winter months. The risk of disease is much higher in infants and elderly people, and more frequent in individuals with predisposing conditions such as viral upper respiratory tract infections, or underlying conditions such as immune deficiency states. Mortality is highest in patients with underlying conditions, where infection may lead to meningitis or bacteraemia. These conditions include congenital or acquired immune deficiency, splenic dysfunction or asplenia (see section 1.8), sickle cell anaemia, Hodgkin’s disease, human immunodeficiency virus (HIV) infection, cochlear implants, or following organ transplantation. Other conditions that increase the risk of pneumococcal infection include diabetes mellitus, congestive heart failure, chronic pulmonary disease and renal failure. Patients with cerebrospinal fluid (CSF) leakage due to a fracture at the base of the skull or following a neurosurgical procedure are at risk of recurrent pneumococcal meningitis.

The World Health Organization (WHO) estimates that pneumococcus causes over one million deaths per year, mostly in children under five years of age in non-industrialised countries. In industrialised countries it causes an estimated 100 cases of pneumonia, 15–19 cases of febrile bacteraemia and 1–2 cases of meningitis per 100,000 people per year. Even in industrialised countries the mortality rate from
bacteraemic pneumococcal pneumonia averages 10–20 percent, and may exceed 50 percent in the high risk groups. Many studies have identified pneumococcus as the commonest cause of community acquired pneumonia, in adults causing between 30 and 50 percent of all cases. Many cases of pneumonia that do not have the causative organism identified are likely to be pneumococcal. S. pneumoniae is the major bacterial cause of otitis media in children, accounting for 30–60 percent of culture positive episodes.

New Zealand epidemiology

An analysis of hospitalisation data from 1986 to 1996 found that pneumonia is an important illness in the first year of life, with high rates for children up to five years of age. After this the incidence declines over the first decade of life and remains at low levels until the age of 50, then starts rising steeply from 65 years of age. The hospitalisation data also shows that only 18 percent of the 8995 hospitalisations with pneumonia in 1995 had a cause identified, with pneumococcal pneumonia the most commonly coded organism in 734 (8 percent) of hospitalisations. This may underestimate the proportion of cases of pneumonia caused by S. pneumoniae as the organism is not identified in all cases, and not all are coded accurately where the organism is found.

A population based Auckland review of invasive pneumococcal disease (IPD) in children from 1984 to 1992 found an average annual incidence of 22 per 100,000 for children under 15 years, 56 per 100,000 in children under five years and 110 per 100,000 in children under two years. The rates were higher in Māori and Pacific children. The rates of invasive disease for Māori and Pacific children under 15 years were 28 per 100,000 and 49 per 100,000, and the rate was especially high in Pacific children under two years of age with a rate of 215 per 100,000. Rates of pneumococcal meningitis in all children under the age of two years was 23 per 100,000, and was 46 per 100,000 in Pacific children.

Further data from Auckland prospective surveillance during 2000/01 found the rate of invasive disease in all children under the age of two years was 191 per 100,000. For Māori children the rate was 217 per 100,000 and for Pacific 296 per 100,000. The rate of pneumococcal meningitis in children under the age of two years in Auckland remains high with a rate of 30 per 100,000 in all children, and rates of 43 per 100,000 and 49 per 100,000 in Māori and Pacific children. Lower rates for all New Zealand of 80 per 100,000 are likely to reflect less than complete referral of isolates in a passive surveillance system, and different rates of disease through the country.

More recent information comes from isolates from invasive disease, which are serogrouped and serotyped at the Institute of Environmental Science and Research (ESR) reference laboratory. The most common serogroups/serotypes in 2003/04 were 14, 9, 19, 4 and 23F. Table 16.1 below shows the proportion of invasive pneumococcal isolates that would be covered by either a seven-valent conjugate vaccine or a 23-valent polysaccharide vaccine at different ages. Note that although
the table gives the percentage of isolates covered by the 23-valent polysaccharide vaccine in children under five years, this vaccine is not effective in children under the age of two years when disease rates are highest. Although not all isolates from invasive disease are sent for reference testing, these results do provide an assessment of the burden of severe disease caused by \textit{S. pneumoniae} in New Zealand and the likely benefit from vaccines directed against specific serogroups/serotypes.

Table 16.1: Number of isolates of invasive pneumococcal disease, and serotypes covered by a vaccine, by age

<table>
<thead>
<tr>
<th>Year</th>
<th>Number of isolates from children &lt; 5 years</th>
<th>Percent covered by PCV7 and 23PPV vaccines:</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>PCV7 23PPV</td>
</tr>
<tr>
<td>2003</td>
<td>176</td>
<td>77% 95%</td>
</tr>
<tr>
<td>2004</td>
<td>161</td>
<td>79% 95%</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Year</th>
<th>Number of isolates from children 5–15 years</th>
<th>Percent covered by 23PPV vaccine</th>
</tr>
</thead>
<tbody>
<tr>
<td>2003</td>
<td>21</td>
<td>81%</td>
</tr>
<tr>
<td>2004</td>
<td>20</td>
<td>95%</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Year</th>
<th>Number of isolates from adults 15+</th>
<th>Percentage covered by 23PPV vaccine</th>
</tr>
</thead>
<tbody>
<tr>
<td>2003</td>
<td>325</td>
<td>95%</td>
</tr>
<tr>
<td>2004</td>
<td>363</td>
<td>95%</td>
</tr>
</tbody>
</table>

Key: PCV7 = pneumococcal conjugate vaccine; 23PPV = pneumococcal polysaccharide vaccine

In New Zealand, as in other countries, there has been concern at the increase in the prevalence of antimicrobial resistance in \textit{S. pneumoniae}. Antibiotic resistance data is collected and collated by ESR, and the antibiotic resistance of New Zealand isolates of \textit{S. pneumoniae} is given in Table 16.2.

Table 16.2: Increase in antibiotic resistance of \textit{Streptococcus pneumoniae} disease isolates, 1988–2004

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Invasive isolates % resistance to:</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Penicillin</td>
<td>1</td>
<td>15</td>
<td>16.6</td>
<td>16.4</td>
</tr>
<tr>
<td>Cefotaxime</td>
<td>0.8</td>
<td>4.1</td>
<td>7.5</td>
<td>12.1</td>
</tr>
<tr>
<td>Non-invasive isolates % resistance to:</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Penicillin</td>
<td>1.8</td>
<td>19</td>
<td>25.7</td>
<td>27.6</td>
</tr>
<tr>
<td>Tetracycline</td>
<td>5.6</td>
<td>11.2</td>
<td>15.5</td>
<td>18.9</td>
</tr>
</tbody>
</table>

When the \textit{S. pneumoniae} isolates from 2004 were analysed by serotype and by their resistance pattern, it was found that 98 percent of penicillin resistant serotypes would be covered by the serotypes of the seven-valent vaccine and 100 percent would be covered by the 23-valent vaccine. Similarly, 94 percent of the serotypes
resistant to third generation cephalosporins would be covered by serotypes in the seven-valent vaccine and 100 percent by the 23-valent vaccine.\textsuperscript{10} This suggests that if pneumococcal vaccines were more widely used in New Zealand, disease caused by resistant isolates would be reduced.

In a study of adults with community acquired pneumonia admitted to Christchurch and Waikato Hospitals in 1999/2000,\textsuperscript{11} the pneumonia rate among Māori was 3.03 times higher than that among non-Māori. The age specific rates were significantly higher among Māori for each 10-year age band from 45 to 74 years, and the mean age of Māori who were admitted to hospital was lower at 50 years, compared with the mean age of non-Māori of 66 years. Overall, 58 percent of the participants in the study had a comorbidity such as chronic obstructive pulmonary disease, diabetes, heart failure or asthma, and 21 percent were smokers. The Māori participants were more likely to have a comorbid condition (63 percent compared with 57 percent in non-Māori), although the difference was not significant, and were more likely to be smokers (35 percent Māori compared with 19 percent of non-Māori). Both smoking and having a comorbid illness are known to be risk factors for pneumococcal disease.

16.4 Vaccines

There are two types of vaccine available against \textit{S. pneumoniae}: the 23-valent polysaccharide vaccine licensed for adults and children from two years of age, and the newer seven-valent protein conjugate vaccine (Prevenar\textsuperscript{®}) licensed for use in children aged six weeks to nine years.

From 2006 the pneumococcal conjugate vaccine and pneumococcal polysaccharide vaccine will be fully funded for a group of children at special risk of the disease (see section 16.5A); and the pneumococcal polysaccharide vaccine will be funded for individuals with asplenia and pre- and post-splenectomy (see section 16.5B).

16.4A Seven-valent conjugate vaccine (PCV7)

A seven-valent pneumococcal polysaccharide protein conjugate vaccine (PCV7, Prevenar\textsuperscript{®}, Wyeth Lederle) is effective in infants and young children against \textit{S. pneumoniae} and is licensed in New Zealand for infants and children aged six weeks to nine years.

The pneumococcal polysaccharide is conjugated to a carrier protein, as in the \textit{Haemophilus influenzae} type b vaccines, and induces increased production of antibodies, immunological memory and maturation of the antibody response. The resulting antibodies have high avidity in contrast to the poor antibody response when polysaccharide vaccine alone is given. Each candidate polysaccharide is coupled individually to the protein, and this limits the number of serotypes covered. The seven-valent protein conjugate vaccine contains the saccharides of the capsular antigen of \textit{S. pneumoniae} serotypes 4, 6B, 9V, 14, 18C, 19F and 23F individually.
conjugated to diphtheria CRM$_{197}$ protein, a non-toxic variant of diphtheria toxin. These serotypes caused 88 percent of invasive disease in children under the age of five years in 2002.$^{12}$

One dose (0.5 mL) contains 2 µg of saccharide for serotypes 4, 9V, 14, 18C, 19F and 23F, and 4 µg of serotype 6B per dose (16 µg total saccharide) conjugated to the CRM$_{197}$ carrier protein and adsorbed on aluminium phosphate (0.5 mg), and is administered intramuscularly. (See section 2.3 for needle sites and sizes.)

PCV7 was recommended for the infant schedule in the United States (US) in February 2000 for all children from two to 23 months of age, and for children from 24 to 59 months of age who are at increased risk of pneumococcal disease.$^{13}$ Other countries are now including pneumococcal conjugate vaccine on their infant immunisation schedule, including Australia and the Scandinavian countries.

**Efficacy of the seven-valent conjugate vaccine**

In a large controlled trial among infants attending the Northern California Kaiser Permanente (NCKP) medical centres in the US,$^{14}$ PCV7 had a 97.4 percent efficacy (95 percent confidence interval [CI]: 83–100 percent) against $S.~pneumoniae$ invasive disease in children who had completed a four-dose vaccine course at two, four, six and 12 to 15 months of age, and 85.7 percent efficacy (95 percent CI: 0–100 percent) in partially vaccinated children who had received one dose or more of vaccine against the seven vaccine serotypes.

It was also found that in children who had received one or more doses of PCV7 there were 11 percent fewer episodes of clinical pneumonia and a reduction of 33 percent of episodes of pneumonia confirmed by X-ray. Among children who had clinical pneumonia and X-ray evidence of consolidation ($\geq 2.5$ cm), the efficacy of PCV7 was estimated at 73 percent.$^{15}$ In the same trial there was a 7 percent reduction overall in episodes of acute otitis media.

A further efficacy study$^{16}$ with PCV7 against IPD in American Indian children showed a primary efficacy of 76.8 percent (95 percent CI: 9.4–95.1 percent), and the intention to treat analysis was 82.6 percent (95 percent CI: 21.4–96.1 percent). Importantly, there was no increase in disease from non-vaccine serotypes.

In the US further studies have been published examining the effect of introducing pneumococcal vaccine to the infant schedule. In one large study,$^{17}$ the rate of IPD decreased after the vaccine was introduced (in early 2000) from 24.3 per 100,000 persons to 17.3 per 100,000 in 2001. The largest decrease was in children less than two years of age, where the disease rate decreased 69 percent in 2001 compared to the baseline. The rate of disease from vaccine serotypes decreased by 78 percent, and the rate of disease from vaccine related serotypes decreased by 50 percent. The rates of IPD also decreased in adults (unimmunised) by 32 percent in those aged 20–39 years, by 8 percent in those aged 40–64 years, and by 18 percent in those aged 65 years and older.
aged 65 years and older. Disease from penicillin resistant strains decreased by 35 percent. Ongoing monitoring is in place to monitor both this decline in disease incidence and any shift to non-vaccine serotype disease.

Following the introduction of PCV7 into the infant immunisation schedule in Massachusetts,\textsuperscript{18} the rate of IPD in children under the age of five years declined by 69 percent: from 56.9 per 100,000 in 1990–2001 to 17.4 per 100,000 in 2001–03, in spite of some vaccine shortages. Infants under the age of one year had the highest rate of disease, at 36.5 per 100,000, a 7.8 fold risk compared with children older than one year. Immunised children who developed disease caused by one of the vaccine serotypes were more likely to have a comorbid disease, and the African-American and children of Hispanic descent in the study had a 2.3 and 1.9 fold greater incidence rate than whites.

The US and some European countries recommend three doses of PCV7 in the first year and a fourth dose in the second year of life. In contrast, the schedules in Sweden, Denmark, Norway and Italy, and in Finland from 2005, recommend primary vaccination with PCV7 at ages three and five months and a third dose at 12 months of age. The immunogenicity and tolerability of this regime was studied in Swedish children.\textsuperscript{19} The results suggest that a two-plus-one course of PCV7 may be sufficient, although follow up studies to assess ongoing efficacy are needed.

A study of Gambian children\textsuperscript{20} has shown some evidence that children who are primed with two or three doses of a pneumococcal conjugate vaccine respond with a higher antibody response when the polysaccharide vaccine is given at age two years. This supports the use of a booster of polysaccharide vaccine.

Other conjugate pneumococcal vaccines, including a nine-valent vaccine, are being studied in clinical trials, and a significant effect on pneumonia was seen in the Gambia.\textsuperscript{21} In South Africa,\textsuperscript{22} a nine-valent pneumococcal conjugate vaccine was given at six, 10 and 14 weeks of age. Among children without HIV infection, the vaccine reduced the incidence of a first episode of invasive pneumococcal disease (caused by vaccine serotypes) by 83 percent (95 percent CI: 39–97 percent), and the efficacy among HIV infected children was 65 percent (95 percent CI: 24–86 percent). The vaccine also reduced the incidence of vaccine serotype and antibiotic resistant invasive pneumococcal disease among children both with and without HIV infection.

The South African study also reported the incidence of viruses associated with pneumonia.\textsuperscript{23} The nine-valent vaccine prevented 31 percent (95 percent CI: 15–43 percent) of pneumonias associated with any of seven respiratory viruses, influenza A, respiratory syncytial virus, adenovirus and parainfluenza viruses types 1–3 in the hospitalised children. The results suggest that pneumococcus has a major role in the development of pneumonia associated with viruses, and that these viruses may contribute to the pathogenesis of bacterial pneumonia.
A study from Finland suggested that boosting with polysaccharide vaccine at 12 months of age following priming doses of a conjugate vaccine in infancy was as effective as boosting with the conjugate vaccine in protection against acute otitis media. This raises the possibility of boosting with polysaccharide vaccine as a less costly option, though further studies are needed.

**Administration with other vaccines**

The pneumococcal conjugate vaccine PCV7 may be administered at the same time as other routine childhood vaccinations, in a separate syringe at a separate injection site.

### 16.4B Pneumococcal polysaccharide 23-valent vaccine (23PPV)

The polysaccharide vaccine (23PPV, PNEUMOVAX®23, MSD) is made from the purified capsular polysaccharide antigens of 23 serotypes of *S. pneumoniae*. It is available in New Zealand for adults and children from two years of age. PNEUMOVAX®23 includes the 23 serotypes responsible for about 90 percent or more of cases of invasive disease in industrialised countries: 1, 2, 3, 4, 5, 6B, 7F, 8, 9N, 9V, 10A, 11A, 12F, 14, 15B, 17F, 18C, 19A, 19F, 20, 22F, 23F and 33F. The Auckland study of paediatric invasive disease found that the 23-valent vaccine would cover 98 percent of serotypes, but because two-thirds of these children were under two years of age the vaccine would be of limited value. Cross reactivity may allow for protection against additional serotypes.

One dose (0.5 mL) contains 25 µg of each capsular polysaccharide antigen, dissolved in isotonic saline solution with phenol (0.25 percent) added as a preservative, and no adjuvant. The vaccine can be administered either intramuscularly or subcutaneously. (See section 2.3 for needle sites and sizes.)

**Efficacy of the polysaccharide 23-valent vaccine**

The assessment of the efficacy of pneumococcal vaccination depends on whether immune competent or immune compromised patients are compared, and whether the end point is pneumococcal pneumonia or bacteraemia.

#### Healthy adults

The early pneumococcal vaccine trials were performed in South African gold miners and US military recruits, and at least 90 percent of these healthy young adults responded to a single dose of vaccine. Results of a more recent trial with the 23-valent vaccine show that about 80 percent or more of young, healthy adults respond to the vaccine with type specific antibodies within two to three weeks. A meta-analysis of trials with a total of over 21,000 participants confirmed that pneumococcal vaccine was effective in immunocompetent subjects under 65 years in preventing both all cause pneumonia, pneumococcal pneumonia and deaths and bacteraemias. This meta-analysis failed to show any benefit for the elderly.
Children under the age of two years

Bacterial capsular polysaccharides induce antibodies primarily by T-cell independent mechanisms, which are not mature before two years of age, and so children less than two years of age respond poorly and inconsistently to the polysaccharide vaccine. Age specific immune responses also vary by serotype, and the response to some common paediatric pneumococcal serotypes (eg, 6A and 14) is decreased in children aged between two and five years of age.

Older people

Most healthy older people respond well to the vaccine, although there it is unclear how long the antibody response lasts. The consensus appears to be that most older people will require a second vaccination after five years. In a large community based study of adults over the age of 65 years, the vaccine reduced the risk of pneumococcal bacteraemia (hazard ratio: 0.56; 95 percent CI: 0.33–0.93), there was no reduction in pneumonia. A meta-analysis confirmed that in observational studies there was a protective effect against bacteraemia, and a non-significant protective effect in the trial data. No benefit was demonstrated against pneumonia. A two-year retrospective cohort study of older people with chronic lung disease found that vaccination prevented 43 percent of pneumonia hospitalisations and 31 percent of deaths, resulting in both health and economic benefits.

Immune compromised people

Response to vaccination is generally less than normal in immune compromised individuals. Many will show no response, and antibody response in those who do respond often declines rapidly. Patients with advanced HIV disease are less likely to respond. However, people with HIV are a high risk group for pneumococcal infection (the risk is 100 times greater than in non-HIV adults of a similar age), and it is felt that the risk of infection justifies vaccination. In a case control study of people with HIV infection, the vaccine was 70 percent effective against pneumonia.

Chronic conditions

The response to vaccination has been studied in patients with chronic cardiovascular and respiratory conditions, with diabetes, and in alcoholics. In these conditions most studies have reported adequate response to vaccination, although the response has been reduced in patients with chronic obstructive pulmonary disease.

Haematological neoplasm

Patients with Hodgkin’s disease normally respond to vaccination if it is given prior to radiation or chemotherapy, but seldom respond after treatment is completed. The response to vaccination is poor in patients with multiple myeloma and almost non-existent in those with chronic lymphocytic leukaemia.
Other population studies
A 1999 meta-analysis that included 13 randomised or quasi-randomised controlled trials (RCTs) estimated that immunisation reduced invasive disease caused by the \textit{S. pneumoniae} types in the vaccine by 83 percent, and invasive disease from all \textit{S. pneumoniae} types by 73 percent, but had no effect on the other outcomes.\textsuperscript{40} It has been argued that the failure of the controlled studies to show an effect was due to the studies being too small, and there being a lack of specificity and sensitivity in the diagnosis of pneumococcal pneumonia.

A Swedish RCT also failed to show an effect on preventing pneumonia in 691 non-immune compromised patients between 50 and 85 years of age who had received the vaccine and been treated as inpatients for community acquired pneumonia.\textsuperscript{41}

The problems with the polysaccharide vaccine have been summarised as:\textsuperscript{42}

- reduced efficacy in high risk individuals
- uncertain efficacy against pneumonia
- only suitable for children two years of age and over (there is high pneumococcal disease burden in the first year of life).

Administration with other vaccines
The polysaccharide vaccine may be given with the influenza vaccine or the other childhood vaccines. If not given at the same time, there is no need for a minimum interval after any other vaccine.
### 16.5 Vaccine recommendations

Pneumococcal vaccine recommendations are given below and in the text.

#### Table 16.3: Individual recommendations for pneumococcal immunisation

<table>
<thead>
<tr>
<th>Funded Vaccine* Recommendations</th>
<th>Not Funded but Recommended</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Splenectomy or functional asplenia</strong></td>
<td><strong>Children with high risk conditions (&lt; 5 years)</strong></td>
</tr>
<tr>
<td>Children (0–16 years) pre- or post-splenectomy or with functional asplenia</td>
<td>On immunosuppressive therapy or radiation therapy</td>
</tr>
<tr>
<td>Adults pre- or post-splenectomy</td>
<td>Primary immune deficiencies</td>
</tr>
<tr>
<td></td>
<td>HIV</td>
</tr>
<tr>
<td></td>
<td>Renal failure or nephrotic syndrome</td>
</tr>
<tr>
<td></td>
<td>Organ transplants</td>
</tr>
<tr>
<td></td>
<td>Cochlear implants or intracranial shunts</td>
</tr>
<tr>
<td></td>
<td>With chronic CSF leaks</td>
</tr>
<tr>
<td></td>
<td>On corticosteroid therapy for more than 2 weeks, at daily dose of prednisone of 2 mg/kg or greater, or a total daily dosage of 20 mg or more</td>
</tr>
</tbody>
</table>

* Vaccine administration is also funded

Key: CSF = cerebrospinal fluid
<table>
<thead>
<tr>
<th>Funded Vaccine Recommendations</th>
<th>Not Funded but Recommended</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pre- and post-splenectomy (all ages)</td>
<td>High risk children (&lt; 5 years of age)</td>
</tr>
<tr>
<td>Children under the age of 5 years</td>
<td>PCV7** + 23PPV at age 2 years and 5 years</td>
</tr>
<tr>
<td>Children 5–9 years</td>
<td>PCV7 +23PPV</td>
</tr>
<tr>
<td>Older children (10–16 years)</td>
<td>23PPV</td>
</tr>
<tr>
<td>Adults (16 years and above)</td>
<td>23PPV</td>
</tr>
</tbody>
</table>

* See Table 16.5 for pneumococcal vaccine schedule.
** See age appropriate schedule (Table 16.5) for timing and dosage.
Key: PCV7 = pneumococcal conjugate vaccine; 23PPV = pneumococcal polysaccharide vaccine.

16.5A Seven-valent conjugate vaccine recommendations for children

Pneumococcal conjugate vaccine (PCV7, Prevenar®) is not yet funded for all children and is not on the National Immunisation Schedule. However, a small number of doses of PCV7 have been purchased, so that from 2006 children with specific conditions that put them at greater risk of pneumococcal invasive disease may be offered vaccination.
Recommended and funded immunisation schedules for children at special risk

From 2006 pneumococcal conjugate vaccine (PCV7) and pneumococcal polysaccharide vaccine (23PPV) will be fully funded for a group of children at special risk of the disease. The vaccines are available on the recommendation of a paediatrician or other secondary care specialist, and will be delivered in primary care. A child in the risk group is eligible for the age appropriate vaccine schedule, and both the PCV7 and the 23PPV vaccine boosters are publicly funded (see Tables 16.5 and 16.6).

The PCV7 may be given at the same time as other vaccines on the National Immunisation Schedule.

Children of any age pre- or post-splenectomy or with functional asplenia

PCV7 and 23PPV, including boosters, are funded for those children aged six weeks to 16 years, pre- or post-splenectomy or with functional asplenia. Where possible the vaccine should be administered at least 14 days before splenectomy (see section 1.8). Use Table 16.5 below for the recommended vaccine schedules. Boosters of 23PPV are recommended five-yearly and are funded.

Table 16.5: Schedule for pneumococcal vaccines for adults pre- and post-splenectomy and children pre- and post-splenectomy or with functional asplenia

<table>
<thead>
<tr>
<th>Age of child at start of course</th>
<th>Conjugate pneumococcal vaccine (PCV7)</th>
<th>Polysaccharide pneumococcal vaccine (23PPV)</th>
</tr>
</thead>
<tbody>
<tr>
<td>6 weeks to 6 months</td>
<td>3 doses PCV7 at least 6–8 weeks apart, or at same time as the usual schedule; plus a 4th dose at age 15 months</td>
<td>One dose of 23PPV at age 2 years and a second dose at age 4–5 years Booster dose of 23PPV 5 yearly</td>
</tr>
<tr>
<td>7–11 months</td>
<td>2 doses of PCV7 at least 6–8 weeks apart; plus a 3rd dose at age 15 months</td>
<td>One dose of 23PPV at age 2 years and a second dose at age 4–5 years Booster dose of 23PPV 5 yearly</td>
</tr>
<tr>
<td>12–59 months</td>
<td>2 doses of PCV7 given at 6–8 weeks apart</td>
<td>One dose of 23PPV at age 2 years and a second dose at age 4–5 years Booster dose of 23PPV 5 yearly</td>
</tr>
<tr>
<td>5–9 years</td>
<td>One dose of PCV7</td>
<td>One dose of 23PPV 6–8 weeks after PCV7 Booster dose of 23PPV 5 yearly</td>
</tr>
<tr>
<td>10–16 years</td>
<td>(A dose of PCV7 may be recommended for some children)</td>
<td>One dose of 23PPV Booster dose of 23PPV 5 yearly</td>
</tr>
<tr>
<td>Adults &gt;16 years</td>
<td></td>
<td>One dose of 23PPV Booster dose of 23PPV 5 yearly</td>
</tr>
</tbody>
</table>
Note that for these individuals the quadrivalent meningococcal vaccine (ACYW135) and Hib vaccine are now publicly funded (vaccine and administration), and the meningococcal B vaccine MeNZB™ is publicly funded while the vaccine is available in New Zealand (see section 1.8 and individual vaccine chapters).

