The Australian Immunisation Handbook provides clinical advice for health professionals on the safest and most effective use of vaccines in their practice. These recommendations are developed by Australian Technical Advisory Group on Immunisation (ATAGI) (immunisation-advisory-bodies) and approved by the National Health and Medical Research Council (NHMRC) (http://www.nhmrc.gov.au/).

The Handbook’s clinical recommendations are based on the best scientific evidence available at the time of publication from published and unpublished literature. Where specific empirical evidence was unavailable, recommendations were formulated using the best available expert opinion relevant to Australia.

In some instances, the ATAGI recommendations differ from vaccine product information sheets (PI); these differences are detailed in the relevant vaccine chapters under the heading ‘Variations from product information’. Where a variation exists, the ATAGI recommendation should be considered best practice.

Public Consultation on changes to the recommended use of meningococcal and Haemophilus influenzae type B (Hib) vaccines

Key Points:

- The Australian Technical Advisory Group on Immunisation is consulting with stakeholders on proposed changes to meningococcal and Haemophilus influenzae type B vaccination recommendations for inclusion in the Australian Immunisation Handbook.
- The public consultation will remain open until 11:59pm on 06 May 2018.
- Comments from all parties are welcomed.

PDF printable version of The Australian Immunisation Handbook (PDF 12241 KB large file)(7B28E87511E08905CA257D4D001DB1F8/$File/Aus-Imm-Handbook.pdf)

Please note: This PDF is not up to date. The most recent information is available at the chapters within the Table of Contents. Each chapter contains a PDF print friendly version which can be downloaded and/or printed.
Updates to the 10th edition of The Australian Immunisation Handbook

Advice included in the 10th edition of The Australian Immunisation Handbook has been updated since this edition was first published in 2013. A list of updates is provided below by the date they were published. These updates have been made in response to specific issues requiring amendment; amended chapters have not been reviewed in their entirety unless specified.

The most up-to-date version of the 10th edition Handbook is the online version within the individual chapters. If you have a hard copy of the 10th edition Handbook this list can be printed for easy reference or used to annotate updates in your hard copy.

Updates:

- 1 August 2016/[Internet/immunise/publishing.nsf/Content/Handbook10-home-handbook10-updates-handbook10-updates-01-08-2016-1]
- 21 March 2016/[Internet/immunise/publishing.nsf/Content/Handbook10-home-handbook10-updates-handbook10-updates-21-03-2016-1]
April 2018

Updates to the 10th edition of The Australian Immunisation Handbook

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Key updates made to the 10th edition Handbook in February 2018 are listed below

Chapter 4.6 Human Papillomavirus

4.6.7 Recommendations

The following replaces the existing Recommendations listed in Chapter 4.6 Human Papillomavirus:

a. All individuals (males and females) who commence vaccination at the age of 9 to 14 years, except immunocompromised individuals (refer to (b) below), should receive two doses of 9vHPV vaccine given 6–12 months apart (0, 6–12 months).

b. The following population groups should receive three doses of 9vHPV vaccine given at 0, 2 and 6 months:
   i. immunocompromised individuals (males and females) at any age;
   ii. males and females who receive their first dose of 9vHPV after turning 15 years of age.

Table 1: Comparison of the ATAGI current and proposed recommendations for HPV vaccination

<table>
<thead>
<tr>
<th>Recommendation</th>
<th>Vaccine</th>
<th>Cohort</th>
<th>Number of doses</th>
<th>Schedule of doses</th>
</tr>
</thead>
<tbody>
<tr>
<td>Previous</td>
<td>2vHPV† vaccine (females only)</td>
<td>Commencing vaccination aged 9–18 years</td>
<td>3 doses</td>
<td>0, 1 and 6 months (2vHPV vaccine)</td>
</tr>
<tr>
<td></td>
<td>4vHPV† vaccine (males and females)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Immuno compromised aged 9–45 years‡</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Current</td>
<td>9vHPV vaccine (males and females)</td>
<td>Commencing vaccination aged 9–14 years</td>
<td>2 doses</td>
<td>0, 6–12 months‡</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Immuno compromised aged 9–45 years‡</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Commencing vaccination aged ≥15 years</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

† HPV vaccine may be administered from 9 years of age, however, the optimal time for vaccination is approximately 12–14 years, as provided under the school-based National Immunisation Program (NIP).

‡ Both 2vHPV and 4vHPV vaccines have been registered in Australia. Only 4vHPV vaccine has been provided under the National Immunisation Program (NIP) since HPV vaccination was funded in 2007.

¶ Immunocompromised individuals include those with primary or secondary immunodeficiencies (B lymphocyte antibody and T lymphocyte complete or partial deficiencies), HIV infection, malignancy, organ transplantation, autoimmune disease, or significant immunosuppressive therapy (but does not include asplenia or hypopsplenia).

If an individual has received two doses of HPV vaccine with an interval of less than 5 months between dose 1 and dose 2, a third dose is required at least 12 weeks after the second dose, ensuring that the minimum intervals for 3 doses have been met. If the second dose is received at <6 months but ≥5 months after the first dose, a third dose is not required, as clinical trial data support this interval still being sufficiently immunogenic.

Minimum intervals recommended for a 3-dose schedule are at least 4 weeks between dose 1 and dose 2 and at least 5 months between dose 1 and dose 3.

c. No catch up is recommended for individuals who have completed a full schedule (either age and interval appropriate 2- or 3- dose schedules) with either 4vHPV or 2vHPV. Refer to evidence following.

d. 9vHPV vaccine can be used to complete an HPV vaccination schedule commenced with either the 4vHPV or 2vHPV vaccine.

e. All individuals (males and females) who receive their first dose of 9vHPV after turning 15 years of age.

Chapter 4.7 Influenza

Updating the text to reflect the 2018 influenza season (Refer to Chapter 4.7 Influenza/Internet/Immunise/publishing.nsf/Content/Handbook10-home-handbook10part4-handbook10-4-7))

Chapter 4.13 Pneumococcal disease

4.13.7 Recommendations

The following replaces the existing Recommendations for infant pneumococcal vaccination schedule listed in Chapter 4.6 Pneumococcal disease:

a. All children, except those specified in (b) below, should receive three doses of 13vPCV at 2, 4 and 12 months of age (called ‘2+1’ schedule) instead of the current schedule with doses at 2, 4 and 6 months of age (called ‘3+0’ schedule).

b. The following population groups at increased risk of pneumococcal infection should continue to receive four doses of 13vPCV at 2, 4, 6 and 12 months* of age (called ‘3+1’ schedule):
   i. Aboriginal and Torres Strait Islander children living in the NT, QLD, SA and WA.
   ii. Children with underlying medical conditions associated with an increased risk of IPD.

*Note the preferred schedule point for the fourth (last) 13vPCV dose is age 12 months rather than 18 months.

Table 1: Comparison of current and proposed ATAGI recommendations for 13vPCV schedules in children

<table>
<thead>
<tr>
<th>Cohort</th>
<th>Schedule in previous recommendation*</th>
<th>Schedule in current recommendation</th>
</tr>
</thead>
<tbody>
<tr>
<td>All children in ACT, NSW, TAS or VIC</td>
<td>3+0 (2, 4 and 6 months)</td>
<td>2+1 (2, 4 and 12 months)</td>
</tr>
<tr>
<td>Children without underlying medical conditions associated with increased risk of IPD</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Aboriginal and Torres Strait Islander children in NT, QLD, SA or WA

<table>
<thead>
<tr>
<th>Number of doses given previously</th>
<th>Age at presentation</th>
<th>Age when previous dose of any PCV&lt;sup&gt;1&lt;/sup&gt; was given</th>
<th>Recommendations&lt;sup&gt;‡&lt;/sup&gt;</th>
<th>Number of further dose(s) required</th>
</tr>
</thead>
<tbody>
<tr>
<td>No previous doses</td>
<td></td>
<td>1st dose</td>
<td>2nd dose</td>
<td>3rd dose</td>
</tr>
<tr>
<td></td>
<td>&lt;12 months</td>
<td>–</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td></td>
<td>12–59 months</td>
<td>–</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>1 previous dose</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>&lt;12 months</td>
<td>Any age</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td></td>
<td>12–59 months</td>
<td>&lt;12 months</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td></td>
<td>≥12 months</td>
<td>–</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>2 previous doses</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>&lt;12 months</td>
<td>Any age</td>
<td>Any age</td>
<td>–</td>
</tr>
<tr>
<td></td>
<td>12–59 months</td>
<td>&lt;12 months</td>
<td>Any age</td>
<td>–</td>
</tr>
<tr>
<td></td>
<td>≥12 months</td>
<td>–</td>
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<td></td>
<td>≥12 months</td>
<td>≥12 months</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>3 previous doses</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>&lt;12 months</td>
<td>Any age</td>
<td>Any age</td>
<td>Any age</td>
</tr>
<tr>
<td></td>
<td>12–59 months</td>
<td>&lt;12 months</td>
<td>Any age</td>
<td>–</td>
</tr>
<tr>
<td></td>
<td>≥12 months</td>
<td>≥12 months</td>
<td>≥12 months</td>
<td>–</td>
</tr>
</tbody>
</table>

<sup>1</sup> Prior PCV doses may have been given as 7vPCV (e.g. from overseas), 10vPCV or 13vPCV. Use 13vPCV as the vaccine formulation for catch-up doses, regardless of which formulation of PCV the child received previously.

<sup>2</sup> Where possible, align doses with the standard schedule points at 2, 4 and 6 months of age for infants. The minimum interval between dose(s) is 1 month if aged <12 months, and 2 months if aged ≥12 months.

<sup>3</sup> The last dose should be given after the child reaches 12 months of age (as a booster dose) with a minimum interval of 2 months after the previous dose of PCV.

Table 3: Catch-up schedule for 13vPCV for all other children aged <5 years (not covered in Table 2a)
| 3 previous doses | <12 months | <12 months | <12 months | 1
|------------------|-----------|------------|------------|---
| 12–59 months     | Any age   | Any age    | ≥12 months | None

1 Prior PCV doses may have been given as 7vPCV (e.g. from overseas), 10vPCV or 13vPCV. Use 13vPCV as the vaccine formulation for catch-up doses, regardless of which formulation of PCV the child received previously.

2 Where possible, align doses with the standard schedule points at 2 months and 4 months of age for infants aged <5 months. The minimum interval between dose(s) is 1 month if aged <12 months, and 2 months if aged ≥12 months.

3 The last dose should be given after the child reaches 12 months of age (as a booster dose) with a minimum interval of 2 months after the previous dose of 13vPCV.
Updates to the 10th edition of The Australian Immunisation Handbook

Advice included in the 10th edition of The Australian Immunisation Handbook has been updated since this edition was first published in 2013. A list of updates is provided below by the date they were published. These updates have been made in response to specific issues requiring amendment; amended chapters have not been reviewed in their entirety unless specified.

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Key updates made to the 10th edition Handbook in August 2017 are listed below by chapter, including chapter sections and subsections. Other minor amendments to those listed below have been made to improve clarity, consistency and accuracy; these changes are not specifically noted. References have been removed, updated or introduced where required.

Note: The updated chapters are available online in HTML and PDF formats.

Chapter 2.1 Pre-vaccination

2.1.5 Catch-up

- The text has been edited due to the discontinuation of the Haemophilus b conjugate (PRP-OMP) vaccine in Australia (PedvaxHIB). (Refer also Chapter 4.3 Haemophilus influenzae type b (internet/immunise/publishing.nsf/Content/Handbook10-home%7EHandbook10part4%7EHandbook10-4-3)).

Chapter 3.3 Groups with special vaccination requirements

3.3.2 Vaccination of women who are planning pregnancy, pregnant or breastfeeding, and preterm infants

- Clarification of advice on the administration of tTpa during the third trimester of each pregnancy.

3.3.3 Vaccination of immunocompromised persons

- Addition of text and a table to clarify the contraindications to use of zoster vaccine in immunocompromised individuals and to provide further detail on what constitutes immunocompromise relevant to all live vaccines. (Refer also Chapter 4.24 Zoster (internet/immunise/publishing.nsf/Content/Handbook10-home%7EHandbook10part4%7EHandbook10-4-24)).

- Addition of text providing more specific detail of CD4 levels at which a person infected with HIV can receive zoster vaccine. (Refer also Chapter 4.24 Zoster (internet/immunise/publishing.nsf/Content/Handbook10-home%7EHandbook10part4%7EHandbook10-4-24)).

3.3.7 Vaccination of persons at occupational risk

- Addition of text clarifying diphtheria vaccination in laboratory workers. (Refer also Chapter 4.2 Diphtheria (internet/immunise/publishing.nsf/Content/Handbook10-home%7EHandbook10part4%7EHandbook10-4-2)).

Chapter 4.2 Diphtheria

4.2.4 Vaccines and 4.2.12 Variations from product information

- Amendment of text due to the discontinuation of a vaccine type, Pediacel. (Refer also Chapters, 4.2 Diphtheria (internet/immunise/publishing.nsf/Content/Handbook10-home%7EHandbook10part4%7EHandbook10-4-2), 4.3 Haemophilus influenzae type b (internet/immunise/publishing.nsf/Content/Handbook10-home%7EHandbook10part4%7EHandbook10-4-3), 4.14 Polio (internet/immunise/publishing.nsf/Content/Handbook10-home%7EHandbook10part4%7EHandbook10-4-14) and 4.19 Tetanus (internet/immunise/publishing.nsf/Content/Handbook10-home%7EHandbook10part4%7EHandbook10-4-19)).

4.2.7 Recommendations

- Addition of text clarifying vaccination in laboratory workers.

Chapter 4.3 Haemophilus influenzae type b

4.3.4 Vaccines

- Addition of text to clarify situations in which vaccine interchangeability will now need to be considered.

4.3.4 Vaccines, 4.3.7 Recommendations, 4.3.12 Variations from product information

- Amendment of text due to the discontinuation of the Haemophilus b conjugate (PRP-OMP) vaccine (PedvaxHIB) (Refer also Chapter 2.1 Pre-vaccination (internet/immunise/publishing.nsf/Content/Handbook10-home%7EHandbook10part2%7EHandbook10-2-1)).

- Amendment of text due to the discontinuation of a vaccine type, Pediacel (Refer also Chapters, 4.2 Diphtheria (internet/immunise/publishing.nsf/Content/Handbook10-home%7EHandbook10part4%7EHandbook10-4-2), 4.12 Pertussis (internet/immunise/publishing.nsf/Content/Handbook10-home%7EHandbook10part4%7EHandbook10-4-12), 4.14 Polio (internet/immunise/publishing.nsf/Content/Handbook10-home%7EHandbook10part4%7EHandbook10-4-14) and 4.19 Tetanus (internet/immunise/publishing.nsf/Content/Handbook10-home%7EHandbook10part4%7EHandbook10-4-19)).

Chapter 4.4 Hepatitis A

4.4.4 Vaccines

- Amendment of text to align with new product information.

4.4.6 Dosage and administration

- Correction of incorrect text, replacing ELISA units with antigen units and changing 12 months to 36 months.

Chapter 4.9 Measles

4.9.4 Vaccines
4.9.5 Transport, storage and handling

- Amendment of text to align with new product information on storage of vaccine at various temperatures (Refer also Chapters, 4.11 Mumps (/immunise/publishing.nsf/Content/Handbook10-home%7EHandbook10part4%7EHandbook10-4-11) and 4.18 Rubella (/immunise/publishing.nsf/Content/Handbook10-home%7EHandbook10part4%7EHandbook10-4-18)).

4.9.10 Precautions, 4.9.11 Adverse events

- Moving text on egg allergy from Precautions to Adverse Events to be consistent with other chapters (Refer also Chapters, 4.11 Mumps (/immunise/publishing.nsf/Content/Handbook10-home%7EHandbook10part4%7EHandbook10-4-11) and 4.18 Rubella (/immunise/publishing.nsf/Content/Handbook10-home%7EHandbook10part4%7EHandbook10-4-18)).

4.11.4 Vaccines

- Correction of text due to incorrect nomenclature (Refer also Chapters, 4.9 Measles (/internet/immunise/publishing.nsf/Content/Handbook10-home%7EHandbook10part4%7EHandbook10-4-9), 4.18 Rubella (/immunise/publishing.nsf/Content/Handbook10-home%7EHandbook10part4%7EHandbook10-4-18) and 4.22 Varicella (/immunise/publishing.nsf/Content/Handbook10-home%7EHandbook10part4%7EHandbook10-4-22)).

4.11.11 Adverse events

- Addition of text on ovalbumin quantity in vaccine.

Chapter 4.11 Mumps

4.11.4 Vaccines

- Amendment of text to align with new product information on storage of vaccine at various temperatures (Refer also Chapters, 4.9 Measles (/internet/immunise/publishing.nsf/Content/Handbook10-home%7EHandbook10part4%7EHandbook10-4-9) and 4.18 Rubella (/immunise/publishing.nsf/Content/Handbook10-home%7EHandbook10part4%7EHandbook10-4-18)).

4.11.11 Adverse events

- Addition of text on egg allergy to Adverse Events to be consistent with other chapters (Refer also Chapters, 4.9 Measles (/internet/immunise/publishing.nsf/Content/Handbook10-home%7EHandbook10part4%7EHandbook10-4-9), 4.18 Rubella (/immunise/publishing.nsf/Content/Handbook10-home%7EHandbook10part4%7EHandbook10-4-18) and 4.22 Varicella (/immunise/publishing.nsf/Content/Handbook10-home%7EHandbook10part4%7EHandbook10-4-22)).

Chapter 4.12 Pertussis

4.12.4 Vaccines and 4.12.12 Variations from product information

- Amendment of text due to the discontinuation of a vaccine type, Pediacel. (Refer also Chapters, 4.2 Diphtheria (/immunise/publishing.nsf/Content/Handbook10-home%7EHandbook10part4%7EHandbook10-4-2), 4.3 Haemophilus influenzae type b (/immunise/publishing.nsf/Content/Handbook10-home%7EHandbook10part4%7EHandbook10-4-3), 4.14 Polio (/immunise/publishing.nsf/Content/Handbook10-home%7EHandbook10part4%7EHandbook10-4-14) and 4.19 Tetanus (/internet/immunise/publishing.nsf/Content/Handbook10-home%7EHandbook10part4%7EHandbook10-4-19)).

Chapter 4.14 Polio

4.14.4 Vaccines and 4.14.12 Variations from product information

- Amendment of text due to the discontinuation of a vaccine type, Pediacel. (Refer also to Chapters, 4.2 Diphtheria (/immunise/publishing.nsf/Content/Handbook10-home%7EHandbook10part4%7EHandbook10-4-2), 4.3 Haemophilus influenzae type b (/immunise/publishing.nsf/Content/Handbook10-home%7EHandbook10part4%7EHandbook10-4-3), 4.12 Pertussis (/internet/immunise/publishing.nsf/Content/Handbook10-home%7EHandbook10part4%7EHandbook10-4-12) and 4.19 Tetanus (/internet/immunise/publishing.nsf/Content/Handbook10-home%7EHandbook10part4%7EHandbook10-4-19)).

Chapter 4.16 Rabies

4.16.5 Rabies immunoglobulin

- Amendment of text relating to the use of immunoglobulin.

4.16.7 Dosage and administration

- Clarification of text relating to administration of the vaccine and immunoglobulin.

4.16.8 Recommendations

4.17.6 Dosage and administration

- Amendment of text relating to the need for a third dose of vaccine.

Chapter 4.18 Rubella

4.18.4 Vaccines

- Amendment of text to align with new product information. In particular the source of animal derived gelatin was updated to specify porcine gelatin. (Refer also Chapters, 4.9 Measles (immunise/publishing.nsf/Content/Handbook10-home%7EHandbook10-part4%7EHandbook10-4-9), 4.11 Mumps (immunise/publishing.nsf/Content/Handbook10-home%7EHandbook10-part4%7EHandbook10-4-11), 4.21 Typhoid (immunise/publishing.nsf/Content/Handbook10-home%7EHandbook10-part4%7EHandbook10-4-21), 4.22 Varicella (immunise/publishing.nsf/Content/Handbook10-home%7EHandbook10-part4%7EHandbook10-4-22) and Appendices 3 & 4 (immunise/publishing.nsf/Content/Handbook10-home%7EHandbook10-tools%7EHandbook10-appendices)).

4.18.5 Transport, storage and handling

- Amendment of text to align with new product information on storage of vaccine at various temperatures (Refer also Chapters, 4.9 Measles (immunise/publishing.nsf/Content/Handbook10-home%7EHandbook10-part4%7EHandbook10-4-9) and 4.11 Mumps (immunise/publishing.nsf/Content/Handbook10-home%7EHandbook10-part4%7EHandbook10-4-11)).

4.18.11 Adverse events

- Addition of text on egg allergy to Adverse Events to be consistent with other chapters (Refer also Chapters, 4.9 Measles (internet-immunise/publishing.nsf/Content/Handbook10-home%7EHandbook10-part4%7EHandbook10-4-9), 4.11 Mumps (immunise/publishing.nsf/Content/Handbook10-home%7EHandbook10-part4%7EHandbook10-4-11), 4.18 Rubella (immunise/publishing.nsf/Content/Handbook10-home%7EHandbook10-part4%7EHandbook10-4-18) and 4.22 Varicella (immunise/publishing.nsf/Content/Handbook10-home%7EHandbook10-part4%7EHandbook10-4-22)).

Chapter 4.19 Tetanus

4.19.4 Vaccines and 4.19.12 Variations from product information

- Amendment of text due to the discontinuation of a vaccine type, Pediacel. (Refer also Chapters, 4.2 Diphtheria (immunise/publishing.nsf/Content/Handbook10-home%7EHandbook10-part4%7EHandbook10-4-2), 4.3 Haemophilus influenzae type b (immunise/publishing.nsf/Content/Handbook10-home%7EHandbook10-part4%7EHandbook10-4-3), 4.12 Pertussis (immunise/publishing.nsf/Content/Handbook10-home%7EHandbook10-part4%7EHandbook10-4-12) and 4.14 Polio (immunise/publishing.nsf/Content/Handbook10-home%7EHandbook10-part4%7EHandbook10-4-14)).

Chapter 4.20 Tuberculosis

4.20.10 Precautions

- Addition of text to clarify when BCG vaccination should be deferred in people with skin conditions.

Chapter 4.21 Typhoid

4.21.4 Vaccines

- Amendment of text to align with new product information. In particular the source of animal derived gelatin was updated to specify bovine gelatin. (Refer also Chapters, 4.9 Measles (internet-immunise/publishing.nsf/Content/Handbook10-home%7EHandbook10-part4%7EHandbook10-4-9), 4.11 Mumps (immunise/publishing.nsf/Content/Handbook10-home%7EHandbook10-part4%7EHandbook10-4-11), 4.18 Rubella (immunise/publishing.nsf/Content/Handbook10-home%7EHandbook10-part4%7EHandbook10-4-18) and 4.22 Varicella (immunise/publishing.nsf/Content/Handbook10-home%7EHandbook10-part4%7EHandbook10-4-22)).

Chapter 4.22 Varicella

4.22.4 Vaccines

- Amendment of text to align with new product information. In particular the source of animal derived gelatin was updated to specify porcine gelatin. (Refer also Chapters, 4.9 Measles (internet-immunise/publishing.nsf/Content/Handbook10-home%7EHandbook10-part4%7EHandbook10-4-9), 4.11 Mumps (immunise/publishing.nsf/Content/Handbook10-home%7EHandbook10-part4%7EHandbook10-4-11), 4.18 Rubella (immunise/publishing.nsf/Content/Handbook10-home%7EHandbook10-part4%7EHandbook10-4-18), 4.21 Typhoid (immunise/publishing.nsf/Content/Handbook10-home%7EHandbook10-part4%7EHandbook10-4-21) and Appendices 3 & 4 (immunise/publishing.nsf/Content/Handbook10-home%7EHandbook10-tools%7EHandbook10-appendices)).

4.22.11 Adverse events

- Addition of text on egg allergy to Adverse Events to be consistent with other chapters. (Refer also Chapters, 4.9 Measles (internet-immunise/publishing.nsf/Content/Handbook10-home%7EHandbook10-part4%7EHandbook10-4-9), 4.11 Mumps (immunise/publishing.nsf/Content/Handbook10-home%7EHandbook10-part4%7EHandbook10-4-11), 4.18 Rubella (immunise/publishing.nsf/Content/Handbook10-home%7EHandbook10-part4%7EHandbook10-4-18)).
4.22.12 Public health management of varicella

- Addition of text to section regarding giving neonates zoster immunoglobulin (ZIG) to clarify it is after primary varicella-zoster virus (VZV) infection of the mother.

Chapter 4.23 Yellow fever

4.23.4 Vaccine

- Amendment of text describing vaccine failure.

4.23.7 Recommendations

- Editing of text relating to a booster dose to provide clarity.