*Children under the age of five years with specific risk conditions*

Pneumococcal conjugate and polysaccharide vaccines are funded for the following children aged under five years:

- on immunosuppressive therapy or radiation therapy, when there is expected to be sufficient immune response
- with primary immune deficiencies
- with HIV infection
- with renal failure, or nephrotic syndrome
- immune suppressed following organ transplantation
- with cochlear implants or intracranial shunts
- with chronic cerebrospinal fluid leaks
- receiving corticosteroid therapy for more than two weeks, who are on an equivalent daily dosage of prednisone of 2 mg/kg per day or greater, or children who weigh more than 10 kg on a total daily dosage of 20 mg or greater.

The pneumococcal vaccine schedules recommended for this group of children at higher risk of pneumococcal disease are shown in Table 16.6. These schedules are for children who have not previously received any pneumococcal vaccine.

Some children in these groups may have received a previous dose of a pneumococcal vaccine. For recommendations for catch up schedules for these children, see Appendix 2.
**Table 16.6: Schedule for pneumococcal vaccines for children at higher risk of pneumococcal disease with no prior history of pneumococcal vaccines**

<table>
<thead>
<tr>
<th>Age of child at start of course</th>
<th>Conjugate pneumococcal vaccine (PCV7)</th>
<th>Polysaccharide pneumococcal vaccine (23PPV)</th>
</tr>
</thead>
<tbody>
<tr>
<td>6 weeks to 6 months</td>
<td>3 doses PCV7 at least 6–8 weeks apart, or at same time as the usual schedule; plus a 4th dose at age 15 months</td>
<td>One dose of 23PPV at age 2 years and a second dose at age 4–5 years</td>
</tr>
<tr>
<td>7–11 months</td>
<td>2 doses of PCV7 at least 6–8 weeks apart; plus a 3rd dose at age 15 months</td>
<td>One dose of 23PPV at age 2 years and a second dose at age 4–5 years</td>
</tr>
<tr>
<td>12–59 months</td>
<td>2 doses of PCV7 given at 6–8 weeks apart</td>
<td>One dose of 23PPV at age 2 years and a second dose at age 4–5 years</td>
</tr>
<tr>
<td>Older children up to the age of 16 years in high risk groups*</td>
<td>One dose of PCV7</td>
<td>One dose of 23PPV 6–8 weeks after PCV7</td>
</tr>
</tbody>
</table>

* not currently funded

**Recommendations for other children at increased risk of invasive pneumococcal disease (not funded)**

Pneumococcal vaccine is recommended, but not yet funded, for the following children at increased risk of pneumococcal disease:

- preterm infants, born at under 28 weeks’ gestation
- premature infants with chronic lung disease who are discharged home on domiciliary oxygen.
- children with cardiac disease associated with cyanosis or cardiac failure
- bronchiectasis
- insulin dependent diabetes
- Down’s syndrome.

The vaccine programme will be extended when funds are available, and practitioners will be informed of any changes. The schedules in Table 16.6 should be used for these children.

**Recommendations for healthy children not in the risk groups (not funded)**

Māori and Pacific children have higher rates of pneumococcal disease than children of other ethnicities, and children attending early childhood services have also
been reported with higher rates of disease. The pneumococcal vaccine schedule for healthy children is detailed below. Pneumococcal vaccine is not funded except for children at special risk of disease, as in the special programme above. However, some parents may wish to pay for pneumococcal vaccine for their child. The vaccine may be given at the same time as the usual childhood immunisations.

The following schedule is for healthy children not at increased risk of pneumococcal disease.

Table 16.7: Schedule for pneumococcal vaccines for healthy children

<table>
<thead>
<tr>
<th>Age of healthy child at start of course</th>
<th>Conjugate pneumococcal vaccine (PCV7) schedule</th>
</tr>
</thead>
<tbody>
<tr>
<td>6 weeks to 6 months</td>
<td>3 doses PCV7 at least 6-8 weeks apart, or at the same time as the usual schedule; plus a booster 4th dose at age 12–15 months, at least 2 months after the primary series</td>
</tr>
<tr>
<td>7–11 months</td>
<td>2 doses of PCV7 at least 6–8 weeks apart; plus a third dose at age 12–15 months</td>
</tr>
<tr>
<td>12–23 months</td>
<td>2 doses of PCV7 given 6–8 weeks apart</td>
</tr>
<tr>
<td>24–59 months</td>
<td>One dose of PCV7</td>
</tr>
</tbody>
</table>

### 16.5B Pneumococcal polysaccharide 23-valent vaccine recommendations for children and adults

The polysaccharide vaccine is recommended for children two years of age and older, as below.

**Funded programme for pneumococcal polysaccharide vaccine for adults pre- and post-splenectomy and children pre- and post-splenectomy or with functional asplenia**

From 2006 pneumococcal polysaccharide 23-valent vaccine (23PPV, PNEUMOVAX®23) is funded (vaccine and administration) on the recommendation, or a prior recommendation, of a secondary care specialist (such as haematologist or infectious diseases physician) for:

- adults pre- and post-splenectomy – where possible the vaccine should be administered at least 14 days before splenectomy (see section 1.8 and 16.5)
- children and young people up to the age of 16 years pre- and post-splenectomy or with functional asplenia (see Table 16.5 above for recommendations for PCV7 and 23PPV)

Reimmunisation with pneumococcal polysaccharide vaccine for individuals with asplenia is recommended five-yearly. The booster doses are also funded.
Note that for these individuals, the quadrivalent meningococcal vaccine (ACYW135) and Hib vaccine are now publicly funded (vaccine and administration), and the meningococcal B vaccine (MeNZB™) is publicly funded while the vaccine is available in New Zealand (see section 1.8 and individual vaccine chapters).

Other recommendations for pneumococcal polysaccharide vaccine
Pneumococcal polysaccharide vaccine is recommended, but not publicly funded, for patients, at special risk, including:

- immune competent people at increased risk of pneumococcal disease or its complications because of chronic illness (eg, chronic cardiac, renal or pulmonary disease, diabetes, and alcoholism)
- people with chronic cerebrospinal fluid leaks
- immune compromised patients at increased risk of pneumococcal disease (eg, those with nephrotic syndrome, multiple myeloma, lymphoma and Hodgkin’s disease, or those who are immune suppressed following organ transplantation)
- individuals with HIV infection, who are recommended to receive a dose of pneumococcal conjugate vaccine and a booster dose of the polysaccharide vaccine
- people who have had one episode of invasive pneumococcal disease
- people 65 years of age and over.

Reimmunisation/ booster doses
One time reimmunisation with polysaccharide vaccine should be considered after three to five years in children younger than 10 years of age when first immunised, and after five years in older children and adults belonging to particularly high risk groups, who frequently exhibit a poor immune response. Examples of such high risk individuals include those with sickle cell anaemia, nephrotic syndrome and renal failure, and transplant recipients. Seek expert advice in such situations. Boosters are recommended five-yearly after a splenectomy.

Revaccination of immunocompetent individuals previously vaccinated with polysaccharide vaccine is not routinely recommended.

Special considerations
In patients with Hodgkin’s disease or other malignant lymphomas, the vaccine should be given at least two weeks before any contemplated splenectomy (see section 1.8), and, if possible, before any significant chemotherapy or nodal irradiation. Similar considerations apply to patients undergoing organ transplantation. If a patient is immunised during chemotherapy, they should be reimmunised three months after the completion of chemotherapy.
Penicillin prophylaxis

Because of the relatively poor response to vaccination with pneumococcal vaccine in splenectomised children and individuals with nephrotic syndrome or sickle cell disease, it is recommended that such patients receive continuous penicillin prophylaxis in addition to pneumococcal vaccine (see section 1.8). The age at which prophylaxis can be discontinued must be decided empirically because no studies on this question have been carried out (see also section 16.8). Some experts continue prophylaxis throughout childhood and into adulthood for particularly high risk patients.

16.6 Expected responses and adverse events following immunisation (AEFI)

16.6A Seven-valent conjugate vaccine (PCV7)

Expected responses

Expected responses to PCV7 pneumococcal vaccine are generally mild and limited to local reactions of redness or swelling. There was no increase in reactogenicity through the primary series. In the NCKP vaccine trial there was an increase in tenderness following the booster in 36 percent of children, and in 18.5 percent this affected limb movement.

This large US trial showed that local reactions to PCV7 were higher than local reactions to the diphtheria, tetanus and acellular pertussis vaccine (DTaP): around 10 percent of children had erythema at the site after PCV7 compared to 6.7 percent with erythema after DTaP. The rate of fever over 39°C in infants who received DTaP plus the second dose of PCV7 vaccine was 2.5 percent, compared with 0.8 percent of children who received a control vaccine.

Adverse events following immunisation

Rare events (≥ 0.01 percent and < 0.1 percent) included febrile seizures and hypotonic, hyporesponsive episode. Very rare events (< 0.01 percent) included urticaria, angioneurotic oedema, erythema multiforme, and hypersensitivity including anaphylaxis. For further information, see the manufacturer’s data sheet.

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 http://carm.otago.ac.nz. If the patient or parent/caregiver does not consent to being identified, the report should be made without personal identification.
16.6B Pneumococcal polysaccharide 23-valent vaccine (23PPV)

Pneumococcal polysaccharide vaccine is well tolerated. Expected responses following immunisation occur in small numbers of recipients (1–10 percent), and consist primarily of local discomfort, erythema and induration lasting a couple of days. Side effects requiring a general practitioner consultation occur in approximately 8 per 1000 vaccinations, and more severe side effects in 1 per 100,000.

Revaccination with the current vaccine is not associated with an increase in systemic events. A recent study that compared rates in first time and repeat vaccination did find an increase in large (> 10 cm) local reactions (3 percent versus 11 percent), but no other differences. The reactions mostly did not cause limitation and lasted a few days. The reactions were associated with immune competence and high levels of antibody pre-immunisation. A large study compared hospitalisation rates after first or repeat vaccination and found no significant difference. Therefore, it appears that revaccination may be safely given, with a small increased risk of self limiting large local reactions.

Any severe or unexpected reactions should be reported to CARM, PO Box 913, Dunedin, using the prepaid postcard H3442 (see section 2.4) or via online reporting at http://carm.otago.ac.nz. If the patient or parent/caregiver does not consent to being identified, the report should be made without personal identification.

16.7 Contraindications to pneumococcal conjugate and polysaccharide vaccines

See section 1.9 for general contraindications for all vaccines. There are no specific contraindications to the polysaccharide or conjugate vaccines apart from a severe reaction to a previous dose or known hypersensitivity to any components of either vaccine.

Because the safety of pneumococcal polysaccharide vaccine has not been confirmed in pregnant women, deferral of immunisation is recommended unless the risk of infection is substantial.

16.8 Passive immunisation and prophylaxis

Intramuscular or intravenous immunoglobulin is recommended for the prevention of pneumococcal infection in individuals who have had recurrent pneumococcal infections and are unable to mount an immune response to vaccine because of congenital or acquired immune deficiency disease.

Antimicrobial prophylaxis with twice daily penicillin (co-trimoxazole or erythromycin for penicillin allergic people) should be considered for those likely to have a poor immune response to pneumococcal vaccine (see sections 1.8 and 16.5 for information about splenectomy).
References


17 Varicella (Chickenpox and Shingles)

17.1 Introduction
Varicella was at first confused with smallpox, and the first clinical differentiation was by Heberden in 1767. The varicella zoster virus (VZV) was first isolated in cell culture in 1952. Varicella (chickenpox) is a highly infectious disease caused by human herpes virus type 3 (varicella-zoster virus). It is usually, but not invariably, a mild, self limited disease in otherwise healthy children, but the severity of disease and risk of complications are usually greater in adolescents and adults. Varicella can also cause severe and even fatal disease in immune suppressed individuals (eg, children with acute leukaemia), in whom the mortality may be as high as 7–10 percent. Mortality in normal children is less than 2 per 100,000 cases, increasing up to 15-fold in adults. Reactivation of latent VZV results in herpes zoster (shingles), a disease with considerable morbidity.

17.2 The illness
A maculo-papular rash, which becomes vesicular, appears first on the face and scalp, later spreading to the trunk and abdomen and eventually to the limbs. The vesicles dry after three to four days, but may be followed by further lesions. A wide variation in the number of lesions is possible, ranging from a few to many hundred. The hallmark of the disease is the presence of lesions at all stages. Lesions may be found in the mouth and at times in the vagina, where they can be the cause of considerable distress. The rash is pruritic and is usually associated with mild fever, malaise, anorexia and listlessness.

The majority of hospitalisations from varicella are from severe chickenpox or bacterial superinfection of the skin lesions. Superinfection with Group A beta haemolytic streptococci is a potentially serious complication, which may be fatal. Other complications include varicella pneumonia (more common in adolescents and adults), acute cerebellar ataxia (more common in infants and children, and almost always self limited), and, rarely, encephalitis, with permanent neurological disability or fatal outcome. Transverse myelitis, thrombocytopenia and, rarely, involvement of the viscera and joints may also occur.

Salicylates (aspirin containing analgesics) should not be given to children with chickenpox, because of the association between Reye syndrome (an acute encephalopathy with hepatic failure) developing after an infectious illness such as influenza or natural varicella infection and the use of salicylates.

The incubation period of varicella is 10–21 days (usually 14–16 days). The virus is plentiful in the naso-pharynx initially and in the vesicles before they dry up. The infectious period is from one to two days before the rash emerges until the rash dries up about seven days later. The infectious period may be more prolonged in immune suppressed individuals.
The disease may be more serious in adults, particularly in pregnant women, and the risk of severe disease is greatly increased in neonates and immune suppressed individuals. Transplacental transmission is rare. Congenital varicella syndrome has been reported after varicella infections in the first half of pregnancy and may result in congenital malformations, skin scarring, other anomalies, abortion or fetal death. The observed incidence of congenital varicella syndrome, in retrospective and prospective studies, ranges from 0.7 percent to 2 percent.\textsuperscript{1} There is a higher risk when maternal infection occurs between 13 and 20 weeks gestation compared with 0 and 12 weeks (2 percent compared with 0.4 percent).\textsuperscript{2}

The onset of chickenpox in pregnant women, from five days before delivery to two days after delivery, is estimated to result in severe varicella in 17 to 30 percent of their newborn infants. Half the deaths from chickenpox before one year of age occur during the first month of life.

Herpes zoster (shingles) is due to reactivation of latent varicella virus infection. The majority of cases of zoster occur in adults over 40 years of age. The dermatomal distribution of the vesicular rash is the key diagnostic feature. Herpes zoster is uncommon in infants and children but may occur after chickenpox in infancy. When it occurs in those under two years of age it may reflect \textit{in utero} chickenpox with the greatest risk following exposure between 25 and 36 weeks’ gestation, with reactivation in early life. Herpes zoster occurs more commonly in immune suppressed individuals, and there is some evidence that up to 10 percent of children treated for a malignant neoplasm may develop herpes zoster.

\section*{17.3 Epidemiology}

The epidemiology of this infection appears to be similar in all industrialised countries with temperate climates. Epidemics occur each winter/spring, with some variability from year to year. Approximately 3 percent of each birth cohort are infected during infancy. Thereafter, 8–9 percent of the birth cohort are infected each year throughout childhood, so that by 10 years of age less than 15 percent, and by 14 years of age less than 10 percent, remain susceptible. The average age for infection is seven years. The infection rate drops rapidly in adolescence and young adulthood to about 1 percent per year. By 40 years of age almost the entire birth cohort (over 97 percent) have been infected, so that only a few adults remain susceptible. Transmission of the virus is less efficient in tropical climates. Adolescent and adult immigrants to New Zealand from such countries are more likely to be susceptible, placing them at risk of contracting chickenpox in their new environment.

By contrast, herpes zoster is a sporadic disease occurring as a reactivation of the VZV in individuals who have previously had chickenpox. VZV is present in lesions of herpes zoster, and is transmissible from the vesicles to other susceptible individuals. About 4 percent of individuals will suffer a second episode of shingles. Third episodes are rare.
Varicella vaccine has been introduced into childhood immunisation programmes overseas, including the United States (US) from 1995 and Australia from 2005. Following introduction of varicella vaccine onto the childhood schedule, the incidence of infection with wild type virus decreases, and therefore adults are less likely to boost immunity to latent herpes zoster. It was hypothesised that lack of boosting may lead to an increase in herpes zoster in older adults. However, a study in the US\(^3\) from 1992 to 2002 has shown that although the incidence of varicella decreased in children, from 2.63 cases per 1000 person years in 1992 to 0.92 cases per 1000 person years in 2002, there was no increase in herpes zoster in adults of any age: the age adjusted rate of herpes zoster was 4.05 cases per 1000 person years in 1992 and 3.7 cases per 1000 person years in 2002.

A more potent form of the varicella vaccine has been tested as a zoster vaccine.\(^4\) By boosting cell mediated immunity in older adults, zoster might be prevented. In a large clinical trial of 38,586 adults aged 60 years and over, with either a history of chickenpox or of having lived in the US for more than 30 years, the participants received the high dose zoster vaccine or a placebo. The results showed that the zoster vaccine reduced the burden of illness of zoster by 61 percent in all age groups, and by 65.5 percent in the age group 60–69 years and 55.4 percent in those over 70 years. There was also a 66.5 percent reduction in post-herpetic neuralgia (PHN) in all age groups. Over five years of follow up, the incidences of zoster and PHN was reduced, and in the vaccine recipients who received the zoster vaccine but developed zoster the illness was less severe.

New Zealand epidemiology

In New Zealand it is expected that 90 percent of children would have had varicella infection before adolescence, with peak incidence in the five to nine years age group. With higher participation rates in preschool education, a greater proportion of infections may now be occurring in preschool aged children.

Hospitalisation\(^5\)

New Zealand hospital discharge information for varicella between 1970 and 2004 is shown in Figure 17.1. Only 4 percent of hospitalisations involved people with an underlying disease associated with immune suppression. The rate of hospital discharges for the zero to four and five to nine years age groups was higher compared with older age groups because the disease is most common in childhood. However, adults, adolescents and infants are more likely to suffer severe illness or the complications of chickenpox.\(^6\)
Based on overseas rates, it is estimated that up to one case of congenital varicella syndrome may be expected in New Zealand each year, although few have been reported.

**Mortality**

Mortality data are available for the period 1980 to 2002. Nine deaths were attributed to chickenpox over the 14-year period 1980 to 1993, of which four occurred in children, two in infants and three in adolescents or adults. None of the cases who died had a contributory cause of death recorded. From 1994 to 2002 there were nine deaths associated with varicella, two were children aged five to nine years, four were adults aged 30 to 64 years and three were adults over the age of 65 years. Larger series from other developed temperate climate countries suggest that up to 10 percent of chickenpox deaths may involve individuals with immune suppression.

In summary, in a typical year New Zealand is estimated to experience approximately 50,000 chickenpox infections, of which 150–200 result in hospitalisation, one to two cases result in residual long term disability or death, and 0.5–1 cases result in severe congenital varicella syndrome. About two-thirds of this burden is borne by otherwise healthy children, and less than one-tenth by children with a disease associated with immune suppression.

### 17.4 Vaccines

VZV was first isolated in the 1950s. An attenuated (live) VZV (Oka strain) developed in Japan was found suitable for vaccine use. Currently, both VARILRIX and VARIVAX® (both based on the Oka strain) are licensed and are available in New Zealand.
VARILRIX

VARILRIX (GSK) is a live attenuated virus vaccine presented as a lyophilised powder for reconstitution with the supplied diluent. The vaccine should be stored in the refrigerator at +2°C to +8°C, although the diluent may be stored at room temperature. Reconstituted vaccine must be used immediately.

VARILRIX should be administered by subcutaneous injection. The upper arm (deltoid region) is the preferred site of injection. A single 0.5 mL dose provides protection for individuals nine months to 12 years of age, inclusive, with over 95 percent achieving seroconversion. The vaccine can be administered concurrently with other vaccines, but in a separate syringe and at a different site. If not administered concurrently, the vaccine must be separated from other live vaccines (eg, measles, mumps and rubella – MMR) by at least one month. (See section 2.3 for needle sites and sizes.)

People 13 years of age and over, and immune compromised individuals of all ages when indicated, require two doses of VARILRIX (a minimum of six weeks apart) to achieve a seroconversion rate similar to children.

VARIVAX®

VARIVAX® (MSD) is a live attenuated virus vaccine presented as a lyophilised powder for reconstitution with the supplied diluent. The vaccine should be stored in the refrigerator at +2°C to +8°C, but may also be stored in the freezer. When the vaccine is transferred from the freezer to the refrigerator it should not be refrozen. Reconstituted vaccine must be used immediately.

VARIVAX® should be administered subcutaneously, with the deltoid area the preferred site for injection. A single 0.5 mL dose is sufficient for children 12 months to 12 years of age inclusive; people 13 years of age and older require two doses, given four to eight weeks apart. (See section 2.3 for needle sites and sizes.)

Measles, mumps, rubella and varicella vaccine (MMRV)

In the US an MMRV vaccine (ProQuad®, Merck) that is freezer stable is now licensed and is likely to be available in New Zealand in the next one to three years (see section 9.4). Trials are ongoing to produce a refrigerator stable vaccine.

There is also a refrigerator stable two-dose MMRV vaccine (GSK) recommended for use in the second year of life. It is possible either or both of these vaccines will be licensed for distribution in the next one to three years.

Efficacy

Varicella vaccine is 95–98 percent effective in preventing moderate and severe disease during seven years of follow up post-vaccination. Mild cases of varicella rash and illness have been reported in children who have received vaccine, and the vaccine is estimated as being 70–100 percent effective against all disease. The duration of immunity has been 11 years in the vaccine trial participants in the US.
and up to 20 years in studies from Japan. The estimated hospitalisation rates for varicella have decreased in the US after introducing the varicella vaccine, from 2.3 per 100,000 population in the pre-vaccination era in 1994/95 to 0.3 per 100,000 in 2002 following introduction of the vaccine programme. It is estimated that the varicella related annual national expenditure in the US for ambulatory visits and hospitalisations decreased by 74 percent, to $22.1 million in 2002.

17.5 Recommended immunisation schedule

Varicella vaccine is not yet on the New Zealand National Immunisation Schedule

At present, the varicella vaccine has not been added to the New Zealand National Immunisation Schedule. There are two reasons for this decision: the costs, and the undesirability of adding another injection or immunisation visit to the Schedule. When a tetravalent MMRV vaccine becomes available, this recommendation could change.

Recommendations for use

Varicella immunisation is recommended, but not funded, for:

• adults and adolescents who were born and resident in tropical countries if they have no history of varicella infection
• children with chronic liver disease who may in future be candidates for transplantation – varicella vaccine has been found to be safe and immunogenic in children with chronic liver disease and is therefore recommended early in the disease and prior to liver transplantation
• children with deteriorating renal function, as early as possible before transplantation – varicella immunisation of children with end stage and pre-end stage renal failure results in a high rate of seroconversion and persistence of protective antibody titres
• children likely to undergo solid organ transplant
• children with human immunodeficiency virus (HIV) infection at CDC stage N1 or A1 – a recent study has found varicella vaccine is safe and effective when given to children aged one to eight years who are mildly affected with HIV infection at CDC stage N1 or A1. Two doses were given, four weeks apart.

Immune suppressed individuals

The vaccine should not be given to immune suppressed children except under the direction and care of a paediatric oncologist, following a suitable protocol. Immune suppressed individuals are at highest risk of severe varicella and zoster infections. The original vaccine formulations, in particular VARIVAX®, have been studied in immune suppressed children. Approximately 20 percent of these vaccine recipients required acyclovir because of a rash developing up to one month after vaccination. Despite this, the study concluded that the vaccine VARIVAX® was safe, immunogenic and effective in these children.
Where immune suppressed individuals cannot be vaccinated, it is important to vaccinate the household members and other close contacts (with either vaccine) to provide ‘ring fence’ protection. There is debate regarding the severity of disease that may result if a susceptible immune suppressed person is inadvertently exposed to a person who has a vaccine related rash. If this does occur, the administration of varicella zoster immunoglobulin (ZIG) should be considered, as should the use of acyclovir to treat any disease that develops. Any vaccine related rash or illness that occurs will be far less severe than illness with the wild virus in an immune suppressed child.

Immunisation of children with congenital T-cell immune deficiency syndromes is generally contraindicated, but those with impaired humoral immunity may be immunised (see below for further contraindications).

Health care workers
In 1999 all acute care hospitals were advised that the varicella vaccines were available for use in adults and that hospitals should incorporate the use of varicella vaccine for health care workers in their occupational health programme. All health care workers on obstetric, paediatric and neonatal units, and those caring for immune suppressed children and adults, should be immunised with varicella vaccine if they are susceptible to varicella. When a health care worker has a good history of prior varicella infection, no blood test is required. If there is not a good history of varicella infection, a blood test to assess susceptibility will be necessary.

If a health care worker who has clinical contact with patients develops a rash as a result of the vaccine (around 5 percent), they must be excluded from contact with immune suppressed patients at risk and be allocated other duties, or excluded from their place of work for the duration of the rash.

Whenever exposure to wild chickenpox occurs, previously vaccinated health care workers should examine themselves daily for 21 days for a rash. If a rash appears they should seek advice from their occupational health service.

Healthy children
The varicella vaccine is available, but not publicly funded, for children whose parents/caregivers wish them to avoid having chickenpox. It can be given with the other two vaccines scheduled at 15 months of age. If not given concurrently it should be given at least four weeks after the MMR vaccine. One dose is required for children from nine months up to and including 12 years of age.

Healthy adolescents/adults
Immunisation could be offered to all susceptible adults and adolescents in view of their increased risk of serious varicella outcomes relative to children. Two doses of vaccine, one to two months (or more) apart, are required for adults and adolescents.
from 13 years of age in order to achieve a seroconversion rate greater than 90 percent. To assess susceptibility, it has been found that maternal recall of varicella or characteristic rash is reliable evidence of immunity. In people with no history or recall of the rash, 70–90 percent are found to be immune.\textsuperscript{16}

The US Advisory Committee on Immunization Practices (ACIP) recommends vaccinating susceptible individuals in the following high risk groups:

- people who live or work in environments where transmission of VZV is likely (eg, staff in early childhood services, residents and staff members in institutional settings)
- people who live and work in environments where transmission can occur (eg, college students, inmates and staff members of correctional institutions, and military personnel)
- non-pregnant women of childbearing age
- adolescents and adults living in households with children
- international travellers.\textsuperscript{17}

### 17.6 Expected responses and adverse events following immunisation (AEFI)

Experience with the varicella vaccines used in Japan and other countries indicates that, in general, side effects including local reactions, fever and mild papulo-vesicular rash in normal healthy individuals are mild and self limiting. About 5–7 percent (VARIVAX\textsuperscript{®}) or 2–6 percent (VARILRIX) of healthy child vaccinees develop a mild rash three to four weeks after vaccination. The mean number of vesicles is five, compared with several hundred in wild varicella in an unimmunised child. After VARIVAX\textsuperscript{®,} PCR (polymerase chain reaction) analysis from rashes that occurred within 14 days of vaccination was more likely to identify the presence of wild type VZV, whereas PCR from a rash developing \(>14\) days and \(\leq 42\) days post-vaccine was more likely to identify the vaccine virus.\textsuperscript{18}

Only a small percentage of vaccinees who develop a rash appear able to transmit the Oka virus to susceptible contacts, and then only very inefficiently. Secondary transmission of the vaccine virus has been documented in immune competent people on only four occasions out of 47.5 million doses of the varicella vaccine, VARIVAX\textsuperscript{®,} distributed.\textsuperscript{19} All four vaccinees developed a rash. Disease in the four contacts was mild. Of the four individuals, three were unvaccinated and one individual had a history of mild varicella in the past. One of the four was a pregnant woman who developed a rash with 100 vesicular lesions and subsequently had a therapeutic abortion (PCR negative for VZV). However, when an immune suppressed individual inadvertently comes in contact with a vaccinee who has a varicella like rash, the administration of ZIG should be considered (see below).\textsuperscript{20} Acyclovir may also be considered for the immune suppressed individual if symptoms develop.
The Oka strain of varicella used in the available vaccines can establish latent ganglionic infection in vaccinees and later reactivate to produce clinical zoster (shingles). To date, there has been insufficient follow up time to determine whether the risk of zoster is lower in healthy vaccinees than in naturally infected individuals. However, a cohort study in children with acute lymphoblastic leukaemia (who have a high rate of zoster in childhood) has shown that vaccinees had less than one-fifth the zoster rate of their naturally infected counterparts.\textsuperscript{21}

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 http://carm.otago.ac.nz. If the patient or parent/caregiver does not consent to being identified, the report should be made without personal identification.

17.7 Contraindications

See section 1.9 for general contraindications for all vaccines.

Varicella vaccination is contraindicated for:

- individuals with primary or acquired T-cell immune deficiency states – consult the child’s paediatrician for advice
- children on high dose steroids (ie, children on 2 mg/kg per day or more of prednisone or its equivalent, or 20 mg per day if their weight is over 10 kg)
- children on salicylates, because of the association between Reye syndrome, natural varicella infection and salicylates – the vaccine manufacturers advise against the use of salicylates for six weeks after varicella vaccine is given; there has been no reported association between the vaccine and Reye syndrome, but avoidance of salicylates is recommended as a precaution,\textsuperscript{22} and physicians need to weigh the theoretical risk from the vaccine against the known risk of varicella disease in children receiving long term salicylate therapy
- individuals with known systemic hypersensitivity to neomycin
- women during pregnancy – women should be advised to avoid pregnancy for three months after vaccination, because the vaccine’s safety for the fetus has not yet been demonstrated.

17.8 Control measures

Post-exposure prophylaxis with zoster immunoglobulin (ZIG)

ZIG is a high titre immunoglobulin (IG), available from the New Zealand Blood Service for the passive prevention of varicella in high risk subjects. It is effective if given within 96 hours of exposure, and as soon as possible. Large doses of normal IG are indicated when ZIG is unavailable.
The decision on whether to offer ZIG will depend on:

- the likelihood that infection will result from a given contact
- the exposed individual’s susceptibility to varicella
- the likelihood that an individual will develop serious complications if infected.

Contact can be defined as follows:

- household contact – individuals living in the same house are very likely to be infected if susceptible
- playmate contact – this can be defined as more than one hour of play indoors with an infected individual
- newborn infant contact – this occurs when the mother of a newborn infant develops chickenpox, but not shingles, from one week before to one week after delivery.

**Susceptibility**

In general, a positive past history of chickenpox can be taken as indicating immunity, provided there has not been an intervening bone marrow transplant. Please consult with the local laboratory about the availability and interpretation of tests.

Candidates for ZIG administration, provided exposure has occurred and susceptibility is likely, are:

- immune compromised individuals
- pregnant women (see below)
- newborn infants whose mother had onset of chickenpox but not zoster within seven days before delivery or after delivery (see below)
- hospitalised premature infants whose mothers have no history of chickenpox, or who are less than 28 weeks’ gestation or 1000 g in weight, irrespective of maternal history.

**Care of pregnant women after exposure**

If an immune competent pregnant woman is exposed to varicella, it is recommended, where possible, that her varicella antibodies be assessed if she has no past history of varicella. If there is no evidence of immunity then ZIG should be administered. This is because pregnant women are at higher risk of severe complications, and acyclovir is not generally recommended in pregnancy, although some experts recommend oral acyclovir for pregnant women in the second and third trimesters. Seek specialist advice before administration.

Intravenous acyclovir is recommended for the pregnant patient with severe complications of varicella. ZIG given to a pregnant woman within five days of delivery may not protect the fetus/neonate. The neonate should receive ZIG on delivery and
may need treatment with acyclovir. For further information on the management of exposure to varicella during pregnancy and care of the newborn, see Appendix 10.

**Dosage of ZIG**

The ZIG prepared by CSL in Melbourne, from New Zealand donors, contains 100 IU/mL (ie, 200 IU/2 mL vial). The recommended dose is 6 mL for adults, 4 mL for children aged 6–12 years, and 2 mL for children aged 0–5 years. ZIG should be given intramuscularly, not intravenously.

**Hospital outbreaks**

It is advised that:

- susceptible staff be excluded from contact with high risk patients from day 8 to day 21 after exposure to varicella or zoster
- hospital staff who have no past history of chickenpox and who will be in contact with pregnant women or high risk patients be screened for varicella zoster antibodies; those who are not immune should be offered immunisation.

**Exclusion from school or childcare**

Parents/caregivers should be advised that:

- cases should be excluded from early childhood services or school until fully recovered or all lesions have crusted
- high risk children should be excluded from early childhood services or school for the duration of the outbreak.

**Post-exposure vaccination and outbreak control**

Varicella vaccine may be used for post-exposure prophylaxis.

Data from the US and Japan from household, hospital and community settings indicates that the varicella vaccine is effective in preventing illness or modifying varicella severity if used within three days, and possibly up to five days, of exposure. The US ACIP now recommends the vaccine for use in susceptible individuals following exposure to varicella. If exposure to varicella does not cause infection, post-exposure vaccination should induce protection against subsequent exposure. If the exposure results in infection, no evidence indicates that administration of the varicella vaccine during the pre-symptomatic or prodromal stage of illness increases the risk for adverse events following immunisation. Note that although this method of immunisation may be successful, it is not necessarily reliable. Immunisation before exposure is recommended as the preferred method of preventing outbreaks.

For more details on control measures, refer to the *Control of Communicable Diseases Manual*.25
References


Chapter 18: Passive Immunisation

18.1 Introduction
Passive immunisation involves administering pre-formed antibody as human immune globulin to a recipient who is thought to have either no natural immunity to one or more infections, or has impaired antibody production. Human immune globulin preparations are prepared by fractionating large pools of plasma collected from blood donors to the New Zealand Blood Service. In New Zealand, blood donations are only collected from voluntary, unpaid donors who are in good health and who do not have any conditions identifiable by the standard questionnaire that all blood donors complete, and/or by the mandatory serological testing for HIV/AIDS, hepatitis B, hepatitis C and syphilis on each donation. Blood donations are only used if the tests show no evidence that these infections are present. CSL Bioplasma of Australia manufacture the immune globulins (immunoglobulins) for the New Zealand Blood Service.

18.2 Preparations available in New Zealand
There are two classes of immunoglobulin product available in New Zealand: human normal immunoglobulin for intramuscular use, and human normal immunoglobulin for intravenous use (IVIG). Both products have an excellent safety record in both Australia and New Zealand.

Human normal immunoglobulin for intramuscular use
Normal immunoglobulin is a sterile, preservative free, pasteurised solution containing 160 mg/mL human plasma proteins and 22.5 mg/mL glycine. The solution has a pH of 6.6. At least 98 percent of the protein is immunoglobulins (mainly immunoglobulin G, or IgG). Normal immunoglobulin is intended for intramuscular injection, and is available in 2 mL and 5 mL vials. It is prepared by Cohn cold ethanol fractionation of human plasma. The manufacturing process for normal immunoglobulin contains a specific viral inactivation step (pasteurisation at 60°C for 10 hours) to reduce the possibility of virus transmission.

Human normal immunoglobulin for intravenous use
The current human normal immunoglobulin for intravenous use in New Zealand is Intragam®P, produced by CSL Australia. Intragam®P is a sterile, preservative free solution containing 6 g of human protein and 10 g of maltose in each 100 mL. The solution has a pH of 4.25. Isotonicity is achieved by adding maltose. At least 98 percent of the protein has the electrophoretic mobility of IgG. At least 90 percent of the protein is IgG monomer and dimer. Intragam®P contains only trace amounts of IgA (typically < 18 µg/mL). Intragam®P is intended for intravenous administration. It is made by chromatographic fractionation of large pools of human plasma obtained from voluntary blood donors. The protein has not been chemically or enzymatically...
modified. The manufacturing process contains special steps to reduce the possibility of virus transmission, including pasteurisation (heating at 60°C for 10 hours) and incubation at low pH.

The sterile solution of immunoglobulin is prepared from a large pool of plasma. Both immunoglobulin products provide antibodies representative of those present in the general population: those against measles, varicella zoster, hepatitis A, and other viruses that are prevalent in the community.

**Other immunoglobulin preparations**

There are also a number of specific human immunoglobulin preparations available, including those for tetanus, hepatitis B, varicella zoster and anti-D. These are manufactured from plasma pools containing donations from individuals known to have high levels of the appropriate antibody. Presentation of these preparations is the same as normal immunoglobulin. The volume of the product will be determined by the potency for the appropriate antibody. In unusual circumstances, when supplies of specific immunoglobulin products are not available from the New Zealand Blood Service, commercial products from alternative donor sources may be supplied.

Other products are held in one or two centres for national use. For example, rabies immunoglobulin is held at Christchurch Hospital pharmacy and in Auckland by CSL NZ/Pro Pharma Ltd. The diphtheria antitoxin is held at the Auckland Hospital pharmacy.

### 18.3 Indications for use

**Passive immunisation**

For advice on the use of immunoglobulin products and specific dosages of these products, please contact a transfusion medicine specialist at the New Zealand Blood Service.

Human normal immunoglobulin is available for passive immunisation (pre- or post-exposure prophylaxis) against measles (see section 9.8) and hepatitis A (see section 14.8). It is not recommended for the prevention of rubella or mumps. Guidance on the use of specific preparations is provided in other sections of this Handbook: pre- or post-exposure prophylaxis against hepatitis B (section 3.8), tetanus (section 5.8) and varicella zoster (section 17.8).

Information on rabies is provided in the Ministry of Health publication *Health Advice for Overseas Travellers*, 1996 (see also Appendix 11 for additional websites). Information on a commercial preparation of rabies immunoglobulin is available from Medsafe, at the Ministry of Health.
Management of primary and acquired immune deficiency

Recurrent infections can occur in individuals who have low or absent levels of circulating immunoglobulins – so-called humoral immune deficiency. This can arise as a congenital disorder or can be acquired as a consequence of a number of diseases. Humoral immune deficiency can exist alone or as part of a wider immune deficiency syndrome. Immunoglobulin products can be used to prevent recurrent infections in these patients. In most clinical settings IVIG will be the product of choice for managing these patients.

For replacement therapy in antibody deficiency disorders, monthly administration of IVIG is given, usually at a dosage of 300–400 mg/kg of body weight. The dosage and frequency of infusion should be based on the effectiveness in the individual patient. In general, however, the aim of treatment should be to maintain the serum IgG at or above a level of 5 g/L. IVIG may also be used to treat Kawasaki disease, immune mediated thrombocytopenia, paediatric HIV infection, and conditions in adults such as chronic lymphocytic leukaemia and after a bone marrow transplant. It is important to consult a specialist physician/paediatrician for advice.

18.4 Storage and administration

Immunoglobulin products must be stored at +2°C to +8°C and must not be frozen. They should also be protected from the light. Always check and observe the manufacturer’s expiry date before injecting the product. Discard unused portions of an ampoule. Record the batch number of the dose injected on the recipient’s records.

Intramuscular human normal immunoglobulin should be given using a large (20 G) needle. This product should not be given intravenously because of the possible reactions discussed below.

18.5 Duration of effect

The half-life of immunoglobulin in the circulation is approximately three weeks. It is estimated that at the recommended doses, protective levels will be maintained for three to four weeks.

18.6 Expected responses and adverse reactions

Any severe or unexpected reactions to any immunoglobulin product should be reported on a form obtainable from the New Zealand Blood Service.

Local tenderness and muscle stiffness occasionally occur at the site of injection and may persist for several hours after intramuscular injection. An occasional recipient may react more strongly, with erythema or low grade fever. Systemic reactions, urticaria and angioedema may occur.
Reactions to IVIG tend to be related to the infusion rate and are most likely to occur during the first hour of the infusion. However, delayed reactions can occur, and include nausea, vomiting, chest pains and rigors. Systemic and local reactions are more common in those being treated for hypogammaglobulinaemia than in those with normal gammaglobulin levels who are being treated with immunoglobulin preparations for autoimmune conditions.

There have been occasional reports of renal failure following infusion of IVIG. These largely relate to sucrose containing products. Intragam®P, the product available in New Zealand, does not contain sucrose, but patients should be adequately hydrated prior to administration of Intragam®P. Renal function should be monitored in patients considered to be at increased risk.

Aseptic meningitis has been reported following treatment with IVIG. This may present up to two days following treatment. Anaphylactic reactions, although rare, have been reported following injection of immunoglobulin products, although anaphylaxis is more likely to occur following intravenous infusion (see below).

Immunoglobulin products may interfere with the immune response to live virus vaccines (see section 1.9 and Table 1.11). In general, live vaccines should be given at least three weeks before or up to six months after the immunoglobulin preparation. This does not apply to the yellow fever vaccine, because New Zealand blood donors are very unlikely to have antibodies to this virus. For travellers abroad this interval may not be possible.

### 18.7 Precautions and contraindications

Anaphylactic reactions have been reported following injection of immunoglobulin preparations, and anaphylaxis is more likely to occur following intravenous infusion. In highly allergic individuals, repeated injections may lead to anaphylactic shock. For this reason, adrenaline and other means of treating acute reactions should be immediately available.

Skin tests should not be conducted with immunoglobulin preparations. Intradermal injection of concentrated gammaglobulin may cause a local inflammatory reaction, which can be misinterpreted as a positive allergic reaction. Such allergic responses to normal immunoglobulin given in the prescribed intramuscular route are extremely rare, but may occur in those with immunoglobulin A (IgA) deficiency and in whom anti-IgA is present. Approximately 1 in 1200 individuals in New Zealand are IgA deficient, and a small percentage of these have anti-IgA present. All immunoglobulin preparations contain traces of IgA. If a patient is known to be IgA deficient with anti-IgA present, expert advice should be sought before administering these products. It is not current practice, and it is not recommended, to test for IgA deficiency or anti-IgA prior to administering intramuscular human immunoglobulin.
Reference

19  New Vaccines

19.1 Human papilloma virus

Introduction

Human papilloma virus (HPV) vaccines are now in stage III clinical trials. The pharmaceutical companies expect to apply for licensure overseas, and in Australia and New Zealand in 2006.

Human papilloma virus vaccine

Two vaccines against HPV have been developed and are in stage III clinical trials. One is a bivalent vaccine, containing HPV types 16 and 18, the other quadrivalent, containing HPV types 16, 18, 6 and 11. HPV-6 and 11 are not oncogenic but can cause florid genital warts. The pharmaceutical companies are expecting to apply for licensure in the United States (US), Australia and New Zealand in 2006.

Illness and epidemiology

Cervical cancer is one of the leading causes of cancer morbidity and mortality in women throughout the world. Prior infection with oncogenic HPV is a necessary although not sufficient prerequisite for the development of cervical cancer. Infection with oncogenic HPV types is also implicated in the development of other anogenital cancers, including neoplasms of the vulva, vagina, anus, penis and oropharynx. Non-oncogenic HPV types cause genital warts. Of the oncogenic HPVs, types 16 and 18 account for some 70% of cervical cancers; the remainder are caused by a variety of other oncogenic HPV types, for example, types 31, 33 and 45. HPV infection is common with an estimated 70 percent of sexually active women becoming infected.\textsuperscript{1} International studies have shown that HPV-16 infection is the type most commonly associated with cervical cancer and is found in about 60 percent of cervical cancers. This is followed by HPV type 18, found in about 10 percent of cervical cancers.

Cervical screening programmes are based on regular cytological screening to detect, monitor and treat at an early stage precancerous lesions, or cervical intraepithelial neoplasia (CIN). These programmes have been successful in reducing invasive disease and mortality.

A vaccine to prevent infection with oncogenic HPV types has the potential to reduce the incidence of precursor lesions and cervical cancer\textsuperscript{2}. However, vaccination needs to be administered before HPV infection occurs. Since genital HPV is so common, this means vaccination before the onset of sexual activity – realistically, during early adolescence.

The stage III trial results are encouraging and suggest an HPV vaccine may be effective in preventing persistent HPV infection and therefore may prevent the development of cervical cancer. Further information is needed from ongoing studies.
to define the duration of protection and the optimal timing for the vaccine. It will be important to analyse the effect of the HPV vaccine on the design of cervical screening programmes over a woman’s lifetime, and economic models may be useful\(^3\) in examining the options.

**New Zealand epidemiology**

Both cervical cancer incidence and mortality have fallen dramatically in New Zealand (as in other developed countries) over the last decade, due to cervical screening. New Zealand’s National Cervical Screening Programme, administered by the National Screening Unit of the Ministry of Health, became operational in 1991 and now achieves over 70 percent coverage of eligible women (ie, the 20–69 year age range).

Over the past 10 years cervical screening has led to a 40 percent reduction in the incidence of invasive cervical cancer. However, incidence remains approximately twice as high among Māori than among non Māori women. Over the same period, mortality from cervical cancer has fallen about 60 percent. Again, ethnic inequalities remain, with mortality among Māori still approximately 4 times that of non Māori. Much of the ethnic inequality in the cervical cancer burden reflects lower Programme coverage for Māori women (approximately 55 percent compared to 75 percent).

In New Zealand, the cervical screening programme has led to a reduced incidence of invasive disease and has facilitated recall. The National Cervical Screening Register records the woman’s cytological reports and results of investigations, and sends out recalls for three-yearly cervical screening.

One source of information on the incidence of HPV infection in New Zealand comes from surveillance data collected from sexual health clinics, youth health clinics and some family planning clinics. These data are collated and analysed by the Institute of Environmental Science and Research (ESR). In 2004 there were 3822 new diagnoses of genital warts in males and females in sexual health clinics; population rates cannot be calculated. The age group most affected by genital warts is young adults aged 15–24 years. The number of new cases seen has increased over time, although some of the increase may represent changes in presentation at clinics rather than a change in incidence.

An Auckland study\(^4\) of 513 cervical swabs, mainly from women attending colposcopy clinics, found that 221 specimens (43 percent) were positive for HPV. Twenty-two different types of HPV were detected, and 141 were oncogenic types, representing 14 of the 18 known oncogenic types. Types 16, 18, and 31 were the most common detected, representing 39 percent, 10 and 10 percent of the oncogenic types found, respectively. The other 11 oncogenic HPV types ranged in prevalence from 7.4 to 0.6 percent.
In considering options for timing an HPV vaccine for the immunisation schedule in New Zealand, it is useful to consider the results of the 2001 Youth Health Survey,\(^5\) which provides information on sexual behaviours. Among secondary school students in years 9 to 13, 17 percent of students aged 13 years reported they had had sexual intercourse, 33 percent of those aged 15 years, and 49 percent of students aged 15 years.

**Vaccines**

There are two vaccines currently in stage III clinical trials. One vaccine is bivalent with HPV- types 16 and 18, and the other is a quadrivalent vaccine with HPV types 16, 18, 6 and 11. Trials are underway studying the vaccine in young women, women up to age 45 years and in males.

Both vaccines under trial are recombinant and contain HPV L1 virus like particles (VLPs). The VLPs mimic the true structure of the virion and induce an antibody response after vaccination. An earlier HPV-16 vaccine showed protection against persistent infection with HPV-16 and associated CIN.\(^6\)

**Bivalent vaccine: HPV-16,18 virus like particle vaccine (Cervarix, GSK)**

The bivalent HPV-16,18 vaccine manufactured by GSK contains 20 µg of HPV-16 L1 VLP and 20µg of HPV-18 L1 VLP. Each type of VLP was produced on *Spodoptera frugiperda* Sf-9 and *Trichoplusia ni* Hi-5 cell substrate with AS04 adjuvant containing 500 µg of aluminium hydroxide and 50 µg 3-deacylated monophosphoryl lipid A.

In a randomised controlled trial\(^7\) in North America and in Brazil, three doses of this bivalent vaccine, or a placebo, were given to 1113 women aged between 15 and 25 years at zero, one month and six months. The women were seronegative for HPV-16 and 18 at the study's commencement.

Of the women receiving the vaccine, 100 percent seroconverted to the HPV-16 and 99.7 percent seroconverted to HPV-18. Geometric mean titres (GMT) for naturally occurring infections are 50 ELISA units/mL for HPV-16, and 41 ELISA units/mL against HPV-18. The GMT of the women who received the vaccine were over 80 and 100 times greater than after natural infection with HPV-16 and 18, and the titres remained high at 18 months (10 to 16 times higher than after natural infection). The study found that the vaccine was highly efficacious in preventing incident and persistent HPV-16 and 18 infections in the fully vaccinated women. Efficacy against persistent infection with HPV-16, 18 was assessed as 100 percent in the according to protocol cohorts (95% confidence interval [CI]: 47–100). There was a 91.6 percent efficacy against incident infection (95% CI: 64.5–98.0) after 18 months follow up, which persisted at 27 months. Two women in the vaccine group developed HPV-16 and/or HPV-18 associated cytological abnormalities; one developed low grade squamous intraepithelial lesion and the other developed atypical squamous cells of undetermined significance. This compared with 27 women in the placebo group who developed lesions.
Chapter 19: New Vaccines

Expected reactions and adverse events following immunisation (AEFI) with the bivalent HPV vaccine (GSK)

The bivalent HPV-16,18 vaccine was safe and well tolerated. No serious adverse events were reported in the trial. Local reactions were common, with 34.3 percent of vaccine recipients reporting swelling and 35.6 percent redness at the injection site; 93.4 percent reported pain. Other symptoms reported following vaccination were gastrointestinal, headache, itching and rash. No temperatures over 39°C were reported, although 16.6 percent of vaccine recipients reported a temperature of over 37.5°C.

Quadrivalent vaccine: HPV-6,11,16,18 virus like particle vaccine (GARDASIL, Merck)

This quadrivalent vaccine now manufactured by Merck is based on technology developed by CSL.

Studies involving adult women

The pre-publication results of stage III vaccine trials in women after 17 months of follow up were announced in 2005. The study enrolled 12,167 women in 90 centres around the world, and women were randomised to receive three doses of the HPV vaccine or placebo. The vaccine was 100 percent effective (95% CI: 76−100) in preventing high grade cervical pre-cancers, and non-invasive cervical cancers (CIN 2/3 and adenocarcinoma in situ [AIS]), in 17 months of follow up after completing the course of vaccine. No cases of AIS or CIN 2 or 3 were reported in women who had received three doses of GARDASIL, compared to 21 cases in the control group.

An earlier stage II study compared 275 women who received a placebo to 276 women who received the quadrivalent vaccine, which contained 20 µg HPV type 6, 40 µg type 11, 40 µg type 16, and 20 µg of HPV type 18. The women were followed for 30 months, and the study found a 90 percent decrease of HPV 6, 11, 16 or 18 infection, or genital disease in the vaccine recipients. This study showed that the low dose vaccine, with levels of antigen as above gave comparable immunogenicity to the intermediate and high dose vaccine. There were 40 endpoints of HPV detection in the trial participants, of which four were in the vaccine group. These were: at the last recorded visit at 36 months, three women in the vaccine group had HPV 16 DNA detected in cervicovaginal sample, compared with 10 women with HPV 6, 11, 16 or 18 in the placebo group. One woman in the vaccine group had HPV 18 detected at 12 and 18 months only. The estimated efficacy of the vaccine against all four HPV types was 89 percent (95% CI: 73–96). At month 36, 94 percent of the vaccine recipients were seropositive for HPV type 6, 96 percent for HPV type 11, 100 percent for HPV type 16, and 79 percent for HPV type 18.
Studies involving adolescent males and females, and young women
The results of a non-inferiority study in 1016 adolescent males and females aged 10 to 15 years and 513 young adult women aged 16 to 23 years were presented in 2005. Participants received the quadrivalent vaccine at zero, two and six months. To demonstrate non-inferiority, serology tests on day one and at month seven for serum anti-HPV antibodies on the adolescent study subjects were to be comparable with the results for the young women and the results of a previous study on adult women.

At month seven the seroconversion rates for the girls and boys were 100 percent for anti-HPV-6, 11, and 16, and 99.6 percent for anti-HPV-18. The month seven geometric mean titres (GMT) were 1.67–2.7 times higher (non-inferior, p < 0.001) than in the young adult cohort. Anti-HPV-6, 11, 16 and 18 GMTs in boys were 1.07–1.33 times higher than the GMTs in girls.