Chapter 4.24 Zoster

4.24.7 Recommendations

- Addition of text reiterating importance of obtaining a medical history in patients prior to vaccination, to reiterate the contraindications regarding use of zoster vaccine in immunocompromised individuals and to provide further detail on what constitutes immunocompromise and how to manage inadvertent vaccination in these individuals.

4.24.9 Contraindications

- Addition of text and table to reiterate the contraindications regarding use of zoster vaccine in immunocompromised individuals and to provide further detail on what constitutes immunocompromise and how to manage inadvertent vaccination in these individuals.

4.24.10 Precautions

- Addition of text providing more specific detail of CD4 levels at which a person infected with HIV can receive zoster vaccine. (Refer also Chapter 3.3 Groups with special vaccination requirements/year/immunise/publicating.nsf/Content/Handbook10-home%7EHandbook10-part4%7EHandbook10-3-3).

4.24.11 Adverse events

- Addition of text providing details of select serious outcomes where immunocompromised individuals have received zoster vaccine.

Appendices 3 & 4

- Addition and removal of text due to changes in vaccines on NIP and changes to PI's. In particular, the source of animal derived gelatin was updated to specify porcine gelatin. (Refer also Chapters, 4.9 Measles/year/immunise/publicating.nsf/Content/Handbook10-home%7EHandbook10-part4%7EHandbook10-4-9), 4.11 Mumps (year/immunise/publicating.nsf/Content/Handbook10-home%7EHandbook10-part4%7EHandbook10-4-11), 4.18 Rubella (year/immunise/publicating.nsf/Content/Handbook10-home%7EHandbook10-part4%7EHandbook10-4-18), 4.21 Typhoid (year/immunise/publicating.nsf/Content/Handbook10-home%7EHandbook10-part4%7EHandbook10-4-21) and 4.22 Varicella (year/immunise/publicating.nsf/Content/Handbook10-home%7EHandbook10-part4%7EHandbook10-4-22).
17 February 2017

Key updates made to the 10th edition Handbook in February 2017 are listed below by chapter, including chapter sections and subsections. Other minor amendments to those listed below have been made to improve clarity, consistency and accuracy; these changes are not specifically noted.

References have been removed, updated or introduced where required.

Note: The updated chapter is available online in PDF and HTML formats.

4.7 Influenza

4.7.4 Vaccines

Afluria Quad – Seqirus (quadrivalent inactivated influenza virus) is now available in Australia for adults aged ≥18 years.

Clarification on advice relating to waning immunity following influenza vaccination and the timing of vaccination to provide the maximum protection.

4.7.5 Transport, storage and handling and 4.7.6 Dosage and administration

Advice relating to the timing and importance of discarding vaccines when they reach their expiry date.

4.7.10 Precautions

Clarification of advice on influenza vaccination for persons with egg allergy including the addition of Table 4.7.2 Recommended administration of influenza vaccine in egg allergic individuals.

Persons with egg allergy, including anaphylaxis, can be safely vaccinated with influenza vaccines. Non-anaphylaxis egg allergy or people sensitised but who have not yet eaten egg can be vaccinated with full age appropriate dose in any immunisation setting. Persons with a history of anaphylaxis to egg should be vaccinated in medical facilities with staff experienced in recognising and treating anaphylaxis. Anaphylaxis following a previous dose of influenza vaccine continues to be a contraindication to future influenza vaccination.

4.7.13 Variations from product information

ATAGI’s advice on egg allergies and vaccination during pregnancy varies from the product information.
1 August 2016

Key updates made to the 10th edition Handbook in August 2016 are listed below by chapter, including chapter sections and subsections. Other minor amendments to those listed below have been made to improve clarity, consistency and accuracy; these changes are not specifically noted. References have been removed, updated or introduced where required.

Note: The updated chapter is available online only in HTML formats.

Chapter 2.1 Pre-vaccination
- Updated information on Australia’s immunisation registers to align with the Australian Immunisation Register Act 2015.
- Update in line with A New Tax System (Family assistance) Act 1999:
  - New text updated criteria for eligibility for a medical exemption to vaccination based on natural immunity.
  - Table 2.1.12 Catch-up schedule for persons ≥10 years of age to clarify pertussis catch-up recommendations.

Chapter 2.2 Administration of vaccines
- Aligning with the advice in the Australian Guidelines for the Prevention and Control of Infection in Healthcare (2010).

Chapter 2.3 Post-vaccination
- Updated information on Australia’s immunisation registers to align with the Australian Immunisation Register Act 2015.
- Update to publication timelines for aggregate Therapeutic Goods Administration (TGA) vaccine Adverse Effects Following Immunisation reports in Communicable Diseases Intelligence (CDI).

Chapter 2.3 Vaccination for international travel
- Updated ATAGI advice on 10-yearly booster dose requirements for yellow fever, as well as required updates to supporting data and resources for travel vaccination. Refer also to the Yellow fever chapter.

Chapter 3.2 Vaccination for international travel
- Updated ATAGI advice on 10-yearly booster dose requirements for yellow fever, as well as required updates to supporting data and resources for travel vaccination. Refer also to the Yellow fever chapter.

Chapter 3.3 Groups with special vaccination requirements
- Clarification of advice on the administration of live vaccines to patients who are immunocompromised, including specific advice on biological and non-biological disease modifying anti-rheumatic drugs (DMARDs).
- Relevant changes to align with new updates in other chapters (i.e. Influenza, Pneumococcal and Yellow fever).

Chapter 4.12 Pertussis (also chapters, 4.2 Diphtheria, 4.3 Haemophilus influenzae type b, 4.5 Hepatitis B, 4.14 Poliomyelitis and 4.19 Tetanus, as required)
- Clarification of advice, including:
  - On those who are considered close contacts of young infants and those who are considered contacts of others at increased risk from pertussis.
  - On the appropriate action if the dose of dTpa recommended during pregnancy is administered before the third trimester.
  - On the appropriate action for future pertussis vaccines when a mother receives a dose of dTpa post-partum rather than in the third trimester of pregnancy.
  - On the recommended interval between DT-containing vaccines in two contexts: a) standard catch-up and b) maternal pertussis vaccination.
  - That a history of extensive limb swelling after a booster dose of DTPa is not a contraindication to future recommended doses of pertussis-containing vaccine.
- Factual changes to chapter/s, including:
  - Addition of combination pertussis-containing vaccine, Hexaxim, to the vaccine information box.
  - Updates to Product Information.

Chapter 4.6 Human papillomavirus
- New text noting alternative schedule for 2vHPV in adolescent girls recently registered by the TGA (no change to ATAGI recommendation at this stage).

Chapter 4.13 Pneumococcal disease
- Clarification of advice on the co-administration of trivalent influenza vaccines and 13-valent pneumococcal conjugate vaccines in children, in alignment with update to the Influenza chapter (including new reference).
- Clarification of advice on pneumococcal vaccination during pregnancy and breastfeeding.

Chapter 4.20 Tuberculosis
- New text advising on the event of a shortage of the currently registered BCG vaccine and usage of alternative vaccine products.
- New sub-section providing advice on the co-administration of BCG vaccine with other vaccines.
- New sub-section providing advice on BCG vaccination before or after immunoglobulin or blood product administration.

Chapter 4.23 Yellow fever (Category II update – went out to public consultation)
- Updated ATAGI advice that 10-yearly booster doses are no longer routinely recommended except for groups/circumstances who are specified.
- Clarification of advice, including:
  - On the co-administration of yellow fever vaccine with other parenteral live vaccines.
  - On circumstances when vaccination can be considered for pregnant and breastfeeding women.
  - Of groups for whom yellow fever vaccination is contraindicated and appropriate mosquito avoidance advice for such individuals.
  - On the vaccine requirements that need to be meet under updated International Health Regulations (both in Australia and internationally).

Chapter 4.24 Zoster
- Clarification of advice on the administration of live vaccines to patients receiving or planning treatment with biological and non-biological disease modifying anti-rheumatic drugs (DMARDs).
- Removal of sub-section providing advice on the co-administration of zoster vaccine with other vaccines as information already provided earlier in chapter.
Key updates made to the 10th edition Handbook in March 2016 are listed below by chapter, including chapter sections and subsections. Other minor amendments to those listed below have been made to improve clarity, consistency and accuracy; these changes are not specifically noted.

References have been removed, updated or introduced where required.

Note: The updated chapter is available online only in HTML formats.

4.7 Influenza

Terminology referring to the Seqirus (previously bioCSL) brand of trivalent influenza vaccine has been changed throughout the influenza chapter.

4.7.3 Epidemiology and 4.7.4 Vaccines

Most up-to-date information on influenza epidemiology (including Figure 4.7.1: Average annual influenza notification and hospitalisation rates for 2010 to 2013, Australia, by age group) and evidence on influenza vaccines added.

4.7.6 Dosage and administration

Information added on the appropriate action if a child aged 6 months to <3 years inadvertently receives a 0.5 mL dose of influenza vaccine, including in Table 4.7.1: Recommended doses of influenza vaccine.

Advice on the number of doses of annual influenza vaccine required for children aged 6 months to <9 years, based on their previous vaccination history, has been updated in Table 4.7.1: Recommended doses of influenza vaccine.

4.7.6 Dosage and administration and 4.7.7 Recommendations

Advice specifically on the use of quadrivalent influenza vaccine formulations has been included.

4.7.6 Dosage and administration and 4.7.10 Precautions

Information added on the co-administration of trivalent influenza vaccines and 13-valent pneumococcal conjugate vaccine in children.
22 June 2015

Key updates made to the 10th edition Handbook in June 2015 are listed below by chapter, including chapter sections and subsections. In addition to the updates listed below, other minor amendments have been made to some chapters to improve clarity, consistency and accuracy; these changes are not specifically noted.

References have been removed, updated or introduced where required.

2.1 Pre-vaccination

2.1.4 Pre-vaccination screening

Information on vaccination of infants born to mothers receiving immunosuppressive therapy during pregnancy added to Table 2.1.1: Pre-vaccination screening checklist and Table 2.1.2: Responses to relevant conditions or circumstances identified through the pre-vaccination screening checklist.

2.1.5 Catch-up

Link to resource for international immunisation schedules updated.

Information added on the acceptable minimum intervals and age restrictions for primary hepatitis B vaccine doses in infants and appropriate action if these are not met, including in Table 2.1.7: Minimum acceptable dose intervals for children <10 years of age (refer also to 4.5 Hepatitis B (Handbook10-home-handbook10part4-handbook10-4-5)).

Advice on catch-up vaccination for pertussis-containing vaccines updated, including in Table 2.1.6: Number of vaccine doses that should have been administered by the current age of the child and Table 2.1.7: Minimum acceptable dose intervals for children <10 years of age (refer also to 4.12 Pertussis (Handbook10-home-handbook10part4-handbook10-4-12)).

Advice on catch-up vaccination for meningococcal vaccines updated, including in Table 2.1.5: Minimum acceptable age for the 1st dose of scheduled vaccines in infants in special circumstances and Table 2.1.7: Minimum acceptable dose intervals for children <10 years of age (refer also to 4.10 Meningococcal disease (Handbook10-home-handbook10part4-handbook10-4-10)).

2.2 Administration of vaccines

2.2.2 Equipment for vaccination

Information on the need to shake vials, pre-filled syringes or reconstituted vaccines added.

2.2.3 Route of administration and 2.2.5 Vaccine injection techniques

Information on Intanza intradermal vaccine formulations removed, including from Table 2.2.1: Route of administration for vaccines used in Australia (refer also to 4.7 Influenza (Handbook10-home-handbook10part4-handbook10-4-7)).

2.2.4 Preparation for vaccine administration

Advice on the prophylactic use of paracetamol added (refer also to 4.10 Meningococcal disease (Handbook10-home-handbook10part4-handbook10-4-10)).

2.3 Post-vaccination

2.3.1 Immediate after-care and 2.3.2 Adverse events following immunisation

Advice on the prophylactic use of paracetamol updated (refer also to 4.10 Meningococcal disease (Handbook10-home-handbook10part4-handbook10-4-10)).

Information on complex regional pain syndrome added.

3.1 Vaccination for Aboriginal and Torres Strait Islander people

3.1.1 Children

Recommendation for the use of influenza vaccines updated (refer to 4.7 Influenza (Handbook10-home-handbook10part4-handbook10-4-7)).

3.2 Vaccination for international travel

3.2.2 Infections acquired by travellers, 3.2.4 Vaccines and 3.2.5 Vaccinating the traveller with special risk factors

Information on the risk of Japanese encephalitis to travellers added (refer also to 4.8 Japanese encephalitis (Handbook10-home-handbook10part4-handbook10-4-8)).

3.2.3 Practical aspects of recommending vaccinations for travellers and 3.2.4 Vaccines

Information on international health regulations related to polio added (refer also to 4.14 Poliomyelitis (Handbook10-home-handbook10part4-handbook10-4-14)).

3.2.4 Vaccines

Recommendations on the use of meningococcal vaccines updated (refer also to 4.10 Meningococcal disease (Handbook10-home-handbook10part4-handbook10-4-10)).

Information on Intanza intradermal vaccine formulations removed from Table 3.2.1: Dose and routes of administration of commonly used vaccines in adult travellers (refer also to 4.7 Influenza (Handbook10-home-handbook10part4-handbook10-4-7)), Advice on the ages at which to use Japanese encephalitis vaccines updated in Table 3.2.2: Recommended lower age limits of travel vaccines for children (refer also to 4.8 Japanese encephalitis (Handbook10-home-handbook10part4-handbook10-4-8)).

3.2.4 Vaccines and 3.2.5 Vaccinating the traveller with special risk factors

Recommendations on the use of meningococcal vaccines updated (refer to 4.10 Meningococcal disease (Handbook10-home-handbook10part4-handbook10-4-10)).

3.3 Groups with special vaccination requirements

3.3.2 Vaccination of women who are planning pregnancy, pregnant or breastfeeding, and preterm infants and 3.3.3 Vaccination of immunocompromised persons

Information on the vaccination of infants born to mothers receiving immunosuppressive therapy during pregnancy added.

Recommendations on the use of pertussis-containing vaccines in pregnant women updated, including in Table 3.3.1: Recommendations for vaccination in pregnancy (refer to 4.12 Pertussis (Handbook10-home-handbook10part4-handbook10-4-12)).

3.3.3 Vaccination of immunocompromised persons

Information on Intanza intradermal influenza vaccine formulations removed from Table 3.3.5: Recommendations for vaccination in persons with functional or anatomical asplenia (refer also to 4.7 Influenza (Handbook10-home-handbook10part4-handbook10-4-7)).
3.3.3 Vaccination of immunocompromised persons and 3.3.7 Vaccination of persons at occupational risk

Recommendations on the use of meningococcal vaccines updated (refer to 4.10 Meningococcal disease (Handbook10-home~handbook10part4~handbook10-4-10)).

4.2 Diphtheria

4.2.4 Vaccines, 4.2.7 Recommendations and 4.2.8 Pregnancy and breastfeeding

Recommendations on the use of pertussis-containing vaccines updated (refer to 4.12 Pertussis (Handbook10-home~handbook10part4~handbook10-4-12)).

4.3 Haemophilus influenzae type b

4.3.4 Vaccines, 4.3.6 Dosage and administration and 4.3.7 Recommendations

Information on the use of the Hib-MenCCV combination vaccine added.

4.4 Hepatitis A

4.4.7 Recommendations

Lifestyle risk factors for hepatitis A clarified.

4.5 Hepatitis B

4.5.4 Vaccines

Information on accelerated hepatitis B schedules added.

4.5.7 Recommendations

Clinical course of action for sexual contacts of persons with hepatitis B clarified.

4.5.4 Vaccines and 4.5.7 Recommendations

Acceptable minimum intervals and age requirements for primary hepatitis B vaccine doses and the appropriate action if these are not met has been clarified (refer also to 2.1 Pre-vaccination (Handbook10-home~handbook10part2~handbook10-2-1)).

4.6 Human papillomavirus

4.6.4 Vaccines

Information on next-generation HPV vaccines and schedules under development added.

4.7 Influenza

Terminology referring to the bioCSL brand of trivalent influenza vaccine has been changed throughout the influenza chapter and other chapters if required.

4.7.4 Vaccines and 4.7.11 Adverse events

Information on inactivated quadrivalent influenza vaccine formulations added (including in vaccine information box).

4.7.4 Vaccines and 4.7.6 Dosage and administration

Information on Intanza intradermal vaccine formulations removed.

4.7.6 Dosage and administration

Upper age limit for when children require 2 doses of inactivated influenza vaccine if receiving for the first time clarified.

4.7.7 Recommendations

Number of doses of annual influenza vaccine required in persons with immunocompromising conditions clarified (refer also to 3.3 Groups with special vaccination requirements (Handbook10-home~handbook10part3~handbook10-3-3)).

Information on influenza vaccine recommendations for preterm infants added.

Recommendations on the use of influenza vaccines updated, including:

- Persons at increased risk of complications from influenza infection for whom vaccination is recommended expanded to include individuals with a BMI ≥40 and individuals with chronic liver disease.
- Annual influenza vaccine is now recommended for all Aboriginal and Torres Strait Islander children.

4.8 Japanese encephalitis

4.8.3 Epidemiology and 4.8.7 Recommendations

Information on the risk of Japanese encephalitis to travellers added (refer also to 3.2 Vaccination for international travel (Handbook10-home~handbook10part3~handbook10-3-2)).

4.8.4 Vaccines

Information on accelerated schedule for JEpect added.

4.8.6 Dosage and administration

Information on the interchangeability of Japanese encephalitis vaccines added.

Recommendations on the use of Japanese encephalitis vaccines updated, including:

- JEpect can now be given at the same time as quadrivalent meningococcal vaccine and rabies vaccine, and Imojev can be given at the same time as MMR vaccine.

4.8.4 Vaccines and 4.8.6 Dosage and administration

Advice on the age of use for Japanese encephalitis vaccines updated, including a new table, Table 4.8.1: Recommended doses of JE vaccines (refer also to 3.2 Vaccination for international travel (Handbook10-home~handbook10part3~handbook10-3-2)).

4.8.4 Vaccines, 4.8.6 Dosage and administration and 4.8.7 Recommendations

Recommendations on the use of Japanese encephalitis vaccines updated, including:

A booster dose of Imojev is now recommended in children aged ≥9 months to <18 years and a booster dose of JEspect is recommended in adults aged ≥18 years.

4.8.4 Vaccines, 4.8.6 Dosage and administration and 4.8.13 Variations from product information

Recommendations on the use of Japanese encephalitis vaccines updated, including:

- JEspect can now be given to children aged ≥2 months to <18 years in circumstances where an alternative is not available or contraindicated.

4.8.10 Precautions

Information on vaccination after immunoglobulin or blood product administration added.

4.9 Measles

4.9.10 Precautions and 4.9.11 Adverse events

Advice on the prophylactic use of paracetamol updated (refer also to 4.10 Meningococcal disease).

4.9.12 Public health management of measles

Advice on post-exposure management of measles clarified in Table 4.9.2: Post-exposure prophylaxis required within 72 hours of first exposure for persons exposed to measles.

4.10 Meningococcal disease

This entire Handbook chapter has been reviewed and updated including:

- Addition of two new meningococcal vaccine formulations: meningococcal B vaccine (Bexsero) and quadrivalent meningococcal conjugate vaccine (Nimenrix).
- Recommendations on the use of Bexsero.
- Recommendations for the use of prophylactic administration of paracetamol with Bexsero as an exception to routine Handbook recommendations.
- Recommendations for vaccination of groups at increased risk of meningococcal disease including men who have sex with men, college students, new military recruits and people with HIV.
- Recommendations for vaccination of persons with certain medical conditions (including age of use and booster recommendations by vaccine brand).
- Recommendations for vaccination of travellers (including age of use and booster recommendations by vaccine brand).

4.13 Pneumococcal disease

4.13.4 Vaccines, 4.13.6 Dosage and administration, 4.13.7 Recommendations, 4.13.11 Adverse events and 4.13.12 Variations from product information

Information on registration of 13vPCV for use from 6 weeks of age added.

4.13.6 Dosage and administration

Recommendation for the use of pneumococcal polysaccharide vaccine updated:

Co-administration of 23vPPV and Zostavax is acceptable (refer also to 4.24 Zoster).

4.14 Poliomyelitis

4.14.7 Recommendations

Information on international health regulations related to polio added (refer also to 3.2 Vaccination for international travel).

4.16 Rabies and other lyssaviruses (including Australian bat lyssavirus)

4.16.5 Rabies immunoglobulin

Information added on alternative products for use during potential shortages of rabies immunoglobulin.

4.16.8 Recommendations

Information added on appropriate post-exposure prophylaxis following a potential exposure to a terrestrial animal in an area where rabies is not enzootic.

4.19 Tetanus

4.19.4 Vaccines, 4.19.7 Recommendations, 4.19.8 Pregnancy and breastfeeding and 4.19.14 Variations from product information

Recommendations on the use of pertussis-containing vaccines updated (refer to 4.12 Pertussis).

4.22 Varicella

4.22.11 Adverse events

Advice on the prophylactic use of paracetamol updated (refer also to 4.10 Meningococcal disease).

4.23 Yellow fever

4.23.7 Recommendations

Information on booster dose requirements under International Health Regulations added.

4.24 Zoster (herpes zoster)

4.24.6 Dosage and administration

Recommendations on the use of zoster vaccine updated, including:

Co-administration of 23vPPV and Zostavax is acceptable (refer also to 4.13 Pneumococcal disease).

4.24.7 Recommendations

Recommendations on the use of zoster vaccine updated, including:

Zostavax recommendations now broken down by new age groups.
Key updates made to the 10th edition Handbook in March 2015 are listed below by chapter, including chapter sections and subsections. In addition to the updates listed below, other minor amendments have been made to some chapters to improve clarity, consistency and accuracy; these changes are not specifically noted.

References have been removed, updated or introduced where required.

Note: These updates are available online only in HTML and PDF formats.

4.12 Pertussis

4.12.4 Vaccines
Information on the vaccine formulation Infanrix added to the vaccine information box.
Information on pertussis-containing vaccines containing two pertussis antigen components added.

4.12.7 Recommendations
Recommendations on the use of pertussis-containing vaccines updated, including:

A booster dose of pertussis-containing vaccine is now recommended at 18 months of age (in addition to the booster dose already recommended at 4 years of age).

4.12.7 Recommendations and 4.12.8 Pregnancy and breastfeeding
Recommendations on the use of pertussis-containing vaccines updated, including:

- A dose of dTap (reduced antigen formulation) is now recommended for pregnant women in the third trimester of each pregnancy (optimally between 28 and 32 weeks) as the preferred strategy for reducing the risk of pertussis in young infants.
17 January 2014

17 January 2014

The individual amendments made in the January 2014 update of the 10th edition of the Handbook are listed below by chapter/section heading. The amended text is highlighted for easy identification. Page numbers indicate the page on which the amendment occurs in the hard copy version of the Handbook.

1.4 What's new

1.4.1 New chapters and chapters that no longer appear in the Handbook

The sixth bullet point under this heading (page 7) should read as follows:

- The chapter on smallpox has been deleted. For information on smallpox, see the Guidelines for smallpox outbreak, preparedness, response and management on the Department of Health website (http://www.health.gov.au/).

2.1 Pre-vaccination

2.1.2 Effective cold chain: transport, storage and handling of vaccines

Text in the first shaded box under this heading (page 25) should read as follows:

All immunisation service providers must be familiar with, and adhere to, the National vaccine storage guidelines: Strive for 5 (2nd edition) (IMM77-cnt). This publication can be accessed free of charge.

References

Reference 1 has been updated to:


(NB. This reference has also been updated in the reference lists for all disease chapters in Part 4 of the Handbook)

2.1.5 Catch-up

Under the sub-heading 'Planning catch-up vaccination', the seventh bullet point (page 42), should read as follows:

- When commencing the catch-up schedule, the standard scheduled interval between doses may be reduced or extended, and the numbers of doses required may reduce with age. For example, from 16 months of age, only 1 dose of (any) Hib vaccine is required.

In Table 2.1.5: Minimum acceptable age for the 1st dose of scheduled vaccines in infants in special circumstances, in the MenCCV row, the text in the Action (right hand) column (page 47) should read as follows:

<table>
<thead>
<tr>
<th>Vaccine</th>
<th>Minimum age for 1st dose in special circumstances (weeks)</th>
<th>Action if a vaccine dose is inadvertently administered prior to the recommended minimum age</th>
</tr>
</thead>
<tbody>
<tr>
<td>MenCCV</td>
<td>6</td>
<td>If any MenCCV doses are given before 12 months of age, then a booster dose of MenCCV should be given at 12 months of age or 6 weeks after the last dose, whichever is later. Note: MenCCV is routinely recommended at 12 months of age, although recommendations for children at increased risk of meningococcal disease differ (see 4.10 Meningococcal disease).</td>
</tr>
</tbody>
</table>

In Table 2.1.5: Minimum acceptable age for the 1st dose of scheduled vaccines in infants in special circumstances, the second footnote (†) (page 48) should read as follows:

† If the need to repeat the 1st dose of vaccine is not recognised until the infant is older (e.g. a 4-month-old infant presents for vaccination and has only previously received 1 dose of DTPa-hepB-IPV-Hib or 13vPCV vaccines both at age ≥28 days), repeat these vaccines now (and count these as dose 1), then proceed with subsequent schedule as per NIP and/or catch-up recommendations for these vaccines described in this chapter.