These results in young adolescents prior to sexual activity support the bridging of efficacy data from studies in adult women. Which is to say, if the GMT and seroconversion rates in adolescents are comparable to adult women, then efficacy in adolescents may be inferred from the efficacy in studies of adult women, without lengthy clinical trials in adolescents being necessary for licensure. This finding is important because the vaccine is likely to be of most benefit if given before the initiation of sexual activity, and this study is the first demonstration of seroconversion in adolescent males.

Expected reactions and adverse events following immunisation (AEFI) with the quadrivalent HPV vaccine (Merck)
The quadrivalent vaccine was well tolerated. Pain at the injection site was the most common local reaction, and overall 86 percent of vaccine recipients reported injection site reactions. Headache was the most common systemic reaction, and overall 38 percent of vaccine recipients reported systemic symptoms. Most reactions (94 percent) were mild or moderate. There were no vaccine related serious adverse events.

Immunisation schedule for HPV vaccines
Three doses of vaccine are given. In the reported trials the following schedules were used.

- The bivalent HPV-16,18 vaccine (Cervarix, GSK) was given at zero, one month and six months.
- The quadrivalent HPV-16,18,6,11 vaccine (GARDASIL™, Merck) was given at zero, two months and six months.
19.2 Rotavirus

Introduction
Rotavirus gastroenteritis is a significant cause of infant diarrhoea worldwide, both in developed and in less developed countries. In less developed countries rotavirus is a common cause of mortality, and in developed countries is a cause of hospitalisations.

Illness
Rotavirus causes diarrhoea in infants between the ages of six and 24 months. Accompanying symptoms include vomiting and fever, and the illness lasts from three to eight days. The virus is present in the stool before the development of symptoms and may persist for up to 21 days.

Transmission occurs through the faecal-oral route. In severe cases of rotavirus infection dehydration and electrolyte imbalance may occur, and in immune compromised children and children with human immunodeficiency virus (HIV) infection may become chronic.

Most children will have been infected by the age of three years. Breastfed infants may also become infected with rotavirus but the illness is milder. Adults are infected through contact with infected infants, although most adults will have no symptoms. The incubation period ranges from two to four days.

The rotaviruses are segmented, double stranded RNA viruses of the family Reoviridae. There are seven distinct antigenic groups (groups A to G). Group A viruses are the commonest, causing disease worldwide, but groups B and C are also important in human disease. The virus is also classified into serotypes based on two outer capsid proteins the VP7 (G protein) and VP4 (P protein). Types G1–4 and 9, and P type 1A and 1B are the most common.

Vaccines
The types of virus assessed for use as rotavirus vaccines have included live attenuated virus, both human and animal strains of the virus, as well as human-animal reassortant viruses developed for vaccines. A recent summary has described the progress in rotavirus vaccines and the information below is taken from this paper.12

An oral human-rhesus rotavirus quadrivalent vaccine (Rotashield, Wyeth) was licensed in the US and on the infant schedule in 1999. It was voluntarily withdrawn from the market after reports of an association of this vaccine with intussusception. Other vaccines assessed have been a human-lamb vaccine used in some parts of China, and vaccines with human-bovine strains. Others have been studied, with differing results, in developed and developing countries. The vaccines Rotateq and Rotarix are the most likely to be available first in developed countries.
**Pentavalent WC3 - based bovine - human reassortant vaccine (Rotateq, Merck)**

This vaccine contains five bovine–human reassortants representing the common VP7 types, G1–4 and P(8). The vaccine is administered as a three-dose oral course at the same time as the usual infant schedule. In large trials the vaccine had an efficacy of 74 percent against all disease, and 98 percent against severe disease. A large safety trial found no evidence of intussusception.

**Monovalent human G1 rotavirus vaccine (Rotarix, GSK)**

Rotarix is a monovalent G1 rotavirus vaccine derived from a human G1 strain. The vaccine is given in two oral doses at the same time as the usual schedule vaccines. In trials the efficacy was reported as 72 percent and 85 percent against all and severe disease. Further trials have confirmed good efficacy, and the vaccine was licensed in 2004 in Mexico and the Dominican Republic, and licensure is now being sought in many other countries. The safety trials showed no evidence of intussusception.

Information on the immunisation schedules for these rotavirus vaccines will be available at a later date.

**References**


20 Vaccination Questions and Concerns

This chapter provides information that can be used when responding to concerns from the public and health professionals about how vaccines work and the safety of vaccines. In particular, it addresses some recent concerns about vaccines and the National Immunisation Schedule.

There is a section discussing how the public’s and health professionals’ perceptions and concerns are translated and relayed through the media and how this may affect a parent or caregiver’s decision to immunise their child. Although there have been enormous benefits from immunisation – such as the eradication of smallpox, near eradication of poliomyelitis, and improved prevention and control of other infectious diseases – there are also new and emerging infectious diseases that challenge our understanding of infectious agents and the body’s response to them. These challenges are stimulating research and studies into vaccine safety and any longer term effects of both infectious diseases and vaccines.

The information is grouped under the following headings:

20.1 Some commonly asked questions
20.2 Responding to concerns about immunisation
20.3 Lessons from the past
20.4 Conclusion

20.1 Some commonly asked questions

(a) Which vaccines can be administered together?

There are no known contraindications to administering licensed vaccines together, provided they are administered in separate syringes at different sites. Some liquid vaccines may act as the diluent for a lyophilised vaccine, but this should only be done if specifically recommended by the manufacturer and approved by the licensing authority. If two live vaccines are not given simultaneously, they should be given at intervals of at least four weeks.

(b) How should the rest of the National Immunisation Schedule be handled when a complication occurs after administering a vaccine?

Evaluate the probability that the complication is due to the vaccine and, if appropriate, report the reaction 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.
Consult the relevant section of this Handbook, and if need be seek specialist advice (eg, from the medical officer of health, the Ministry of Health, or the Immunisation Advisory Centre, IMAC).

(c) What steps are required if the immunisation schedule is interrupted?
There is no need to repeat prior doses. Simply continue the vaccine schedule as if no interruption had occurred. Remember that children who miss a vaccine dose may do so again, and that close follow up may be required. (See Appendix 2 for immunisation catch-up schedules).

(d) What if the child had a difficult birth or was premature?
These are not contraindications to vaccination, which should be carried out at the usual chronological age. However, if the child is still in hospital or recently discharged, please seek the advice of the treating specialist. (See also section 1.8, section 3.5 on hepatitis B, and section 7.5 on *Haemophilus influenzae* type b, or Hib.)

(e) What special vaccines are offered to newborn babies?
Babies of mothers who are carriers of hepatitis B virus are given hepatitis B vaccine and hepatitis B immunoglobulin at birth to prevent infection with the virus. They then receive the usual immunisations at six weeks, and at three and five months of age. (See section 3.5 for recommended immunisation schedule for babies of HBsAg positive mothers).

A baby who may be at higher risk of tuberculosis is offered a Bacillus Calmette-Guérin (BCG) immunisation soon after birth. (See section 12.5 for neonatal BCG eligibility criteria.) The lead maternity caregiver will discuss this issue with the mother prior to her baby’s birth, and the BCG immunisation may be given while the baby is in hospital or later at a community clinic.

(f) What if the baby is unwell?
Minor illness or being in the recovery phase are not reasons to postpone immunisation. If immunisation is postponed it is important to ensure the child is not lost from recall (see section 1.9, and the sections in specific chapters for contraindications of the relevant vaccines). Babies with severe illness should have immunisation postponed until they are better, because complications of the original illness may be misinterpreted as a complication of the immunisation.

(g) What if the baby is allergic?
Only anaphylaxis is considered a contraindication or precaution for immunisation. See sections on contraindications, in particular for measles (section 9.7) and influenza (section 13.7). Children with asthma, eczema, hay fever and simple allergies should be immunised in the usual way.
(h) What if the child’s mother is pregnant?
This is not a contraindication to giving National Immunisation Schedule vaccines to a child. In particular, measles, mumps and rubella (MMR) vaccine should be given, because it will reduce the risk of the child developing rubella and then infecting the mother.

(i) What about recent immigrants?
Such children should be immunised according to the National Immunisation Schedule with due account taken of prior vaccine administration (see section 1.7). It is important to err on the side of giving rather than withholding vaccines if the vaccination history is uncertain. (See Appendix 2 for immunisation catch-up schedules.)

(j) What if the child is due to have an operation?
Immunisation should be avoided within three days of an anaesthetic (12 days for MMR) in case an adverse event occurs following immunisation and results in the postponement of the anaesthetic.

Individuals scheduled for splenectomy should be immunised at least two weeks before the operation; from 2006 pneumococcal, meningococcal and Hib vaccines are publicly funded for these individuals (see section 1.8 and relevant vaccine chapters).

(k) What if the child has a chronic disease?
Children with chronic diseases should be immunised in the normal way, especially as they may be more likely to suffer the severe effects of vaccine preventable diseases. However, if the illness or its treatment results in impaired immunity, immunisation with live vaccines should be considered carefully (see section 1.8). Consult the child’s paediatrician before immunisation.

(l) What if the child has had fits or convulsions?
Stable neurological disease is not a contraindication to any vaccine. However, unstable or undiagnosed neurological disease is a contraindication to pertussis immunisation. After any vaccine a febrile response may occur, and it is possible that such a response could result in a febrile convolution in a susceptible child. A family history of fits, or epilepsy of any type, is not a contraindication to immunisation.

(m) Can children be immunised if they are known to develop a rash with antibiotics?
Yes. The currently available vaccines do not contain commonly used antibiotics. Some vaccines contain traces of neomycin and/or polymyxin. However, it is extremely unlikely that any child will have been administered either of these antibiotics, and even more unlikely that a child will be allergic to them.
(n) Is it possible to boost a child’s immune system?
Children who are healthy have an immune system that functions optimally. Eating a healthy diet, getting adequate sleep and exercise, and minimising stress will help keep the immune system healthy.

(o) Are live virus vaccines of measles, mumps, rubella and varicella transmissible?
The live attenuated strains of viruses selected for these vaccines are less likely to cause disease and less likely to be transmitted to a susceptible person. On the very rare occasions when transmission of the vaccine virus has occurred, it has resulted in only minor illness in the person infected (see chapter 9 for MMR and chapter 17 for varicella).

(p) Can all children receive all the vaccines?
Rarely a child may have an underlying illness that is a contraindication to a vaccine. The doctor or nurse will assess each child (ie, the family history) to be certain it is safe to give a vaccine.

For example, BCG is contraindicated until after a baby is fully assessed if there is a family history of an immune deficiency disorder. Another vaccine that is not given to some children is varicella vaccine, which is not given to immunosuppressed children. (See chapters 12 and 17, and section 1.8.)

20.2 Responding to concerns about immunisation

Introduction
This section provides information on concerns that have been raised about immunisation, and outlines what is required for a reasoned response. Although much of the section deals with responding to so called ‘anti-immunisation’ views, the approach should be similar for anyone who has concerns. It is important to understand the nature of the parent’s/caregiver’s concern and to respond appropriately with as much information as possible. Individuals have the right to make decisions for themselves and those in their care, and to accept responsibility for their decisions. It is important to respect this right.

In New Zealand, as elsewhere, there are groups of people and individuals who actively campaign against immunisation. Many of those who are active in the anti-immunisation lobby have become so as a result of personal experience, frequently because their child developed a disease or condition they attribute to immunisation. Some individuals who have raised concerns with health professionals have been dissatisfied with inadequate or superficial responses. It is important for all health professionals to be able to provide accurate information about the benefits and risks of immunisation and to respond with as much information as possible to parent/caregiver concerns.
It may be necessary to accept that parents/caregivers have emotional as well as intellectual concerns, and to accept that their opposition may not be changed by rational argument or presentation of evidence. Anti-immunisation arguments are often based on either rejection of the evidence supporting immunisation or on alternative views of health and health care. In any discussion it may help to acknowledge that science does not have all the answers, and that there is more to preventing disease than immunisation. Though at times it may be difficult for those affected to understand, it is also important to point out that an adverse event that follows immunisation is not necessarily caused by the immunisation. It is always helpful to inform parents/caregivers about additional sources of information (see sections 2.2 and 2.3).

**Understanding anti-immunisation views**

Some of the appeal of the anti-immunisation lobby is based on the increasing popularity of ‘alternative’ views of the world. These views may be summarised in the idea that ‘natural’ is better than ‘man made’. The ecological movement has brought increasing acceptance that technology cannot deal with all of humanity’s problems, and that new problem solving technologies can themselves be the source of new problems.

An Australian analysis identified eight subtexts in press reports of anti-immunisation arguments:¹

- cover-up – information is suppressed to keep the true facts hidden
- excavation of the ‘facts’ – there is a large amount of scientific evidence against immunisation that can be found if searched for, and many medical experts who oppose immunisation
- unholy alliance for profit – doctors, pharmaceutical companies and the government collude for the sake of the profits made from the sale of vaccines
- towards totalitarianism – government uses the law to force immunisation as the first step towards increased state control
- us and them – caring and concerned friends and parents against doctors, pharmaceutical companies and bureaucrats
- poisonous cocktails – vaccines are toxic and made from undesirable products
- cause of idiopathic illnesses – many illnesses of unknown cause are blamed on vaccines
- back to nature – natural (disease) is better than man made (vaccine).

English researchers have identified five key concerns of parents, and have suggested helpful responses to these concerns.² These are summarised in Table 20.1.
Table 20.1: Concerns about vaccination and suggested responses

<table>
<thead>
<tr>
<th>Concern</th>
<th>Response</th>
</tr>
</thead>
<tbody>
<tr>
<td>The disease is not serious.</td>
<td>Healthy children can still die from these diseases.</td>
</tr>
<tr>
<td>The disease is uncommon.</td>
<td>The disease is common in unimmunised populations and can easily recur and spread if immunisation rates drop.</td>
</tr>
<tr>
<td>The vaccine is ineffective.</td>
<td>Studies showing the effectiveness of a vaccine are needed before a vaccine is introduced.</td>
</tr>
<tr>
<td>The vaccine is unsafe.</td>
<td>As with effectiveness, the safety of a vaccine is rigorously tested before, and after, its introduction.</td>
</tr>
<tr>
<td>Other methods of disease prevention, such as homoeopathy are preferable to immunisation.</td>
<td>There is no body of scientific evidence that supports homoeopathy or other methods for preventing the diseases.</td>
</tr>
</tbody>
</table>


Questions and concerns on:

(a) Principles of immunisation and immunity

‘Immunisation is unnatural’

The claim that immunisation is harmful simply because it is artificial is not based on evidence. Some claim that the immune system was not designed to be exposed ‘directly’ to an antigen, in the manner of an injection. The immune system is designed to deal with invaders, wherever they enter the body. For example, the injectable polio vaccine has been shown to work just as well in protecting against disease as the oral vaccine, which enters the body in the same way as the infection. Immunisation by injection has also been shown to be safe and effective at preventing diseases like measles that normally enter the body through the airways.

‘The germ theory of disease is false’

The germ theory of disease was a major scientific advance, which has enabled the understanding of many – and the control of some – infectious diseases. However, when germs (bacteria, viruses, etc.) were first discovered, there was no proof that they caused illness. Germs could have been the result, rather than the cause, of disease, and there was debate in the 19th century about their role. However, the roles of bacteria, viruses and other micro-organisms in causing infectious diseases are now scientifically proven. Nevertheless, some people continue to question the role of micro-organisms. For these people, immunity to specific diseases, and hence immunisation, is irrelevant: one simply keeps healthy to prevent infection. It is true that a person’s state of health may sometimes influence how ill they become when infected, but some individuals in excellent health can suffer the severest effects of infections (eg, young adults who suffer meningococcal disease).
(b) The need for immunisation

‘Immunisation has played a minimal role, if any, in controlling disease’

It is true that improvements in living standards, in particular clean water, have had a great impact on health, but immunisation has played an important role as well. In the 1950s the incidence of paralytic polio was increasing until the Salk injected vaccine was introduced. The use of the oral vaccine from 1961 led to the elimination of wild polio from New Zealand and elsewhere.

Improvements in living conditions and medical care have reduced the chance of dying from infectious disease, but without immunisation most people will still acquire some infections. For example measles, which spreads through the air, is largely unaffected by improvements in living conditions other than reducing overcrowding. Healthy children living in ideal conditions remain at risk of death and disability from infections that can be prevented by vaccination. Smallpox vaccination led to the elimination of smallpox – this would not have occurred with improvements in living standards alone.

A recent example of the impact of immunisation was seen in New Zealand, and elsewhere, following the introduction of the Hib vaccine in 1994. This led to an approximately 95 percent decline in Hib disease – unrelated to any other change (see chapter 7). Indeed, it is possible that a change in living conditions (ie, an increased number of children attending early childhood services) could have led to an increase in the incidence of invasive Hib disease, but this did not happen because of the effective Hib vaccine.

Conversely, when pertussis immunisation coverage dropped in England, Japan and Sweden in the 1970s there were dramatic increases in pertussis disease and deaths. The role of immunisation is discussed in more detail in each chapter, but its overall impact on vaccine preventable diseases and their consequences has been well established. If immunisation coverage is sufficiently high, then polio, measles, mumps, rubella, Hib, and hepatitis B eventually could be eliminated from New Zealand through immunisation.

‘Infectious diseases are not serious, and are needed for normal development’

The morbidity and mortality of vaccine preventable diseases is detailed in each disease chapter. Some claim that measles is important for normal development and that after the illness children have a leap in physical and mental development. There is no evidence to support this, but given the serious impact of measles on a child’s health it is not surprising that a child who has recovered will be noted to have much more energy than during the illness. On the other hand, there is evidence that a child has reduced immunity for weeks to months after measles, and during this time the child is more likely to get other infections.
‘Natural measles prevents cancer later in life’

This claim is based (by people other than the original author) on one small Danish study that found a statistical association between certain chronic diseases and cancers, and early exposure to measles infection, possibly modified by the injection of measles antibodies in measles immunoglobulin. The fact that these children failed to develop a rash has been used to claim that it is essential to develop the rash of measles. The study has also been used to suggest that giving vaccine is dangerous if antibodies are present.

These are not the findings of the study, nor does the study author suggest that measles prevents these diseases. The paper concludes: ‘Several types of evidence need to be examined before one can accept the hypothesis that measles virus causes non-measles associated disease.’ No such evidence has been found for these associations.

‘Vaccines do not work as most cases of disease are in immunised children’

No vaccine is 100 percent effective and some immunised children will get the disease. As immunisation coverage increases, the proportion of cases that occur in children who have been immunised increases. There is a simple relation between vaccine effectiveness, immunisation coverage and the proportion of cases that are immunised.

To see this clearly, imagine a group of 100 children. If 90 percent of children are given a vaccine that is 90 percent effective, then:

- 81 of the 100 children will be immune
- 10 children will be susceptible because of not having the vaccine and another nine because of vaccine failure.

This means that we expect that nearly half the cases of disease will be in immunised children – even though only 10 percent of immunised children were susceptible.

Of course if all 100 children had been vaccinated only 10 would be susceptible to disease. As vaccine uptake rises, the proportion of cases of disease that occur in vaccinated people increases dramatically, but the number of cases of disease falls to very low levels.

For pertussis, where the protection following vaccination lasts only a few years, most immunised children will be reinfected but the resultant illness will be milder, with fewer serious consequences and at an older age than if they had not received vaccine. The disease is most severe in infants.

‘Immunisations are not needed in industrialised countries’

Many diseases prevented by immunisation are spread directly from human to human. Clean water and good hygiene do not stop airborne infections or those spread by direct personal contact. Despite excellent hospital care, long term
complications and death still occur from diseases that can be prevented by immunisation. Although it is true that the impact of immunisation is greater in non-industrialised countries, it remains very important for children in industrialised countries such as New Zealand.

At present the risk of getting some vaccine preventable diseases is low because most children have been vaccinated. The degree of risk depends on the proportion of children who have been immunised. This is termed ‘immunisation coverage’. If enough children have been immunised, the organism will not be able to circulate in the community, and the likelihood that those who have not been immunised, or who have failed to respond to immunisation, will be infected is correspondingly reduced. This is termed ‘herd immunity’. Immunisation offers the possibility of eliminating disease, as has happened with smallpox and, in some areas of the world, with polio and measles (see chapters 8 and 9).

‘Natural immunity is better than vaccine induced immunity’

The duration of immunity following vaccination may be less than the duration of immunity after the disease. However, both are protective, and if immunity following immunisation wanes, booster doses may be given. It is important to note that the ‘lifelong’ immunity following natural measles is in the context of repeated exposure to the organism throughout life. With vaccine induced immunity such boosting is much less likely to occur because of reduced circulation of the organism.

Natural immunity and vaccine induced immunity are virtually identical natural responses of the body’s immune system. Those who suffer ‘natural’ disease run the risks of serious illness, disability and death to acquire immunity. In contrast, the acquisition of vaccine derived immunity is at much lower risk. However, several doses of vaccine, and booster doses, may be necessary to attain and maintain good levels of immunity, and immunisation does fail in a small proportion of vaccinees.

For some organisms (e.g., Hib in children under two years, and tetanus at any age) the immunity following vaccination is better than that following infection. With Hib this is because the vaccine can stimulate immune memory in infants in a way that the disease does not. For tetanus this is because the disease can be caused by a small amount of the toxin insufficient to generate an immune response. In 1995 a 40-year-old man developed tetanus for a second time because he failed to complete the recommended course of immunisation after recovering from an earlier episode of tetanus (see chapter 5).6

‘A healthy lifestyle will protect children from infection’

A healthy lifestyle does not produce the necessary immune response to protect a child from a specific potentially serious infection. Only immunisation or being infected by the organism can do this. Immunisation poses far less risk than natural infection because it is very unlikely to cause an illness, while those suffering natural infection are very likely to become ill.
The living arrangements of a person (eg, overcrowding, inadequate sanitation and hygiene) will affect the likelihood of exposure to infection. For most diseases, the health of a person makes little difference to the likelihood of being infected if exposed. However, those in good health will be less likely to suffer a severe illness, or complications, as a consequence of infection.

Nevertheless, a healthy lifestyle does not provide secure protection against disease or its complications. For example, over half of all the children who died from measles in the United Kingdom (UK) between 1970 and 1983 were previously healthy.7

‘Breastfeeding protects against infection’
There is good evidence that breastfeeding reduces to some degree the frequency and severity of gut, chest and ear infections. The extent to which it protects against other diseases is less clear. The protection from breastfeeding varies from person to person and is of brief duration. Both breastfeeding and immunisation contribute to the health of children.

‘Homoeopathic immunisation prevents infection’
Homoeopathic ‘immunisation’ offers no proven protection against infectious diseases. Dr Hahnemann, the founder of homoeopathy, considered conventional immunisation to be ‘a clear and convincing demonstration of the Law of Similitude’8 – the fundamental principle of homoeopathy. The UK Faculty of Homoeopathy supports conventional immunisation and is not aware of any evidence supporting the use of homoeopathic immunisation.9

Some non-medical homoeopaths do not support conventional immunisation, and state that homoeopathic preparations can prevent disease. There are no published studies to support such beliefs – an extensive review of homoeopathic studies found none on the prevention of the usual childhood immunisation schedule diseases.10 There were some studies on the prevention of influenza, with all but one showing no effect. The single study that did find a protective effect was rated ‘of poor quality’.

Only conventional immunisation has been shown to produce a measurable immune response and protection against disease.

‘Other countries have stopped immunisation’
Every country in the world has some type of immunisation programme, and in some it is compulsory. Individual vaccines have been withdrawn from use in certain countries at different times for differing reasons. In 1979 Sweden stopped using pertussis vaccine because of concerns about the efficacy of the locally produced vaccine and because there were concerns that pertussis vaccine might cause brain damage (see below). Sweden was actively involved in testing acellular pertussis vaccines, and has re-introduced pertussis vaccination. France stopped its school-delivered hepatitis B immunisation programme for adolescents to enable recipients to discuss the issue with their family doctor. Hepatitis B vaccine is still widely used
in France and is part of the routine childhood immunisation schedule. In Japan the use of MMR vaccine was temporarily stopped because of concerns about meningitis following the strains of mumps vaccines used there. In 1992 the Urabe strain of mumps vaccine in MMR vaccine was withdrawn from New Zealand and other countries, and replaced with one that is not associated with an increased risk of meningitis (see chapter 10 Mumps).

(c) Vaccine content

‘Vaccines contain toxic chemicals, viruses and cells’

Vaccine production is highly regulated, requiring extensive testing during manufacture and of the final product. The testing standards are rigorous and internationally regulated by independent authorities. The manufacturer must show that each dose is safe, pure and potent enough to be effective. Any toxic substances (eg, formaldehyde) present in vaccines are only permitted in tiny amounts, too small to cause any harm.

There have been unwanted viruses in vaccines in the past: avian leucosis virus in yellow fever vaccines, SV40 in polio vaccines in the 1950s (see section 20.3), and pestivirus in some Japanese vaccines in the 1980s. All vaccines are carefully tested now to ensure that no other viruses or bacteria are present. The sophistication of this testing continues to improve.

In 1995 there was concern that a previously unidentified virus could have been the source of an enzyme, reverse transcriptase, found in vaccines grown in chick cells. The finding was made when a new test that was a million times more sensitive than the prior test was used. Further work has identified that the source of this enzyme is the chick cells on which the vaccine is grown, not a virus.\(^1\)

Some vaccines (eg, rubella) are grown in cells of human origin. The source of some of these cells was a fetus aborted for medical reasons in the 1960s. By a process of repeated cultivation it is possible to produce an ‘immortal’ self-replicating group of cells known as a ‘cell line’. A cell line is similar but not identical to the original cell, and apart from the origin of the cell there is no connection to any fetus. The cell line can be maintained indefinitely in the laboratory and provides a safe and standardised medium for growing vaccine viruses.

Whether vaccines are grown on cells of human or animal origin, whole cells are not in the final vaccine. Once the virus has been cultivated in cells, it is separated from all cellular material. It is possible that minute traces of cellular material might remain in a vaccine, but not whole cells.

During the early stages of the human immunodeficiency virus (HIV) epidemic it was suggested that an early polio vaccine was cultivated in chimpanzee cells contaminated with the precursor of HIV-1. It was suggested that the use of this polio vaccine resulted in the transfer of the virus to humans, and was the source of
HIV. Investigation of the claim revealed that no chimpanzee tissue was involved in the production of the vaccine. Supplies of the early polio vaccine were discovered in freezers and tested in several laboratories, all of which agreed that no HIV, nor chimpanzee DNA, was present in the vaccine. Thus it has been convincingly demonstrated that polio vaccine was not the source of HIV.12

‘Vaccines contain aluminium – a cause of Alzheimer’s disease’
The cause of Alzheimer’s disease, a degeneration of the brain leading to dementia, is not known. There have been some studies suggesting a link with aluminium in the water supply, but it remains uncertain if aluminium does indeed play a role in causing Alzheimer’s disease. The amount of aluminium in a vaccine is tiny and within accepted safety limits.

‘Vaccines contain aluminium – why is it in a vaccine and does it harm my child?’
Clinical studies have found that the effectiveness of some vaccines is improved by the addition of chemical compounds called adjuvants, which increase the body’s immune response to the vaccine and therefore the level of protection. Aluminium compounds have been used for many years as adjuvants in vaccines, and include aluminium sulphate, aluminium hydroxide and alum (potassium aluminium sulphate). Although there have been some claims of adverse effects from these compounds in vaccines, no major effect has been proven. In a systematic review of the evidence for any adverse events after aluminium containing diphtheria, tetanus and pertussis vaccines, it was found there were no serious or long term adverse effects/illness.13 This review found that aluminium hydroxide containing vaccines did cause more local reactions in infants, including erythema and induration, but that there was no association between aluminium containing vaccines and severe events such as collapse, and persistent crying or screaming. In older children, 10 to 16 years of age, the only differences were that after an aluminium containing vaccine the children were more likely to have pain at the injection site 14 days after the immunisation.

‘Vaccines contain mercury – is it safe?’
The vaccines used on the usual New Zealand National Childhood Immunisation Schedule are all thiomersal free; that is, they do not contain any mercury compound. However, thiomersal is found in both child and adult doses of the combination diphtheria, tetanus vaccines (CDT™ and ADT™; 0.01 percent w/v), and in some influenza vaccines.

Very small quantities of mercury compounds such as thiomersal are used in some vaccines as a preservative. The tiny quantity of mercury in a dose of vaccine is not harmful, but because babies now receive several different vaccines the quantity of mercury that was given in vaccines on the United States (US) immunisation schedule exceeded some exposure guidelines.14 There have been historical reports of adverse developmental outcomes in infants following ingestion of fish with toxic levels of
methyl mercury by pregnant women. Thiomersal is, however, a different organic compound which is metabolised to ethyl mercury and thiosalicylate.

Because there was a desire to avoid using any extra chemicals, the vaccine manufacturers developed vaccines without the mercury compound as preservative. The Immunization Safety Review Committee of the Institute of Medicine in the US reviewed the data and in 2001 concluded that the existing evidence was inadequate either to accept or reject an epidemiological relationship between thiomersal exposure and neurodevelopmental disorders. Nevertheless, the report stated that a link was biologically plausible and recommended the use of thiomersal free vaccines.\textsuperscript{15}

**‘Vaccines may cause mad cow disease’**

Before extensive controls were put in place, the materials used in some vaccines could, in theory, transmit the infectious agent responsible for bovine spongiform encephalopathy (BSE) or mad cow disease, or its human equivalent variant Creutzfeldt-Jakob disease (vCJD). After billions of doses this has not been documented. In addition, for those vaccines that use material from cows, the manufacturer must ensure that these materials come from BSE free areas and have been purified to reduce any risk.

Authorities in the US have reached the following conclusions about the risk of vCJD from vaccination.\textsuperscript{16}

- No evidence exists that cases of vCJD are related to the use of vaccines.
- There is no evidence that any vaccines harbour the BSE agent.
- There have been no reports of BSE contamination of pharmaceutical or biological products.
- No bovine material has ever been used as an active ingredient of any vaccine.
- There is no evidence that vaccines have contributed to cases of vCJD in Europe.
- The distribution of vCJD cases does not support concern regarding vaccines. Vaccines are distributed globally, yet cases of vCJD have almost entirely been restricted to the UK.\textsuperscript{17}

There is a theoretical risk that vaccines that contain human blood products (eg, albumin in MMR) might transmit vCJD. There have been two cases of vCJD in the UK that are thought to be the result of whole blood transfusion from donors who were incubating the disease. In vaccine manufacture the blood donor selection and exclusion policies minimise any risk, as would the extraction and preparation of the blood product. There has so far been no evidence of transmission of vCJD from vaccines.
‘Vaccine viruses persist after immunisation’

Vaccine viruses are supposed by some opponents of immunisation to persist in the body, leading to chronic disease. Varicella vaccine does persist after immunisation and may rarely cause shingles. There is no evidence that the constituents of other vaccines persist after immunisation.

(d) Vaccine risks

‘Vaccine risks are greater than the disease’

When immunisation allows us to gain control over a disease, the risk of being infected becomes very low. For example, there is no risk of getting polio in New Zealand unless it is imported. On the other hand, before the change to inactivated polio vaccine (IPV) in 2002 there was a very small risk of paralysis from oral polio vaccine (OPV) at a rate of about 1 in 2.4 million doses. The risk from OPV was then greater than from natural disease, but this is precisely because immunisation has reduced the risk of natural disease in the first place. It is the consequence of any immunisation programme that the risk of vaccination, if the vaccine is successful in eliminating the disease, will become greater than the risk of disease, which will have been reduced to zero. Such a circumstance is evidence of the success of vaccination. This is the reason for the switch to IPV in 2002 (see chapter 8).

In the US there are now more reports of adverse events following immunisation than there are of vaccine preventable diseases. Even if all the adverse events were caused by immunisation – and they are not – this is not a fair comparison. One needs to compare vaccine risks with disease risks in the absence of immunisation. Vaccinating is far less risky than not vaccinating.

‘Most vaccine reactions are not reported in New Zealand, so vaccine risks are underestimated’

The usual expected reactions following immunisation are not reported. Practitioners are asked to report serious and unusual adverse events following immunisation rather than mild, expected reactions to CARM (see section 2.4). It is likely a few adverse events are not reported. This can be for many reasons, including failure to recognise that the event may be linked to immunisation. However, vaccine risks are estimated from a variety of sources, including controlled studies prior to licensure and post-marketing surveillance following licensure. Studies prior to licensure are not usually undertaken in New Zealand. The rate of adverse events reported in New Zealand has generally been lower than the rate of adverse events documented in prospective studies. Nevertheless, in New Zealand a greater proportion of serious events than minor reactions are reported.

‘The follow up in vaccine studies is too short to detect any long term risks’

In order for a vaccine to be used, a rigorous and extensive process is undertaken to demonstrate that the vaccine is safe and prevents disease. This includes careful follow up to identify any adverse events following immunisation. The nature of these
studies is such that only short term effects can be detected. There are, however, several different sorts of studies that can identify longer term effects. Such studies identified an increased mortality in children who received high dose measles vaccine compared to normal dose measles vaccine. As a result, the use of high dose measles vaccine was stopped. This vaccine was never used in New Zealand. There has also been long term follow up of those people who received polio vaccines contaminated with SV40 virus (see section 20.3).

There have also been allegations of Crohn’s disease, autism, asthma and diabetes following immunisation. These have been investigated, showing that studies of long term effects can be, have been and continue to be undertaken. These studies have not shown any evidence of long term adverse effects.

‘Children are more susceptible to disease after immunisation’
There is little evidence to support this statement. Controlled studies monitor adverse events, including any increased risk of infection. By chance, some studies will identify more infections in the vaccinated group. However, most studies have not shown any significant increase in infection. One study followed up more than 60,000 children given DTwP (diphtheria, tetanus and whole cell pertussis) vaccine, and found no difference in serious bacterial infections after immunisation.19

A new vaccine (rotavirus) was withdrawn in 1999, shortly after its introduction in the US, when it was found that the vaccine led to an increased risk of a bowel obstruction (intussusception) in about 1 in 10,000 children (see section 20.3 and chapter 19).

A recent study conducted in Guinea-Bissau has raised concerns about the non-specific effects of vaccines in developing countries.20,21,22 In this study the association between routine childhood vaccinations and survival was examined. Mortality in the group vaccinated with any vaccine was lower compared with those not vaccinated. However, when effects of specific vaccines were examined, the study showed that recipients of BCG alone and measles vaccine at nine months had reduced mortality, while those who received DTwP or polio vaccines had an increase in mortality compared with unvaccinated children that just reached statistical significance.

There are valid concerns about whether the results of this study reflect a real effect of vaccination. If its findings are true it means that the reduction in mortality occurring as a result of DTwP and polio vaccination may be less than expected: ‘the large decrease in the number of deaths from diphtheria, tetanus, pertussis and polio would be partly offset by increased mortality from other causes’. The study findings have not been confirmed, and other studies have found that measles immunisation overall decreases mortality.23
‘Vaccines cause the disease they are supposed to prevent’

Live vaccines can infrequently cause symptoms similar to but much less severe than the disease caused by natural infection. The exception to this is OPV, which can extremely rarely cause vaccine associated paralytic poliomyelitis (VAPP), which is identical to the disease caused by wild poliovirus (see chapter 8).

Inactivated vaccines generally cannot cause the disease against which they protect.

‘Immunisations “overload” or “overwhelm” the immune system’

There is no evidence of immune system ‘overload’. The immune system is designed to be able to deal with a very large number of different antigens. All children, and adults, come into contact with many viruses, bacteria and other agents to which the immune system responds every day.

The additional demands placed by vaccines are small compared to the ability of the immune system to respond. In addition, the number of immunogenic proteins and polysaccharides in modern vaccines has decreased compared with early vaccines because of advances in vaccine technology. For example, early whole cell pertussis vaccines contained around 3000 immunogenic proteins compared with two to five in the modern acellular pertussis vaccines. In spite of an increase in the vaccines on the schedule, an infant now receives fewer immunogenic proteins and polysaccharides than with earlier vaccines.24

From birth, an infant’s immune system responds to various microbial challenges in the environment. The infant is also able to generate an immune response to vaccines; for example, infants born to mothers infected with hepatitis B virus are protected against infection after receiving the hepatitis B vaccine given after birth (along with HBIG) and at age six weeks, and at three and five months. Eighty-five to 95 percent of infants immunised in the first six months of life against pertussis, diphtheria, tetanus, polio and Hib develop protective vaccine specific antibodies. Conjugation of a vaccine antigen to a carrier protein (eg, Hib or conjugate pneumococcal vaccine) enables the infant to develop a specific immune response using helper T-cells and therefore a specific T-cell memory. The immune response to a polysaccharide vaccine alone is poor in infants under the age of two years.

New technology for producing vaccines has resulted in a more specific and therefore lower antigen load. The table below shows the reduction in antigenic content as the result of using new vaccines.
Table 20.2: Number of immunogenic proteins and polysaccharides contained in vaccines over the past 100 years\textsuperscript{25}

<table>
<thead>
<tr>
<th>Year</th>
<th>Vaccine</th>
<th>Proteins</th>
<th>Year</th>
<th>Vaccine</th>
<th>Proteins</th>
<th>Year</th>
<th>Vaccine</th>
<th>Proteins</th>
<th>Year</th>
<th>Vaccine</th>
<th>Proteins/ polysaccharides</th>
</tr>
</thead>
<tbody>
<tr>
<td>1900</td>
<td>Smallpox</td>
<td>~200</td>
<td>1960</td>
<td>Smallpox</td>
<td>~200</td>
<td>1980</td>
<td>Diphtheria</td>
<td>1</td>
<td>2005</td>
<td>Diphtheria</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>Diphtheria</td>
<td>1</td>
<td></td>
<td>Tetanus</td>
<td>1</td>
<td></td>
<td>Tetanus</td>
<td>1</td>
<td></td>
<td>WC-pertussis</td>
<td>2–5</td>
</tr>
<tr>
<td></td>
<td>WC-pertussis</td>
<td>~3000</td>
<td></td>
<td>Polio</td>
<td>15</td>
<td></td>
<td>Polio</td>
<td>15</td>
<td></td>
<td>Total</td>
<td>~200</td>
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<tr>
<td></td>
<td>Polio</td>
<td>15</td>
<td></td>
<td>Measles</td>
<td>10</td>
<td></td>
<td>Measles</td>
<td>10</td>
<td></td>
<td>Total</td>
<td>~3217</td>
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<tr>
<td></td>
<td>Measles</td>
<td>15</td>
<td></td>
<td>Mumps</td>
<td>9</td>
<td></td>
<td></td>
<td></td>
<td></td>
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<td>Rubella</td>
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<td>Total</td>
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<td></td>
<td></td>
<td></td>
<td></td>
<td>Hib</td>
<td>2</td>
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</tbody>
</table>

Key: AC: acellular pertussis, WC: whole cell pertussis.

The immune system is theoretically able to respond to the simultaneous administration of thousands of vaccine antigens without adverse effects.

(e) Conspiracy for profit

‘The real facts are hidden’

Some people claim that governments and the medical establishment are in an alliance with vaccine manufacturers to hide the real facts about immunisation. No evidence has ever been presented for this claim. There is, however, a shared interest between commerce (selling vaccines) and public health (preventing illness).

‘Many studies show vaccines to be dangerous and ineffective’

Although in direct conflict with the claim of ‘hidden facts’, this claim is often made by the same people. At the extreme is the claim of not being able to find a single paper in the entire medical literature showing that immunisation works.\textsuperscript{26} Many papers have reported cases of immunisation failing to protect (this should be expected, given that no vaccine is 100 percent effective), or that some serious events happened after immunisation. Those opposed to immunisation have used such material to create what appears to be a scientific attack on immunisation, by using selective information. Most scientific papers have demonstrated the safety and effectiveness of vaccines and, where appropriate, noted concerns about vaccines either being unsafe or ineffective, which have led to the withdrawal of specific vaccines. Over time, improved vaccines have replaced vaccines that are unsafe or of
poor effectiveness, as well as those that perform less well or cause more reactions; this is standard scientific progress.

‘Immunisation is only for the profit of multinational drug companies’
The development of new vaccines is an expensive and risky business. The high costs of bringing a vaccine to market can only be justified if the vaccine will be sold at a price that provides a commercial return to the manufacturer. A vaccine can only be profitable if it is shown to be safe and effective. Vaccine manufacturers have a natural interest in producing the best possible vaccine as well as making a profit.

‘Nearly all vaccine research is biased because it is funded by the vaccine manufacturers’
It is true that the pharmaceutical companies fund most research on vaccines. This funding does not mean that the research is biased, as much of it is undertaken by independent researchers operating under international standards of good clinical practice. Nevertheless, the potential for bias is a real one, leading many medical journals to require statements of the funding source and all potential conflicts of interest to be declared and published with any scientific studies.

(f) Immunisation as a cause of idiopathic illnesses
In recent years there have been claims that immunisation causes various diseases. These allegations of a link are usually:

• made for a disease of unknown cause
• made by a single researcher or research group
• not confirmed by other researchers.

It is important to identify all the harmful effects of immunisation. Unfortunately, claims are often made without apparent concern for the potential harm resulting from public loss of confidence in all immunisations. The harm from such claims has been documented in relation to pertussis.27

It is likely that simply because a link has been suggested, especially if it has been published in a well known medical journal, it will be publicised and many people will feel that there must be something to the claim. When other researchers investigate it and fail to confirm the findings, it is likely that the alleged link was the result of a chance association. Publicity tends to refer to the study suggesting the link and to ignore those studies that found the link was the result of chance association. Publication of refutations of claims seldom achieves the same, at times sensational, prominence as the original claim.

‘Immunisation causes brain damage’
Two vaccines, measles and pertussis, have been suggested to be possible causes of brain damage, and we will look at each in turn.
(i) Measles
Measles virus causes encephalitis and brain damage. Because the vaccine can cause a mild measles like illness, it is possible that the vaccine could also cause encephalitis. Encephalitis following measles vaccine has indeed been reported at a rate of about 1 per million doses. However, as this is similar to the background rate, it is not certain that the vaccine causes such events. An analysis of claims for encephalitis following measles vaccination in the US found a clustering of events at eight to nine days after immunisation, which supports, but does not prove, the possibility that the vaccine rarely causes encephalitis. The risk was less than 1 per million doses, or about 1000 times less than the risk of encephalitis from measles disease. Thus any risk of encephalitis caused by vaccination is very much less than the risk of encephalitis caused by the disease.

(ii) Pertussis
There have been reports of serious adverse events following whole cell pertussis vaccine since its first use. Despite considerable research, including some large controlled trials, it remains uncertain if the earlier whole cell pertussis vaccine causes brain damage. If the vaccine is ever responsible for brain damage, this is an exceptionally rare event – less than 1 per million doses. The controversy started after some doctors from Great Ormond Street Hospital, London, published a paper in 1974 suggesting that serious neurological problems, including epilepsy and learning disorders, might be secondary to pertussis immunisation.

The British National Childhood Encephalopathy Study (NCES) aimed to resolve the controversy. In this study all cases of acute encephalopathy that occurred in England and Wales during the period of the study, 1976–79, were included and their association with whole cell pertussis vaccine assessed. The NCES results suggested, but did not prove, that the pertussis vaccine could cause short term brain symptoms, acute encephalopathy, following 1 per 110,000 doses of DTwP and permanent brain damage following 1 per 310,000.

A 1989 court case led to a review of the NCES findings. The NCES conclusion had been based on seven children who were thought in the original study to have suffered permanent damage. Review showed that three were alive and well, and the other four had died from causes unrelated to immunisation. The court concluded, after careful scrutiny of the NCES data, that there was no evidence that pertussis vaccine could cause permanent brain damage.

The Institute of Medicine (IOM) came to a similar conclusion that there was not enough evidence to resolve the issue. The conclusion was based on two years’ work by an expert committee that reviewed all the evidence on adverse events from pertussis vaccines. The IOM did conclude, however, that the evidence was consistent with pertussis vaccine causing an acute encephalopathy – largely based on the NCES findings.
However, on further follow up in 1993, children in the NCES who suffered acute encephalopathy were found to have had long term consequences – whether the acute encephalopathy was vaccine associated or not. As a result, the IOM now considers that the evidence is consistent with pertussis vaccine causing ‘the forms of chronic nervous system dysfunction described by the NCES in those children who experience a serious acute neurological illness within seven days after receiving DPT vaccine’.

The critical word is ‘consistent’, which does not mean that the link is proven. The case against such a link includes the following facts.

- Brain damage often becomes apparent in the first year or two of life – frequently around the times that immunisations are scheduled.
- There is no specific type of brain damage associated with whole cell pertussis immunisation.
- Four studies (following up a total of over half a million doses of pertussis vaccine) found no association with neurological illness.
- A case control study that identified all neurological illness in a population of 218,000 children aged 1–24 months during one year found no increase in risk with pertussis vaccination.
- There have been several controlled trials for the acellular pertussis vaccine, none of which found any cases of brain damage. One found one case of encephalitis among 82,000 children participating in a pertussis vaccine trial. That case happened several months after immunisation. In contrast, three of 17,000 children not participating in the trial had encephalitis – all of them due to pertussis.

It is not surprising that most medical authorities agree that that pertussis vaccine has not been proven to be a cause of brain damage.

‘Immunisation causes cot death’

Sudden Infant Death Syndrome (SIDS) occurs under one year of age, and is most common around three months of age, when many immunisations are given. SIDS may occur by chance within a day or so of immunisation. There have been many studies that have conclusively shown that SIDS is not caused by immunisation. In addition, some studies, including the New Zealand Cot Death Study, found a lower rate of SIDS in immunised children. This is consistent with a Scandinavian study, which found that some cases of SIDS were probably caused by undiagnosed pertussis.

Despite the solid evidence against a link, the claims continue to be made, usually on the basis that the studies are faulty. However, consistent findings from several studies using a range of methods make up for any weakness in any individual study.
‘Immunisation causes asthma’
There have been three studies suggesting a link between immunisation and asthma.\textsuperscript{46,47,48} Other, more definitive, studies found no link.\textsuperscript{49,50,51,52,53} The play of chance, as well as bias in study methodology, may allow for the observation of a link when there is none. This is why the consistent findings of several different studies should be given more weight than the findings of a single study. Later studies and a review article, including a large cohort study,\textsuperscript{54} have examined whether vaccines are linked with the development of asthma.\textsuperscript{55} They concluded there was not the evidence to support the hypothesis that vaccines cause allergic diseases.

‘Immunisation causes diabetes’
It has been claimed that immunisation can cause type I diabetes in rats\textsuperscript{56} and children.\textsuperscript{57} The claim is largely based on the analysis of data from a large Finnish study of Hib vaccine. In response, the Finnish investigators re-analysed their data and concluded that there was no link.\textsuperscript{58} Because it is possible to analyse the Finnish data to support such a link,\textsuperscript{59} there was debate on the issue, stimulating research by other authors.

It was also suggested that the increase in cases on the Christchurch diabetes register after 1989 arose from the introduction of hepatitis B immunisation.\textsuperscript{60} The timing of the increase does not coincide with the time that hepatitis B immunisation was introduced, and the Auckland diabetes register showed no increase at this time (the change in immunisation policy affected the whole country).\textsuperscript{61} A review of all the published papers on diabetes found no evidence to support a link with immunisation.\textsuperscript{62} In fact, evidence from Finland suggests that the elimination of natural mumps by immunisation may have decreased the risk of insulin dependent diabetes.\textsuperscript{63} Studies in Sweden failed to find any change in diabetes incidence as a result of stopping BCG\textsuperscript{64} or pertussis immunisation.\textsuperscript{65} Other studies in Sweden\textsuperscript{66} and Canada\textsuperscript{67} have also failed to find any link between immunisation and diabetes.

In 1998 two workshops were held in the US to review all the evidence on the issue of immunisation and diabetes. Both workshops concluded that there was no evidence for any increased risk of diabetes associated with childhood vaccines.\textsuperscript{68} Several studies are under way to determine if certain vaccines administered early in life might protect high risk children against diabetes, as has been demonstrated in genetically predisposed animals.

‘Immunisation causes autism and Crohn’s (and other bowel) disease’
These allegations came from a single group of researchers at the Royal Free Hospital, London. The initial claim was that measles vaccine causes Crohn’s disease – an inflammatory bowel disease.\textsuperscript{69} The claim was based on evidence of measles virus in diseased bowel, as well as an increased risk in groups who were more likely to have been immunised. However, their studies had several serious flaws, and other studies published since have failed to provide any supporting evidence of a link.\textsuperscript{70,71}
The Royal Free Group then published a report implicating measles, mumps, rubella vaccine (MMR) as a cause of autism.72 Autism is a chronic developmental disorder. The main characteristics of autism are problems in social interaction and communication, and restrictive and repetitive interests and activities. Autism may be initially noted in infancy as impaired attachment, but it is most often first identified in toddlers, mostly boys, from 18 to 30 months of age. Boys are three to four times more likely to be afflicted with autism than girls.

This report was later retracted by all but one of the authors.73 Subsequent studies looked for a possible link between autism and MMR, and all studies failed to find such a link, as did the UK’s Committee on Safety of Medicines, which evaluated hundreds of cases where a claim had been made.74 The studies have included a Welsh review of 18 autistic children,75 a review of clinic records over 25 years of 8889 children, a French survey of 6100 school children,76 a 14 year Finnish follow up of more than three million doses of MMR,77 and a British case control study.78

The British case control study had several lines of evidence that were against a link. First, the diagnosis of autism had been increasing since 1979 but there was no jump after the introduction of MMR in 1988. Second, cases were diagnosed at similar ages whether they were immunised before or after 18 months of age, or not at all. Third, the cases were no more likely to have received MMR than the general population. Finally, the first diagnosis of autism or initial signs of behavioural regression were not more likely to occur within time periods following vaccination than during other time periods. The study did find evidence for some recall bias to link initial parental concern with MMR vaccine. A Swedish study found no difference in the prevalence of autism in children born after the introduction of MMR compared with children born before.79

The consistent findings from these studies show that this appears to be another chance association, to be expected given that both MMR immunisation and diagnosis of autism occur in the second year of life. Recently, the NCES was re-examined and found no indication that measles vaccine contributes to the development of long term neurological damage, including educational and behavioural deficits.80

The Immunization Safety Review Committee of the IOM in the US has published a review of all current sources of evidence concerning a possible association between MMR and autism.81 The Committee concluded that ‘the evidence favours rejection of a causal relationship at the population level between MMR vaccine and autism’. However, because of the public concern about this association, the Committee recommended, and suggested several avenues for, further research. It did not recommend a policy review of the recommendations concerning MMR vaccine.
‘Immunisation causes arthritis’

Arthritis or arthralgia occur after both rubella disease and rubella vaccination, especially in adults. It was previously thought that rubella vaccination might lead to long term arthritis. However, two large controlled studies found no evidence to support a link. \(^{82,83}\) Another study did find a slight increase in risk from rubella vaccination, but this was of borderline statistical significance (i.e., it could have been a chance occurrence). \(^{84}\) The evidence currently suggests that rubella vaccination does not cause chronic arthritis. \(^{85}\) (See chapter 11.)

‘Immunisation causes an increase in autoimmune disease (e.g., multiple sclerosis) and cancer’

After millions of vaccinations over many decades, there is no evidence to suggest that immunisation causes these diseases. In fact hepatitis B immunisation can significantly reduce the risk of liver cancer resulting from chronic hepatitis B. The most common type of childhood cancer is leukaemia. Immunised children may be at lower risk of leukaemia. \(^{86}\) A New Zealand study found no link between vaccination and leukaemia. \(^{87}\)

Reports of adults developing multiple sclerosis (MS) after hepatitis B immunisation in France have led to investigation of this claim. The studies have found no link, and it is likely that the reported cases were chance associations. \(^{88}\) Two large studies have looked at the risk of MS after hepatitis B vaccine \(^{89}\) and the effect of vaccinations on relapse of MS. Both studies found that vaccination neither caused MS nor caused an exacerbation of MS. \(^{90}\)

Guillain-Barré syndrome (GBS) is an autoimmune disease of the nerves that causes a temporary paralysis. Although various vaccines have been suspected of causing GBS, some large studies have failed to find a link with measles, \(^{91}\) polio \(^{92}\) or tetanus vaccines. \(^{93}\) There is some evidence that influenza vaccine may cause GBS in one to two people per million doses. \(^{94}\)

20.3 Lessons from the past

There have been errors in immunisation practice in the past. Lessons learnt from these errors have been used to improve vaccine safety, and to set up better research programmes and clinical trials, as well as systems to monitor vaccine safety.