Table 2.1.8: Catch-up schedule for Haemophilus influenzae type b (Hib) vaccination for children 5 years of age (page 54-55)* - this table has been replaced:

- Table 2.1.8: Catch-up schedule for Haemophilus influenzae type b (Hib) vaccination for children 5 years of age (Handbook10-home~handbook10part2~handbook10-2-1#table-2-1-8)

2.2 Administration of vaccines*

2.2.8 Identifying the injection site

Under the sub-heading 'The ventrogluteal area', the first bullet point (page 81), should read as follows:

- Place the palm over the greater trochanter (the uppermost bony prominence of the thigh bone), with the thumb pointing towards the umbilicus. Point the index finger towards the anterior superior iliac spine, and spread the middle finger so it aims at the iliac crest, thus creating a 'V' outlining the ventrogluteal triangular area. The injection site is at the centre of this area shown in the diagram in Figure 2.2.7. Note: In small children and infants, the placement of the hand in relation to these anatomical markers may vary, as shown in the photograph in Figure 2.2.7.

2.3 Post-vaccination

2.3.2 Adverse events following immunisation

Under the sub-heading 'Uncommon/rare adverse events following immunisation', the third bullet point (page 93) should read as follows:

- Oral rotavirus vaccines are associated with a small increased risk of intussusception (IS), a rare form of bowel blockage caused by telescoping of the intestine into itself. This risk appears to be particularly in the 7 days following the 1st vaccine dose; however, a smaller increased risk in the week following the 2nd dose has also been reported. It is not currently clear whether there is an overall increase in the risk of IS above that which would be expected in the 1st year of infancy without vaccine use. The increased risk represents approximately 6 additional cases of intussusception among every 100 000 infants vaccinated, or 14 additional cases per year in Australia. Children who have had IS are recommended not to receive rotavirus vaccine (see 4.17 Rotavirus).

References


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3.3 Groups with special vaccination requirements

3.3.7 Vaccination of persons at occupational risk

In Table 3.3.7: Recommended vaccinations for persons at increased risk of certain occupationally acquired vaccine-preventable diseases, text in the first row of the Healthcare workers (HCW) column (page 170) should read as follows:

<table>
<thead>
<tr>
<th>Occupation</th>
<th>Vaccine</th>
</tr>
</thead>
<tbody>
<tr>
<td>All HCW</td>
<td>Includes all workers and students directly involved in patient care or the handling of human tissue, blood or body fluids</td>
</tr>
<tr>
<td></td>
<td>Hepatitis B</td>
</tr>
<tr>
<td></td>
<td>Influenza</td>
</tr>
<tr>
<td></td>
<td>MMR (if non-immune)</td>
</tr>
<tr>
<td></td>
<td>Pertussis (dTpa)</td>
</tr>
<tr>
<td></td>
<td>Varicella (if non-immune)</td>
</tr>
</tbody>
</table>

3.3.8 Vaccination of migrants to Australia

The sixth paragraph under this heading (page 174) should read as follows:

Migrant/refugee adults also need to be targeted for vaccination, especially against rubella, using MMR vaccine. This is particularly important for women of child-bearing age. Some refugees aged between 9 months and 54 years may have been offered MMR as part of a pre-departure screening, but may require a subsequent dose on arrival in Australia. It is important to take into account any live attenuated viral vaccines that may have been administered as part of a pre-departure screening, such as measles-containing vaccines or yellow fever vaccine (especially in those persons arriving from central and northern African nations). It is important to allow a minimum 4-week interval before administering any other live attenuated viral vaccines.

References
Reference 170 has been updated to:

4.3 Haemophilus influenzae type b

4.3.7 Recommendations

Under the sub-heading ‘Booster doses’, the second paragraph (page 195) should read as follows:

Children aged >15 months and up to 59 months of age at presentation who have not received a primary course of a Hib or Hib-containing vaccine will only require 1 dose of vaccine as catch-up, irrespective of the number of previous doses administered. There should be a minimum 2-month interval between their last dose and the catch-up dose. Catch-up for Hib vaccination for children up to 59 months of age is outlined in Table 2.1.8 Catch-up schedule for Hib vaccination for children <5 years of age in 2.1.5 Catch-up.

4.5 Hepatitis B

4.5.7 Recommendations

Under the sub-heading ‘Persons at occupational risk’, the first paragraph (page 223) should read as follows:

The risk to persons in certain occupations differs considerably from setting to setting in different parts of Australia. However, it is recommended that all staff directly involved in patient care and/or the handling of human tissue, blood or body fluids should be vaccinated. In addition, standard precautions against exposure to human tissue, blood or body fluids should be used as a matter of routine. Under the sub-heading ‘Persons at occupational risk’, the first bullet point (page 223) should read as follows:

- police, members of the armed forces, emergency services staff and staff of correctional facilities; these persons should be vaccinated if they are assigned to duties that may involve exposure to human tissue, blood or body fluids

Under the sub-heading ‘Serological testing following hepatitis B vaccination’ the first bullet point (page 225) should read as follows:

- those at significant occupational risk (e.g. healthcare workers whose work involves frequent exposure to human tissue, blood or body fluids)

4.5.11 Public health management of hepatitis B

In Table 4.5.3: Post-exposure prophylaxis for non-immune persons exposed to a HbsAg-positive source, in the Perinatal exposure row, text in the Vaccine (right hand) column (page 229) should read as follows:

<table>
<thead>
<tr>
<th>Type of exposure</th>
<th>Hepatitis B immunoglobulin</th>
<th>Vaccine</th>
</tr>
</thead>
<tbody>
<tr>
<td>Perinatal (exposure of babies during and after birth)</td>
<td>100 IU, by IM injection</td>
<td>Single dose immediately after birth (preferably within 12 hours of birth and certainly within 48 hours)</td>
</tr>
</tbody>
</table>

4.9 Measles

4.9.7 Recommendations

Under the sub-heading ‘Infants aged <12 months’, the second paragraph (page 272) should read as follows:
Two doses of measles-containing vaccine should be administered at ≥12 months of age. Maternal antibodies to measles are known to persist in many infants until approximately 11 months of age and may interfere with active immunisation before 12 months of age. However, there is some evidence that a dose provided at ≥11 months (but prior to 12 months) of age is sufficiently immunogenic; as such, doses given in this timeframe may not need to be repeated in all circumstances (see also Table 2.1.5 Minimum acceptable age for the 1st dose of scheduled vaccines in infants in special circumstances).

Under the sub-heading 'Children', the fifth paragraph (page 272) should read as follows:

If MMRV vaccine is inadvertently administered as dose 1 of MMR–containing vaccine, the dose does not need to be repeated (providing it was given at ≥12 months of age; see Table 2.1.5 Minimum acceptable age for the 1st dose of scheduled vaccines in infants in special circumstances). However, parents/carers should be advised regarding the small but increased risk of fever and febrile seizures (compared with that expected following MMR vaccine).

4.13 Pneumococcal disease

4.13.6 Dosage and administration

The fourth paragraph under this heading (page 323) should read as follows:

13vPCV (Prevenar 13) is registered for use in infants and children aged 6 weeks up to 17 years and adults aged ≥50 years.

4.13.12 Variations from product information

The second paragraph under this heading (page 336) should read as follows:

13vPCV is registered for use in children up to 17 years of age and adults aged ≥50 years. The ATAGI recommends a dose of 13vPCV for adults of any age who have a condition(s) associated with the highest risk of IPD (see List 4.13.1, Category A). This is based on the likely benefit outweighing uncertainties and risks, and on immunogenicity and safety data in children.

4.17 Rotavirus

4.17.11 Adverse events

Under the sub-heading 'Intussusception', the sentence beginning 'The increased risk of IS...’ in the first paragraph (page 382) should read as follows:

The increased risk of IS following rotavirus vaccination, from the most recent Australian study, is estimated as approximately 6 additional cases of intussusception among every 100 000 infants vaccinated, or 14 additional cases per year in Australia.14

References


References

Reference 74 has been updated to:

3.3 Groups with special vaccination requirements

3.3.5 Vaccination of persons with bleeding disorders

The first paragraph under this heading (page 168) should read as follows:

Persons who are receiving anticoagulant therapy may develop haematomas in IM injection sites. The length of anticoagulant therapy should be clarified and immunisation delayed if therapy is going to be of short-term duration. Unless warfarin or low molecular weight heparin (LMWH) doses are known to be stable, persons receiving anticoagulants should have appropriate levels checked before vaccine administration, if possible. Intramuscular injections should be deferred if the INR is >3.0 (warfarin) or the anti-Xa (LMWH) level 4 hours post dose is >0.5 Units/mL.
1.1 Background
1.2 Development of the 10th edition of the Handbook
1.3 How to use the 10th Edition Handbook
1.4 What's new
1.5 Fundamentals of immunisation
1.1 Background

This chapter has been amended on 22 June 2015.

For more than 200 years, since Edward Jenner first demonstrated that vaccination offered protection against smallpox, the use of vaccines has continued to reduce the burden of many infectious diseases. Vaccination has been demonstrated to be one of the most effective and cost-effective public health interventions. Worldwide, it has been estimated that immunisation programs prevent approximately 2.5 million deaths each year.\(^1\) The declaration of the global eradication of smallpox in 1980, near elimination of poliomyelitis and global reduction in other vaccine-preventable diseases, are model examples of disease control through immunisation.

Vaccination not only protects individuals, but also protects others in the community by increasing the overall level of immunity in the population and thus minimising the spread of infection. This concept is known as 'herd immunity'. It is vital that healthcare professionals take every available opportunity to vaccinate children and adults. Australia has one of the most comprehensive publicly funded immunisation programs in the world. As a result of successful vaccination programs in Australia, many diseases, for example, tetanus, diphtheria, Haemophilus influenzae type b and poliomyelitis, do not occur now or are extremely rare in Australia.\(^2\)

The purpose of The Australian Immunisation Handbook is to provide clinical guidelines for health professionals on the safest and most effective use of vaccines in their practice. These recommendations are developed by the Australian Technical Advisory Group on Immunisation (ATAGI, (Australian Technical Advisory Group on Immunisation)) and were considered for approval by the National Health and Medical Research Council (NHMRC, (National Health and Medical Research Council)) (under section 14A of the NHMRC (National Health and Medical Research Council) Act 1992).

The Handbook provides guidance based on the best scientific evidence available at the time of publication from published and unpublished literature. Further details regarding the Handbook revision procedures are described below in 1.2 Development of the 10th edition of the Handbook. The reference lists for all chapters are included in the electronic version of the Handbook, which is available via the Immunise Australia website (http://www.immunise.health.gov.au).

Information is provided in the Handbook for all vaccines that are available in Australia at or near the time of publication. These include many vaccines that are funded under the National Immunisation Program (NIP, (National Immunisation Program)). A copy of the current NIP (National Immunisation Program) schedule is provided with the hard copy of the Handbook. However, the NIP (National Immunisation Program) schedule may also be updated regularly; immunisation service providers should consult the Immunise Australia website (http://www.immunise.health.gov.au) for changes. A number of vaccines included in this Handbook are not part of the routine immunisation schedule; these vaccines may be given to, for example, persons travelling overseas, persons with a medical condition placing them at increased risk of contracting a vaccine-preventable disease, or those at occupational risk of disease.

The information contained within the hard copy of the Handbook (published in 2013) was correct as at October 2012. However, the content of the Handbook is reviewed regularly. The 10th edition of The Australian Immunisation Handbook will remain current unless amended electronically via the Immunise Australia website or until the 11th edition of the Handbook is published.

Electronic updates to the 10th edition of The Australian Immunisation Handbook will be available via the Immunise Australia website(http://www.immunise.health.gov.au)

References

1.2 Development of the 10th edition of the Handbook

The 10th edition of the Handbook has been developed by the Australian Technical Advisory Group on Immunisation (ATAGI), which provides advice to the Federal Minister for Health on the Immunisation Australia Program and other vaccine-related issues. In addition to technical experts from many fields, the ATAGI (Australian Technical Advisory Group on Immunisation) membership includes a consumer representative and general practitioners. Staff of the National Centre for Immunisation Research and Surveillance of Vaccine Preventable Diseases (NCIRS) (National Centre for Immunisation Research and Surveillance) provided the technical support to the ATAGI (Australian Technical Advisory Group on Immunisation) to develop the Handbook.

It is important to note that recommendations contained within the Handbook do not formally address the cost-effectiveness of different vaccines or different vaccine schedules. Since January 2006, the cost-effectiveness of vaccines is assessed by the Pharmaceutical Benefits Advisory Committee (PBAC), which advises government on the funding of vaccines under the National Immunisation Program and/or Pharmaceutical Benefits Scheme (PBS). Most, but not all, of the recommendations made within the Handbook will be funded under the NIP (National Immunisation Program). PBAC (Pharmaceutical Benefits Advisory Committee) or via other means, such as through special schemes and state- or territory-based programs.

1.2.1 Process of developing Handbook recommendations

The Handbook is designed as a general guide to inform clinicians on the safest and most effective vaccination strategies, using the highest quality evidence available. In the absence of high-quality evidence, such as well-conducted randomised controlled trials and meta-analyses, the ATAGI (Australian Technical Advisory Group on Immunisation) based its recommendations on less rigorous studies, such as uncontrolled clinical trials, case-series and/or other observational studies. Where clinical guidelines were available on specific topics, these were also consulted to help frame recommendations, if relevant, in the Australian setting. Further details on literature search strategies utilised for the production of this edition can be found in Appendix 2 (Handbook10-tools-handbook10-appendices-handbook10-appendix2). The ATAGI (Australian Technical Advisory Group on Immunisation) also consulted immunisation handbooks produced by comparable countries. When published sources were inadequate, recommendations were based on expert opinion. However, limitations and challenges to developing recommendations continue to exist when there are unaddressed scientific questions, complex medical practice issues and continuous new information, as well as differences in expert opinion. Despite these limitations, the ATAGI (Australian Technical Advisory Group on Immunisation) has sought to provide clear and relevant recommendations wherever possible.

The 1st edition of The Australian Immunisation Handbook was published in 1975. Due to its longevity, scope and complexity, the Handbook does differ from other NHMRC (National Health and Medical Research Council) guidelines. As such, recommendations contained in the Handbook do not contain formal levels or grades of evidence or evidence tables. The grades of evidence assigned to recommendations for the three newly vaccine-preventable diseases (human papillomavirus (HPV), rotavirus and herpes zoster) that were included in the 9th edition Handbook (and its electronic amendments) have now been removed and replaced with an evidence statement for consistency with other chapters in the 10th edition of the Handbook. The ATAGI (Australian Technical Advisory Group on Immunisation) has developed new recommendations for the Handbook after considering clinical questions, reviewing available evidence, as described above, and through extensive consultation with other experts (described below). Evidence statements for recommendations, with cross reference to other relevant sections of the Handbook, have been included wherever possible.

1.2.2 Consultation and input into the draft 10th edition Handbook

Prior to completion of the draft 10th edition Handbook, the ATAGI (Australian Technical Advisory Group on Immunisation) sought expert review of individual chapters by leading Australian experts. These reviewers, who are acknowledged in the front of this Handbook, provided input to further refine each chapter. The ATAGI (Australian Technical Advisory Group on Immunisation) also, where relevant, consulted members of each of its current disease-based Working Parties. Other peak advisory groups, in particular the National Immunisation Committee, were also consulted and provided valuable input into the development of this revised edition. The draft 10th edition of the Handbook was available for public consultation over a 4-week period during July–August 2012. The ATAGI (Australian Technical Advisory Group on Immunisation) reviewed all public comments received and, where necessary, incorporated these as changes to the Handbook. The NHMRC (National Health and Medical Research Council) was also consulted throughout the development of the 10th edition of the Handbook, prior to the Handbook being proposed for submission to the NHMRC (National Health and Medical Research Council) for consideration of approval (under section 14A of the NHMRC (National Health and Medical Research Council) Act 1992).

1.2.3 Implementation of recommendations in the 10th edition Handbook

The 10th edition of the Handbook is disseminated directly to all registered medical practitioners in Australia. Additional hard copies are distributed to other immunisation service providers via their state or territory health authority. An electronic version of the Handbook is freely accessible on the Immunise Australia Program website (home). Implementation of the recommendations as stated in the Handbook is undertaken by immunisation service providers in conjunction with their state or territory health authority and the Immunise Australia Program of the Australian Government Department of Health.
There are a number of appendices, including contact details for state and territory health departments (Appendix 1), the literature search strategies used for the 10th edition of the Handbook (Appendix 2); some commonly asked questions (Appendix 4); a glossary of terms used in the Handbook (Appendix 5); abbreviations used in the Handbook (Appendix 6); and a list of dates when various vaccines became available in Australia (Appendix 7).
1.4 What's new

A 'Pregnancy and breastfeeding' section has been added to all disease chapters. Where relevant, information on co-administration with other vaccines and interchangeability of vaccines is now included in the 'Dosage and administration' section of disease chapters.

- Advice is now provided on the use of vaccines in multi-dose vials.
- Information on the burden of influenza in Indigenous children, and the rationale for vaccination of those, especially ≥6 months to <5 years of age, has been included.

The Evidence Grades assigned in the 9th edition to recommendations contained within three chapters – Human papillomavirus, Rotavirus and Zoster (online only) – have been removed (see discussion in 1.2 Development of the 10th edition of the Handbook regarding Handbook development).

1.4.1 New chapters and chapters that no longer appear in the Handbook

- Part 1 (Handbook10-home-handbook10part1) now includes the development process for the Handbook (previously in Appendix 2).
- Part 2 (2.3.2) Handbook10-home-handbook10appendices-handbook10-appendix2) and information on the fundamentals of immunisation, including passive and active immunisation, vaccine efficacy and vaccine safety.
- The chapter on Australian bat lyssavirus and rabies is now listed under Rabies and other lyssaviruses (including Australian bat lyssavirus) in the alphabetical list of diseases in Part 4 (Handbook10-home-handbook10part4).
- The chapter on zoster (herpes zoster) is now included as a disease chapter in Part 4 (Handbook10-home-handbook10part4) in this printed version of the 10th edition. It had previously been available as an online update to the 9th edition.
- The chapter on smallpox has been deleted. For information on smallpox, see the Guidelines for smallpox outbreak, preparedness, response and management on the Department of Health website (http://www.health.gov.au/).

- Some appendices contained in the 9th edition have been deleted:
  - Definitions of adverse events following immunisation (previously Appendix 6): some common adverse events are now defined in the glossary of technical terms and an expanded section on adverse events following immunisation is now provided in Part 2 (2.3.2) Handbook10-home-handbook10part2-handbook10-2-3E2-3-2).
  - Summary table – for a vaccination encounter (previously Appendix 10): this information is now incorporated throughout Part 2 (Handbook10-home-handbook10part2).

1.4.2 Changes to the format of disease chapters in Part 4

- Where relevant, information on reconstitution and stability of reconstituted vaccines has been included in the 'Transport, storage and handling' section of disease chapters.
- Where relevant, information on co-administration with other vaccines and interchangeability of vaccines is now included in the 'Dosage and administration' section of disease chapters.
- A 'Pregnancy and breastfeeding' section has been added to all disease chapters.
- Information on the public health management of each disease is only given in detail where there are specific additional recommendations for vaccine use in the context of disease control and/or post-exposure prophylaxis. The reader is referred to published guidelines from the Communicable Diseases Network Australia (CDNA) (Communicable Diseases Network Australia), where available.
- The Evidence Grades assigned in the 9th edition to recommendations contained within three chapters – Human papillomavirus, Rotavirus and Zoster (online only) – have been removed (see discussion in 1.2 Development of the 10th edition of the Handbook regarding Handbook development).

1.4.3 Overview of major changes to recommendations

The following list summarises major changes to recommendations and other important information that have occurred in each part of the 10th edition of the Handbook.

### Part 2 Vaccination procedures

#### 2.1 Pre-vaccination

- The checklist table (Table 2.1.5) containing information on the minimum acceptable age for the 1st vaccine doses in infants now provides advice on action required in case of early administration.
- Catch-up recommendations and tables are now for children aged <10 years (previously <8 years).
- Catch-up guidelines have been included for new vaccines (MMRV, MenB, MenC, MenW, Rubella and Varicella), Hib-MenCCV, 13vPCV and 10vPCV).
- Updated pneumococcal catch-up tables (Tables 2.1.9 (Handbook10-home-handbook10part2-handbook10-2-14#table-2-1-9), 2.1.10 (Handbook10-home-handbook10part2-handbook10-2-14#table-2-1-10) and 2.1.11 (Handbook10-home-handbook10part2-handbook10-2-14#table-2-1-11)) provide recommendations for use of pneumococcal vaccines up to the age of 5 years.
- Information is provided on the HALO (health, age, lifestyle, occupation) (health, age, lifestyle, occupation) principle for use when considering catch-up vaccination for adults.
- Additional vaccines (MenCCV, 13vPCV, 23vPPV, zoster) have been added to the catch-up table (Table 2.1.12 (Handbook10-home-handbook10part2-handbook10-2-14#table-2-1-12)) for adolescents and adults and this table now applies to persons ≥10 years of age (previously 8 years).

#### 2.2 Administration of vaccines

- Advice is now provided on the use of vaccines in multi-dose vials.
- Advice is provided on what to do if a vaccine is inadvertently administered via a route (e.g. intramuscular (IM) or subcutaneous (SC)) other than for which it is recommended.
- Information is now provided on vaccinating children with congenital limb malformation, children in spica casts, patients undergoing treatment for breast cancer, and patients with lymphoedema.
- The section on administration of multiple vaccine injections at the same visit now includes advice on the order in which to give sequential vaccines and advice on simultaneous injections by two providers.

#### 2.3 Post-vaccination

- The section on adverse events following immunisation has been enhanced and expanded, including use of adrenaline autoinjectors for anaphylaxis treatment and more information on reporting of adverse events following immunisation.
- Contact details are provided for obtaining HPV (human papillomavirus) vaccination history from the National HPV Vaccination Program Register (NHVPR) (National), or the HPV (human papillomavirus) Vaccine Program Register and other registers.

### Part 3 Vaccination for special risk groups

#### 3.1 Vaccination for Aboriginal and Torres Strait Islander people

- Information on the burden of influenza in Indigenous children, and the rationale for vaccination of those, especially ≥5 years to <5 years of age, has been included.
- It is now recommended that Aboriginal and Torres Strait Islander people have their risks and vaccination status for hepatitis B reviewed, be offered testing for previous hepatitis B
4.6 Human papillomavirus

HPV vaccination is now recommended for girls at the optimal age for vaccination of 11–13 years. A new table (Table 3.1.1) has been added summarising additional vaccines recommended for Aboriginal and Torres Strait Islander people.

3.2 Vaccination for international travel

This section has been updated and expanded and information on recommended vaccines is now divided into routinely recommended vaccines (that are not specifically related to travelling overseas) and selected vaccines that are recommended based on travel itinerary, activities and likely risk of disease exposure.

Information on more vaccines, including new vaccines, has been added to the tables outlining the dose and routes of administration (Table 3.2.1) (Handbook10-home-handbook10part3-handbook10-3-2#table-3-2-1)) and recommended lower age limits (Table 3.2.2) (Handbook10-home-handbook10part3-handbook10-3-2#table-3-2-2)) for vaccines for travellers.

3.3 Groups with special vaccination requirements

The section on vaccination of persons with a prior adverse event following immunisation has been expanded. Advice is provided on vaccination of persons with allergies, including egg allergy.

The section on vaccination of women who are planning pregnancy, pregnant or breastfeeding, and preterm infants has been updated and expanded.

The table of recommendations for vaccination in pregnancy (Table 3.3.1) (Handbook10-home-handbook10part3-handbook10-3-3#table-3-3-1)) has been updated to include all vaccines.

dTPa vaccine can be given during the third trimester of pregnancy as an alternative to post-partum or pre-conception vaccination.

The section on vaccination of immunocompromised persons, including transplant recipients and oncology patients, has been updated and expanded.

All immunocompromised persons, irrespective of age, who receive influenza vaccine for the first time are now recommended to receive 2 vaccine doses, at least 4 weeks apart, and 1 dose annually thereafter.

The tables of recommendations for vaccinations in solid organ transplant (Table 3.3.2) summarising vaccine recommendations in this group.

The section on vaccination of persons with autoimmune diseases has been expanded to include those undergoing treatment with immunosuppressive agents and those with Guillain-Barré syndrome and other chronic conditions (hypothyroidism and metabolic diseases).

The section on vaccination of recent recipients of normal human immunoglobulin and other blood products has been expanded.