The SV40 contamination of early polio vaccines

The early polio vaccines of the 1950s and early 1960s were grown on monkey kidney cells, which, in some instances, were shown to be contaminated with the monkey virus, simian virus 40 (SV40). By 1962 around 98 million individuals had been given polio vaccine, of whom 10–30 million may have received vaccine contaminated with SV40. Soon after its discovery, measures to exclude the virus from polio and other vaccines were rapidly introduced and no vaccine manufactured after 1963 contained SV40. SV40 has been shown to cause cancers in animals, and virus traces have
been found in some rare human cancers, mesotheliomas, osteosarcomas and brain tumours. There is no evidence, however, that SV40 causes cancer in humans: several studies have failed to show an association between exposure to SV40 contaminated vaccines and human cancer, the latest after more than 30 years of follow up.\textsuperscript{95}

**The Cutter polio vaccine incident – insufficiently inactivated vaccine**

The first polio vaccine was made from virus that was inactivated. In the early days of manufacture (1955), vaccine from Cutter laboratories was inadequately inactivated. This was because clumping of the virus led to a failure of those viruses in the centre of the clump to come into contact with the inactivating agent, formaldehyde. As a result, children were injected with vaccine contaminated by live virus and 260 children developed polio from the vaccine. There have been no cases of polio from inactivated polio vaccine since the Cutter incident.

**Killed measles vaccine causing atypical measles**

The first measles vaccine used in the US (from 1963 to 1967) was an inactivated (killed) vaccine. This inactivated vaccine produced immunity that was short lived and placed the recipients at risk of atypical measles. The killed measles vaccine was not used in New Zealand.

**High dose measles vaccine**

In an attempt to use a vaccine that could be given at an earlier age to infants in developing countries, the World Health Organization (WHO) in 1990 recommended the use of high dose measles vaccine. This vaccine was effective from six months of age. However, the vaccine was found to lead to increased late mortality in girls.\textsuperscript{96,97} As a result the WHO advised against its use.\textsuperscript{98}

**Rubini mumps vaccine – failed to protect**

The Rubini strain of mumps vaccine was shown to produce good levels of antibodies against mumps and so was licensed for use. However, studies in Europe and Singapore have shown that it provides virtually no protection against mumps and it is no longer used in most countries (see section 9.4).

**Mumps vaccine meningitis**

Some strains of mumps vaccine cause aseptic meningitis. Complete recovery after a few days’ illness is the norm and sequelae are rare or absent. Taking into account intensity of surveillance, it is likely that rates of meningitis following mumps vaccination with the Urabe strain vary from 1 per 1000 to 1 per 20,000. A rate of 1 per 11,000 vaccinations, as measured in the UK, following immunisation with the Urabe strain (compared to 1 in 800,000 for the Jeryl Lynn strain) led to the withdrawal of vaccines containing the Urabe strain from several countries, including New Zealand. Rates following vaccination with other Japanese strains vary from 1 in 120,000 to 1 in 5000 doses. For the Leningrad-3 strain, rates of 1 in 1000 have been reported.\textsuperscript{99}
**Pertussis vaccines – variable protection**

Until recently, whole cell pertussis vaccines were considered to be generic products (ie, all provided broadly similar levels of protection). However, in the acellular pertussis vaccine trials, conducted during the last decade, it was shown that this was not the case and that one whole cell vaccine provided low levels of protection. This vaccine has not been used in New Zealand.

**Rotavirus vaccine**

Rotavirus vaccine was introduced onto the US schedule in August 1998. Because it had been observed in pre-licensure trials that intussusception had occurred following administration of the vaccine, the incidence of intussusception was closely monitored using an adverse event reporting system. In 1999, when it was suspected that there was an increased risk of intussusception associated with the vaccine in infants, it was withdrawn.100 (See chapter 19.)

**20.4 Conclusion**

Vaccines are not perfect. They cause reactions. Local reactions occur frequently, systemic reactions less commonly, and severe reactions rarely. But vaccines do prevent disease. It is to be expected that agents that are so effective in reducing disease incidence – including the elimination of smallpox, and the potential elimination of polio and measles – produce some adverse events. However, in comparison to natural disease such events are infrequent and almost always less severe. There is no doubt that the benefits of immunisation far outweigh the risks.
References
16 http://www.fda.gov/cber/BSE/bseqa.htm
26 Scheibner V. 1993. Vaccination: 100 years of research shows that vaccines represent a medical assault on the immune system. Victoria: Australian Print Group.


## Appendix 1: The History of Immunisation in New Zealand

<table>
<thead>
<tr>
<th>Vaccine</th>
<th>Year the vaccine was introduced</th>
<th>Details</th>
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<tr>
<td>Diphtheria</td>
<td>1926</td>
<td>Became available in New Zealand for selected schools and orphanages</td>
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<td></td>
<td>1941</td>
<td>Offered routinely to children less than seven years of age</td>
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<tr>
<td>Tetanus</td>
<td>1940–45</td>
<td>Tetanus toxoid became available as a voluntary vaccination</td>
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<tr>
<td>Pertussis</td>
<td>1945</td>
<td>Introduced by the Department of Health – given on request</td>
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<td></td>
<td>1953</td>
<td>Combined pertussis-diphtheria vaccine became available, although usage was restricted</td>
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<tr>
<td>BCG</td>
<td>1948</td>
<td>Initially introduced for nurses, then later extended to all adolescents</td>
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<td></td>
<td>1963</td>
<td>Adolescent BCG programme was discontinued in the South Island and phased out in the North Island by 1990</td>
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<td></td>
<td>1976</td>
<td>Neonatal BCG was introduced, initially in high risk districts, and then variably implemented throughout New Zealand</td>
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<tr>
<td>Salk poliomyelitis (IPV)</td>
<td>1956</td>
<td>Became available; initially 8–9 year olds were targeted, then 5–10 year olds, then 11–15 year olds</td>
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<tr>
<td></td>
<td>1959</td>
<td>Offered to all those between 6 months and 29 years of age</td>
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<td></td>
<td>2002</td>
<td>IPV replaced OPV on the National Immunisation Schedule, either as IPV or combined with the DTaP vaccine</td>
</tr>
<tr>
<td>Universal DTwP</td>
<td>1958</td>
<td>DTwP became available and the first schedule commenced</td>
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<tr>
<td></td>
<td>1960</td>
<td>DTwP was supplied to medical practitioners free of charge</td>
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<tr>
<td>Sabin poliomyelitis (OPV)</td>
<td>1961</td>
<td>Initially introduced for children under 12 months of age, administered by the Department of Health</td>
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<tr>
<td></td>
<td>1962</td>
<td>In April 95 percent of all school children received two doses; in September it was offered to all adults and adolescents (administered by the Department of Health)</td>
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<td></td>
<td>1967</td>
<td>From April general practitioners were able to administer OPV along with DTwP</td>
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<tr>
<td></td>
<td>2002</td>
<td>OPV was replaced by IPV on the National Immunisation Schedule</td>
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<tr>
<td>Measles</td>
<td>1969</td>
<td>Due to adverse reactions, the measles programme was suspended in late 1969 until the Edmonston B strain vaccine became available in February 1970</td>
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<tr>
<td></td>
<td>1974</td>
<td>The recommended age changed to 12 months</td>
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<td></td>
<td>1981</td>
<td>The recommended age changed to 12–15 months</td>
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<td></td>
<td>1990</td>
<td>MMR Introduced to the Schedule for all infants at 15 months of age</td>
</tr>
<tr>
<td>Vaccine</td>
<td>Year the vaccine was introduced</td>
<td>Notes</td>
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<tr>
<td>Rubella</td>
<td>1970</td>
<td>Introduced to the Schedule for all children at four years of age</td>
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<tr>
<td></td>
<td>1979</td>
<td>Low uptake at 4 years, especially for boys, spurred a change to an 11-year-old (year 7/form 1) girl vaccination</td>
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<td></td>
<td>1990</td>
<td>MMR Introduced to the schedule for all infants at 15 months of age</td>
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<tr>
<td>Hepatitis B</td>
<td>1985</td>
<td>Plasma derived vaccine was introduced for newborn babies born to HBeAg positive mothers</td>
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<td></td>
<td>1987</td>
<td>Extended to newborns of hepatitis B surface antigen positive mothers and newborns in high risk districts (eg, Northland, South Auckland, Rotorua, Napier, Gisborne)</td>
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<td>1988</td>
<td>In February it was introduced to the Schedule for all infants (catch up programmes for pre-schoolers were implemented during 1988)</td>
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<tr>
<td></td>
<td>1989</td>
<td>In December recombinant hepatitis B vaccine replaced the plasma derived vaccine</td>
</tr>
<tr>
<td></td>
<td>1990</td>
<td>Publicly funded hepatitis B immunisation was extended to all children under 16 years of age (catch up school programmes were also implemented)</td>
</tr>
<tr>
<td>MMR</td>
<td>1990</td>
<td>Introduced to the schedule for all infants at 15 months of age</td>
</tr>
<tr>
<td></td>
<td>1992</td>
<td>A second dose was introduced for 11-year-old (year 7/form 1) boys and girls</td>
</tr>
<tr>
<td></td>
<td>2001</td>
<td>The second dose of MMR was changed from 11 years of age to 4 years of age. A school based catch up programme was offered for all 5–10 year olds.</td>
</tr>
<tr>
<td>Hib</td>
<td>1994</td>
<td>Introduced to the schedule as DTwPH at 6 weeks, 3 months and 5 months of age, and as monovalent Hib at 18 months of age. All children under 5 years of age were offered vaccination against Hib</td>
</tr>
<tr>
<td></td>
<td>1996</td>
<td>Given as DTwPH at 6 weeks, 3 and 5 months, and a booster at age 15 months</td>
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<tr>
<td></td>
<td>2000</td>
<td>Given as Hib-Hep B at 6 weeks and 3 months, and as DTaP/Hib at 15 months</td>
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<tr>
<td></td>
<td>2006</td>
<td>Given as Hib-Hep B at 6 weeks and 3 months, and as Hib alone at age 15 months</td>
</tr>
<tr>
<td>Tetanus/diphtheria (Td)</td>
<td>1994</td>
<td>Introduced to the Schedule, replacing tetanus toxoid</td>
</tr>
<tr>
<td>Influenza</td>
<td>1997</td>
<td>Introduced to the Schedule for adults 65 years of age and over</td>
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<tr>
<td></td>
<td>1999</td>
<td>Introduced to the Schedule for those under 65 years of age with certain medical conditions</td>
</tr>
<tr>
<td>Acellular pertussis</td>
<td>1999</td>
<td>Introduced for infants/children under 7 years of age who had a previous reaction to whole cell pertussis in DTwPH</td>
</tr>
<tr>
<td>DTaP (Infanrix)</td>
<td>2000</td>
<td>In August DTaP was introduced for all infants</td>
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<tr>
<td>Adult dose acellular</td>
<td>2006</td>
<td>Introduced to the schedule at 11 years of age, combined with IPV as dTap-IPV</td>
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<tr>
<td>pertussis dTap</td>
<td></td>
<td>(Boostrix(-IPV))</td>
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<td>(Boostrix(-IPV))</td>
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### Previous National Childhood Immunisation Schedules

#### February 2002 Immunisation Schedule

<table>
<thead>
<tr>
<th></th>
<th>DTaP-IPV</th>
<th>Hib-Hep B</th>
<th>Hep B</th>
<th>DTaP/Hib</th>
<th>Polio (IPV)</th>
<th>MMR</th>
<th>Td</th>
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<tbody>
<tr>
<td>6 weeks</td>
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<td>3 months</td>
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<td>5 months</td>
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<td>15 months</td>
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<td>4 years</td>
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<tr>
<td>11 years</td>
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</tbody>
</table>

* For those children who had not received a fourth dose of polio vaccine.

#### January 2001 Immunisation Schedule

<table>
<thead>
<tr>
<th></th>
<th>DTaP</th>
<th>Hib-Hep B</th>
<th>Hep B</th>
<th>DTaP/Hib</th>
<th>Polio (OPV)</th>
<th>MMR</th>
<th>Td</th>
</tr>
</thead>
<tbody>
<tr>
<td>6 weeks</td>
<td>•</td>
<td>•</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>3 months</td>
<td>•</td>
<td>•</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>5 months</td>
<td>•</td>
<td></td>
<td>•</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>15 months</td>
<td></td>
<td></td>
<td>•</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>4–5 years</td>
<td></td>
<td></td>
<td>•</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>11 years</td>
<td></td>
<td></td>
<td>•</td>
<td>*</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

* For those children who had not received OPV4.

#### August 2000 Immunisation Schedule

<table>
<thead>
<tr>
<th></th>
<th>DTaP</th>
<th>Hib-Hep B</th>
<th>Hep B</th>
<th>DTaP/Hib</th>
<th>Polio (OPV)</th>
<th>MMR</th>
<th>Td</th>
</tr>
</thead>
<tbody>
<tr>
<td>6 weeks</td>
<td>•</td>
<td>•</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>3 months</td>
<td>•</td>
<td>•</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>5 months</td>
<td>•</td>
<td></td>
<td>•</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>15 months</td>
<td></td>
<td></td>
<td>•</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>11 years</td>
<td></td>
<td></td>
<td>•</td>
<td></td>
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<td></td>
<td></td>
</tr>
</tbody>
</table>

#### 1996 Immunisation Schedule

<table>
<thead>
<tr>
<th></th>
<th>DTPH</th>
<th>Hep B</th>
<th>Polio (OPV)</th>
<th>MMR</th>
<th>Td</th>
</tr>
</thead>
<tbody>
<tr>
<td>6 weeks</td>
<td>•</td>
<td>•</td>
<td>•</td>
<td></td>
<td></td>
</tr>
<tr>
<td>3 months</td>
<td>•</td>
<td>•</td>
<td>•</td>
<td></td>
<td></td>
</tr>
<tr>
<td>5 months</td>
<td>•</td>
<td>•</td>
<td>•</td>
<td></td>
<td></td>
</tr>
<tr>
<td>15 months</td>
<td>•</td>
<td></td>
<td>•</td>
<td></td>
<td></td>
</tr>
<tr>
<td>11 years</td>
<td>•</td>
<td>•</td>
<td>•</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
### 1994 Immunisation Schedule

<table>
<thead>
<tr>
<th>Age</th>
<th>DTP</th>
<th>Hep B*</th>
<th>Polio (OPV)</th>
<th>MMR**</th>
<th>DT</th>
<th>Hib</th>
<th>Td</th>
</tr>
</thead>
<tbody>
<tr>
<td>6 weeks</td>
<td>•</td>
<td>•</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>3 months</td>
<td>•</td>
<td>•</td>
<td>•</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>5 months</td>
<td>•</td>
<td>•</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>12–15 months</td>
<td>•</td>
<td>•</td>
<td></td>
<td>•</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>18 months</td>
<td>•</td>
<td>•</td>
<td>•</td>
<td>•</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>5 years</td>
<td></td>
<td>•</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>11 years</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Girls only</td>
<td></td>
</tr>
<tr>
<td>15 years</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>*</td>
</tr>
</tbody>
</table>

* Hepatitis B was introduced for all neonates with catch up to children under five years in 1988.
** MMR was introduced at 15 months in 1990 and at age 11 years in 1992.

### 1984 Immunisation Schedule*

<table>
<thead>
<tr>
<th>Age</th>
<th>DTP</th>
<th>Polio (OPV)</th>
<th>Measles</th>
<th>DT</th>
<th>Rubella</th>
<th>Tetanus</th>
</tr>
</thead>
<tbody>
<tr>
<td>6 weeks</td>
<td>•</td>
<td></td>
<td></td>
<td></td>
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</tr>
<tr>
<td>3 months</td>
<td>•</td>
<td>•</td>
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<tr>
<td>5 months</td>
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<tr>
<td>12–15 months</td>
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<tr>
<td>18 months</td>
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<td></td>
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<td></td>
</tr>
<tr>
<td>5 years</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>11 years</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Girls only</td>
<td></td>
</tr>
<tr>
<td>15 years</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>*</td>
</tr>
</tbody>
</table>

* See notes in the 1994 Immunisation Schedule table above

### 1980 Immunisation Schedule

<table>
<thead>
<tr>
<th>Age</th>
<th>DTP</th>
<th>Polio (OPV)</th>
<th>Measles</th>
<th>DT</th>
<th>Rubella</th>
<th>Tetanus</th>
</tr>
</thead>
<tbody>
<tr>
<td>3 months</td>
<td>•</td>
<td>•</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>5 months</td>
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<td></td>
<td></td>
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<td></td>
</tr>
<tr>
<td>12 months</td>
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<td></td>
<td></td>
<td>•</td>
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<tr>
<td>18 months</td>
<td>•</td>
<td>•</td>
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<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>5 years</td>
<td></td>
<td></td>
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<td></td>
<td></td>
</tr>
<tr>
<td>11 years</td>
<td></td>
<td></td>
<td></td>
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<td>Girls only</td>
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</tr>
<tr>
<td>15 years</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>*</td>
</tr>
</tbody>
</table>
### 1971 Immunisation Schedule

<table>
<thead>
<tr>
<th>Age</th>
<th>DTP</th>
<th>Polio</th>
<th>Measles</th>
<th>DT</th>
<th>Rubella</th>
<th>Tetanus</th>
</tr>
</thead>
<tbody>
<tr>
<td>3 months</td>
<td>•</td>
<td>•</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>5 months</td>
<td>•</td>
<td>•</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>10 months</td>
<td></td>
<td></td>
<td>•</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>18 months</td>
<td>•</td>
<td>•</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>4 years</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>•</td>
<td></td>
</tr>
<tr>
<td>5 years</td>
<td>•</td>
<td></td>
<td></td>
<td></td>
<td>•</td>
<td></td>
</tr>
<tr>
<td>15 years</td>
<td>•</td>
<td></td>
<td>•</td>
<td></td>
<td>•</td>
<td></td>
</tr>
</tbody>
</table>

### 1967 Immunisation Schedule

<table>
<thead>
<tr>
<th>Age</th>
<th>DTP</th>
<th>Polio</th>
<th>DT</th>
</tr>
</thead>
<tbody>
<tr>
<td>3 months</td>
<td>•</td>
<td>•</td>
<td></td>
</tr>
<tr>
<td>4 months</td>
<td>•</td>
<td>•</td>
<td></td>
</tr>
<tr>
<td>5 months</td>
<td>•</td>
<td>•</td>
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<tr>
<td>18 months</td>
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<td></td>
</tr>
<tr>
<td>5 years</td>
<td></td>
<td></td>
<td>•</td>
</tr>
</tbody>
</table>

### 1961 Immunisation Schedule

<table>
<thead>
<tr>
<th>Age</th>
<th>DTP</th>
<th>DT</th>
</tr>
</thead>
<tbody>
<tr>
<td>3 months</td>
<td>•</td>
<td></td>
</tr>
<tr>
<td>4 months</td>
<td>•</td>
<td></td>
</tr>
<tr>
<td>5 months</td>
<td>•</td>
<td></td>
</tr>
<tr>
<td>5 years</td>
<td>•</td>
<td></td>
</tr>
</tbody>
</table>

Note: between 1961 and 1967 polio was administered by the Department of Health.
**Appendix 2: Immunisation Catch Up Schedules**

**A) National Childhood Immunisation Schedule catch up schedules**

<table>
<thead>
<tr>
<th>First dose at 3–7 months</th>
<th>DTaP-IPV</th>
<th>Hib-HepB</th>
</tr>
</thead>
<tbody>
<tr>
<td>First dose</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1 month interval</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1 month interval</td>
<td></td>
<td></td>
</tr>
<tr>
<td>At age 15 months</td>
<td></td>
<td></td>
</tr>
<tr>
<td>At age 4 years</td>
<td></td>
<td></td>
</tr>
<tr>
<td>At age 11 years</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

* Adult diphtheria, tetanus, pertussis and inactivated polio vaccine.

<table>
<thead>
<tr>
<th>First dose at 8–11 months</th>
<th>DTaP-IPV</th>
<th>Hib-HepB</th>
</tr>
</thead>
<tbody>
<tr>
<td>First dose</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1 month interval</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1 month interval</td>
<td></td>
<td></td>
</tr>
<tr>
<td>6 month interval</td>
<td></td>
<td></td>
</tr>
<tr>
<td>At age 15 months</td>
<td></td>
<td></td>
</tr>
<tr>
<td>At age 4 years</td>
<td></td>
<td></td>
</tr>
<tr>
<td>At age 11 years</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

* Adult diphtheria, tetanus, pertussis and inactivated polio vaccine.

<table>
<thead>
<tr>
<th>First dose at 12–14 months</th>
<th>DTaP-IPV</th>
<th>Hib-HepB</th>
</tr>
</thead>
<tbody>
<tr>
<td>First dose</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1 month interval</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1 month interval</td>
<td></td>
<td></td>
</tr>
<tr>
<td>At age 15 months</td>
<td></td>
<td></td>
</tr>
<tr>
<td>At age 4 years</td>
<td></td>
<td></td>
</tr>
<tr>
<td>At age 11 years</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

* Adult diphtheria, tetanus, pertussis and inactivated polio vaccine.

<table>
<thead>
<tr>
<th>First dose at 15 months – 3 years</th>
<th>DTaP-IPV</th>
<th>Hib-HepB</th>
<th>MMR</th>
</tr>
</thead>
<tbody>
<tr>
<td>First dose</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1 month interval</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1 month interval</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>At age 4 years</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>At age 11 years</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

* Adult diphtheria, tetanus, pertussis and inactivated polio vaccine.
### First dose at 4 years

<table>
<thead>
<tr>
<th>First dose</th>
<th>First dose at 4 years</th>
<th>DTaP-IPV</th>
<th>Hib-HepB</th>
<th>MMR</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 month interval</td>
<td>DTaP-IPV</td>
<td>Hep B</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1 month interval</td>
<td>DTaP-IPV</td>
<td>Hep B</td>
<td></td>
<td></td>
</tr>
<tr>
<td>6 month interval</td>
<td>DTaP-IPV</td>
<td>MMR</td>
<td></td>
<td></td>
</tr>
<tr>
<td>At age 11 years</td>
<td>dTap-IPV*</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

* Adult diphtheria, tetanus, pertussis and inactivated polio vaccine.

### First dose at 5–7 years

<table>
<thead>
<tr>
<th>First dose</th>
<th>First dose at 5–7 years</th>
<th>DTaP-IPV</th>
<th>HepB</th>
<th>MMR</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 month interval</td>
<td>DTaP-IPV</td>
<td>HepB</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1 month interval</td>
<td>DTaP-IPV</td>
<td>HepB</td>
<td></td>
<td></td>
</tr>
<tr>
<td>6 months interval</td>
<td>DTaP-IPV (or Td and IPV &gt; 7 years)</td>
<td>MMR</td>
<td></td>
<td></td>
</tr>
<tr>
<td>At age 11 years</td>
<td>dTap-IPV*</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

* Adult diphtheria, tetanus, pertussis and inactivated polio vaccine.

### First dose at 7 years and older**

<table>
<thead>
<tr>
<th>First dose</th>
<th>First dose at 7 years and older**</th>
<th>Td and IPV</th>
<th>HepB</th>
<th>MMR</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 month interval</td>
<td>Td and IPV</td>
<td>HepB</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1 month interval</td>
<td>dTap-IPV*</td>
<td>HepB</td>
<td>MMR</td>
<td></td>
</tr>
<tr>
<td>10 year interval</td>
<td>dTap-IPV*</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

* Adult diphtheria, tetanus, pertussis and inactivated polio vaccine.
** dTap-IPV may be considered for all three doses of the primary series. See note 9.

Notes

1. There is considerable flexibility in these schedules, and the recommended intervals between doses are not sacrosanct. Vaccines may be given simultaneously and/or the schedule shortened to monthly intervals if this is deemed necessary to ensure the required numbers of doses are administered.

2. If the schedule is interrupted it is not necessary to repeat prior doses; simply resume the schedule as if no dose has been missed.

3. If the immunisation status of a vaccine recipient is uncertain or unknown then the vaccine provider should err on the side of giving rather than not giving the vaccine.

4. If a child attends infrequently, and failure to return for future immunisation is of concern, it is prudent to administer as many antigens as possible at the first visit.

5. In the catch-up schedule for children 12–14 months of age, the third hepatitis B vaccine dose may be moved to a six month interval if the MMR dose at 15 months coincides with the third catch-up visit and 3 injections are not accepted.

6. MMR, Hib and pertussis are given as a priority for children 15 months of age and over because these diseases pose the greatest immediate risk.
7. MMR should be given either at 15 months, or if the child/adult is older than 15 months, at the first immunisation visit.

8. A single dose of Hib vaccine administered at 15 months of age and over is sufficient to induce immunity.

9. After the seventh birthday, Td should be used. The dTap-IPV vaccine is given at age 11 years as a booster. As at 2006, dTap and dTap-IPV are licensed for distribution for booster doses only. However, there are expected to be no safety concerns to giving three doses of dTap-IPV to previously unimmunised older children and adults. Therefore, using dTap should be considered for all catch up and adult schedules for primary and booster immunisations.

B) Pneumococcal Immunisation Programme Catch Up Schedules

Following are recommendations for pneumococcal vaccines for children at higher risk of pneumococcal disease who have received a dose of a pneumococcal vaccine previously.