The section on vaccination of persons with bleeding disorders has been updated to include new recommendations for when IM (intramuscular) injections should be deferred and advice regarding vaccination of persons with haemophilia.

The section on vaccination of migrants to Australia has been expanded.

A new section has been added to provide recommendations for vaccination for sex industry workers.

Part 4 Vaccine-preventable diseases

4.1 Cholera

If the interval between primary immunisation and booster dose is more than 6 months in children aged 2–6 years, or more than 2 years in adults and children aged >6 years, primary immunisation must be repeated.

4.2 Diphtheria, 4.19 Tetanus and 4.12 Pertussis

The 1st dose of DTaP-containing vaccines due at 2 months of age can be given as early as 6 weeks of age.

Advice is provided that an additional dose of pertussis-containing vaccine is given in the 2nd year of life (e.g. at 18 months of age) if parents wish to minimise the likelihood of their child developing pertussis.

The booster dose of DTaP-containing vaccine recommended at 4 years of age can be given as early as 3.5 years.

DTaP-containing vaccines can be used for primary or booster doses in children aged <10 years (previously 8 years). Unvaccinated or partially vaccinated contacts of pertussis cases should be offered DTaP-containing vaccines up to their 10th birthday (previously 8th); dTpa should be offered to those aged ≥10 years.

The 2nd booster dose recommended for adolescents (using dTPa) should preferably be given between 11 and 13 years of age.

Adults aged ≥65 years should be offered a single dTPa booster if they have not received one in the previous 10 years.

For adults who are in certain risk categories for acquiring pertussis, or transmitting it to vulnerable persons, revaccination with dTPa is recommended 10 years after receipt of a prior pertussis-containing vaccine. This interval can be shortened to 5 years in the context of pregnancy.

Information is provided on maternal vaccination with dTPa during the third trimester of pregnancy as an alternative to post-partum or pre-conception vaccination.

For persons undertaking high-risk travel, a 5-yearly booster dose with dT or dTPa should be considered for protection against tetanus. In other travellers, a booster dose of tetanus-containing vaccine should be provided if 10 years have elapsed since the previous dose.

More information on the definition of ‘tetanus-prone wounds’ is provided, and the Table (4.19.1) summarising vaccine recommendations in this group.

4.3 Haemophilus influenzae type b

Combination Hib-meningococcal C vaccine (Hib-MenCCV) included.

Hib vaccination recommendations apply to all children, including Aboriginal and Torres Strait Islander children, as only PRP-T Hib vaccines have been in use in recent years.

4.4 Hepatitis A

The section on serological testing for hepatitis A prior to vaccination has been expanded, and more detail provided as to rationale for vaccination of certain groups.

Hepatitis A vaccination is recommended in preference to N/HIG (normal human immunoglobulin) for use in post-exposure prophylaxis in immunocompetent persons ≥12 months of age.

4.5 Hepatitis B

Different schedules for hepatitis B vaccination, including minimum intervals between doses, have been described in more detail.

Advice is provided regarding the validity of a hepatitis B vaccine schedule used for children born overseas, who were vaccinated at birth, 1 month and 6 months of age.

Information is provided on checking for infection/immunocompetence to hepatitis B in infants born to mothers with chronic hepatitis B infection 3 to 12 months after the primary vaccine course.

It is now recommended that Aboriginal and Torres Strait Islander people have their risks and vaccination status for hepatitis B reviewed, be offered testing for previous hepatitis B infection, and be offered vaccination if non-immune.

Migrants from hepatitis B endemic countries should be offered testing for hepatitis B, and vaccination if appropriate.

The section on serological testing for hepatitis B prior to vaccination has been expanded, and more detail provided as to rationale for testing and/or vaccination of certain groups, including hepatitis B vaccine non-responders.

4.6 Human papillomavirus

HPV (human papillomavirus) vaccination is now recommended for girls at the optimal age for vaccination of 11–13 years.
4.16 Rabies and other lyssaviruses (including Australian bat lyssavirus)

Recommendations for use of HPV (human papillomavirus) vaccine in immunocompromised persons and men who have sex with men are now included.

4.15 Q fever

Information and recommendations on management of all potential lyssavirus exposures, including lyssavirus infection from exposure to bats in non-rabies-enzootic countries, is now included. Algorithms are provided with details of the recommended management pathways for post-exposure prophylaxis for lyssavirus infections, including lyssavirus infection from exposure to bats in non-rabies-enzootic countries. Guidance in use of pre-exposure prophylaxis has been added.

A table (http://www.immunise.health.gov.au/internet/immunise/publishing.nsf/Content/Handbook10-home~handbook10part4~handbook10-4-16#table-4-16-2) summarising recommendations for vaccination of adults with 23vPPV has been revised and expanded to include more specific age ranges.

More information on serological testing and revaccination of women of child-bearing age who are non-immune to rabies is included.

4.14 Poliomyelitis

A booster dose of IPV (inactivated poliovirus vaccine) is recommended at 4 years of age, but can be given as early as 3.5 years.

4.13 Pneumococcal disease

- 10-valent (10vPCV) and 13-valent (13vPCV) pneumococcal conjugate vaccines are included.
- For Aboriginal and Torres Strait Islander children living in the Northern Territory, South Australia or Western Australia, a booster dose of 13vPCV at 12–18 months of age replaces the booster dose of 23vPPV at 18–24 months of age.
- The list of conditions associated with increased risks of invasive pneumococcal disease is updated, and changed from the recommendations provided in the 9th edition. It is stated that MMRV (Measles, Mumps, Rubella and Varicella) vaccines will be available in Australia from July 2013.

Information on the disease burden and benefits of influenza vaccination in pregnancy and in children aged 6 months and <5 years has been expanded.

The list of persons at increased risk of complications from influenza infection has been expanded to include persons with significant obesity and persons with Down syndrome. Alcoholism has been added to the list of chronic illnesses increasing the risk of complications from influenza infection.

Immune compromised persons, irrespective of age, who receive influenza vaccine for the first time are now recommended to receive 2 vaccine doses, at least 4 weeks apart, and 1 dose annually thereafter.

Influenza vaccination is now also recommended for staff working in early childhood education and care and for persons working in the pork industry.

4.12 Meningococcal disease

- For young children with medical risk factors for meningococcal disease, meningococcal C conjugate vaccine (MenCCV) is recommended in those aged 6 weeks to <12 months; thereafter 4vMenCV is recommended in a 2-dose schedule at approximately 12 and 18 months of age.
- 4vMenCV is preferred over the quadrivalent meningococcal polysaccharide vaccine (4vMenPV) for use in persons aged ≥9 months who are at increased risk of meningococcal disease.
- Quadrivalent meningococcal conjugate vaccines (4vMenCV) have been included.
- For Aboriginal and Torres Strait Islander children living in the Northern Territory, Queensland, South Australia or Western Australia, a booster dose of 13vPCV at 12–18 months of age replaces the booster dose of 23vPPV at 18–24 months of age.
- The list of conditions associated with increased risks of invasive pneumococcal disease (IPD) has been revised and expanded to include more specific age ranges,
- More information on serological testing and revaccination of women of child-bearing age who are non-immune to rabies is included.

4.11 Measles, Mumps and Rubella

- The 1st dose of MMR (Measles, Mumps, Rubella) vaccine is to be used for the 1st dose at 12 months of age. MMRV (Measles, Mumps, Rubella and Varicella) vaccines are not recommended for use as the 1st dose of MMR (Measles, Mumps and Rubella)-containing vaccine in children <4 years of age.

Information and recommendations on management of all potential lyssavirus exposures, including lyssavirus infection from exposure to bats in non-rabies-enzootic countries, is now included. Algorithms are provided with details of the recommended management pathways for post-exposure prophylaxis for lyssavirus infections, including lyssavirus infection from exposure to bats in non-rabies-enzootic countries. Guidance in use of pre-exposure prophylaxis has been added.

A table (http://www.immunise.health.gov.au/internet/immunise/publishing.nsf/Content/Handbook10-home~handbook10part4~handbook10-4-13#list-4-13-1) summarising recommendations for vaccination of adults with 23vPPV has been revised and expanded to include more specific age ranges.

More information on serological testing and revaccination of women of child-bearing age who are non-immune to rabies is included.

4.10 Influenza

4.9 Measles, Mumps and Rubella

- 2 new JE (Japanese Encephalitis) vaccines are included.
- Advice on booster doses and information on adverse events have been updated.

4.8 Japanese encephalitis

- 2 new JE (Japanese Encephalitis) vaccines are included.
- Advice on booster doses and information on adverse events have been updated.

4.7 Influenza

4.6 Measles, 4.11 Mumps, 4.18 Rubella and 4.22 Varicella

Information and recommendations on management of all potential lyssavirus exposures, including lyssavirus infection from exposure to bats in non-rabies-enzootic countries, is now included. Algorithms are provided with details of the recommended management pathways for post-exposure prophylaxis for lyssavirus infections, including lyssavirus infection from exposure to bats in non-rabies-enzootic countries. Guidance in use of pre-exposure prophylaxis has been added.

A table (http://www.immunise.health.gov.au/internet/immunise/publishing.nsf/Content/Handbook10-home~handbook10part4~handbook10-4-13#list-4-13-1) summarising recommendations for vaccination of adults with 23vPPV has been revised and expanded to include more specific age ranges.

More information on serological testing and revaccination of women of child-bearing age who are non-immune to rabies is included.

4.5 Poliomyelitis

- The 1st dose of IPV (inactivated poliovirus vaccine) containing combination vaccine due at 2 months of age can be given as early as 6 weeks of age.
- A booster dose of IPV (inactivated poliovirus vaccine) containing combination vaccine is recommended at 4 years of age, but can be given as early as 3.5 years.

4.4 Q fever

- Q fever vaccination is now not routinely recommended for women aged >50 years of age.
- Immunocompromised persons, irrespective of age, who receive influenza vaccine for the first time are now recommended to receive 2 vaccine doses, at least 4 weeks apart, and 1 dose annually thereafter.

Influenza vaccination is now also recommended for staff working in early childhood education and care and for persons working in the pork industry.

4.3 Pneumococcal disease

- Combination Hib-meningococcal C vaccine (Hib-MenCCV) has been included.
- Quadrivalent meningococcal conjugate vaccines (4vMenCV) have been included.
- 4vMenCV is preferred over the quadrivalent meningococcal polysaccharide vaccine (4vMenPV) for use in persons aged ≥9 months who are at increased risk of meningococcal disease.
- For young children with medical risk factors for meningococcal disease, meningococcal C conjugate vaccine (MenCCV) is recommended in those aged 6 weeks to <12 months; thereafter 4vMenCV is recommended in a 2-dose schedule at approximately 12 and 18 months of age.
- 5 yearly booster doses of 4vMenCV are recommended for persons at ongoing high risk of meningococcal infection.
- For persons at ongoing risk of meningococcal infection who have previously received 4vMenPV, a booster dose of 4vMenCV should be given 3 years after the 4vMenPV and then every 5 years.

4.2 Rabies and other lyssaviruses

- Recommendations for use of HPV (human papillomavirus) in males have been included. HPV (human papillomavirus) vaccination is recommended for males aged 9–18 years, with the optimal age for vaccination being 11–13 years.
- Specific recommendations regarding the use of HPV (human papillomavirus) vaccine in immunocompromised persons and men who have sex with men are now included.

4.1 Meningococcal disease

- The 1st dose of MMR (Measles, Mumps and Rubella) vaccine in children ≥9 years of age is now not routinely recommended for women aged >50 years of age.
- Immunocompromised persons, irrespective of age, who receive influenza vaccine for the first time are now recommended to receive 2 vaccine doses, at least 4 weeks apart, and 1 dose annually thereafter.

Influenza vaccination is now also recommended for staff working in early childhood education and care and for persons working in the pork industry.

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- 2 new JE (Japanese Encephalitis) vaccines are included.
- Advice on booster doses and information on adverse events have been updated.
Persons who have completed a primary course of a currently available cell culture-derived rabies vaccine no longer routinely require booster doses if travelling or living in an area of high risk.

Information on the role of serological testing has been more clearly presented.

4.17 Rotavirus

- The upper age limits for each dose of rotavirus vaccines are more clearly defined.
- Contraindications to rotavirus vaccination now include previous history of intussusception (IS) and severe combined immunodeficiency in infants.
- Information on the safety of rotavirus vaccines in infants with underlying conditions and infants who are immunocompromised has been updated.
- Information on adverse events following rotavirus vaccination has been updated and expanded, including new information on the low, but increased, risk of IS occurring following the 1st or 2nd dose of either rotavirus vaccine.

4.20 Tuberculosis

- Bacille Calmette-Guérin (BCG) vaccination is no longer routinely recommended for neonates weighing <2.5 kg.
- Generalised septic skin disease, skin conditions such as eczema, dermatitis and psoriasis, and significant febrile illness are no longer contraindications to BCG vaccination but, if present, vaccination should be deferred.

4.23 Yellow fever

- Yellow fever vaccine is not recommended in women who are breastfeeding infants aged <9 months.
- More detail is provided on how to access the WHO information regarding areas of high yellow fever activity and requirements for travel.

4.24 Zoster

- Information on the efficacy of vaccination in persons aged 50–59 years has been included.

Part 5 Passive immunisation

- Information regarding the use of intravenous immunoglobulins as treatment for disease conditions (such as Kawasaki disease) or as replacement therapy for immunodeficient individuals is no longer included in the Handbook. Readers are referred to National Blood Authority guidelines.
1.5 Fundamentals of immunisation

1.5.1 Overview

Vaccines are complex biological products designed to induce a protective immune response effectively and safely. Vaccines contain one or more antigens (or immunogens) that stimulate an active immune response. These are generally protein- or polysaccharide (sugar)-based substances. The number and derivation of the antigen(s) contained in each vaccine vary. Most vaccines work by inducing B-lymphocytes to produce antibodies that bind to and inhibit pathogenic organisms or their toxins. Generation of T-cell-mediated (cellular) immunity is also important for some vaccines.

Vaccines, like all medicines, are regulated in Australia by the Therapeutic Goods Administration (TGA). Before they are made available for use they are rigorously tested in human clinical trials to confirm that they are safe and that they stimulate protective immune responses. Vaccines are also evaluated to ensure compliance with strict manufacturing and production standards. This testing is required by law and is usually conducted both during the vaccine's development and after its registration. In addition, once they are in use, the safety of vaccines is monitored by the TGA and other organisations using different methods, including passive and active surveillance for adverse events following immunisation (see 1.5.5 Vaccine safety and adverse events following immunisation).

1.5.2 Passive immunisation

Passive immunity is the direct transfer or administration of antibodies to a non-immune person to provide immediate protection. One example of passive immunity is the transfer of maternal antibodies to the fetus, which provides some short-lived protection of the newborn infant against certain infections. Another example is the administration of a product containing antibodies (or immunoglobulins, IgG) pooled from blood donors, in order to provide temporary protection to a non-immune person who has recently been exposed to infection. The protection afforded is immediate, but lasts for only a few weeks as the half-life of IgG is approximately 3 to 4 weeks. Regular immunoglobulin infusions are also indicated for some immuno-compromised persons who are deficient in antibody. A separate use of immunoglobulins is in the treatment of a number of specific immune-mediated conditions in order to modulate the disease course.

For further information regarding the use of intravenous immunoglobulin for this purpose, see the Clinical practice guidelines for the use of intravenous immunoglobulin in Australia (http://www.nba.gov.au/vig/index.html).

For more information on passive immunisation see Part 5 Passive immunisation (Handbook 10-home-handbook10part5).

1.5.3 Active immunisation

Active immunisation involves the use of vaccines to stimulate the immune system to produce a protective immune response. Vaccines usually induce an immune response that mimics the host's response to natural infection, but without the harmful consequences of the infection itself. In addition to antibody responses, many vaccines also stimulate cell-mediated immunity. Immunisation following active immunisation generally lasts for months to many years, depending on the nature of the vaccine as well as host factors. Protective immunity is induced by antigen(s) contained within the vaccine. This may be a toxoid (a bacterial toxin that has been rendered non-toxicogenic, e.g. for tetanus or diphtheria); killed or inactivated bacteria or viruses, such as hepatitis A vaccines; live attenuated bacteria or viruses, such as measles, mumps and rubella vaccines; or subunit components of a pathogen that only contain the antigen(s) of interest, such as the hepatitis B vaccine.

In addition to containing the immunising antigen(s), vaccines may also contain the following:

- Adjuvants, which enhance the immune response to an antigen; an example is aluminium hydroxide.
- Preservatives, which reduce the risk of contamination; some examples are 2-phenoxethanol, which is also used in many cosmetics and pharmaceuticals, and thiomersal, which is used in the Q fever vaccine but is not present in any of the vaccines on the National Immunisation Program for young children.
- Stabilisers, which improve the shelf-life and help to protect the vaccine from adverse conditions; examples are sucrose, mannitol, lactose and gelatin. Stabilisers are also used in most confectionery and many pharmaceuticals.
- Emulsifiers or surfactants, which alter the surface tension of the liquid vaccine; examples are polysorbate-80 or sorbitol. Emulsifiers are added to most ice creams and many pharmaceuticals.
- Residuals, which are minute or trace amounts of substances that remain after the manufacture of the vaccine; examples of residuals detectable in some vaccines are formaldehyde, antibiotics such as neomycin or polymyxin, and egg proteins.

Further details of a particular vaccine's constituents can be found in either the product information (PI) or the consumer medicines information (CMI) for individual vaccines. This information is presented in the shaded box for each vaccine under the disease-specific chapters in Part 4 (Handbook 10-home-handbook10part4) of this Handbook (current June 2012); however, it is important to note that PI (Product Information) and CMI (consumer medicines information) are updated periodically. The most current versions of the PI (Product Information) and CMI (consumer medicines information) for vaccines (and other medicines) are available from the TGA website (http://www.tga.gov.au).

In addition, information on the components contained in vaccines that are available under the Australian National Immunisation Program is provided in Appendix 3 (Handbook 10-home-handbook10-tools-handbook10-appendices-handbook10-appendix3) of this Handbook, and further details on vaccine composition can be found in Appendix 4 (Commonly asked questions about vaccination-handbook10-home-handbook10-tools-handbook10-appendices-handbook10-appendix4).

The recommended number of doses and age of administration vary for each vaccine. These recommendations are based on the type of vaccine, disease epidemiology (the age-specific risk for infection and for complications), and the anticipated immune response of the recipient (including whether transplacental transfer of maternal antibodies will inhibit the immune response in an infant). Several doses of a vaccine may be required to induce protective immunity, particularly in younger children.

Homeopathic preparations do not induce immunity and are never an alternative to vaccination (see Appendix 4 (Commonly asked questions about vaccination-handbook10-home-handbook10-tools-handbook10-appendices-handbook10-appendix4)).

Detailed information on the background, available vaccines and recommendations for vaccines used in active immunisation are provided in the disease-specific chapters in Part 4 (Handbook 10-home-handbook10part4) of this Handbook.

1.5.4 Vaccine efficacy, vaccine effectiveness and vaccine failure

The terms vaccine efficacy and vaccine effectiveness are often used interchangeably. However, in general terms, vaccine efficacy refers to estimates of protection obtained under the idealised conditions of a randomised controlled trial (RCT). It is usually expressed as the percentage reduction in a person's risk of disease if vaccinated compared to the risk if not vaccinated. Vaccine effectiveness refers to estimates of protection obtained under 'real world' rather than trial conditions, for example, in immunisation programs after vaccine registration. Sometimes vaccine effectiveness is also taken to include the broader impact of a vaccination program on overall disease incidence in the population, including any additional herd protection conferred to unvaccinated individuals.

The extent and duration of protection provided by vaccination varies and is influenced by many factors. For example, some vaccines, such as the pneumococcal and meningococcal polysaccharide vaccines, provide protection for a few years only. This is because polysaccharide antigens induce antibodies without the involvement of T-lymphocytes (T-cell independent response). T-cell lymphocyte involvement is needed for long-term immune memory; without it, protection is relatively short-lived and immunity wanes, sometimes requiring revaccination. In addition, polysaccharide vaccines are less immunogenic in children aged <2 years. The process of conjugating (or linking) capsular polysaccharides to a protein carrier creates conjugate vaccines that can induce antibody production with the help of T-lymphocytes (T-cell dependent response). This results in higher-quality and longer-term immunity, including in children <2 years of age.

Conjugated vaccines are available for Haemophilus influenzae type b, Neisseria meningitidis (serogroups A, C, W135, and Y) and pneumococcal disease.

Vaccine failure can be due to either vaccine failure or failure to vaccinate (i.e. that an indicated vaccine was not administered appropriately for any reason). Sometimes a vaccinated person may develop infections despite being vaccinated (vaccine failure). Often such infections result in a milder or more attenuated form of disease, for example, chickenpox developing despite varicella vaccination or whooping cough developing after 2 or more doses of pertussis vaccine. Vaccine failure can be categorised in two ways. Primary vaccine failure occurs when
What is an adverse event following immunisation?

The term 'adverse event following immunisation' (AEFI) (adverse events following immunisation) refers to any untoward medical occurrence that follows immunisation, whether expected or unexpected, and whether triggered by the vaccine or only coincidentally occurring after receipt of a vaccine. The adverse event may be of any unfavourable and unintended sign, abnormal clinical laboratory finding, symptom or disease.7

Adverse events following immunisation (AEFI (adverse events following immunisation)) should be reported promptly, either according to relevant state or territory protocols or directly to the TGA (Therapeutic Goods Administration) (for detailed information on reporting and management of AEFI (adverse events following immunisation), see 2.3 Post-vaccination (Handbook 10-home–handbook10part2–handbook10-2-3)).

The safety of vaccines is very important as vaccines are given to prevent disease and target all or many members of the population, most of whom are healthy. All vaccines available in Australia must pass stringent safety testing before being approved for use by the TGA (Therapeutic Goods Administration). This testing is required by law and is usually done over many years during the vaccine’s development. In addition, the TGA’s Adverse Events Following Immunisation (AEFI) monitors the safety of vaccines once they are registered.

From the time a vaccine comes into use, there is ongoing review of both vaccine safety and efficacy through a variety of mechanisms, such as further clinical trials and surveillance of disease and vaccine adverse events. One important component of ensuring that vaccines are safe is to monitor the occurrence of AEFI (adverse events following immunisation). In Australia, there are regional and national surveillance systems that collect reports of any adverse events following immunisation. All AEFI (adverse events following immunisation) reported are added to the national Adverse Drug Reactions System (ADRS) database, which is operated by the TGA (Therapeutic Goods Administration). (See also 2.3 Post-vaccination (Handbook 10-home–handbook10part2–handbook10-2-3)). Each year, reports presenting data and analysis of AEFI (adverse events following immunisation) in Australia are published in the journal Communicable Diseases Intelligence, accessible via the Australian Government Department of Health website (http://www.health.gov.au/internet/main/publishing.nsf/Content/cda-pubs-cdi-cdintro.htm).

In some cases, other specific studies will be conducted to ensure that vaccine safety is closely monitored once a vaccine is in use. For example, the risk of intussusception (intussusception) following rotavirus vaccines has been closely monitored in Australia and elsewhere because of the association of a previously licensed vaccine with an unacceptably high risk of IL (intussusception).

Adverse reactions to vaccines (also known as 'vaccine side effects') do sometimes occur. It is usually not possible to predict which individuals may have a mild or, rarely, a serious reaction to a vaccine. However, by following guidelines regarding when vaccines should and should not be used, the risk of adverse events can be minimised. As vaccines are usually given to healthy people, any adverse event that follows soon after immunisation may be perceived as due to the vaccine. The fact that an adverse event occurs after an immunisation does not prove the vaccine caused the event. A causal association is rarely certain, but is most likely when the AEFI (adverse events following immunisation) is both typical (even if very rare) and when there is no other plausible explanation, for example, an injection site reaction occurring a day after vaccination or typical anaphylaxis occurring within minutes of vaccination. Many AEFI (adverse events following immunisation) are less specific and/or have plausible alternative explanations, including coincidence. Such associations can only be assessed by large-scale epidemiological studies or specific tests, for example, in the case of allergy, by allergy testing or challenge. Even when an AEFI (adverse events following immunisation) is typical, it may be nonetheless unrelated to vaccination (see 2.3 Post-vaccination (Handbook 10-home–handbook10part2–handbook10-2-3)).

Vaccine adverse events fall into two general categories: local or systemic. Local reactions are defined as reactions occurring at the site of vaccine administration (usually pain, redness or swelling at the injection site) and are generally the least severe and most frequently occurring AEFI (adverse events following immunisation). Systemic reactions most commonly include fever, headache and lethargy.8,9 Allergic reactions can also occur, although anaphylaxis, the most severe form of an allergic response, is rarely caused by vaccination. It is not possible to completely predict which individuals may have a reaction to a vaccine.

Each chapter in the Handbook indicates under which circumstances vaccine administration is contraindicated or where precautions are required. A contraindication to vaccination usually occurs when a pre-existing condition that significantly increases the chance that a serious adverse event will occur following receipt of a specific vaccine. A contraindication may also occur when there is insufficient safety data regarding a vaccine’s use and there is a theoretical risk of harm. In general, vaccines should not be given where a contraindication exists, except under advice from your local state or territory health department (Appendix 1 Contact details for Australian, state and territory government health authorities and communicable disease control (Handbook10-home–handbook10-tools–handbook10-appendices–handbook10-appendix1)).

A precondition is that a may increase the chance of an adverse event following immunisation or one that may compromise the ability of the vaccine to produce immunity. When a precaution exists, there may still be circumstances when the benefits of giving the vaccine outweigh the potential risks; however, special care and the provision of appropriate advice to the vaccine recipient may be required (see 3.3.1 Vaccination of persons who have had an adverse event following immunisation (Handbook10-home–handbook10part1–handbook10-3-383-3-1)).

In 2010, a national review of the management of adverse events that occurred following influenza vaccine administration was performed.10 The review made a number of recommendations to further improve the monitoring of vaccine safety in Australia. Any changes to the system(s) for monitoring or reporting of AEFI (adverse events following immunisation) in Australia will be reflected in future updates to the Handbook and will also be available from the Immunise Australia website (home).

References

Part 2 Vaccination Procedures

In Australia, vaccination is undertaken predominantly through general practices, but in some jurisdictions vaccines may be given through local council clinics, community centres or through school-based immunisation programs. In some situations, vaccinations may also be given in travel medicine clinics, public hospitals, staff occupational health clinics and aged care facilities. State or territory legislation outlines who can access and administer vaccines. All vaccines must be administered in accordance with the relevant legislation, best practice and the following Handbook guidelines and recommendations. Other relevant guidelines such as the National vaccine storage guidelines: Strive for 5 and the Australian guidelines for the prevention and control of infection in healthcare should also be followed (refer below and to 2.2. Administration of vaccines).

- 2.1 Pre-vaccination (Handbook10-home~handbook10part2~handbook10-2-1)
- 2.2 Administration of vaccines (Handbook10-home~handbook10part2~handbook10-2-2)
- 2.3 Post-vaccination (Handbook10-home~handbook10part2~handbook10-2-3)
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The following sections discuss steps and procedures that should occur before a vaccination encounter.

- 2.1.1 Preparing an anaphylaxis response kit
- 2.1.2 Effective cold chain: transport, storage and handling of vaccines
- 2.1.3 Valid consent
- 2.1.4 Pre-vaccination screening
- 2.1.5 Catch-up
- References

2.1.1 Preparing an anaphylaxis response kit

The availability of protocols, equipment and drugs necessary for the management of anaphylaxis should be checked before each vaccination session. An anaphylaxis response kit should be on hand at all times and should contain:

- adrenaline 1:1000 (minimum of three ampoules – check expiry dates)
- minimum of three 1 mL syringes and 25 mm length needles (for intramuscular (IM) injection)
- cotton wool swabs
- pen and paper to record time of administration of adrenaline
- laminated copy of adrenaline doses (Table 2.3.2 or back cover of this Handbook)
- laminated copy of ‘Recognition and treatment of anaphylaxis’ (back cover of this Handbook).

Refer to 2.3.2 Adverse events following immunisation (Handbook10-home~handbook10part2~handbook10-2-3) for details on recognition and treatment of adverse events following immunisation (in particular, refer to ‘Use of adrenaline’ and ‘Use of adrenaline autoinjectors for anaphylaxis treatment’ in that section).

2.1.2 Effective cold chain: transport, storage and handling of vaccines

The cold chain is the system of transporting and storing vaccines within the temperature range of +2°C to +8°C from the place of manufacture to the point of administration. Maintenance of the cold chain is essential for maintaining vaccine potency and, in turn, vaccine effectiveness. It is vital, not only for those vaccines provided as part of the National Immunisation Program, but also for vaccines purchased by the patient via prescription from a pharmacist. In such cases, both the doctor issuing the prescription and the pharmacist dispensing the vaccine must inform the patient of the need for maintaining, and how to maintain, the cold chain for the vaccine they have purchased.

All immunisation service providers must be familiar with, and adhere to, the National vaccine storage guidelines: Strive for 5 (2nd edition)(IMM77-cnt). This publication can be accessed free of charge from (www.immunise.health.gov.au/internet/immunise/publishing.nsf/Content/IMM77-cnt)

The National vaccine storage guidelines: Strive for 5 contains specific details on setting up the infrastructure for a vaccination service, and immunisation service providers should refer to this document to ensure that satisfactory equipment and procedures are in place before commencing vaccination services.

These guidelines also provide instructions on how best to transport vaccines from the main storage facility to outreach or external clinics. Purpose-built vaccine refrigerators (PBRs) (Purpose-built vaccine refrigerators) are the preferred means of storage for vaccines. Domestic refrigerators are not designed for the special temperature needs of vaccine storage.

Cold chain breaches

Despite best practices, cold chain breaches sometimes occur. It is important to report any cold chain breaches so that revaccination of patients or recall of unused vaccines can be undertaken, if required.

Do not discard or use any vaccines exposed to temperatures below +2°C or above +8°C without obtaining further advice. Isolate vaccines and contact the state/territory health authorities (refer to Appendix 1 (Handbook10-home~handbook10part2~handbook10-appendices~handbook10-appendix1)) for advice on the National Immunisation Program vaccines and the manufacturer/supplier for privately purchased vaccines. Recommendations for the discarding of vaccines may differ between health authorities and manufacturers.

2.1.3 Valid consent

Valid consent can be defined as the voluntary agreement by an individual to a proposed procedure, given after sufficient, appropriate and reliable information about the procedure, including the potential risks and benefits, has been conveyed to that individual. As part of the consent procedure, persons to be vaccinated and/or their parents/carers should be given sufficient information (preferably written) on the risks and benefits of each vaccine, including what adverse events are possible, how common they are and what they should do about them (the table inside the front cover of this Handbook, Side effects following immunisation for vaccines used in the National Immunisation Program (NIP), can be used for this purpose).

For consent to be legally valid, the following elements must be present:

1. It must be given by a person with legal capacity, and of sufficient intellectual capacity to understand the implications of being vaccinated.
2. It must be given voluntarily in the absence of undue pressure, coercion or manipulation.
3. It must cover the specific procedure that is to be performed.
4. It can only be given after the potential risks and benefits of the relevant vaccine, risks of not having it and any alternative options have been explained to the individual.

The individual must have sufficient opportunity to seek further details or explanations about the vaccine(s) and/or its administration. The information must be provided in a language or by other means the individual can understand. Where appropriate, an interpreter and/or cultural support person should be involved.

Consent should be obtained before each vaccination, once it has been established that there are no medical condition(s) that contraindicate vaccination. Consent can be verbal or written. Immunisation providers should refer to their state or territory's policies on obtaining written consent (refer to Appendix 1 Contact details for Australian, state and territory government health authorities and communicable disease control (Handbook10-home~handbook10part2~handbook10-appendices~handbook10-appendix1)).

Consent on behalf of a child or adolescent

In general, a parent or legal guardian of a child has the authority to consent to vaccination of that child; however, it is important to check with your state or territory authority where any doubt exists. A child in this context is defined as being under the age of 18 years in Tasmania, Victoria and Western Australia; under the age of 14 years in New South Wales; and under the age of 16 years in the Australian Capital Territory, South Australia and the Northern Territory. Queensland follows common law principles.

For certain procedures, including vaccination, persons younger than the ages defined above may have sufficient maturity to understand the proposed procedure and the risks and benefits associated with it, and thus may have the capacity to consent under certain circumstances. Refer to the relevant state or territory immunisation service provider guidelines for more information.

Should a child or adolescent refuse a vaccination for which a parent/guardian has given consent, the child/adolescent’s wishes should be respected and the parent/guardian informed.
Resources to help communicate the risks and benefits of vaccines

Plain language should be used when communicating information about vaccines and their use. The person to be vaccinated (or their parent/guardian) must be encouraged and allowed to ask for further information and have sufficient time to make a decision about whether to consent or not. It is preferable that printed information is available to supplement any verbal explanations. The summary table Comparison of the effects of diseases and the side effects of NIP (National Immunisation Program) vaccines inside the back cover of this Handbook provides some basic information necessary to communicate the risks and benefits of vaccination. The table can be photocopied and used freely as required.

More detailed information concerning vaccines and their use is available from the following sources:

- The Immunise Australia website (http://www.immunise.health.gov.au) (www.immunise.health.gov.au) includes the booklet Understanding childhood immunisation, which contains frequently asked questions and links to state and territory health department websites. Several of these sites offer multilingual fact sheets.
- The National Centre for Immunisation Research and Surveillance of Vaccine Preventable Diseases website (http://www.ncirs.edu.au) (www.ncirs.edu.au) includes fact sheets related to specific vaccines, vaccine-preventable diseases and vaccine safety. The website also hosts online decision aids to assist patients in deciding whether to vaccinate or not.

Refer also to Appendix 4 Commonly asked questions about vaccination (Handbook10-home+handbook10-tools+handbook10-appendices+handbook10-appendix4).

Evidence of consent

General practice or public immunisation clinics

Consent may be given either in writing or verbally, according to the protocols of the health facility, but it must meet the criteria for valid consent. Evidence of verbal consent should be documented in the clinical records. If a standard procedure is routinely followed in a practice or clinic, then a stamp, a sticker or a provider’s signature indicating that the routine procedure has been followed may be used. For paperless medical records, a typed record of verbal consent may be made in the patient’s file, or a copy of written consent scanned into the file.

Explicit verbal consent is required before administration of any vaccine, even when written consent has been given at previous vaccination encounters for the same vaccine. Verbal consent should be documented in the patient’s file each time it is given.

School-based vaccination programs

Consent is required for provision of individual vaccines or a vaccine course offered in school-based vaccination programs. In school-based, and other large-scale, vaccination programs, the parent or guardian usually does not attend with the child on the day the vaccination is given, and written consent from the parent or guardian is desirable in these circumstances. However, if written consent is not able to be provided, or if further clarification is required, verbal consent may be sought by telephone from the parent or guardian by the immunisation service provider. This should be clearly documented on the child’s consent form. In some jurisdictions, older adolescents may be able to provide their own consent for vaccinations offered through school-based vaccination programs (refer to ‘Consent on behalf of a child or adolescent’ above). Consent requirements and vaccines offered in these programs vary between jurisdictions. Refer to the relevant state or territory school-based vaccination program guidelines for more information.

2.1.4 Pre-vaccination screening

Immunisation service providers should perform a comprehensive pre-vaccination health screen of all persons to be vaccinated. For some individuals, alterations to the routinely recommended vaccines may be necessary to either eliminate or minimise the risk of adverse events, to optimise an individual’s immune response, or to enhance the protection of a household contact against vaccine-preventable diseases.

Providers should:

- ensure that they have the right person to be vaccinated
- ensure which vaccine(s) are indicated, including any previously missed vaccine doses
- consider whether alternative or additional vaccines should be given
- check if there are any contraindications or precautions to the vaccines that are to be given
- ensure that the patient to be vaccinated is the appropriate age for the vaccines to be given
- check that the correct time interval has passed since any previous vaccine(s) or any blood products were given.

Refer also to 2.1.5 Catch-up and relevant disease chapters for further details.

Steps for pre-vaccination screening

Follow these steps to complete the pre-vaccination screening process:

- Provide the person to be vaccinated or the parent/carer with the Pre-vaccination screening checklist (Table 2.1.1).
- The checklist may be photocopied and handed to the person to be vaccinated or the parent/carer just before vaccination.
- The checklist may also be photocopied and displayed in the clinic/surgery for easy reference for the immunisation service provider.
- For vaccination of adults, seek additional information about the occupation and lifestyle factors that may influence vaccination requirements. This is discussed in more detail in 2.1.5 Catch-up below under ‘Catch-up schedules for persons ≥10 years of age’.
- If you identify the presence of a condition or circumstance indicated on the pre-vaccination screening checklist, refer to Table 2.1.2, which lists the specific issues pertaining to such condition(s) or circumstances and provides the appropriate action with a rationale.
- Where necessary, seek further advice from a specialist immunisation clinic, a medical practitioner with expertise in vaccination, the immunisation section within your state or territory health authority, or your local Public Health Unit (refer to Appendix 1 Contact details for Australian, state and territory government health authorities and communicable disease control (Handbook10-home+handbook10-tools+handbook10-appendices+handbook10-appendix1)).
Rationale

Refer to the Australian Immunisation Handbook for more information.

Note: The recommended responses for immunisation service providers to make if any conditions or circumstances are identified by using the pre-screening checklist are summarised in Table 2.1.2.

Table 2.1.2: Responses to relevant conditions or circumstances identified through the pre-vaccination screening checklist

| Condition or circumstance of person to be vaccinated | Action | Rational

### Is unwell today:
- **Acute febrile illness (current T ≥38.5°C)**
- **Acute systemic illness**

- **Defer all vaccines until afebrile.**
  - **Note:** Children with minor illnesses (without acute systemic symptoms/signs) should be vaccinated.
  - **To avoid an adverse event in an already unwell child, or to avoid attributing symptoms to vaccination.**

### Has a disease that lowers immunity, is receiving treatment that lowers immunity or is an infant of a mother who received immunosuppressive therapy during pregnancy

- **Refer to 3.3.3 Vaccination of immunocompromised persons**
  - (Handbook10-home–handbook10-part3–handbook10-3-3). 3.3.3.2 Vaccination of women who are planning pregnancy, pregnant or breastfeeding, and preterm infants (Handbook10-home–handbook10-part3–handbook10-3-3).
  - In some cases, expert advice may need to be sought before vaccination (refer to Appendix 1 (Handbook10-home–handbook10-tools–handbook10-appendices–handbook10-appendix1)).
  - **Note:** Persons living with someone with lowered immunity should be vaccinated, including with live viral vaccines (refer to below).
  - **The safety and effectiveness of the vaccine may be suboptimal in persons who are immunocompromised. Live attenuated vaccines may be contraindicated.**

### Has had anaphylaxis following a previous dose of the relevant vaccine

- **Do not vaccinate. Seek further medical advice to confirm causality and to assist with other vaccinations.**
- **Refer also to ‘Contraindications to vaccination’ below.**
  - **Anaphylaxis to a previous dose of vaccine is a contraindication to receiving the same vaccine.**

### Has a severe allergy to a vaccine component

- **Refer to Appendix 3 (Handbook10-home–handbook10-tools–handbook10-appendices–handbook10-appendix3) for a vaccine component checklist.**
- **Do not vaccinate but seek specialist advice (refer to Appendix 1 (Handbook10-home–handbook10-tools–handbook10-appendices–handbook10-appendix1)).**
  - The patient may still be able to be vaccinated, dependent on the allergy.
  - **Anaphylaxis to a vaccine component is generally a contraindication to receiving the vaccine.**

### Has received a live attenuated viral parenteral vaccine* or BCG (bacille Calmette-Guérin) vaccine in past 4 weeks

- **Delay live attenuated viral parenteral vaccines by 4 weeks.**
  - **The immune response to a live attenuated viral vaccine (given parenterally) may interfere with the response to a subsequent live viral vaccine given within 4 weeks of the first.**

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Note: Please discuss this information or any questions you have about vaccination with your doctor/nurse before the vaccines are given.

Before any vaccination takes place, your doctor/nurse should ask you:

- Did you understand the information provided to you about vaccination?
- Do you need more information to decide whether to proceed?
- Did you bring your/your child's vaccination record card with you?

It is important for you to receive a personal record of your or your child's vaccinations. If you do not have a record, ask your doctor/nurse to give you one. Bring this record with you every time you or your child visit for vaccination. Make sure your doctor/nurse records all vaccinations on it.

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Note: Refer to the Australian Immunisation Handbook for more information.

Conditions or circumstances identified using the pre-vaccination screening checklist

The recommended responses for immunisation service providers to make if any conditions or circumstances are identified by using the pre-screening checklist are summarised in Table 2.1.2.

**Note:** Only vaccines recommended on the NIP (National Immunisation Program) schedule are included in Table 2.1.2. For information on other vaccines, refer to the relevant disease-specific chapter in Part 4 (Handbook10-home–handbook10-part4) of this Handbook or to vaccine product information.

For reference, Table 2.1.3 provides a list of live attenuated vaccines.
### Condition or circumstance of person to be vaccinated

<table>
<thead>
<tr>
<th>Action</th>
<th>Immunise - The Australian Immunisation Handbook 10th Edition</th>
<th>Rationale</th>
</tr>
</thead>
<tbody>
<tr>
<td>Has had any blood product in the past 7 months, or has had IM (intramuscular) or IV (intravenous) immunoglobulin in the past year</td>
<td>Check which product the person received and the interval since administration. Refer to Table 3.3.6 Recommended intervals between either immunoglobulins or blood products and MMR (Measles, Mumps and Rubella), MMRV (Measles, Mumps, Rubella and Varicella) or varicella vaccination (Handbook10-home<del>handbook10part3</del>handbook10-3-3#table-3-3-6). If not eligible, make a return appointment for this vaccination, and send a reminder later if necessary.</td>
<td>Antibodies in these products may interfere with the immune response to MMR (Measles, Mumps and Rubella), MMRV (Measles, Mumps, Rubella and Varicella) and varicella vaccines. The recommended interval to vaccination varies depending on the immunoglobulin or blood product administered.</td>
</tr>
<tr>
<td>Is planning a pregnancy or anticipating parenthood</td>
<td>Ensure women planning pregnancy and household members have received vaccines recommended for their age group. For example, 2nd dose of MMR vaccine (Measles, Mumps and Rubella) if born after 1966; varicella; dTpa (diphtheria-tetanus-acellular pertussis) vaccine, and/or have had appropriate pre-conception serological testing. Refer to 3.3.2 Vaccination of women who are planning pregnancy, pregnant or breastfeeding, and preterm infants (Handbook10-home<del>handbook10part3</del>handbook10-3-3). Advise women not to become pregnant within 28 days of receiving live viral vaccines.</td>
<td>Vaccinating before pregnancy may prevent maternal illness, which could affect the infant, and may confer passive immunity to the newborn.</td>
</tr>
<tr>
<td>Is pregnant</td>
<td>Refer to Table 3.3.1 Recommendations for vaccination in pregnancy (Handbook10-home<del>handbook10part3</del>handbook10-3-3#table-3-3-1). Influenza and pertussis vaccines are recommended for all pregnant women. Live vaccines should be deferred until after delivery. Vaccination of household contacts of pregnant women may also be required (refer to recommendations in relevant disease chapter).</td>
<td>There is insufficient evidence to ensure the safety of administering live vaccines during pregnancy. Inactivated vaccines are generally not contraindicated in pregnancy.</td>
</tr>
<tr>
<td>Has a history of Guillain-Barré syndrome (GBS)</td>
<td>Refer to 3.3.3 Vaccination of immunocompromised persons (Handbook10-home<del>handbook10part3</del>handbook10-3-3) and 4.7 Influenza (Handbook10-home<del>handbook10part4</del>handbook10-4-7). Risks and benefits of influenza vaccine should be weighed against the potential risk of GBS (Guillain-Barré syndrome) recurrence (seek further advice as per Appendix 1 (Handbook10-home<del>handbook10-tools</del>handbook10-appendices~handbook10-appendix1)).</td>
<td>Persons with a history of GBS (Guillain-Barré syndrome) may be at risk of recurrence of the condition following influenza vaccine.</td>
</tr>
<tr>
<td>Was born preterm</td>
<td>Refer to 3.3.2 Vaccination of women who are planning pregnancy, pregnant or breastfeeding, and preterm infants (Handbook10-home<del>handbook10part3</del>handbook10-3-3). Preterm infants born at &lt;28 weeks gestation and/or with chronic lung disease require extra pneumococcal vaccinations (refer to 4.13 Pneumococcal disease (Handbook10-home<del>handbook10part4</del>handbook10-4-13)). Preterm infants born at &lt;32 weeks gestation and/or &lt;2000 g birth weight may require an extra dose of hepatitis B vaccine (refer to 4.5 Hepatitis B (Handbook10-home<del>handbook10part4</del>handbook10-4-5)).</td>
<td>Preterm infants may be at increased risk of vaccine-preventable diseases (e.g. invasive pneumococcal disease), and may not mount an optimal immune response to certain vaccines (e.g. hepatitis B).</td>
</tr>
<tr>
<td>Has a severe or chronic illness</td>
<td>Refer to 3.3 Groups with special vaccination requirements (Handbook10-home<del>handbook10part3</del>handbook10-3-3). These persons should receive recommended vaccines such as pneumococcal vaccine and annual influenza vaccination. If there is significant immunocompromise, they should not receive live vaccines* (refer to above).</td>
<td>Persons with a severe or chronic illness may be at increased risk of vaccine-preventable diseases (e.g. invasive pneumococcal disease), but may not mount an optimal immune response to certain vaccines. The safety and effectiveness of some vaccines may be suboptimal in persons who are immunocompromised (refer to above).</td>
</tr>
<tr>
<td>Has a bleeding disorder</td>
<td>Refer to 3.3.5 Vaccination of persons with bleeding disorders (Handbook10-home<del>handbook10part3</del>handbook10-3-3). The subcutaneous route could be considered as an alternative to the intramuscular route; seek specialist advice (refer to Appendix 1 (Handbook10-home<del>handbook10-tools</del>handbook10-appendices~handbook10-appendix1)).</td>
<td>Intramuscular injection may lead to haematomas in patients with disorders of haemostasis.</td>
</tr>
<tr>
<td>Identifies as an Aboriginal or Torres Strait Islander</td>
<td>Refer to 3.1 Vaccination for Aboriginal and Torres Strait Islander people (Handbook10-home<del>handbook10part3</del>handbook10-3-1). Refer to the National Immunisation Program for specific recommendations for Aboriginal and Torres Strait Islander people.</td>
<td>Some Indigenous persons are at increased risk of some vaccine-preventable diseases, such as influenza, pneumococcal disease and hepatitis A.</td>
</tr>
<tr>
<td>Does not have a functioning spleen</td>
<td>Refer to 3.3.3 Vaccination of immunocompromised persons, (Handbook10-home<del>handbook10part3</del>handbook10-3-3) ‘Persons with functional or anatomical asplenia’. Check the person’s vaccination status for pneumococcal, meningococcal, influenza and Hib (&lt;em&gt;Haemophilus influenzae&lt;/em&gt; type b) vaccinations.</td>
<td>Persons with an absent or dysfunctional spleen are at an increased risk of severe bacterial infections, most notably invasive pneumococcal disease.</td>
</tr>
</tbody>
</table>

---

**Rationale**

**Live attenuated oral vaccines**

- **Bacterial**
  - Japanese encephalitis (Imojev)
  - BCG (bacille Calmette-Guerin)
- **Viral**
  - Measles-mumps-rubella (MMR, Measles, Mumps and Rubella)
  - Yellow fever

**Live attenuated parenteral vaccines**

- **Bacterial**
  - Oral rotavirus vaccine
- **Viral**
  - Measles-mumps-rubella-varicella (MMRV, Measles, Mumps, Rubella and Varicella)
  - Varicella
  - Zoster

**Contraindications to vaccination**

- There are only two absolute contraindications applicable to all vaccines:
  - Anaphylaxis following a previous dose of the relevant vaccine
  - Anaphylaxis following any component of the relevant vaccine.

- There are two further contraindications applicable to live (both parenteral and oral) vaccines:
  - Live vaccines (refer to Table 2.1.3) should not be administered to persons who are significantly immunocompromised, regardless of whether the immunocompromise is caused by disease or treatment. The exception is that, with further advice, MMR (Measles, Mumps and Rubella), varicella and zoster vaccines can be administered to HIV-infected persons in whom immunocompromise is mild. (Refer to 3.3.3 Vaccination of immunocompromised persons, and individual disease-specific chapters.)
  - In general, live vaccines should not be administered during pregnancy, and women should be advised not to become pregnant within 28 days of receiving a live vaccine (refer to Table 3.3.1 Recommendations for vaccination in pregnancy (Handbook 10-home handbok10part3-handbook10-3-3#table-3-3-1)) in 3.3 Groups with special vaccination requirements) (Handbook 10-home handbok10part3-handbook10-3-3).

**False contraindications to vaccination**

- No-one should be denied the benefits of vaccination by withholding vaccines for inappropriate reasons.

- Conditions listed in Table 2.1.4 below are not contraindications to vaccination. Persons with these conditions should be vaccinated with all recommended vaccines.