<table>
<thead>
<tr>
<th>Age of child</th>
<th>Previous dose(s) of any pneumococcal vaccine</th>
<th>Recommendations</th>
</tr>
</thead>
<tbody>
<tr>
<td>23 months or under</td>
<td>Any or none</td>
<td>As in Table 16.6, chapter 16</td>
</tr>
<tr>
<td>24–59 months</td>
<td>4 doses of conjugate vaccine</td>
<td>1 dose of polysaccharide vaccine at 24 months of age, 6–8 weeks after the last dose of conjugate vaccine; and 1 dose of polysaccharide vaccine 3–5 years after the first dose</td>
</tr>
<tr>
<td>24–59 months</td>
<td>1–3 doses of conjugate vaccine</td>
<td>1 dose of conjugate vaccine; 1 dose of polysaccharide vaccine 6–8 weeks after the last dose of conjugate vaccine; and 1 dose of polysaccharide vaccine 3–5 years after the first dose</td>
</tr>
<tr>
<td>24–59 months</td>
<td>1 dose of polysaccharide vaccine</td>
<td>2 doses of conjugate vaccine, 6–8 weeks apart, beginning at 6–8 weeks after the dose of polysaccharide vaccine; 1 dose of polysaccharide vaccine 3–5 years after the first dose of polysaccharide vaccine</td>
</tr>
<tr>
<td>24–59 months</td>
<td>No previous dose of conjugate or polysaccharide vaccine</td>
<td>2 doses of conjugate vaccine 6–8 weeks apart; 1 dose of polysaccharide vaccine 6–8 weeks after the last dose of conjugate vaccine; and 1 dose of polysaccharide vaccine 3–5 years after the first dose of polysaccharide vaccine</td>
</tr>
</tbody>
</table>
Appendix 3: Immunisation Standards 2006

Purpose

The National Immunisation Schedule for children and adults protects against nine serious vaccine preventable diseases. In addition, the Schedule offers publicly funded immunisation to individuals at risk of influenza, tuberculosis and pneumococcal disease. Immunisation against meningococcal B disease is offered as part of a special immunisation programme. These Immunisation Standards apply to the delivery of all the Schedule vaccines.

Immunisation involves many individuals and organisations. The following information aims to identify their roles and responsibilities, and to set standards for service delivery.

Roles and responsibilities

Parents/caregivers

Parents/caregivers roles are to:

- ensure the child receives age appropriate immunisations at six weeks; 3 months, 5 months and 15 months; and 4 and 11 years of age, and the MeNZB™ vaccine at six weeks, three, five and ten months of age (the parents/guardians need to consent to each immunisation)

- agree to the delivery of two or three injections at one visit (extra visits will be required if immunisations are not given at the same time, to ensure full protection from the diseases)

- agree to the collection of their child’s immunisation information on the National Immunisation Register (NIR) or be given the opportunity to opt off the collection of this information on the NIR (for NIR birth cohort children)

- when requested, provide the child’s Immunisation Certificate to an early childhood service or primary school.

Parents/caregivers who choose not to have their children immunised should explain this decision to their children. If they so wish, children may be immunised when they reach an age at which they are competent to make their own informed choice.1

Early childhood service and primary schools

Early childhood service and primary schools’ roles are to:

- request the parent/caregiver at the time of enrolment, for children born after 1 January 1995, to provide the child’s Immunisation Certificate
• document the information from the Immunisation Certificate on the early childhood service/school immunisation register. Information includes the child's name, date of birth, and immunisation status, and confirmation as to whether the Certificate was shown or not.

Vaccinators

Vaccinators include general practitioners, practice nurses (vaccinating under the direction of a medical practitioner) and authorised independent vaccinators, such as public health nurses, and some practice nurses or occupational health nurses, authorised by a medical officer of health to practise independently.

The vaccinator is responsible for the delivery and administration of the vaccines on the National Immunisation Schedule, including the MeNZBTM vaccine. The vaccinator should also ensure that all individuals under their care are given the opportunity to receive all their immunisations on time by operating a recall system and providing written and/or phone recalls.

To be effective the vaccines must be:
• stored and transported within the correct temperature range (+2°C to +8°C) (see chapter 2)
• given before the vaccine expiry date
• correctly reconstituted (where necessary) and given using strict aseptic technique
• administered using the correct dose, appropriate needle length, angle and injection site for the vaccinee (see chapter 2).

As with all health care, informed consent must be obtained. Consent need not always be written, but the vaccinator must keep a written record of the immunisations delivered. Where the vaccinee is a child, the vaccinator must record the immunisations given in the child’s Well Child Tamariki Ora Health Book and accurately complete the child’s Immunisation Certificate. For those children born within the NIR birth cohort, or all those receiving the MeNZBTM vaccine their immunisation history will be collected on the NIR unless the parent/caregiver has opted off the collection of this information (for the purposes of safety monitoring all those receiving the MeNZBTM vaccine must have their information collected on the NIR).

Organisations offering immunisation services

Organisations offering immunisation services include general medical practices, primary health organisations, independent practice associations, outreach immunisation service providers, iwi providers, public health services, Plunket, and lead maternity carers (for specific vaccines only).
For immunisation services to achieve high coverage levels of effective vaccines, the service should:

- have links to comprehensive primary health care
- reduce barriers to access
- have either electronic or manual links to the NIR, in order to:
  - provide ongoing monitoring of immunisation coverage of children attending their service and measuring coverage at two years of age
  - operate a reminder and recall system
  - have systems allowing identification of those behind on immunisations
- monitor influenza immunisation coverage for those 65 years of age and over, and the ‘at risk groups’
- at every opportunity offer immunisations to those who are behind on the National Immunisation Schedule
- have systems for follow up of non-immunised children
- meet cold chain accreditation requirements and continue to maintain the procedures for cold chain management. If there are cold chain failures, discuss with the medical officer of health, and/or local immunisation co-ordinator/facilitator to determine if the vaccines need to be discarded or if patient follow up is required.

**Immunisation co-ordinators/facilitators**

Immunisation co-ordination varies throughout New Zealand, but the key components of the role may include:

- providing support and co-ordination between different providers
- monitoring cold chain management, including cold chain accreditation
- providing support and co-ordination for the education of providers in delivery of immunisations
- establishing a mechanism for follow up and immunisation of non-immunised children.

**Medical officers of health and public health services**

The medical officer of health has statutory responsibilities for:

- surveillance and control of vaccine preventable diseases (including outbreak control)
- approval of authorised independent vaccinators.
A medical officer of health also provides advice to vaccinators and the public.

Public health services (or public health nurses working outside these units) may provide:

- school based immunisation programmes
- assistance with the follow up of children who do not respond to recall.

**Institute of Environmental Science and Research (ESR)**

ESR operates the national vaccine store. ESR's responsibilities include ensuring that the quality of vaccines arriving in New Zealand meet the prescribed specifications, distributing the vaccines through vaccine distributor networks, and the ongoing cold chain audit process. ESR also has a role in the collation of information on notifiable diseases, including the vaccine preventable diseases.

**District Health Boards (DHBs)**

There are 21 DHBs in New Zealand, responsible for providing publicly funded health care services, including immunisation services, for the population of their geographical region. The statutory objectives of DHBs are to:

- improve, promote and protect the health of communities
- promote the integration of health services, especially primary and secondary care services
- promote effective care or support of those in need of personal health services or disability support.

The DHB funding obligations under primary health services are to:

- provide services to help children stay well, including the immunisations on the National Immunisation Schedule
- provide all the immunisation services listed on the National Immunisation Schedule (as contained in the Ministry of Health Immunisation Handbook) at no charge
- co-ordinate immunisation services at the regional level
- achieve maximum target immunisation coverage levels for their population.

**Ministry of Health**

The Ministry of Health is responsible for:

- ensuring the adequacy of the immunisation programme at the national level through a national co-ordination function
- monitoring and analysing information on immunisation coverage, the vaccine preventable diseases (including implied vaccine effectiveness) and adverse events following immunisation
• purchasing health education materials to assist individuals to make an informed choice about immunisation
• monitoring DHB performance
• national promotion of immunisation
• advising the Minister of Health on immunisation policy and developing and co-ordinating *Immunisation in New Zealand: Strategic directions*, including issues relating to:
  – the National Immunisation Schedule
  – the National Immunisation Register
  – strategies for improving coverage
  – purchase of programmes to promote immunisation
  – auditing the performance of cold chain management and accreditation
  – providing technical support to medical officers of health on matters relating to vaccines and immunisation.

The Ministry of Health currently undertakes vaccine purchase for all National Immunisation Schedule vaccines (including the MeNZB™ vaccine), except the influenza vaccine.

**Minister of Health**

The Minister has overall responsibility for all aspects of the National Immunisation Programme, through funding agreements with the purchasers. The following target has been set for immunisation: 95 percent of children will be fully immunised at two years of age.

**Standards for vaccinators**

**Standard 1:** The vaccinator is competent in the immunisation technique and has the appropriate knowledge and skills for the task

**Required characteristics**

1.1 The vaccinator completes an appropriate training programme. If a vaccinator is working as an independent vaccinator they should have a current authorisation certificate from a medical officer of health or the Director-General of Health.

1.2 The vaccinator administers sufficient immunisations to maintain competence, and demonstrates his/her competence biennially to an approved peer.

1.3 The vaccinator is able to deal with anaphylactic and other reactions, resuscitation, spillages (blood or vaccine) and the safe disposal of needles, syringes and vaccines (see chapter 2 and Appendix 6).
1.4 The vaccinator remains current with developments in immunisation theory, practice and policy with at least four hours of self directed learning or immunisation education/training every two years.

1.5 The vaccinator communicates immunisation information effectively and in a culturally appropriate way to families and individuals.

1.6 The vaccinator has had education and training to use the NIR to check a child's immunisation records, administer the correct vaccines, and follow up.

Standard 2: The vaccinator obtains informed consent to immunise (see chapter 2).

Required characteristics

2.1 The vaccinator obtains consent for each immunisation episode and records that the patient/parent/guardian has been informed of the benefits and risks of immunisation in order to make an informed decision about immunisation and the immunisation programme. (Children can give consent if they have the understanding and maturity to form a balanced judgement about immunisation. Parents/guardians should be encouraged to be involved in their child’s decision.)

2.2 The vaccinator communicates using clear, simple terminology appropriate to the listener’s values, beliefs and culture. Communication should be supported by suitable health education material.

2.3 The vaccinator allows time to answer questions and obtains feedback indicating that the patient/parent/guardian understands which vaccine is being given and why.

2.4 Consent need not always be written consent, but the vaccinator should keep a written record that verbal consent was obtained.

2.5 Adequate information about the disease and vaccination must be given to patients/parents/guardians to enable informed consent.

2.6 The vaccinator informs the parent/caregiver that vaccinations given will be recorded on the NIR (for birth cohort children) unless the parent/caregiver chooses to opt off the NIR.

Standard 3: The vaccinator provides safe immunisation

Required characteristics

3.1 The venue is appropriate for the patient/parent/caregiver with facilities available for assessment and management of adverse events, including anaphylaxis (see chapter 2).

3.2 The vaccinator can treat AEFIIs (adverse events following immunisation), including anaphylaxis, and has a contingency plan for seeking emergency assistance.
3.3 Because of the potential for anaphylactic reactions, vaccinees with their parents/caregivers are required to remain under observation for a minimum of 20 minutes after immunisation.

3.4 The vaccinator ensures continuity of the cold chain and the practice's participation in cold chain accreditation (see chapter 2).

3.5 Before vaccinating, the vaccinator:
- ascertains the date of the last immunisation, to ensure doses are spaced correctly
- enquires about any reactions following previous vaccine doses
- checks for true contraindications (see chapter 1 and the specific disease chapters)
- determines the current health of the vaccinee and the possible immune suppressed status of contacts.

See the prevaccination checklist in chapter 2.

3.6 The vaccinator uses aseptic techniques in preparation and administration of all vaccines (see chapter 2 and Appendix 6), visually checks the vaccine, reconstitutes vaccines with the diluent supplied (as appropriate) and uses vaccines within the recommended period after reconstitution.

3.7 The vaccinator provides verbal and written information about care after immunisation, including management of expected vaccine responses and accessing advice and medical attention, if required, during office and after office hours (see chapter 2).

3.8 The vaccinator carries indemnity insurance for their personal/professional protection and that of the vaccinee.

Standard 4: The vaccinator documents information on the vaccine(s) administered, and maintains patient confidentiality

Required characteristics

4.1 The vaccinator documents the patient’s personal details, including: NHI, name, date of birth, address, contact telephone number, next of kin details, and general practitioner (if the vaccinator is not the usual primary care provider).

4.2 The vaccinator will ensure the immunisation information is sent to the NIR (ie, electronically or manually), where applicable.

4.3 The vaccinator documents the following details:
- date administered
- consent obtained
• vaccine type and number in the series
• batch number and expiry date
• injection site (e.g., deltoid not upper arm)
• needle length
• the patient was observed for 20 minutes post-vaccination
• if the vaccine is given by a non-standard route, the reason must be well documented
• the date for the next immunisation (if required) for the patient/parent/caregiver, in the *Well Child Tamariki Ora Health Book*.

4.3 The vaccinator ensures the Immunisation Certificate is accurately completed.

4.4 If the vaccinator is not the usual primary care provider, and the patient/parent/guardian consents, the patient’s general practitioner or other primary care provider is informed, within four weeks, of the receipt of the vaccine(s). When a child is registered on the NIR all associated providers will be notified that an immunisation event has occurred.

4.5 The vaccinator ensures the Immunisation Benefit Claim Form is accurately completed.

4.6 The vaccinator ensures all immunisations are reported with NHI number, as agreed by the Ministry of Health.

4.7 All personal documentation is appropriately treated and stored to maintain confidentiality, and is made available to the patient/parent/caregiver on request.

**Standard 5:** The vaccinator administers all vaccine doses for which the vaccinee is due at each visit and only follows true contraindications

*Required characteristics*

5.1 The vaccinator follows the National Immunisation Schedule and delivers the immunisations recommended for that visit, unless the patient/parent/guardian does not consent to this.

5.2 When catch up immunisation is required, this is planned with the minimum number of visits.

5.3 A dose of vaccine is deferred or avoided only when contraindicated. The reason for deferral or avoidance must be well documented (see chapter 1 and the specific disease chapter).
Standard 6: The vaccinator reports adverse events following immunisation promptly, accurately and completely

Required characteristics

6.1 Any severe or unexpected reactions are reported to the Medical Assessor, Centre for Adverse Reactions Monitoring, PO Box 913, Freepost no. 112002, Dunedin, on the reply paid postcard HP3442 (copies can be found in the MIMS New Ethicals, or Figure 2.7 of the Immunisation Handbook 2006, or obtained from the local immunisation co-ordinator/facilitator) or via online reporting at http://carm.otago.ac.nz, and to the patient’s general practitioner (if the vaccinator is another person). If the patient/parent/guardian does not consent to being identified, the report should be made without personal identification. Other significant events occurring in association with vaccination, which may or may not be caused by immunisation, should also be reported (recognised reactions from vaccines are listed in the specific disease chapters).

6.2 If uncertain about the safety of further doses, the vaccinator seeks specialist (e.g., paediatrician, infectious disease physician or medical officer of health) opinion.

6.3 The vaccinator ensures the adverse event, and any subsequent decisions relating to the event, are clearly documented in the child’s Well Child Tamariki Ora Health Book and in the vaccinator’s records, and are fully explained to the patient/parent/caregiver.

6.4 Informs the DHB NIR administrator of CARM Report feedback so that it can be recorded on the NIR.

Standards for organisations offering vaccination services

Standard 7: The organisation, which employs vaccinators to offer vaccination services, has links to comprehensive primary health care and the Well Child programme

Required characteristics

7.1 Immunisation is delivered, not in isolation, but as an integrated part of Well Child activities through primary health care.

7.2 If possible, at the time of immunisation the organisation undertakes other health promotion and/or disease prevention activities, in accordance with the recommended New Zealand Well Child schedules.
Standard 8: The organisation achieves high immunisation coverage of its population

*Required characteristics*

8.1  The organisation has an effective, secure, NHI-based system for recording and reporting immunisations and identifying patients requiring immunisation.

8.2  The organisation has electronic linkage to the NIR or a paper-based process for registration and immunisation event notification and uses the NIR to assist with follow up.

8.3  The organisation provides reminders and recalls when immunisations are overdue.

8.4  Attendance at the organisation is used as an opportunity to remind patients/parents/caregivers of the importance of immunisation, and, if appropriate, to check and bring up to date the individual’s immunisation status.

8.5  Those who do not respond to recall are appropriately referred to the outreach immunisation service, as per local protocol.

Standard 9: The organisation supports vaccinators

*Required characteristics*

9.1  The organisation provides back up and support for vaccinators working in the community.

9.2  The organisation supports the need for practice nurses/vaccinators to have access to ongoing education and training on immunisation and vaccines.

Standard 10: The service is readily available, with no barriers to access

*Required characteristics*

10.1  No fee is charged to the parent/caregiver for the child’s immunisations that are on the National Immunisation Schedule (or for completing the child’s Immunisation Certificate).

10.2  Where possible, immunisations are provided at all times when the service is open.

10.3  Where possible, immunisations are provided without the need for an appointment.

10.4  Where possible, immunisation should also be offered out of normal working hours.

10.5  The service is culturally appropriate.

10.6  Sources for further information include:

- Health Immunisation Regulations 1995
- Medicines Act 1981
• Medicines Regulations 1984

• Health (Infectious and Notifiable Diseases) Regulations 1966, Amendment No. 2, regulation 44A

• National Immunisation Register Privacy Policy

• Ministry of Health Cold Chain Accreditation Practice Assessment Form (October 2004)

• Ministry of Health Cold Chain Accreditation Reviewer Form (October 2004)

• IMAC Vaccine Storage and Distribution National Standards

• IMAC Standards for Delivery of Vaccinator Training Courses for Non-Medical Vaccinators, 2nd edition, 2002. (Note: these standards will be updated during 2006)

• IMAC Standards for Delivery of Updates for Trained Non-Medical Vaccinators, 1st edition, 2003

• Guardianship Act 1968.

Reference

1  Consent in Child and Youth Health: Information for practitioners is available from the Ministry of Health website (www.moh.govt.nz). Duties regarding informed consent are more fully outlined in the Code of Health and Disability Services Consumers’ Rights.
Appendix 4: Authorisation as an Independent Vaccinator

Authorisation as an independent vaccinator
Protocol for authorisation of vaccinators in New Zealand
November 2004

Authority

Medicines Regulations 1984, clause 44A (2) states ‘The Director-General or a medical officer of health may authorise any person to administer a vaccine for the purposes of an approved immunisation programme if that person, following written application, provides documentary evidence satisfying the Director-General or the medical officer of health as the case may be, that that person:

i. Can carry out basic emergency techniques including resuscitation and the treatment of anaphylaxis and

ii. Has knowledge of the safe and effective handling of immunisation products and equipment and

iii. Can demonstrate interpersonal skills and

iv. Has knowledge of the relevant diseases and vaccines in order to be able to explain the vaccination to the patient, parent or guardian of the patient who is to consent to the vaccination on behalf the patient, to ensure that the patient or parent or guardian of the patient can give informed consent to the vaccination’.

Any authorisation given by the Director-General or a medical officer of health under subclause (2) of the regulation shall be valid for a period of two years (from the date of training) and shall be subject to such conditions as the Director-General or the medical officer of health, as the case may be, thinks fit.

Successful applicants will be authorised to administer either all or specific vaccines on the National Immunisation Schedule and any other vaccine as authorised by medical officer of health or the Director-General. This would not normally include travel vaccines. Authorisation is equivalent to ‘certified’ as referred to in Schedule 3, clause 2.1 (s) of the Section 88 Notice to General Practitioners (February 2002).

Authorisation for vaccinating other populations, for example influenza or hepatitis B vaccination of workplace staff, as part of a locally approved schedule, will be subject to whatever conditions the medical officer of health, or Director-General of Health, decides. The authorised vaccinator will have to apply to the local medical officer of health for the approval of a local vaccination programme.
Process for initial authorisation

Applicants applying for authorisation as an independent vaccinator will be required to:

1. Demonstrate that within the preceding 12 months, they have attended, completed and passed a vaccinator training course that meets the Standards for Delivery of Vaccinator Training Courses published by the Immunisation Advisory Centre (IMAC) in 1998 and any subsequent revisions. Specifically the course should consist of:
   - a minimum 16 hours educational input
   - a written test (minimum one hour duration consisting of a combination of multiple choice and short answers, and may be oral at the facilitator’s discretion)
   - clinical assessment (by the immunisation co-ordinator/facilitator or an appropriately authorised independent vaccinator). Information about the practice environment will be collected at the time of this assessment.

2. Provide evidence of current practising certificate and indemnity insurance.

Competencies for the Registered Nurse Scope of Practice (Nursing Council 2004) require that all nurses have appropriate competencies for their practice and can access and use emergency equipment.

Health professionals providing vaccination for specific groups or individuals or work settings may be authorised to administer only certain vaccines on the National Immunisation Schedule or on a locally approved schedule.

Process for reauthorisation

The Standards for Immunisation Providers (Vaccinators) in the Immunisation Handbook 2006 (see Appendix 3):

(1.2) The vaccinator administers sufficient immunisations to maintain competence and demonstrates his/her competence biennially to an approved peer.

(1.4) The vaccinator remains current with developments in immunisation theory, practice and policy with at least four hours of self-directed learning or immunisation education/training every two years.

Independent vaccinators may meet these educational requirements through self-directed learning such as:

- attending vaccination related lectures
- reading relevant articles
- being peer reviewed
• analysing critical events
• anaphylaxis/resuscitation practice.

The purpose of the ongoing training is to:
• bring them up to date with new and recent developments
• revise key areas of the vaccination process
• reviews the essential skills required to undertake vaccination.

Applicants for reauthorisation will be required to:

1. demonstrate that within the preceding 12 months, they have undertaken specific education update(s) for trained vaccinators; the training should be of a minimum of 4 hours duration
2. the Medical Officer of Health and the immunisation co-ordinator/facilitator will agree on a process for the regular assessment of clinical competency.
3. provide evidence of current practising certificate and indemnity insurance.

Competencies for the Registered Nurse Scope of Practice (Nursing Council 2004) require that all nurses have appropriate competencies for their practice and can access and use emergency equipment.

Process when authorisation has not been maintained i.e. where the authorisation expired more than six months previously

In general where five years or more have elapsed since the applicant completed their initial vaccinator training, they will be required to attend, complete and pass a vaccinator training course that complies with the IMAC Standards for Delivery of Vaccinator Training Courses because:
• there will have been significant developments in vaccination delivery in the intervening interval and
• prior to 1998 there were no national standards for the delivery of vaccinator training courses.

If the applicant has attended update sessions at least every two years but has never requested Authorisation as a Vaccinator, they will be assessed on a case-by-case basis by the Medical Officer of Health and the immunisation co-ordinator/facilitator.

If the applicant has completed a vaccinator training course within the last five years, they will be required to:
1. attend the first available vaccinator Update training course and submit evidence of attendance to the Medical Officer of Health
2. provide evidence that they have attended specific vaccination education sessions of a minimum of 4 hours duration during the last two years
3. demonstrate their clinical competency in vaccination (within the 3 months prior to application) to the immunisation co-ordinator/facilitator or an appropriately authorised independent vaccinator

4. provide evidence of current practising certificate and indemnity insurance. Competencies for the Registered Nurse Scope of Practice (Nursing Council 2004) require that all nurses have appropriate competencies for their practice and can access and use emergency equipment.

Process where applicant is new to the health district in which they intend to practise

If an authorised independent vaccinator wishes to practice in another health district, they must get authorisation from the local Medical Officer of Health before practising independently. The applicant will be required to:

1. provide evidence of current practising certificate and indemnity insurance. Competencies for the Registered Nurse Scope of Practice (Nursing Council 2004) require that all nurses have appropriate competencies for their practice and can access and use emergency equipment

2. provide details of their proposed work in the district.

This protocol was initially developed by John Holmes, Ann Shaw and Lyn Smith and incorporated comments and suggestions from Drs Derek Bell, Maree Leonard, Ed Kiddle, Phil Shoemack, Mel Brieseman and Daniel Williams (Medical Officers of Health).

It was further reviewed by the Medical Officers of Health from all the health districts in New Zealand at their national meeting in November 2004 and also discussed with Loretta Roberts, Regional Immunisation Coordinator for IMAC and their comments have been incorporated.

It will be reviewed in July 2006 unless there are changes to legislation. Any comments should be sent to John Holmes, Medical Officer of Health (Otago/Southland), PO Box 5144, Dunedin.
Independent vaccinators delivering an immunisation service

Authorised independent vaccinators should be aware that the following details of practice will be considered if they decide to seek medical officer of health approval for a local immunisation programme.

<table>
<thead>
<tr>
<th>1. Location/s (specify)</th>
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<td>Office Use Only</td>
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<th>2. Staff</th>
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<tr>
<td>There must be two people present for outreach or offsite immunisation – one of whom must be an approved non-medical vaccinator; the other must be either a registered nurse or have first aid and basic life support training.</td>
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<th>3. Linkages with the local immunisation co-ordinator/ facilitator</th>
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<tr>
<td>• Do you have processes for regular contact with your local immunisation co-ordinator/facilitator?</td>
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<tr>
<td>• current approval as an independent vaccinator issued by the local medical officer of health*.</td>
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<tr>
<td>• current practising certificate*</td>
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<tr>
<td>• current certificate in basic life support* (normally valid for 12 months)</td>
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<td>• indemnity insurance.*</td>
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<th>5. Legal</th>
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<tr>
<td>You should have knowledge of the Provisions contained in the following legislation:</td>
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<tr>
<td>• The Code of Health and Disability Consumers’ Rights Regulation 1996</td>
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<td>• Privacy Act 1993 (storage and transfer of information)</td>
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<tr>
<td>• The Health and Safety in Employment Act 1992 (suitable area for post vaccination observation, correct disposal of vaccines, etc)</td>
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<td>• Medicines Act 1981.</td>
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<th>6. Venue</th>
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<tr>
<td>Venue must allow for safe management of delivery of immunisations.</td>
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<td>• Privacy</td>
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<td>• Resting space</td>
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<td>• Waiting space</td>
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<tr>
<td>• Maintenance of privacy of records.</td>
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7. Documentation
You should have documented processes for the following

a. Pre vaccination:
   • What information is provided to patients (including consent)?*
   • How do you identify persons eligible for free vaccination?*

b. Post vaccination:
   • How will patient details be recorded?*.
   • What are the means of recording administration of a vaccine(s) and any post-vaccination adverse events?*
   • How will notice of administration be provided to the primary care provider?*
   • What information will be provided to the vaccinee post-vaccination (including provision of emergency care)?*
   • How will information on adverse reactions be reported*.