**Table 2.1.3: Live attenuated parenteral and oral vaccines**

<table>
<thead>
<tr>
<th>Vaccine</th>
<th>Bacterial</th>
<th>Viral</th>
<th>Bacterial</th>
</tr>
</thead>
<tbody>
<tr>
<td>Japanese encephalitis (Imojev)</td>
<td></td>
<td>BCG (bacille Calmette-Guerin)</td>
<td>Oral rotavirus vaccine</td>
</tr>
<tr>
<td>Measles-mumps-rubella (MMR, Measles, Mumps and Rubella)</td>
<td></td>
<td></td>
<td>Oral typhoid vaccine</td>
</tr>
<tr>
<td>Measles-mumps-rubella-varicella (MMRV, Measles, Mumps, Rubella and Varicella)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Varicella</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yellow fever</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Zoster</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Table 2.1.4: False contraindications to vaccination**

- Mild illness without fever (T <38.5°C)
- Family history of any adverse events following immunisation
- Past history of convulsions
- Treatment with antibiotics
- Treatment with locally acting (inhaled or low-dose topical) steroids
- Replacement corticosteroids
- Asthma, eczema, atopy, hay fever or ‘s屋里es’
- Previous infection with the same pathogen
- Prematurity (vaccination should not be postponed and can be given if the infant is medically stable). Refer also to 3.3.2 Vaccination of women who are planning pregnancy, pregnant or breastfeeding, and preterm infants (Handbook 10-home handbok10part3-handbook10-3-3).
- History of neonatal jaundice
- Low weight in an otherwise healthy child
- Neurological conditions, including cerebral palsy and Down syndrome
- Contact with an infectious disease
- Child’s mother is pregnant

* Live attenuated vaccines are classified in Table 2.1.3 below.
† Refer to 4.9 Measles (Handbook 10-home-handbok10part4-handbook10-4-9). 4.11 Mumps (Handbook 10-home-handbok10part4-handbook10-4-11) or 4.18 Rubella (Handbook 10-home-handbok10part4-handbook10-4-18) for further information.
‡ Refer to 4.2 Diphtheria (Handbook 10-home-handbok10part4-handbook10-4-2). 4.12 Pertussis (Handbook 10-home-handbok10part4-handbook10-4-12) or 4.19 Tetanus (Handbook 10-home-handbok10part4-handbook10-4-19) for further information.
2.1.5 Catch-up

Every opportunity should be taken to review a person's vaccination history and to administer the appropriate vaccine(s). If the person has not had documented receipt of vaccines scheduled in the NIP (National Immunisation Program) appropriate for his/her age, plan and document a catch-up schedule and discuss this with the person to be vaccinated or their parent/carer. The assessment of vaccination status should be based on the schedule for the state or territory in which the person to be vaccinated is residing. The objective of catch-up vaccination is to complete a course of vaccination and provide optimal protection as quickly as possible. The information and tables below will assist in planning a catch-up schedule.

An online ‘catch-up calculator’ for NIP (National Immunisation Program) vaccines is hosted by South Australia Health (http://immunisationcalculator.sahealth.sa.gov.au/) (at immunisationcalculator.sahealth.sa.gov.au) and is available to assist in determining appropriate catch-up schedules for children ≤ 7 years of age across Australia. When using such resources, also check the accuracy of information provided by referring to your current state/territory immunisation schedule and the current edition of the Handbook.

If still uncertain about how to plan the catch-up schedule, or for more complicated catch-up scenarios, seek further advice (refer to Appendix 1 Contact details for Australian, state and territory government health authorities and communicable disease control (Handbook10-home-handbook10-tools-handbook10-appendices-handbook10-appendindx)).

For recently arrived migrants, the World Health Organization website (http://apps.who.int/immunization_monitoring/globalsummary) lists immunisation schedules provided by other countries, which may supplement information regarding which vaccines a child/adult arriving from overseas may have received (refer also to 3.3.8 Migration of Migrants to Australia (Handbook10-home-handbook10-part3-handbook10-3-3)).

**Confirmation of vaccination history**

The most important requirement for assessment of vaccination status is to have written documentation of vaccination. The approach of immunisation service providers to the problem of inadequate records should be based on the age of the person to be vaccinated, whether previous vaccines have been given in Australia or overseas, and the vaccines being considered for catch-up.

Detailed information on the vaccine registers used in Australia and how to obtain vaccination records is provided in 2.3.4 Immunisation registers (Handbook10-home-handbook10-part2-handbook10-2-3), but is also described briefly below.

**Children, adolescents and young adults <2 years of age**

The Australian Childhood Immunisation Register (ACIR) commenced on 1 January 1996 and holds records of vaccinations given since then to children (between birth and their 7th birthday). From 1 January 2016, the register will accept records of vaccinations given to older children, adolescents and young adults <20 years of age (referred to as ‘young individuals’ in ACIR legislation) if the vaccination was given after 1996. Details of a child’s, adolescent’s or young adult’s immunity history can be obtained via the ACIR secure site within the Health Professionals Online Services (HPOS) (www.humanservices.gov.au/hpos) or the ACIR Enquiry Line (1800 653 809). If it is believed that vaccines have been given but are not recorded on the ACIR, every effort should be made to contact the relevant immunisation service provider. If confirmation from the nominated provider or the ACIR cannot be obtained, and no written records are available, the vaccine(s) should be considered as not received, and the individual should be offered catch-up vaccination appropriate for their age.

Prior to January 2016, vaccination information was not recorded on the ACIR for children, adolescents or young adults aged ≥7 years. Documented vaccinations given to a child, adolescent or young adult <20 years of age that are not captured on the ACIR can be added to the register by immunisation service providers. This is done through the ACIR secure site within HPOS or by completing an Immunisation History form. (Refer also to 2.3.4 Immunisation registers (Handbook10-home-handbook10-part2-handbook10-2-3), ‘Reporting to the Australian Childhood Immunisation Register’.)

Certain vaccinations received during adolescence may be recorded by other registers. For example, the National HPV Vaccination Program Register (the HPV Register) holds details of human papillomavirus (HPV) vaccinations reported to the Register since the commencement of the HPV Vaccination Program in April 2007. The HPV Register initially only recorded vaccinations for females, but since 2013 also records vaccinations given to males. Details of HPV vaccinations held by the HPV Register can be obtained by phoning the Register on 1800 478 734 (1800 HPV REG). (Refer also to 2.3.4 Immunisation registers (Handbook10-home-handbook10-part2-handbook10-2-3)).

Some states and territories also maintain records of vaccinations delivered through school-based programs. Information on how to obtain such records can be obtained from state and territory government health departments (refer to Appendix 1 Contact details for Australian, state and territory government health authorities and communicable disease control).

From the 2017 school year, the HPV Register will become the Australian School Vaccination Register, which will capture adolescent vaccinations given through school programs (refer to 2.3.4 Immunisation registers (Handbook10-home-handbook10-part2-handbook10-2-3), ‘School vaccination program registers’).

**Adults (≥20 years of age)**

From September 2016, all vaccinations given in general practice or community clinics over the life of an individual will be captured in the Australian Immunisation Register (AIR), which is an expansion of the AIR. Adults who received vaccinations prior to September 2016 may only have patient-held and/or provider-held documentation of previous vaccination history or, in some instances, these may not be available. Information for certain vaccinations may be available from other sources, such as the HPV Register (which from the 2017 school year will become the Australian School Vaccination Register (ASVR) and also capture other adolescent vaccinations which are given through school programs) and the Australian Q Fever Register. (Refer also to 2.3.4 Immunisation registers (Handbook10-home-handbook10-part2-handbook10-2-3)).

**Incomplete documentation of prior vaccination**

If receipt of prior vaccination cannot be confirmed via the above methods, it should generally be assumed that the vaccine(s) required have not been given previously. All efforts should be made to confirm and ensure appropriate documentation of prior receipt of vaccines.

For most vaccines (except Q fever), there are no adverse events associated with additional doses if given to an already immune person. In the case of diphtheria-, tetanus- and pertussis-containing vaccines and pneumococcal polysaccharide vaccines, frequent additional doses may be associated with an increase in local adverse events; however, the benefits of protection may outweigh the risk of an adverse reaction. (Refer also to 4.2 Diphtheria (Handbook10-home-handbook10-part4-handbook10-4-2), 4.12 Pertussis, (Handbook10-home-handbook10-part4-handbook10-4-12) 4.13 Pneumococcal disease (Handbook10-home-handbook10-part4-handbook10-4-13) or 4.19 Tetanus (Handbook10-home-handbook10-part4-handbook10-4-19).) Additional doses of MMR (Measles, Mumps and Rubella), varicella, inactivated poliomyelitis (IPV (inactivated poliomyelitis vaccines)) or hepatitis B vaccines are rarely associated with significant adverse events.

**Use of laboratory testing to guide catch-up vaccination**

Laboratory testing (via serology, antigen detection or polymerase chain reaction (PCR)) can be reliably used for certain diseases (hepatitis A, hepatitis B, measles, mumps, rubella and varicella) to determine immunity from prior vaccination and/or infection and may be useful to guide the need for catch-up vaccination. However, for other diseases, laboratory testing is not routinely recommended to guide the need for catch-up vaccination as it is not necessarily reliable and/or detection of a previous infection (e.g., due to one serotype) does not protect against subsequent disease. As a previous infection is not a contraindication to immunisation against that same disease, in most circumstances, and for most vaccines, it is more practical to offer vaccination rather than laboratory testing. Refer also to recommendations regarding serological testing before and after vaccination in various disease chapters.

If serological testing is performed, interpretation of the results may be enhanced by discussion with the laboratory that performed the test, ensuring that relevant clinical information is provided.

Determining when a vaccine dose is valid according to age and interval since last dose

A ‘valid’ vaccine dose is a dose that is considered immunogenic (and safe) given the age and health status of the recipient and the interval since the recipient’s last dose of the same vaccine. For children who are vaccinated at an age younger than that routinely recommended, or for children and adults in whom the interval between vaccine doses is shorter than the usual recommended interval, information regarding both the minimum acceptable age for the 1st dose of an infant vaccine (Table 2.1.5) and the minimum acceptable intervals between vaccine doses (Tables 2.1.7 to 2.1.12) can be used to determine whether additional vaccine doses and/or catch-up vaccination is required. For more details refer to the following sections.

Planning catch-up vaccination

This and the following two sections are dedicated to planning catch-up vaccination. In the following two sections information is presented by age of the vaccine recipient (children aged <10 years and persons aged ≥10 years). A number of tables and figures are provided to help plan a catch-up schedule:

- Table 2.1.1 is a worksheet for calculating and recording which vaccines are required in children aged <10 years, the number of doses outstanding and the timing of these doses (refer to ‘Using the catch-up worksheet’ (Figure 2.1.1) for children <10 years of age) below.
- Table 2.1.5 lists the minimum acceptable ages for the 1st dose of scheduled vaccines in infants.
- Table 2.1.6 can be used to assess the number of doses a child should have received if they were on schedule. Check under the current age of the child to see how many doses they should have already received and use that number as the starting point for calculating a catch-up schedule. For example, a child who is 18 months old now should have received 3 doses of DTPa (diphtheria-tetanus-acellular pertussis vaccine), 3 doses of IPV (inactivated poliovirus vaccine), etc.
- Table 2.1.7 lists the minimum acceptable interval between doses under special circumstances, such as catch-up vaccination. Vaccine doses should not be administered at less than the acceptable minimum interval. In the majority of instances, doses administered earlier than the minimum acceptable interval should not be considered as valid doses and should be repeated, as appropriate, using Table 2.1.6.
- Table 2.1.8 to Table 2.1.11 are for calculating catch-up for Haemophilus influenzae type b (Hib) and pneumococcal vaccination of children.
- Table 2.1.12 can be used to calculate a catch-up schedule for persons aged ≥10 years.

In addition, the following principles should generally be applied when planning catch-up vaccination:

- When commencing the catch-up schedule, the standard scheduled interval between doses may be reduced or extended, and the numbers of doses required may reduce with age. For example, from 16 months of age, only 1 dose of (any) Hib-containing vaccine is required.
- As a child gets older, the recommended number of vaccine doses may change (or even be omitted from the schedule), as the child becomes less vulnerable to specific diseases.
- For incomplete or overdue vaccinations, build on the previous documented doses. In almost every circumstance, it is advisable to not start the schedule again, regardless of the interval since the last dose, but to count previous doses. One exception to this rule is for oral cholera vaccine (refer to 4.1.1 Cholera (Handbook10-home-handbook10-part4-handbook10-4-1)).
- If more than one vaccine is overdue, 1 dose of each due or overdue vaccine should be given at the first catch-up visit. Further required doses should be scheduled after the appropriate minimum interval (refer to Table 2.1.7).
- A catch-up schedule may require multiple vaccinations at a visit. Give all the due vaccines at the same visit – do not defer. Refer to 2.2.9 Administering multiple vaccine injections at the same visit (Handbook10-home-handbook10-part2-handbook10-2-2).
- The administration of two combination vaccines containing the same antigen is not recommended but may be acceptable when providing catch-up vaccinations where no alternative vaccine(s) or schedules are available. For example, catch-up vaccination for multiple infant vaccines using Hib-MenCCV and another Hib-containing combination vaccine.
- The standard intervals and ages recommended in the NIP (National Immunisation Program) schedule should be used once the child or adult is up to date with the schedule.
- Some persons will require further doses of antigens that are available only in combination vaccines. In general, the use of the combination vaccine(s) is acceptable, even if this means the number of doses of another antigen administered exceeds the required number.
- For some vaccines, catch-up vaccination is not recommended. For example, rotavirus vaccination is not recommended if the 1st (and subsequent) vaccine doses are not able to be provided within the prescribed upper age limits (refer to ‘Catch-up guidelines for individual vaccines for children <10 years of age’ below).

Using the catch-up worksheet (Figure 2.1.1) for children <10 years of age

A catch-up schedule for a child <10 years of age should be planned by taking into account the guidelines above in conjunction with the catch-up tables (listed above). The catch-up worksheet (Figure 2.1.1) provides a method of recording these steps.

To use the catch-up worksheet:

1. Record the child’s details, including date of birth and current age in the top left corner of the worksheet.
2. For each vaccine, determine how many doses have been received and the date that the last dose was given. Record this in the ‘Last dose given’ column of the worksheet. If documentation is adequate, include previous vaccinations given in another country (receipt of these vaccines should be entered onto the ACIR (Australian Childhood Immunisation Register) for a child <7 years of age – refer to 2.3.4 Immunisation registers (Handbook10-home-handbook10-part2-handbook10-2-3)).
3. Refer to Table 2.1.6 to check how many doses of each vaccine are required for the child’s current age. Enter this number in the ‘Number of doses required at current age’ column of the worksheet.
4. Assess other factors that may affect the type or number of vaccines required. These should have been ascertained during pre-vaccination screening (refer to 2.1.4 Pre-vaccination screening above, the pre-vaccination screening check list (Table 2.1.1) and table of responses (Table 2.1.2) and may include:
   - anaphylaxis to any vaccine or one of its components (that vaccine is contraindicated)
   - immunocompromise due to disease or treatment (refer to 3.3 Groups with special vaccination requirements (Handbook10-home-handbook10-part3-handbook10-3-3)).
   - children identifying as Aboriginal or Torres Strait Islander (refer to 3.1 Vaccination for Aboriginal and Torres Strait Islander people (Handbook10-home-handbook10-part3-handbook10-3-1)).
   - children with underlying medical risk condition(s) that predispose them to invasive pneumococcal disease (refer to 4.13 Pneumococcal disease (Handbook10-home-handbook10-part4-handbook10-4-13)).
   - preterm infants born at <32 weeks gestation (refer to ‘Hepatitis B vaccine’ and ‘Pneumococcal conjugate vaccines (13vPCV)’).
   - children identifying as Aboriginal or Torres Strait Islander (refer to 3.1 Vaccination for Aboriginal and Torres Strait Islander people (Handbook10-home-handbook10-part3-handbook10-3-1)).
   - children with underlying medical risk condition(s) that predispose them to invasive pneumococcal disease (refer to 4.13 Pneumococcal disease (Handbook10-home-handbook10-part4-handbook10-4-13)).
5. Record any factors that affect the comments column beside the relevant vaccine.
6. If any variations to the schedule are necessary due to recorded factors (e.g. a child who is immunocompromised may require different vaccines), adjust the ‘number of doses required’ accordingly.
7. For each vaccine, compare the number of doses received, as recorded in the ‘Last dose given’ column, with the number of doses required for the child’s current age.
8. If the child has already received the number of doses required for a particular vaccine, cross through the relevant ‘Dose number due now’ and ‘Further doses’ columns. Ensure that the minimum acceptable interval has been observed for all doses previously received, particularly if the child commenced their vaccination program overseas.
9. If the number of doses received, as recorded in the ‘Last dose given’ column, is less than the number of doses required, administer a dose of the relevant vaccine now, and record this in the ‘Dose number due now’ column. If this dose still does not complete the required doses, enter the further dose numbers in the ‘Further doses’ column.
10. To schedule the next dose at the most appropriate time (usually at the earliest opportunity), refer to Table 2.1.7 for the minimum acceptable interval required between doses. Record when the next dose is due in the ‘Further doses’ column.
11. Convert this information into a list of proposed appointment dates, detailing vaccines and dose number needed at each visit on the ‘Catch-up appointments’ section of the worksheet.
12. Once a child has received relevant catch-up vaccines, give the remaining scheduled vaccines as per the recommended NIP (National Immunisation Program) schedule. For example, for a 12-month-old child who is brought up to date with all vaccines including the 12-month vaccinations, the 2nd dose of MMR (Measles, Mumps and Rubella) containing vaccine should be given at 18 months of age, not 4 weeks after the last received dose.
Figure 2.1.1: Catch-up worksheet for children <10 years of age for NIP vaccines

CATCH-UP WORKSHEET

<table>
<thead>
<tr>
<th>Name:</th>
<th>Last dose given</th>
<th>Number of doses required at current age*</th>
<th>Dose number due now</th>
<th>Further doses Interval or date</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>DOB:</td>
<td>Dose number and date</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age:</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

DTPa (diphtheria-tetanus-acellular pertussis vaccine)

Poliomyelitis (IPV (inactivated poliomyelitis vaccine))

Hepatitis A

Hepatitis B

Hib (Haemophilus influenzae type b)

Pneumococcal (13vPCV (13-valent pneumococcal conjugate vaccine))

Pneumococcal (23vPPV (23-valent pneumococcal polysaccharide vaccine))

MenCCV (meningococcal serogroup C conjugate vaccine)

MMR (Measles, Mumps and Rubella)

Rotavirus

DO NOT give after upper age limits for each dose. Refer to Table 4.17 (Handbook10-home#handbook10part4#handbook10-4-17), Table 4.17.1 (Handbook10-home#handbook10part4#handbook10-4-17#table-4-17-1).

Varicella

CATCH-UP APPOINTMENTS

<table>
<thead>
<tr>
<th>Date</th>
<th>Vaccines and dose number</th>
<th>Interval to next dose</th>
<th>Comments</th>
</tr>
</thead>
</table>

* Refer to Table 2.1.6 Number of vaccine doses that should have been administered by the current age of the child and Table 2.1.7 Minimum acceptable dose intervals for children <10 years of age.
† Refer to Table 2.1.8 for Hib (Haemophilus influenzae type b) vaccine catch-up recommendations.
‡ Refer to Tables 2.1.9, 2.1.10 and 2.1.11 for pneumococcal vaccine catch-up recommendations.
§ Previous doses of pneumococcal conjugate vaccine may have been given using 7-valent (7vPCV (7-valent pneumococcal conjugate vaccine)) or 10-valent (10vPCV (10-valent pneumococcal conjugate vaccine)) vaccine(s).

Table 2.1.5: Minimum acceptable age for the 1st dose of scheduled vaccines in infants in special circumstances*

<table>
<thead>
<tr>
<th>Vaccine</th>
<th>Minimum age for 1st dose in special circumstances*</th>
<th>Action if a vaccine dose is inadvertently administered prior to the recommended minimum age‡</th>
</tr>
</thead>
</table>

<table>
<thead>
<tr>
<th>Vaccine</th>
<th>Minimum age for 1st dose in special circumstances*</th>
<th>Action if a vaccine dose is inadvertently administered prior to the recommended minimum age</th>
</tr>
</thead>
<tbody>
<tr>
<td>DTPa (diphtheria-tetanus-acellular pertussis vaccine)</td>
<td>6 weeks</td>
<td>If the 1st dose of DTPa (diphtheria-tetanus-acellular pertussis vaccine)-containing vaccine was administered at ≤28 days of age, it is recommended that the dose is repeated. This repeat dose should be given at 2 months of age. The NIP (National Immunisation Program) schedule should be followed thereafter, with the next dose of DTPa (diphtheria-tetanus-acellular pertussis vaccine)-containing vaccine given at 4 months of age.†&lt;sup&gt;11&lt;/sup&gt; If the 1st dose of DTPa (diphtheria-tetanus-acellular pertussis vaccine)-containing vaccine was administered between &gt;28 days and &lt;42 days (6 weeks) of age, it does not necessarily need to be repeated. Limited data suggest that administration at this age will still be safe and immunogenic. The NIP (National Immunisation Program) schedule should be followed thereafter, with the next dose of DTPa (diphtheria-tetanus-acellular pertussis vaccine)-containing vaccine given at 4 months of age.†&lt;sup&gt;11&lt;/sup&gt;</td>
</tr>
<tr>
<td>Poliomyelitis (IPV (inactivated poliomyelitis vaccine))</td>
<td>6 weeks</td>
<td>Refer to DTPa (diphtheria-tetanus-acellular pertussis vaccine)-containing vaccines above.</td>
</tr>
<tr>
<td>Hib (Haemophilus influenzae type b)</td>
<td>6 weeks</td>
<td>Refer to DTPa (diphtheria-tetanus-acellular pertussis vaccine)-containing vaccines above.</td>
</tr>
<tr>
<td>Hepatitis B§</td>
<td>6 weeks&lt;sup&gt;§&lt;/sup&gt;</td>
<td>Refer to DTPa (diphtheria-tetanus-acellular pertussis vaccine)-containing vaccines above.</td>
</tr>
<tr>
<td>Pneumococcal (10vPCV 13-valent pneumococcal conjugate vaccine)</td>
<td>6 weeks</td>
<td>If the 1st dose of PCV (pneumococcal conjugate vaccine) was administered at ≤28 days of age, it is recommended that the dose is repeated. This repeat dose should be given at 2 months of age. The NIP (National Immunisation Program) schedule should be followed thereafter, with the next dose of PCV (pneumococcal conjugate vaccine) given at 4 months of age.† If the 1st dose of PCV (pneumococcal conjugate vaccine) was administered between &gt;28 days and &lt;42 days (6 weeks) of age, it does not necessarily need to be repeated. Limited data suggest that administration at this age will still be safe and immunogenic. The NIP (National Immunisation Program) schedule should be followed thereafter, with the next dose of pneumococcal conjugate vaccine given at 4 months of age.†</td>
</tr>
<tr>
<td>Rotavirus</td>
<td>6 weeks</td>
<td>If the 1st dose of rotavirus vaccine was administered at ≤28 days of age, it is recommended that the dose is repeated. This repeat dose should be given at 2 months of age. The NIP (National Immunisation Program) schedule should be followed thereafter, with the next dose of rotavirus vaccine given at 4 months of age. If the 1st dose of rotavirus vaccine was administered between &gt;28 days and &lt;42 days (6 weeks) of age, it does not necessarily need to be repeated. Limited data suggest that administration at this age will still be safe and immunogenic. The NIP (National Immunisation Program) schedule should be followed thereafter, with the next dose of rotavirus vaccine given at 4 months of age. For all doses of rotavirus vaccine it is important to ensure the upper age limits for dose administration are not exceeded (refer to 4.17 Rotavirus(Handbook10-home=handbook10part4=handbook10-4-17), Table 4.17.1).</td>
</tr>
<tr>
<td>Meningococcal®</td>
<td>6 weeks&lt;sup&gt;®&lt;/sup&gt;</td>
<td>If the 1st dose of either 4vMenCV or MenB is administered between &gt;28 days and &lt;42 days (6 weeks) of age, the dose does not necessarily need to be repeated; however, expert advice should be sought.</td>
</tr>
<tr>
<td>Hepatitis A (Indigenous children in NT, Qld, SA and WA only)</td>
<td>12 months</td>
<td>If the 1st dose of hepatitis A vaccine is administered at &lt;12 months of age, and ongoing protection against hepatitis A is required, the 1st dose should be repeated.</td>
</tr>
<tr>
<td>MMR (Measles, Mumps and Rubella)</td>
<td>12 months</td>
<td>MMR (Measles, Mumps and Rubella) vaccine may be given from 9 months of age, in certain circumstances, such as for post-exposure prophylaxis for measles (refer to 4.9 Measles(Handbook10-home=handbook10part4=handbook10-4-9), but it is recommended that the 1st dose be repeated if it was given at &lt;12 months of age† Refer to note on MMRV (Measles, Mumps, Rubella and Varicella) below.††</td>
</tr>
<tr>
<td>Varicella††</td>
<td>12 months</td>
<td>If a varicella-containing vaccine is administered at &lt;12 months of age, the dose should be repeated, preferably at 18 months of age. Refer to note on MMRV (Measles, Mumps, Rubella and Varicella) below.††</td>
</tr>
</tbody>
</table>

* Special circumstances may include infants/children being vaccinated during an outbreak of a certain disease, before overseas travel, or opportunistic vaccination following early attendance to a provider. These ages will often differ from routinely recommended ages of administration under the NIP (National Immunisation Program) schedule. In some instances, these ages will also result in the dose not being considered by the Australian Childhood Immunisation Register (ACIR (Australian Childhood Immunisation Register)) as valid for the purpose of calculating immunisation status. If the ACIR (Australian Childhood Immunisation Register) age requirement differs from the minimum ages in this table, this is noted.†† If the need to repeat the 1st dose of vaccine is not recognised until the infant is older (e.g. a 4-month-old infant presents for vaccination and has only previously received 1 dose of DTPa (diphtheria-tetanus-acellular pertussis vaccine) and IPV (inactivated poliomyelitis vaccine)-containing vaccines above.|

†‡ The minimum age from which the combination vaccine given at ≤28 days of age, it is recommended that the dose is repeated. This repeat dose should be given at 2 months of age. The NIP (National Immunisation Program) schedule should be followed thereafter, with the next dose of DTPa (diphtheria-tetanus-acellular pertussis vaccine)-containing vaccine given at 4 months of age.†‡ If the 1st dose of DTPa (diphtheria-tetanus-acellular pertussis vaccine)-containing vaccine was administered between >28 days and <42 days (6 weeks) of age, it does not necessarily need to be repeated. Limited data suggest that administration at this age will still be safe and immunogenic. The NIP (National Immunisation Program) schedule should be followed thereafter, with the next dose of DTPa (diphtheria-tetanus-acellular pertussis vaccine)-containing vaccine given at 4 months of age.†‡ |

†‡ The minimum age from which the combination vaccine given at ≤28 days of age, it is recommended that the dose is repeated. This repeat dose should be given at 2 months of age. The NIP (National Immunisation Program) schedule should be followed thereafter, with the next dose of DTPa (diphtheria-tetanus-acellular pertussis vaccine)-containing vaccine given at 4 months of age.†‡ If the 1st dose of DTPa (diphtheria-tetanus-acellular pertussis vaccine)-containing vaccine was administered between >28 days and <42 days (6 weeks) of age, it does not necessarily need to be repeated. Limited data suggest that administration at this age will still be safe and immunogenic. The NIP (National Immunisation Program) schedule should be followed thereafter, with the next dose of DTPa (diphtheria-tetanus-acellular pertussis vaccine)-containing vaccine given at 4 months of age.†‡ |

†‡ The minimum age from which the combination vaccine given at ≤28 days of age, it is recommended that the dose is repeated. This repeat dose should be given at 2 months of age. The NIP (National Immunisation Program) schedule should be followed thereafter, with the next dose of DTPa (diphtheria-tetanus-acellular pertussis vaccine)-containing vaccine given at 4 months of age.†‡ If the 1st dose of DTPa (diphtheria-tetanus-acellular pertussis vaccine)-containing vaccine was administered between >28 days and <42 days (6 weeks) of age, it does not necessarily need to be repeated. Limited data suggest that administration at this age will still be safe and immunogenic. The NIP (National Immunisation Program) schedule should be followed thereafter, with the next dose of DTPa (diphtheria-tetanus-acellular pertussis vaccine)-containing vaccine given at 4 months of age.†‡ |

†‡ The minimum age from which the combination vaccine given at ≤28 days of age, it is recommended that the dose is repeated. This repeat dose should be given at 2 months of age. The NIP (National Immunisation Program) schedule should be followed thereafter, with the next dose of DTPa (diphtheria-tetanus-acellular pertussis vaccine)-containing vaccine given at 4 months of age.†‡ If the 1st dose of DTPa (diphtheria-tetanus-acellular pertussis vaccine)-containing vaccine was administered between >28 days and <42 days (6 weeks) of age, it does not necessarily need to be repeated. Limited data suggest that administration at this age will still be safe and immunogenic. The NIP (National Immunisation Program) schedule should be followed thereafter, with the next dose of DTPa (diphtheria-tetanus-acellular pertussis vaccine)-containing vaccine given at 4 months of age.†‡ |

†‡ The minimum age from which the combination vaccine given at ≤28 days of age, it is recommended that the dose is repeated. This repeat dose should be given at 2 months of age. The NIP (National Immunisation Program) schedule should be followed thereafter, with the next dose of DTPa (diphtheria-tetanus-acellular pertussis vaccine)-containing vaccine given at 4 months of age.†‡ If the 1st dose of DTPa (diphtheria-tetanus-acellular pertussis vaccine)-containing vaccine was administered between >28 days and <42 days (6 weeks) of age, it does not necessarily need to be repeated. Limited data suggest that administration at this age will still be safe and immunogenic. The NIP (National Immunisation Program) schedule should be followed thereafter, with the next dose of DTPa (diphtheria-tetanus-acellular pertussis vaccine)-containing vaccine given at 4 months of age.†‡ |
Table 2.1.6: Number of vaccine doses that should have been administered by the current age of the child

This table can be used in conjunction with Figure 2.1.1 Catch-up worksheet for children <10 years of age for NIP (National Immunisation Program) vaccines.

<table>
<thead>
<tr>
<th>Vaccine</th>
<th>Current age</th>
<th>0 to &lt;2 months</th>
<th>2 to &lt;4 months</th>
<th>4 to &lt;6 months</th>
<th>6 to &lt;12 months</th>
<th>12 to 18 months</th>
<th>&gt;18 months to &lt;4 years</th>
<th>4 years to &lt;10 years</th>
</tr>
</thead>
<tbody>
<tr>
<td>DTPa (diphtheria-tetanus-acellular pertussis vaccine)</td>
<td></td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>3</td>
<td>4</td>
<td>5*</td>
<td></td>
</tr>
<tr>
<td>Poliomyelitis (IPV (inactivated poliomyelitis vaccine))</td>
<td></td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>3</td>
<td>3</td>
<td>4†</td>
<td></td>
</tr>
<tr>
<td>Hepatitis A §</td>
<td></td>
<td>1†</td>
<td>2†</td>
<td>2†</td>
<td>2†</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hepatitis B §</td>
<td></td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>3</td>
<td>3</td>
<td>3</td>
<td></td>
</tr>
<tr>
<td>Hib (cervical Haemophilus influenzae type b)</td>
<td></td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>3</td>
<td>3</td>
<td>3</td>
<td></td>
</tr>
<tr>
<td>Pneumococcal (13-valent pneumococcal conjugate vaccine) and 23vPPV (23-valent pneumococcal polysaccharide vaccine)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Complex – refer to Table 2.1.8 for Hib (cervical Haemophilus influenzae type b) vaccine catch-up</td>
<td></td>
</tr>
<tr>
<td>MenCCV (meningococcal serogroup C conjugate vaccine)</td>
<td></td>
<td>1</td>
<td>1</td>
<td>1</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>MMR (Measles, Mumps and Rubella) ‡</td>
<td></td>
<td>1</td>
<td>2 ‡</td>
<td>2 ‡</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Rotavirus #</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Complex – refer to Tables 2.1.9, 2.1.10 and 2.1.11 for pneumococcal vaccine catch-up</td>
<td></td>
</tr>
<tr>
<td>Varicella †</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>There are specific age limits as per 4.17</td>
<td>NO CATCH-UP</td>
</tr>
</tbody>
</table>

* A total of 5 doses of DTPa-containing vaccine are recommended for children <10 years of age: 3 doses as part of the primary schedule for infants (recommended at 2, 4 and 6 months of age) and 2 booster doses (recommended at 18 months and 4 years of age); refer to 4.12 Pertussis. If the 1st booster dose recommended at 18 months of age (dose 4) is given after the child is 3.5 years of age, the 2nd booster dose recommended at age 4 years (dose 5) is not required.
† If the 3rd dose of IPV (inactivated poliomyelitis vaccine) is given after 3.5 years of age, a 4th dose is not required. However, if using a combination vaccine it is acceptable to give a 4th dose.
‡ Indigenous children resident in the Northern Territory, Queensland, South Australia and Western Australia only. Dependent on jurisdiction, the 1st dose is given at 12–18 months of age, followed by the 2nd dose 6 months later at 18–24 months of age. Consult relevant state/territory health authorities for advice regarding catch-up in children >2 years of age.
§ A birth dose of monovalent hepatitis B vaccine is recommended for all infants; however, if this was not given, a catch-up birth dose is not necessary. Where the birth dose was given, in the usual circumstances where hepatitis B-containing combination vaccines for children are used for catch-up, a further 3 doses of hepatitis B-containing vaccine are recommended. In the unusual circumstance where a child requires catch-up only for hepatitis B vaccination, the standard monovalent hepatitis B vaccination schedule of 0, 1, 6 months can be adopted to work out the remaining number of doses required and intervals of the catch-up schedule (refer to 4.5 Hepatitis B (Handbook 10-home-handbook 10-part4-handbook 10-4-5)).
¶ MMRV (Measles, Mumps, Rubella and Varicella) can be given as the 2nd dose of MMR (Measles, Mumps and Rubella) containing vaccine where both MMR (Measles, Mumps and Rubella) and varicella are required (refer to 4.9 Measles (Handbook 10-home-handbook 10-part4-handbook 10-4-9) and 4.22 Varicella (Handbook 10-home-handbook 10-part4-handbook 10-4-22)).
†† One monovalent varicella vaccine, Varilrix, is registered for use from 9 months of age, and can be provided from 9 months of age in special circumstances, for example, prior to travel. However, if a dose has been provided at <12 months of age, it should be repeated.

Table 2.1.7: Minimum acceptable dose intervals for children <10 years of age

This table can be used in conjunction with Figure 2.1.1 Catch-up worksheet for children <10 years of age for NIP (National Immunisation Program) vaccines and Table 2.1.6 Number of vaccine doses that should have been administered by the current age of the child.

Note: These are not the routinely recommended intervals between vaccine doses. These minimum intervals are only to be used under special circumstances, such as when catch-up vaccination is required or when a child is back on schedule for their age. These intervals may differ from the routinely recommended intervals between doses under the NIP (National Immunisation Program) schedule. If providing catch-up using a combination vaccine, it is important to ensure that minimum intervals are met for all antigens.

<table>
<thead>
<tr>
<th>Vaccine</th>
<th>Minimum interval between dose 1 and 2</th>
<th>Minimum interval between dose 2 and 3</th>
<th>Minimum interval between dose 3 and 4</th>
<th>Minimum interval between dose 4 and 5</th>
</tr>
</thead>
<tbody>
<tr>
<td>DTPa (diphtheria-tetanus-acellular pertussis vaccine)</td>
<td>4 weeks</td>
<td>4 weeks</td>
<td>6 months</td>
<td>6 months</td>
</tr>
<tr>
<td>Poliomyelitis (IPV (inactivated poliomyelitis vaccine))</td>
<td>4 weeks</td>
<td>4 weeks</td>
<td>4 weeks†</td>
<td></td>
</tr>
<tr>
<td>Hepatitis A §</td>
<td>6 months</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Catch-up guidelines for individual vaccines for children <10 years of age

The advice below on catch-up for individual vaccines should be considered with the general principles for planning catch-up vaccination described in more detail in ‘Planning catch-up vaccination’ above.

DTPa (diphtheria-tetanus-acellular pertussis vaccine) vaccine

Monovalent pertussis vaccine is not available in Australia. DTPa-containing vaccines can be used for catch-up of primary or booster doses in children aged <10 years, where required.

Children <10 years of age should receive a total of 5 doses of DTPa-containing vaccine; 3 doses as part of the primary schedule for infants (recommended at 2, 4 and 6 months of age) and 2 booster doses (recommended at 18 months and 4 years of age) (refer to 4.12 Pertussis(Handbook10-home-handbook10part4-handbook10-4-12)). However, if the 1st booster dose recommended at 18 months of age (dose 4) is given after the child is 3.5 years of age, the 2nd booster dose recommended at 4 years of age (dose 5) is not required.

Because the 18-month booster dose was not routinely recommended between 2003 and 2015, there will be children who have only had 3 primary doses of DTPa-containing vaccine prior to a booster dose at 4 years of age. In these circumstances, providing the child’s 4th dose of DTPa-containing vaccine was administered after 3.5 years of age, they do not require any further doses until the single booster dose recommended during adolescence (refer to 4.12 Pertussis(Handbook10-home-handbook10part4-handbook10-4-12)) However, any child aged ≥18 months to 3.5 years who has not previously received a booster dose of DTPa-containing vaccine at 18 months of age should receive their 1st booster dose (dose 4) now, followed by a 2nd booster dose at 4 years of age (with a minimum interval of 6 months between these doses). These children should then receive their next booster dose during adolescence as routinely recommended (refer to 4.12 Pertussis(Handbook10-home-handbook10part4-handbook10-4-12)).

Hepatitis B vaccine

Australian-born infants typically receive a monovalent hepatitis B vaccine birth dose (which can be regarded as dose 0 [zero] for the purposes of this table) followed by a primary course of hepatitis B-containing vaccine consisting of 3 doses at 2, 4 and 6 months of age (given as DTPa-hepB-IPV-Hib). In addition to the minimum intervals between doses outlined in this table, the minimum recommended interval between dose 1 and dose 2 is 4 months (refer to 4.5 Hepatitis B(Handbook10-home-handbook10part4-handbook10-4-5)). The final dose of the primary hepatitis B vaccine course (with or without a birth dose) should preferably be administered at ≥24 weeks of age. However, if the final dose is given at <24 weeks but ≥16 weeks (approximately 4 months) of age, it is not necessary to repeat the dose for the child to be considered as fully immunised by the ACIR. Note: The ACIR accepts a minimum interval of 4 weeks between any hepatitis B vaccine dose to allow children who have been immunised using 3-dose schedules (typically provided overseas) to be considered as fully immunised.

The recommended schedule for meningococcal vaccines varies for different formulations (refer to 4.10 Meningococcal disease(Handbook10-home-handbook10part4-handbook10-4-10)). The minimum acceptable interval between conjugate vaccines containing meningococcal serogroup C (MenCV, Hib-MenCCV and 4vMenCV) is 8 weeks. The minimum acceptable interval between primary doses of MenB is 4 weeks for infants aged <6 months. There is no clinical trial data in older children for minimum intervals less than the routinely recommended interval of 8 weeks. In circumstances where MenB and 4vMenCV are indicated, the vaccines can be administered concurrently based on first principles. (Refer also 4.10 Meningococcal disease(Handbook10-home-handbook10part4-handbook10-4-10)).

MRM (Measles, Mumps and Rubella)†† is recommended as the 1st dose of MMR (Measles, Mumps and Rubella)-containing vaccine in children <4 years of age (refer to 4.9 Measles (Handbook10-home-handbook10part4-handbook10-4-9)), MMR / Measles, Mumps, Rubella and Varicella is recommended to be given as the 2nd dose of MMR (Measles, Mumps and Rubella)-containing vaccine. MMRV / Measles, Mumps, Rubella and Varicella can be given 4 weeks following the 1st catch-up dose of MMR (Measles, Mumps and Rubella) vaccine or as catch-up for the 2nd dose of MMR (Measles, Mumps and Rubella) where varicella is also required.

Varicella**†† Two doses of varicella-containing vaccine are not routinely recommended in children <14 years of age; however, a 2nd dose can be provided to offer increased protection against varicella (refer to 4.22 Varicella(Handbook10-home-handbook10part4-handbook10-4-22)).
The same brand of Hib-containing vaccine should be used for all doses of Hib vaccine. If different Hib vaccines (i.e. PRP-OMP and PRP-T vaccines) are used in the primary series, for example, in a child born overseas, then 3 doses (of any Hib vaccine) are required for the primary series, at 2, 4 and 6 months of age, with a booster of a Hib-containing vaccine at 12 months of age (provided as either the combination vaccine Hib-MenCCV or monovalent Hib vaccine – refer also to Meningococcal C conjugate vaccine (MenCCV) below).

For extremely preterm and/or low-birth-weight infants (<28 weeks gestation or <1500 g birth weight), 4 doses of a Hib (<em>Haemophilus influenzae</em> type b)-containing vaccine (irrespective of the brand used) should be given, at 2, 4, 6 and 12 months of age (refer to 3.3.2 Vaccination of women who are planning pregnancy, pregnant or breastfeeding, and preterm infants(http://wcmprd01.central.health/internet/immunise/publishing.nsf/Content/Handbook10-home-handbook10part3-handbook10-3-3)). Refer also to 4.3 Haemophilus influenzae type b (http://wcmprd01.central.health/internet/immunise/publishing.nsf/Content/Handbook10-home-handbook10part4-handbook10-4-3).

MMR (Measles, Mumps and Rubella) vaccine, MMRV (Measles, Mumps, Rubella and Varicella) vaccine and varicella vaccine

If no previous documented doses have been given, catch-up for MMR (Measles, Mumps and Rubella) vaccine consists of 2 doses of MMR (Measles, Mumps and Rubella)-containing vaccine, given at least 4 weeks apart (refer to 4.9 Measles(Handbook10-home-handbook10part4-handbook10-4-8)). If no previous documented varicella vaccination has been given, a single dose of varicella-containing vaccine is recommended in children aged <14 years (refer to 4.22 Varicella(Handbook10-home-handbook10part4-handbook10-4-22)).

If a child receives varicella vaccination at <12 months of age, a further dose should be given at 18 months of age. In this circumstance MMRV (Measles, Mumps, Rubella and Varicella) vaccine may be given where the 2nd dose of MMR (Measles, Mumps and Rubella) and varicella of a dose of varicella vaccine are both required (refer below and to 4.22 Varicella (Handbook10-home-handbook10part4-handbook10-4-22)).

Meningococcal C conjugate vaccine (MenCCV)

A single dose of MenCCV (meningococcal serogroup C conjugate vaccine)-containing vaccine is recommended for children at 12 months of age (as either MenCCV (meningococcal serogroup C conjugate vaccine) or the combination vaccine Hib-MenCCV). If a dose has not been given at ≥12 months of age (or if dose(s) were given at <12 months of age), a single dose of MenCCV (meningococcal serogroup C conjugate vaccine) is recommended (refer to 4.10 Meningococcal disease(Handbook10-home-handbook10part4-handbook10-4-10)). Both MenCCV (meningococcal serogroup C conjugate vaccine) and Hib-MenCCV can be used for catch-up vaccinations for either meningococcal C or Hib in children <10 years of age, if required. 4vMenCV and MenBv are recommended for certain children at increased risk of meningococcal disease due to age and/or other risk factors (refer to 3.3 Groups with special vaccination requirements(Handbook10-home-handbook10part3-handbook10-3-3) and 4.10 Meningococcal disease(Handbook10-home-handbook10part4-handbook10-4-10)).

Pneumococcal conjugate vaccines (13vPCV (13-valent pneumococcal conjugate vaccine)) and 10vPCV (10-valent pneumococcal conjugate vaccine))

The number of doses and recommended intervals of 13vPCV (13-valent pneumococcal conjugate vaccine) required for catch-up vaccination vary with the age of the child, their health and Indigenous status, and the state or territory of residence (Refer to Tables 2.1.9, 2.1.10 and 2.1.11 below).

Table 2.1.9 is for children who are not at increased risk of invasive pneumococcal disease (IPD (invasive pneumococcal disease)) (including Indigenous children living in the Australian Capital Territory, New South Wales, Victoria and Tasmania). Table 2.1.10 is for Indigenous children residing in the Northern Territory, Queensland, South Australia and Western Australia. Table 2.1.11 provides catch-up details for children with a medical condition(s) associated with an increased risk of IPD (invasive pneumococcal disease). (Refer also to 4.13 Pneumococcal disease(Handbook10-home-handbook10part4-handbook10-4-13).)

If 13vPCV (13-valent pneumococcal conjugate vaccine) is not available, and 10vPCV (10-valent pneumococcal conjugate vaccine) is being used, 10vPCV (10-valent pneumococcal conjugate vaccine) is recommended in a 4-dose schedule. (Refer also to 4.13 Pneumococcal disease(Handbook10-home-handbook10part4-handbook10-4-13).) If catch-up is required for 10vPCV (10-valent pneumococcal conjugate vaccine), vaccination can be done according to the information provided in Table 2.1.10.

Children aged ≥5 years who are not at increased risk of invasive pneumococcal disease (including Indigenous children aged ≥5 years) do not require catch-up doses of PCV (pneumococcal conjugate vaccine).

Poliomyelitis vaccine

If no previous doses of poliomyelitis vaccine have been given, give 3 doses of IPV (inactivated poliomyelitis vaccine) or IPV-containing vaccines at least 4 weeks apart (refer to 4.14 Poliomyelitis). (Previous doses of OPV (oral poliomyelitis vaccine) are interchangeable with IPV (inactivated poliomyelitis vaccine). )

If the 3rd dose of IPV (inactivated poliomyelitis vaccine) is administered at ≤3.5 years of age, give the 4th (booster) dose at the 4th birthday. If the 3rd dose is given after 3.5 years, the 4th dose is not required. However, if the use of combination vaccines is necessary, a further IPV (inactivated poliomyelitis vaccine)-containing dose may be given.

Rotavirus vaccine

Catch-up rotavirus vaccination of older infants or children is not recommended. Infants should commence the course of rotavirus vaccination within the recommended age limits for the 1st dose; that is, the 1st dose of Rotarix should be given between 6 and 12 weeks of age (i.e. before turning 13 weeks old), and the 1st dose of Rotavirus should be given between 6 and 14 weeks of age (i.e. before turning 15 weeks old). It is recommended that vaccine doses are not given beyond the upper age limits specified in Table 4.17.1 (refer to 4.17 Rotavirus (Handbook10-home-handbook10part4-handbook10-4-17)).

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Table 2.1.8: Catch-up schedule for <em>Haemophilus influenzae</em> type b (Hib) vaccination for children <5 years of age

<table>
<thead>
<tr>
<th>Number of Hib (&lt;em&gt;Haemophilus influenzae&lt;/em&gt; type b) doses given previously</th>
<th>Current age</th>
<th>Age when previous dose(s) of Hib (&lt;em&gt;Haemophilus influenzae&lt;/em&gt; type b) vaccine given</th>
<th>Recommendations</th>
</tr>
</thead>
<tbody>
<tr>
<td>No previous doses</td>
<td>&lt;7 months</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>7–11 months</td>
<td>–</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>12–15 months</td>
<td>–</td>
<td>–</td>
<td>–</td>
</tr>
</tbody>
</table>

### Number of Hib (\textit{Haemophilus influenzae} type b) doses given previously

<table>
<thead>
<tr>
<th>Current age</th>
<th>1st dose</th>
<th>2nd dose</th>
<th>3rd dose</th>
<th>Number of further primary dose(s) required</th>
<th>Number of booster doses required at age ≥12 months</th>
</tr>
</thead>
<tbody>
<tr>
<td>16–59 months</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>Not needed ⁵</td>
</tr>
<tr>
<td>1 previous dose</td>
<td>&lt;7 months</td>
<td>–</td>
<td>–</td>
<td>2 ⁴</td>
<td>1</td>
</tr>
<tr>
<td>7–11 months</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>12–15 months</td>
<td>&lt;12 months</td>
<td>–</td>
<td>–</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>≥12 months</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>Not needed</td>
<td>–</td>
</tr>
<tr>
<td>16–59 months</td>
<td>&lt;16 months</td>
<td>–</td>
<td>–</td>
<td>Not needed</td>
<td>–</td>
</tr>
<tr>
<td>2 previous doses</td>
<td>≤12 months</td>
<td>&lt;7 months</td>
<td>&lt;12 months</td>
<td>1 ⁴</td>
<td>1</td>
</tr>
<tr>
<td>7–11 months</td>
<td>7–11 months</td>
<td>–</td>
<td>–</td>
<td>Not needed</td>
<td>–</td>
</tr>
<tr>
<td>12–15 months</td>
<td>&lt;7 months</td>
<td>&lt;12 months</td>
<td>–</td>
<td>1 ⁴</td>
<td>1</td>
</tr>
<tr>
<td>≥12 months</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>Not needed</td>
<td>–</td>
</tr>
<tr>
<td>16–59 months</td>
<td>≤16 months</td>
<td>–</td>
<td>–</td>
<td>Not needed</td>
<td>–</td>
</tr>
<tr>
<td>3 previous doses</td>
<td>7–11 months</td>
<td>Any age</td>
<td>Any age</td>
<td>Any age</td>
<td>Not needed</td>
</tr>
<tr>
<td>12–59 months</td>
<td>&lt;7 months</td>
<td>&lt;12 months</td>
<td>&lt;12 months</td>
<td>Not needed</td>
<td>–</td>
</tr>
<tr>
<td>≥12 months</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>Not needed</td>
<td>–</td>
</tr>
<tr>
<td>≥12 months</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>Not needed</td>
<td>–</td>
</tr>
<tr>
<td>7–11 months</td>
<td>7–15 months</td>
<td>–</td>
<td>–</td>
<td>Not needed</td>
<td>–</td>
</tr>
<tr>
<td>Any age</td>
<td>≤16 months</td>
<td>–</td>
<td>–</td>
<td>Not needed</td>
<td>–</td>
</tr>
</tbody>
</table>

* Recommendations for vaccination of haematopoietic stem cell transplant (HSCT) recipients differ; refer to Table 3.3.3 Recommendations for revaccination following haematopoietic stem cell transplant (HSCT) in children and adults, irrespective of previous immunisation history.