NOTE: For influenza vaccinations
It will be necessary to provide the following information to the MOH:
• number of recipients who were >65 years (free vaccines)
• number of <65 years eligible for free influenza vaccine
• number of non-eligible influenza vaccines given.

8. Equipment
The following should be available:

• Cell phone/phone access Yes / No
• Oxygen cylinder, flow meter, tubing and paediatric/adult masks Yes / No
• Airways – infant through to adult Yes / No
• Ambubag (Adult /Infant) Yes / No
• Adrenaline Yes / No
• Syringes (1mL, 2.5mL, 5mL), Needles (1.58cm to 3.8cm) Yes / No
• Sharps box Yes / No
• Alcohol swabs, Cotton wool balls/gauze etc Yes / No
• Thermometer/sphygmomanometer Yes / No
• Vaccines Yes / No
• Appropriately monitored vaccine storage# Yes / No
• Min-Max thermometer or recording device for monitoring Yes / No
• Gloves Yes / No
• 0.5% Hypochlorite Yes / No
• Approved biohazard bag Yes / No
9. Optional Additional Emergency Equipment

<table>
<thead>
<tr>
<th>Equipment</th>
<th>Yes / No</th>
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<tbody>
<tr>
<td>Intravenous cannula and administration sets</td>
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<tr>
<td>Intravenous fluids</td>
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<tr>
<td>Hydrocortisone for injection</td>
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<tr>
<td>Antihistamine for injection</td>
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<tr>
<td>Soda bicarbonate</td>
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<td>Saline Flush</td>
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*See the IMAC Cold Chain Standards.

Applicant: .................................................. Date: .........................

NOTE: Please ensure that you have included the documentation marked with an *
Appendix 5: Immunisation Certificate

The Health (Immunisation) Regulations 1995 require parents of children born from 1 January 1995 to show their child’s Immunisation Certificate when these children start at an early childhood service and on school entry.

The Immunisation Certificate shows whether a child is fully immunised or not. Information must be recorded at 15 months of age when the early childhood vaccinations are complete, and after the immunisations at four years of age or at school entry. For those parents who decline to have their child vaccinated, the certificate may be completed at any time.

Parent/caregiver responsibilities
Parents or caregivers remain free to choose whether or not to vaccinate their child, but they must make a choice, and get a certificate to provide documentation of their choice.

Vaccinator responsibilities
When completing and signing the Immunisation Certificate, vaccinators should be confident that a child is fully vaccinated. The primary concern is the child’s protection. If the previous vaccination history is uncertain and parents/guardians do not wish their child to be vaccinated, the child should be certified as ‘not fully’ vaccinated. Children who have not received the necessary doses of a vaccine or have no evidence of laboratory proven disease should be recorded as not fully vaccinated.

The Immunisation Certificate is included in the Well Child Tamariki Ora Health Book. This book also contains the record of the child’s vaccinations. Vaccinators should ensure they record vaccination and other relevant health information in this book. This becomes particularly important if the child sees different health professionals. If the child’s book is lost, it should be replaced. Copies of the Well Child Tamariki Ora Health Book and Immunisation Certificate pads can be obtained from the authorised provider of health education materials – usually the local public health service.

Early childhood services and school responsibilities
All early childhood services and primary schools, including kohanga reo, independent schools and kura kaupapa Māori, must keep an immunisation register for children born from 1 January 1995. The register is a tool to help reduce the spread of vaccine preventable diseases in early childhood services and schools, as well as in the wider community.
The early childhood service or school has the responsibility to:

- advise the child's parent/caregiver that an Immunisation Certificate is required
- ensure the parent or caregiver is requested to provide the Certificate
- record the information from the certificate (or the fact that it was not shown) on the register
- advise the parent/caregiver that a general practitioner, practice nurse or public health nurse can help them get a certificate if they do not have one.
Appendix 6:
Vaccine Presentation, Preparation and Disposal

Presentation of vaccines
The vaccines in current use are supplied in pre-filled syringes, single dose ampoules and vials. An ampoule is made of clear glass with a narrow neck, which is snapped off to allow access to a single dose of vaccine. A vial is a glass container with a rubber seal on the top protected by a metal or plastic cap until it is ready for use. Vials contain either liquid or dry preparations.

Vaccines should not be mixed in the same syringe, unless the manufacturer’s information sheet specifically states it is permitted.

Preparation and administration of vaccines
In order to minimise the risk of spread of infection and needle-stick injury, vaccinators should observe standard occupational health and safety guidelines.

Needles must always be changed between drawing up and administering the vaccine, as the passage of needles through rubber seals causes blunting, resulting in increased tissue trauma if the same needle is used to administer the injection. A new needle prevents tracking the vaccine through the skin and subcutaneous tissues where absorbed vaccines are more likely to cause local reactions. Do not expel the air contained in the new needle – it is sterile and minute in quantity.

Drawing up vaccine from ampoules
• Most inactivated vaccines contain an adjuvant and must be shaken vigorously prior to being drawn up, to obtain a uniform suspension.
• Flick the top of the ampoule with a finger to bring the fluid down into ampoule from the neck.
• Snap the ampoule neck quickly and firmly. A small gauze pad may be placed around the neck of ampoule to protect fingers from trauma.
• Draw up the vaccine quickly to prevent contamination by airborne contaminants. Do not scrape the needle tip on the inside of ampoule, nor allow the needle tip or shaft to touch the contaminated rim of the ampoule. The ampoule may be held upside-down as long as the needle tip or shaft does not touch the rim, otherwise surface tension is broken and the fluid will drip out.
• Change the needle, choosing the appropriate gauge and length for administration.
• After noting the batch number and expiry date, dispose of the empty vaccine ampoules and used needles into the sharps container.
Drawing up vaccine from vials

- Most inactivated vaccines contain an adjuvant and to obtain a uniform suspension must be shaken vigorously prior to being drawn up.
- Flip the plastic cap off the vial, taking care not to touch rubber seal.
- With the vial upright, insert tip of needle through the centre of rubber seal where it is thinner and easier to penetrate. Keeping firm pressure on the needle during insertion prevents cutting the rubber core from the seal.
- Withdraw the contents of the vial into the syringe.
- Draw back slightly on the plunger (to empty the needle of vaccine) and tap the barrel of syringe to dislodge any air bubbles. Expel air from the syringe and needle until the vaccine is visible at the needle connection part of the syringe.
- Change the needle, choosing the appropriate gauge and length for administration.
- After noting the batch number and expiry date, dispose of the empty vaccine vials and used needles into the sharps container.

Reconstitution and drawing up of freeze-dried vaccine, such as MMR

Freeze-dried vaccine must be reconstituted with the diluent supplied and used within the recommended period after reconstitution. For the single dose MMR vaccine in current use, this is eight hours (providing it is protected from light and stored at +2°C to +8°C).

- Flip the plastic cap off the diluent vial, taking care not to touch rubber seal.
- With the vial upright, insert needle tip through the centre of rubber seal where it is thinner and easier to penetrate. Keeping firm pressure on the needle during insertion prevents cutting the rubber core from the seal.
- Invert the vial and draw up the entire volume of diluent.
- Flip the cap off the vaccine vial and then slowly, to avoid frothing, empty the contents of the syringe into the vial, using the vial entry technique mentioned above.
- Swirl the vial gently to dissolve. The needle and syringe may be removed or left in place.
- After reconstitution the vaccine should be checked to see that the colour compares with the information supplied by the manufacturer on the package insert and that there is no particulate matter present. The MMR vaccine in current use should be clear yellow.
- Withdraw the contents of the vial into the syringe.
• Draw back slightly on the plunger (to empty the needle of vaccine) and tap the barrel of the syringe to dislodge any air bubbles. Expel air from the syringe and needle until the vaccine is visible at the needle connection part of the syringe.

• Change the needle, choosing the appropriate gauge and length for administration.

• After noting the batch number and expiry date, dispose of the empty vaccine vials and used needles into the sharps container.

Disposal of needles, syringes, and vaccine vials/ampoules

Do not separate needles from syringes or recap needles, unless a recapping device is used. All empty, partly used vials/ampoules, syringes and needles should be discarded into the sharps container.

Sharps containers

• Sharps containers should be made of rigid, leak and puncture proof material. They must be fitted with a carrying handle and have an opening that is wide enough to allow disposable materials to be dropped into the container with one hand while still preventing removal of the contents.

• Sharps containers should be situated out of children’s reach and available in every area where vaccinations take place.

• Sharps containers should be filled only to the indicated line, then sealed and given to an approved hazardous waste disposal person for incineration (as per the Resource Management Act 1991).

Spillages

• For blood or vaccine splashes on the skin – thoroughly wash the area under cold running water then wash with the iodine-based hand wash vaccinators have available.

• For spills on work surfaces, put on gloves and treat the spill by wiping the area with a pad soaked in 0.5 percent hypochlorite (household bleach diluted 1 to 9 parts water). Repeat with the hypochlorite solution and a fresh pad then clean up with water or a commercial detergent. Alternatively granular hypochlorite can be used for liquid spills, by applying sufficient granules to absorb the spilt fluid and then cleaning up after 10 minutes contact time. Carefully seal all contaminated material in approved biohazard bag for incineration by an approved hazardous waste disposal person.

• Contaminated linen is adequately treated by a routine hot wash cycle (60°C–70°C) using an ordinary bleach concentration.
Appendix 7: Medicines Act 1981, Section 47

The Medicines Act 1981, section 47, Storage and delivery of medicines states:

1) No person who is in possession or charge of any prescription medicine or restricted medicine shall put it:
   a) In any cupboard, box, shelf, or other place of storage in which articles of food or drink are stored or kept for ready use; or
   b) In any place to which young children or unauthorised persons have ready access.

2) No person shall pack any medicine, or prepare it for use in any room or on any bench that is used for the purpose of packing, preparing or consuming any food or drink.

3) Except as otherwise provided in any regulations made under this Act, no person who is in possession, for the purposes of any business, of a prescription medicine or a restricted medicine that is kept for the time being within any building or vehicle shall leave that building or vehicle unattended, unless he has taken all reasonable steps to secure that building or vehicle, or the part of it in which the medicine is kept, against unlawful entry.

4) No person shall deliver on retail sale, or in circumstances corresponding to retail sale, any medicine otherwise than through the post or by handing it or causing it to be handed to the person, or another person reasonably believed to be acting on that person’s behalf, to whom it is addressed or for whose use it is intended.

5) Every person commits an offence against this Act who, without reasonable excuse, contravenes any of the provisions of this section.
Appendix 8: Hepatitis B Antibody Levels in Infants

Testing of infants born to mothers at risk of passing hepatitis B infection (chronic carriers and acute HBV cases in the third trimester) is recommended at five months of age at the time of their fourth dose of hepatitis B vaccine (see Chapter 3).

Interpretation of test results taken at five months of age:

- Where an infant has hepatitis B antibody present at a level above 100 IU/L the infant has an effective immune response to hepatitis B surface antigen. (If the level is above 2000 IU/L it is a very strong response.)

- Where the infant has a hepatitis B antibody level below 10 IU/L there is no evidence of an immune response to the hepatitis B vaccine. The low level of antibody detected in the test may be due to residual passively injected immunoglobulin given at birth. Additional doses of hepatitis B vaccine should be provided, with follow-up to monitor antibody levels. (This should be only a small group of infants.)

- Until further information becomes available to narrow the range, where the infant has a hepatitis B antibody level between 10–100 IU/L the result should be regarded as indeterminate. Residual injected immunoglobulin cannot be distinguished from a modest vaccine-induced response. For indeterminate results, additional vaccine doses, with follow up testing of antibody levels, are recommended.

The following theoretical calculations for clearance of a dose of injected IgG immunoglobulin are provided. It should be noted that higher levels of immunoglobulin may be present if clearance is slower in an individual infant.

- The half-life for most IgG antibodies is of the order of three weeks. A 100 IU dose of hepatitis B immunoglobulin will produce measurable levels of hepatitis B antibody, which will be higher in smaller infants. After five months, the level of injected IgG will fall to approximately 2 IU/L if the half-life is three weeks and to approximately 22 IU/L if the half-life is around six weeks.

Note: If an infant who has received HBig at birth is found at five months of age to have anti-HBs in the range 10–100 IU/L, the result must be regarded as being indeterminate. Possible interpretations are:

- a recent acute infection with HBV from which the infant is recovering. In this case, IgM anti-HBc will be present and a rising level of anti-HBs will be detected on follow-up testing. (Note: detectable IgG anti-HBc of maternal origin may persist in an infant for more than 12 months and is of no diagnostic value.)

- an unusually long half-life for HBIG. In this case IgM anti-HBc will be absent and, further tests after 2–3 months will show a falling level of anti-HBs.
Appendix 9: Meningococcal Invasive Disease

The information provided below has been updated from the Ministry of Health Meningococcal Disease Circular Letter June 1998: To General Practitioners, Medical Officers of Health and Paediatricians. For an update on the epidemiology of meningococcal disease see Chapter 15.

Control of meningococcal disease

Early diagnosis and treatment of meningococcal disease is important, because the disease may be fulminant.

The available evidence favours pre-hospital administration of parenteral antibiotics in cases of suspected meningococcal disease.

Prompt treatment with antibiotics may prevent death and permanent disability, such as damage to the brain, or deafness. Practitioners are reminded of the advice provided in Chapter 15 of the Immunisation Handbook 2006 to administer parenteral antibiotics to suspected cases.

Recommended antibiotics

Prior to transfer to hospital, practitioners should administer parenteral antibiotics to:

- all suspected cases of meningococcal disease in whom there is any haemorrhagic rash
- all other suspected cases for whom the delay to assessment in hospital is likely to be greater than 30 minutes.

The recommended antibiotics are:

- benzyl penicillin  
  - adults: 1.2 g IV (or IM)
  - children: 25–50 mg/kg IV (or IM)
- amoxycillin  
  - adults: 1–2 g IV (or IM)
  - children: 50–100 mg/kg IV (or IM)

Do not be deterred if these antibiotics are not available. Almost any parenterally administered antibiotic in appropriate dosage will inhibit the growth of meningococci.

If possible, take a throat swab (the swab should sample the nasopharyngeal area) when antibiotics are administered, as it may be of assistance in establishing an aetiological diagnosis. The swab should be sent to the hospital with the patient.

Those most at risk from meningococcal disease are children under five years of age. In infants the illness may be non-specific.
Clinical description

*Neisseria meningitidis* causes meningitis or meningococcal septicaemia. The disease presents as an acute illness with fever, nausea, vomiting and headache, and may progress rapidly to shock and death. Petechial rash is seen in about 50 percent of cases.

Symptoms and signs
These may include:

- fever, malaise, prostration
- nausea, vomiting and headache
- rash – petechial or purpuric or maculopapular
- neck stiffness
- young children refusing drinks or feeds
- being sleepy, difficult to rouse
- photophobia
- arthritis/arthralgia.

Because the illness may progress rapidly, early diagnosis and treatment of meningococcal disease is of great importance.

The following points may assist practitioners.

- Examine all the skin of everyone in whom the diagnosis is suspected, as even a single petechial or purpuric lesion may be of significance.
- For individuals with darker skin colouring, it may be more difficult to see petechiae, and a more careful examination will be required. Parents may notice a rash that may otherwise be overlooked.
- The prognosis of meningococcal meningitis is better than that of meningococcal septicaemia. Although neck stiffness and meningococcal irritation are important, their absence does not exclude meningococcal septicaemia or meningitis and is not necessarily reassuring.
- If the practitioner has considered the diagnosis and decided that the clinical features do not merit assessment in hospital, caregivers should be warned to seek urgent medical help, no matter what the time, if there is significant deterioration in the individual’s condition or if any petechial or purpuric lesions develop.
Alternative to penicillin pre-admission antibiotic for suspected meningococcal disease

For patients with a documented history of a severe reaction (such as anaphylaxis), to penicillins, neither penicillin nor amoxycillin should be used. Any of the third-generation cephalosporins would be an acceptable alternative to penicillin. These drugs are known to have a low cross-reactivity with the penicillin-allergic patient. However, there is potential for antibiotic resistance to develop if parenteral cephalosporin use is widespread.

The Ministry of Health recommends that patients with a documented history of anaphylaxis to penicillin, and who are suspected of suffering from meningococcal disease, should be sent immediately to hospital without pre-admission antibiotics.

Ceftriaxone is available on the Medical Practitioners Supply Order.

Acute management and public health control measures

Following arrangements for immediate admission of cases of meningococcal disease to hospital, all cases should be notified immediately on suspicion to the Medical Officer of Health, Public Health Service. The Public Health Service will arrange contact tracing and antibiotic prophylaxis. All adults and children in close contact with primary cases of meningococcal disease should receive antibiotic prophylaxis, preferably within 24 hours of the initial diagnosis, although it may be effective up to 10 days after contact.

Those at particular risk include:

- household contacts
- early childhood service contacts
- those living in close contact in semi-closed communities and institutions
- persons who have had contact with the patient’s oral secretions through kissing and sharing of food or beverages.

Chemoprophylaxis

Rifampicin – recommended dose of 10 mg/kg (maximum dose 600 mg) every 12 hours for two days. For infants less than one month of age: four doses of 5 mg/kg/day over two days.
Vaccine for serogroups A, C, Y and W135

Vaccine may be considered for close contacts of cases of serogroup C meningitis. If there are clusters of cases of serogroups A, C, Y and W135 in the community, the need for a vaccine programme will be assessed by the Medical Officer of Health.

Ministry of Health meningococcal disease national prevention and control plan

The Ministry of Health is coordinating a multi-year national prevention and control plan. This is outlined below:

- Intensified epidemiological surveillance.
- Promoting public awareness to encourage early medical intervention.
- Promoting professional and public awareness to encourage early diagnosis and treatment.
- Prevention of secondary cases by notification, contact tracing and offering prophylactic antibiotics.
- Meningococcal B Immunisation Programme.

The Ministry of Health has agreed on the following key public and professional messages and encourages the use of these messages in the media, to achieve national consistency.
Meningococcal Disease

Key Messages (Public)

• If your child is sick – check them often.
• Do not wait – take action. Doctors’ visits are free for children under six.*
• Meningococcal disease – early treatment saves lives.
• Children may be seriously ill if they:
  – have a fever
  – refuse drinks or feeds
  – are sleepy or floppy – or harder to wake
  – vomit
  – are crying or unsettled
  – have a rash/spots
  – have a headache.
• Anyone can get meningococcal disease – though those at greatest risk are children under five and young adults.
• The MeNZB™ vaccine does not provide protection from other strains of meningococcal disease.
• IF YOUR CHILD GETS WORSE – TAKE THEM STRAIGHT BACK TO THE DOCTOR.
* Note – there may be a change to this policy in the future.

Meningococcal Disease

Key Messages (Professionals)

• Meningococcal disease is a killer; early intervention saves lives.
• It is a year-round disease, but cases of meningococcal disease increase during winter and spring.
• Have a high index of suspicion for meningococcal disease.
• Check all skin areas for the presence of a rash.
• Be aware of the febrile child – suspect meningococcal disease.
Meningococcal Disease
Key Messages (Professionals) cont.

- Accurately assess severity of illness – and ensure treatment.
- Give advice to parents/caregivers on checking the child at regular intervals.
- Advise young adults not to remain on their own if they are sick.
- In suspected cases of meningococcal disease start intravenous or intramuscular antibiotic treatment as soon as possible.
- Prior to transfer to hospital, practitioners should administer parenteral antibiotics to:
  - all suspected cases of meningococcal disease in whom there is any haemorrhagic rash
  - all other suspected cases for whom the delay in reaching the hospital is likely to be greater than 30 minutes.
- If you do not suspect meningococcal disease:
  - encourage early return
  - plan a review.
- The Meningococcal B Immunisation Programme is completed on 30 June 2006. However, children and young people aged 5–19 years should complete a course of MeNZB™ up to 31 December 2006. After that the vaccine is not available to them.
- From 1 July 2006 MeNZB™ vaccine will be available to infants as a four dose course at age six weeks, three, five and ten months. Children under the age of five years should complete a course of MeNZB™ vaccine whilst the vaccine is available. The Ministry of Health will communicate with practitioners if there are changes or additions to this programme.
- The MeNZB™ vaccine does not provide protection against other strains of meningococcal disease eg, A, C, Y, W135. Immunisation is available for these other strains. Note these vaccines are not available on the National Immunisation Schedule. However, they are publicly funded as part of the Pre- and Post-Splenectomy Programme for eligible individuals.
- *Haemophilus influenzae* type b (Hib)/other vaccines do not protect against meningococcal disease.
Appendix 10: Management of Exposure to Varicella During Pregnancy and Care of the Newborn

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Figure 1: Exposure to varicella zoster virus during pregnancy

![Diagram](https://via.placeholder.com/150)

1. Previous maternal chickenpox
2. No history or uncertain past history of chickenpox
3. Check serology urgently
4. Seronegative
5. Access time of exposure
6. Expose < 96 hours earlier
7. Expose > 96 hours earlier
8. Passive immunisation ZIG
9. Oral acyclovir if at risk, ie:
   - second half of pregnancy
   - underlying lung disease
   - immunocompromised
   - smoker
10. Advise to seek medical attention immediately if chickenpox develops
11. Remains well
12. Develops chickenpox
13. Clinical treatment of mother

Notes: Exposure to varicella or zoster for which ZIG is indicated for susceptible persons:
- living in the same household as a person with active chickenpox or herpes zoster
- face-to-face contact with a case of chickenpox or uncovered zoster lesions for at least 5 minutes.
Figure 2: Fetal medicine counselling following varicella zoster in pregnancy

Risk of fetal varicella syndrome (FVS) following maternal chickenpox in pregnancy

Incidence of FVS following varicella in pregnancy
Large case studies suggest rates of 2—2.8% in first 20 weeks gestation

Timing of maternal infection may be important

<12 weeks gestation 0.4%  12—20 weeks gestation 2%  >20 weeks gestation isolated case reports only

• No single diagnostic/prognostic test available
• Regular fetal ultrasound for developing anomalies is recommended
• VZV fetal serology is unhelpful
• Consider amniocentesis: –ve VZV PCR may be reassuring

Sequelae FVS

<table>
<thead>
<tr>
<th>Abnormalities</th>
<th>Frequency</th>
</tr>
</thead>
<tbody>
<tr>
<td>Skin scars</td>
<td>78%</td>
</tr>
<tr>
<td>Eye abnormalities</td>
<td>60%</td>
</tr>
<tr>
<td>Limb abnormalities</td>
<td>68%</td>
</tr>
<tr>
<td>Prematurity, low birthweight</td>
<td>50%</td>
</tr>
<tr>
<td>Cortical atrophy, mental retardation</td>
<td>46%</td>
</tr>
<tr>
<td>Poor sphincter control</td>
<td>32%</td>
</tr>
<tr>
<td>Early death</td>
<td>29%</td>
</tr>
</tbody>
</table>
Appendix 10: Management of Exposure to Varicella During Pregnancy and Care of the Newborn

Figure 3: Management of infants from mothers with perinatal varicella zoster

Treat infant according to timing of maternal chickenpox

Maternal chickenpox > 7 days before delivery
- No ZIG required
- No special interventions
- No isolation of infant from mother
- Breast feeding encouraged
- Even if baby has chickenpox at birth or very soon after usually no interventions are required unless infant is very preterm*
- Very preterm infants born with chickenpox should receive IV acyclovir

Maternal chickenpox ≤ 7 days before delivery
- ZIG required immediately
- Should be given <24 hours after birth but may be given up to 72 hours
- Discharge term infants as soon as possible
- No other interventions
- No isolation of infant from mother
- Breast feeding encouraged

Maternal chickenpox 0—28 days after delivery
- ZIG required immediately
- Should be given <24 hours after development of maternal rash but may be given up to 72 hours
- No other interventions
- No isolation of infant from mother
- Breast feeding encouraged

Develops chickenpox

Every preterm infant in nursery
- IV acyclovir
- Treatment of neonate

Term infant at home or on postnatal ward
- Admit to paediatric unit

Mild disease and ZIG given <24 hours after birth
- Keep under observation
- Treatment with IV acyclovir if respiratory symptoms develop

Severe disease or ZIG given >24 hours after birth
- Treat with IV acyclovir
- Supportive care as required

Notes
- Transplacentally acquired VZV is high-risk and severity reduced by ZIG
- Risk also high for seronegative baby <28 days old
- ZIG not always effective in preventing severe disease
- Very preterm ≤28 weeks gestation

Reference
Appendix 11: Websites

- New Zealand Ministry of Health (www.moh.govt.nz)
- Medsafe (www.medsafe.govt.nz)
- ESR (www.esr.cri.nz)
- Immunisation Advisory Centre (www.immune.org.nz)
- WHO (www.who.int)
- United States (US) Centers for Disease Control and Prevention (www.cdc.gov)
- US National Foundation for Infectious Diseases (www.nfid.org)

**Influenza websites**

- WHO Collaborating Centre for Reference and Research on Influenza, Melbourne, Australia (www.influenzacentre.org)

  Information on national influenza centres and vaccine manufacturers around the world, as well as links to reports of the Weekly Epidemiological Record, which are also downloadable as pdf files.

- FluNet (http://oms.b3e.jussieu.fr/)

  WHO’s geographical information system for monitoring global influenza activity. Recent activity is featured in a series of animated maps and news reports, and listings of participating centres, influenza vaccine manufacturers, and related websites are provided.

- US Centers for Disease Control and Prevention (www.cdc.gov/flu)

  Information for the general public and health professionals on influenza viruses, vaccines, and antiviral agents, and on the clinical features and natural history of human influenza.
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