† This column lists the number of further primary doses that should be scheduled for the child, based on their current age. The recommended interval between primary doses for catch-up is 1 month. Where possible, it is recommended to schedule the required remaining primary doses to be given prior to 12 months of age. If there are further delays in the scheduled catch-up primary dose(s), the number of doses required should be checked again against the child’s age at each presentation.

‡ This column lists the number of booster doses that should be scheduled for the child, based on their current age. Booster doses are to be given at age 12 months or 2 months after the last dose of Hib (\textit{Haemophilus influenzae} type b) vaccine, whichever is later.

§ One less dose is required if PRP-OMP has been used for the entire primary course. If PRP-T has been given as one or more of the doses in the primary course, plan for the number of doses as specified in this table.

¶ A booster dose is not needed if the last previous dose was given at ≥16 months of age.

# This booster dose is not required if PRP-OMP (PRP conjugated to the outer membrane protein of Neisseria meningitidis) was used for both the 1st and the 2nd (primary) doses of Hib (\textit{Haemophilus influenzae} type b) vaccine in infancy, since the 3rd dose of Hib (\textit{Haemophilus influenzae} type b) vaccine received at age 12–15 months would have served as the booster dose for these children.

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**Table 2.1.9: Catch-up schedule for 13vPCV(Prevenar 13) for non-Indigenous children, and Indigenous children residing in the Australian Capital Territory, New South Wales, Tasmania and Victoria, who do not have any medical condition(s) associated with an increased risk of invasive pneumococcal disease (IPD), aged <5 years**

<table>
<thead>
<tr>
<th>Number of doses given previously</th>
<th>Age at presentation</th>
<th>Age when previous dose of any PCV (pneumococcal conjugate vaccine)* was given</th>
<th>Number of further dose(s) required ¹</th>
</tr>
</thead>
<tbody>
<tr>
<td>No previous doses</td>
<td>&lt;7 months</td>
<td>1st dose: –  2nd dose: –  3rd dose: –</td>
<td>3</td>
</tr>
<tr>
<td>1 previous dose</td>
<td>7–11 months</td>
<td>1st dose: –  2nd dose: –  3rd dose: –</td>
<td>2</td>
</tr>
</tbody>
</table>

* Recommendations for vaccination of haematopoietic stem cell transplant (HSCT) recipients differ; refer to Table 3.3.3 Recommendations for revaccination following haematopoietic stem cell transplant (HSCT) in children and adults, irrespective of previous immunisation history.
<table>
<thead>
<tr>
<th>Number of doses given previously</th>
<th>Age at presentation</th>
<th>Age when previous dose of any PCV (pneumococcal conjugate vaccine)* was given</th>
<th>Recommendations</th>
<th>Number of further dose(s) required</th>
<th>Number of booster 13vPCV (13-valent pneumococcal conjugate vaccine) doses required §</th>
</tr>
</thead>
<tbody>
<tr>
<td>No previous doses</td>
<td></td>
<td>1st dose</td>
<td>2nd dose</td>
<td>3rd dose</td>
<td>Number of further primary dose(s) required</td>
</tr>
<tr>
<td>&lt;7 months</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>3</td>
</tr>
<tr>
<td>7–11 months</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>2</td>
</tr>
<tr>
<td>12–23 months</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>1</td>
</tr>
<tr>
<td>24–59 months</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>Not needed</td>
</tr>
<tr>
<td>&lt;7 months</td>
<td>&lt;7 months</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>2</td>
</tr>
<tr>
<td>7–11 months</td>
<td>&lt;7 months</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>2</td>
</tr>
<tr>
<td>1 previous dose</td>
<td>12–59 months</td>
<td>≥12 months</td>
<td>–</td>
<td>–</td>
<td>Not needed</td>
</tr>
<tr>
<td>7–11 months</td>
<td>&lt;7 months</td>
<td>&lt;12 months</td>
<td>–</td>
<td>–</td>
<td>1</td>
</tr>
<tr>
<td>1 previous dose</td>
<td>12–59 months</td>
<td>&lt;12 months</td>
<td>–</td>
<td>–</td>
<td>Not needed</td>
</tr>
<tr>
<td>7–11 months</td>
<td>&lt;7 months</td>
<td>&lt;12 months</td>
<td>–</td>
<td>–</td>
<td>1</td>
</tr>
<tr>
<td>2 previous doses</td>
<td>12–23 months</td>
<td>≥12 months</td>
<td>–</td>
<td>–</td>
<td>Not needed</td>
</tr>
<tr>
<td>24–59 months</td>
<td>Any age</td>
<td>Any age</td>
<td>–</td>
<td>–</td>
<td>Not needed</td>
</tr>
<tr>
<td>3 previous doses</td>
<td>7–59 months</td>
<td>Any age</td>
<td>Any age</td>
<td>Any age</td>
<td>Not needed</td>
</tr>
</tbody>
</table>

* Prior PCV (pneumococcal conjugate vaccine) doses may have been given as 7vPCV (7-valent pneumococcal conjugate vaccine) (e.g. from overseas), 10vPCV (10-valent pneumococcal conjugate vaccine) or 13vPCV (13-valent pneumococcal conjugate vaccine). Use 13vPCV (13-valent pneumococcal conjugate vaccine) as the vaccine formulation for further catch-up doses required, regardless of which formulation of PCV (pneumococcal conjugate vaccine) the child received previously.

† Recommended interval between primary doses for catch-up is 1–2 months. Where possible, it is recommended to align doses with the standard schedule points at 4 months and 6 months of age for infants aged <7 months. The minimum interval between dose(s) is 1 month if aged <12 months, and 2 months if aged ≥12 months.

Table 2.1.10: Catch-up schedule for 13vPCV* (Prevenar 13) for Indigenous children residing in the Northern Territory, Queensland, South Australia or Western Australia ONLY, who do not have any medical condition(s) associated with an increased risk of invasive pneumococcal disease (IPD), aged <5 years

### Table 2.1.11: Catch-up schedule for 13vPCV (Prevenar 13) and 23vPPV (Pneumovax 23) in children with a medical condition(s) associated with an increased risk of invasive pneumococcal disease (IPD),* presenting at age <2 years

For children with a medical condition(s) associated with an increased risk of IPD (invasive pneumococcal disease) presenting at age ≥2 years, refer to recommendations in 4.13 Pneumococcal disease (Handbook10-home=handbook10part4-handbook10-4-13) and Table 4.13.2.1

**Table 2.1.11: Catch-up schedule for 13vPCV (Prevenar 13) and 23vPPV (Pneumovax 23) in children with a medical condition(s) associated with an increased risk of invasive pneumococcal disease (IPD),* presenting at age <2 years**

#### Number of doses given previously

<table>
<thead>
<tr>
<th>Number of doses given previously</th>
<th>Age at presentation</th>
<th>1st dose</th>
<th>2nd dose</th>
<th>3rd dose</th>
<th>Number of further primary dose(s) required</th>
<th>Number of booster doses of 13vPCV (13-valent pneumococcal conjugate vaccine) required at age ≥12 months</th>
<th>Number of doses of 23vPPV (23-valent pneumococcal polysaccharide vaccine) required at age 4–5 years</th>
</tr>
</thead>
<tbody>
<tr>
<td>No previous doses</td>
<td>&lt;7 months</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>3</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>7–11 months</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>2</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>12–23 months</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>1</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>&lt;7 months</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>2</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>&lt;7 months</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>2</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>&lt;7 months</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>2</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>7–11 months</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>1</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>12–23 months</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>1</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>≥12 months</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>Not needed</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>1 previous dose</td>
<td>&lt;12 months</td>
<td>&lt;7 months</td>
<td>–</td>
<td>–</td>
<td>1</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>&lt;12 months</td>
<td>&lt;7 months</td>
<td>–</td>
<td>–</td>
<td>1</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>2 previous doses</td>
<td>&lt;12 months</td>
<td>&lt;7 months</td>
<td>&lt;12 months</td>
<td>–</td>
<td>1</td>
<td>1</td>
<td>1</td>
</tr>
</tbody>
</table>

* If 13vPCV (13-valent pneumococcal conjugate vaccine) is not available, and 10vPCV (10-valent pneumococcal conjugate vaccine) is being used for all/any children, 10vPCV (10-valent pneumococcal conjugate vaccine) is recommended in a 4-dose schedule for infants (i.e. at ages 2, 4, 6 and 12–18 months). If catch-up is required for 10vPCV (10-valent pneumococcal conjugate vaccine), vaccination can be done according to the information provided in this Table. (Refer also to 4.13 Pneumococcal disease (Handbook10-home=handbook10part4-handbook10-4-13).)

† Prior PCV (pneumococcal conjugate vaccine) doses may have been given as 7vPCV (7-valent pneumococcal conjugate vaccine) (e.g. from overseas), 10vPCV (10-valent pneumococcal conjugate vaccine) or v. 13vPCV (13-valent pneumococcal conjugate vaccine) should be used as the vaccine formulation for further catch-up doses required, regardless of which formulation of PCV (pneumococcal conjugate vaccine) the child received previously.

‡ Recommended interval between primary doses for catch-up is 1–2 months. Where possible, it is recommended to align doses with the standard schedule points at 4 months and 6 months of age for infants aged <7 months. The minimum interval between dose(s) is 1 month if aged <12 months, and 2 months if aged ≥12 months.

§ A minimum interval of 2 months is required after the last dose of 13vPCV (13-valent pneumococcal conjugate vaccine) in the primary course.
**Catch-up schedules for persons ≥10 years of age**

Catch-up is much less commonly required for this age group than for young children. Nevertheless, issues surrounding booster doses or revaccinations are common, particularly in adults. Persons who did not have natural infection as children but were not vaccinated remain at unnecessary risk of vaccine-preventable diseases. In general, the same principles for catch-up vaccination apply as for younger children. For example, if a vaccine course is incomplete, do not start the course again, regardless of the interval since the last dose. One exception to this rule is for oral cholera vaccine (refer to Table 2.1.2). The booster dose of PCV (13-valent pneumococcal conjugate vaccine) should be given at the earliest opportunity after the child reaches 12 months of age, but a minimum interval of 2 months is required after the last dose of PCV (13-valent pneumococcal conjugate vaccine) in the primary course.

### Catch-up schedules

<table>
<thead>
<tr>
<th>Number of doses given previously</th>
<th>Age at presentation</th>
<th>1st dose</th>
<th>2nd dose</th>
<th>3rd dose</th>
<th>Number of further primary dose(s) of 13vPCV (13-valent pneumococcal conjugate vaccine) required</th>
<th>Number of booster doses of 13vPCV (13-valent pneumococcal conjugate vaccine) required at age ≥12 months</th>
<th>Number of doses of 23vPPV (23-valent pneumococcal polysaccharide vaccine) required at age 4–5 years</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>7–11 months</td>
<td>7–11</td>
<td>–</td>
<td>–</td>
<td>Not needed</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>&lt;7 months</td>
<td>&lt;7</td>
<td>–</td>
<td>–</td>
<td>1</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>≥12 months</td>
<td>≥12</td>
<td>–</td>
<td>–</td>
<td>Not needed</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>12–23 months</td>
<td>Any age</td>
<td>Any age</td>
<td>Any age</td>
<td>–</td>
<td>Not needed</td>
<td>Not needed</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>&lt;7 months</td>
<td>&lt;7</td>
<td>&lt;12</td>
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</tr>
<tr>
<td></td>
<td>≥12 months</td>
<td>≥12</td>
<td>≥12</td>
<td>≥12</td>
<td>Not needed</td>
<td>Not needed</td>
<td>1</td>
</tr>
<tr>
<td>7–11 months</td>
<td>Any age</td>
<td>Any age</td>
<td>Any age</td>
<td>Any age</td>
<td>Not needed</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>&lt;7 months</td>
<td>&lt;7</td>
<td>&lt;12</td>
<td>&lt;7</td>
<td>1</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>≥12 months</td>
<td>≥12</td>
<td>≥12</td>
<td>≥12</td>
<td>Not needed</td>
<td>Not needed</td>
<td>1</td>
</tr>
</tbody>
</table>

* Refer to List 4.13.1 in 4.13 Pneumococcal disease (Handbook10-home~handbook10part4~handbook10-4-13) for the list of specified conditions.
† Recommendations for vaccination of haematopoietic stem cell transplant (HSCT) recipients differ; refer to Table 3.3.3 Recommendations for revaccination following HSCT in children and adults, irrespective of previous immunisation history (Handbook10-home~handbook10part3~handbook10-3-3)Table 3.3.3.
‡ Prior PCV (pneumococcal conjugate vaccine) doses may have been given as 7vPCV (7-valent pneumococcal conjugate vaccine) (e.g. from overseas), 13vPCV (13-valent pneumococcal conjugate vaccine), or 23vPPV (23-valent pneumococcal polysaccharide vaccine). Where possible, it is recommended to align doses with the standard schedule points at 4 months and 6 months of age for infants aged <7 months. The minimum interval between dose(s) is 1 month if age <12 months, and 2 months if age ≥12 months.
§ The booster dose of PCV (13-valent pneumococcal conjugate vaccine) should be given at the earliest opportunity after the child reaches 12 months of age, but a minimum interval of 2 months is required after the last dose of PCV (13-valent pneumococcal conjugate vaccine) in the primary course.
¶ The booster dose of PCV (13-valent pneumococcal conjugate vaccine) was given.

The above schedule can be used for anyone who has received all doses of 7vPCV (7-valent pneumococcal conjugate vaccine) or 13vPCV (13-valent pneumococcal conjugate vaccine), 23vPPV (23-valent pneumococcal polysaccharide vaccine) or AMR (Australia meningococcal vaccine) vaccine. Where possible, it is recommended to align doses with the standard schedule points at 4 months and 6 months of age for infants aged <7 months. The minimum interval between dose(s) is 1 month if age <12 months, and 2 months if age ≥12 months.

### Recommendations for vaccination of adults

- **Health**: the person to be vaccinated has a medical condition(s) that places them at increased risk of acquiring a particular vaccine-preventable disease or experiencing complications from that disease, for example, influenza.
- **Age**: older age groups may require extra vaccines, such as influenza or pneumococcal vaccination, or certain age groups may be targeted for immunisation against a particular vaccine-preventable disease, such as HPV (human papillomavirus). Another example is young to middle-aged adults who may have missed out on vaccine doses due to schedule changes, such as the 2nd dose of MMR (Measles, Mumps and Rubella) vaccine.
- **Lifestyle**: the person may have missed vaccines because they moved location of residence, may require extra vaccines because they travel frequently, or have other lifestyle risk factors that increase their risk of acquiring a vaccine-preventable disease, for example, smoking or injecting drugs.
- **Occupation**: the person may be employed in an occupation for which certain vaccines are recommended because of the increased risk of acquiring a vaccine-preventable disease and/or transmitting it to others, such as in healthcare or early childhood education and care.

The HALO (health, age, lifestyle, occupation) principle is also incorporated, to some extent, into questions used in the pre-vaccination screening checklist (refer to Tables 2.1.1 and 2.1.2). The HALO (health, age, lifestyle, occupation) principle is also incorporated, to some extent, into questions used in the pre-vaccination screening checklist (refer to Tables 2.1.1 and 2.1.2).

Table 2.1.12 contains information on vaccine doses and intervals between doses for persons aged ≥10 years in whom catch-up vaccination for a particular disease antigen is required. This table only contains information on diseases for which vaccination is recommended at a population level, and for which catch-up is required if doses have been missed earlier in life. The table does not include information on all diseases for which vaccines are required for adults. Recommended vaccines and catch-up vaccination that might be required when assessed using the [Immunise](http://www.immunise.health.gov.au/internet/immunise/publishing.nsf/Content/Handbook10-home)
Table 2.1.12 can be used as follows:

- determine how many vaccine doses for a particular disease antigen a person should have received to be considered completely vaccinated (refer to ‘Doses required’ column)
- check the appropriate ‘Minimum interval’ column to schedule further doses
- refer to the relevant disease-specific chapter(s) in Part 4 (Handbook 10-home-handbook10part3-handbook10-3-3), 3.1 Vaccination for Aboriginal and Torres Strait Islander people (Handbook 10-home-handbook10part3-handbook10-3-1), 3.2 Vaccination for international travel (Handbook 10-home-handbook10part3-handbook10-3-2), and 3.3 Groups with special vaccination requirements (Handbook 10-home-handbook10part3-handbook10-3-3), for additional recommendations, as required.

For example, a 32-year-old woman (Age) is returning to nursing (Occupation) but has only ever had 1 dose of hepatitis B vaccine, 4 doses of the oral poliomyelitis vaccine, 1 dose of MMR (Measles, Mumps and Rubella) vaccine and 2 doses of DTPw vaccine as a child and recently had a splenectomy (Health) following an accident. This person would require:

- 1 dose of 
  1) Tdap (diphtheria-tetanus-acellular pertussis vaccine)
- 2 adult doses of hepatitis B; 1 dose given now and a further dose in 4 weeks
- no further doses of poliomyelitis vaccine (as fully vaccinated against poliomyelitis)
- 1 dose of MMR (Measles, Mumps and Rubella) vaccine
- 2 doses of varicella vaccine if non-immune; 1 dose given now and a further dose in 4 weeks
- 1 dose of influenza vaccine, and 1 dose annually thereafter
- pneumococcal vaccine: 1 dose of 13vPCV (13-valent pneumococcal conjugate vaccine), followed by 23vPPV (23-valent pneumococcal polysaccharide vaccine) approximately 2 months later (because of splenectomy).
- 1 dose of Hib (Haemophilus influenzae type b) vaccine (because of splenectomy)
- 2 doses of 13vPCV (13-valent pneumococcal conjugate vaccine); 1 dose given now and a further dose in 8 weeks (because of splenectomy).
- 2 doses of MenB, 1 dose given now and a further dose in 8 weeks (because of splenectomy).

For additional details on these recommendations, refer to 3.3.7 Vaccination of persons at occupational risk (Handbook 10-home-handbook10part3-handbook10-3-3); ‘Persons with functional or anatomical asplenia’ in 3.3.3 Vaccination of immunocompromised persons (Handbook 10-home-handbook10part3-handbook10-3-3), and relevant disease-specific chapters in Part 4 (Handbook 10-home-handbook10part4).

Where several vaccines are required for an adolescent or adult – for example, dTpa (diphtheria-tetanus-acellular pertussis vaccine), hepatitis B and poliomyelitis vaccines – childhood combination vaccines recommended for use in those <10 years of age should not be used as their antigen content differs and there may be an increased risk of adverse event(s), such as injection site reactions. The childhood combination vaccines are not registered for use in children aged ≥10 years, adolescents or adults.

### Table 2.1.12: Catch-up schedule for persons ≥10 years of age (for vaccines recommended on a population level)

This table is to be used to guide catch-up vaccination for persons ≥10 years of age in conjunction with the guidance provided in the section ‘Catch-up schedules for persons ≥10 years of age’ above.

<table>
<thead>
<tr>
<th>Antigen</th>
<th>Doses required*</th>
<th>Minimum interval between dose 1 and 2</th>
<th>Minimum interval between dose 2 and 3</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diphtheria and tetanus†</td>
<td>3 doses†</td>
<td>4 weeks</td>
<td>4 weeks</td>
</tr>
<tr>
<td>Pertussis‡</td>
<td>1 dose‡</td>
<td>Not required</td>
<td>Not required</td>
</tr>
<tr>
<td>Hepatitis B - Aged 10–19 years</td>
<td>3 paediatric doses</td>
<td>1 month</td>
<td>2 months §</td>
</tr>
<tr>
<td>Hepatitis B - Aged 11–15 years</td>
<td>2 adult doses</td>
<td>4 months</td>
<td>Not required</td>
</tr>
<tr>
<td>Hepatitis B - Aged ≥20 years</td>
<td>3 adult doses</td>
<td>1 month</td>
<td>2 months §</td>
</tr>
<tr>
<td>Poliomyelitis</td>
<td>3 doses</td>
<td>4 weeks</td>
<td>4 weeks</td>
</tr>
<tr>
<td>Human papillomavirus</td>
<td>3 doses</td>
<td>4 weeks</td>
<td>12 weeks</td>
</tr>
<tr>
<td>Measles, mumps and rubella</td>
<td>2 doses</td>
<td>4 weeks</td>
<td>Not required</td>
</tr>
<tr>
<td>Meningococcal¶</td>
<td>1 dose</td>
<td>Not required</td>
<td>Not required</td>
</tr>
<tr>
<td>Pneumococcal</td>
<td>Depends on age of person, Indigenous status and if they have medical condition(s) associated with an increased risk of invasive pneumococcal disease (refer to Table 4.13.3 in 4.13 Pneumococcal disease, and 3.3 Groups with special vaccination requirements)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Varicella #**</td>
<td>At least 1 dose if aged &lt;14 years</td>
<td>If 2nd dose given, a 4-week interval is required #</td>
<td>Not required</td>
</tr>
<tr>
<td>Zoster</td>
<td>1 dose if aged ≥80 years ††</td>
<td>Not required</td>
<td>Not required</td>
</tr>
</tbody>
</table>

* This column outlines the number of vaccine doses required for a person who has not previously received any vaccine doses for that antigen. To determine how many further doses are required for a person who has received previous vaccine doses, the number of previous doses should be deducted from the number in this column. Refer to footnotes below for specific guidance on using this table for catch-up vaccinations for pertussis.

† One of the doses should be given as dTpa-containing vaccine and the course completed with dT. This dose would also provide the single catch-up dose for pertussis (refer to footnote ‡ below). In the unlikely event that dT is not available, dTpa or dTpa-IPV may be used for all 3 primary doses.17

‡ If a person ≥10 years of age has not received the number of pertussis vaccine doses recommended prior to 10 years of age, they only require 1 dose to be considered up-to-date (irrespective of the number of previous doses of pertussis-containing vaccine they received prior to 10 years of age). A single booster dose of pertussis-containing vaccine is routinely recommended for all adolescents, optimally delivered between 11 and 13 years of age, which should be taken into account when planning catch-up for pertussis (refer to 4.12 Pertussis).
¶ The required catch-up dose for meningococcal disease is specific to meningococcal C conjugate vaccine (MenCCV). 4vMenCV and MenBV are indicated for those at increased risk of meningococcal disease; refer to recommendations in 4.10 Meningococcal disease and 3.3 Groups with special vaccination requirements.

# Varicella vaccine is recommended for all non-immune persons. At least 1 dose should be given to those aged <14 years, and all persons aged ≥14 years should receive 2 doses. (Refer also to 4.22 Varicella.)

** MMRV is suitable to provide varicella vaccination in children aged <14 years. This vaccine is not recommended for use in persons ≥14 years of age. (Refer also to 4.22 Varicella.)

†† Routine vaccination of persons aged 70–79 years is expected to obtain the greatest benefits against HZ and its complications. However, vaccination is also recommended for persons aged 60–69 years and ≥80 years (refer to 4.24 Zoster).

References


2.2 Administration of vaccines

This chapter has been amended on July 2016.

- 2.2.1 - Occupational health and safety issues
- 2.2.2 - Equipment for vaccination
- 2.2.3 - Route of administration
- 2.2.4 - Preparation for vaccine administration
- 2.2.5 - Vaccine injection techniques
- 2.2.6 - Recommended injection site
- 2.2.7 - Positioning for vaccination
- 2.2.8 - Identifying the injection site
- 2.2.9 - Administering multiple vaccine injections at the same visit
- References

2.2.1 Occupational health and safety issues

The standard principles of infection prevention and control should always be followed during vaccination to prevent the transmission of infectious organisms. These principles include recommendations for routine hand hygiene, the use of personal protective equipment as appropriate, the handling and disposal of sharps, and routine cleaning of the work environment (refer to the National Health and Medical Research Council’s Australian guidelines for the prevention and control of infection in healthcare).¹

All immunisation service providers must be familiar with, and adhere to, the National Health and Medical Research Council’s Australian guidelines for the prevention and control of infection in healthcare.¹ This publication can be accessed free of charge from www.nhmrc.gov.au/node/30290 (http://www.nhmrc.gov.au/node/30290).

If exposure to blood or body fluids does occur, appropriate guidelines for post-exposure prophylaxis should be followed.

2.2.2 Equipment for vaccination

Preparing for vaccination

Depending on the vaccine(s) that are to be administered, and the age and size of the person to be vaccinated, decide on the appropriate injection site and route, and the injection equipment required (e.g. syringe size, needle length and gauge).

The equipment chosen will vary depending on whether the vaccine is a reconstituted vaccine, a vaccine from an ampoule or vial, or a vaccine in a pre-filled syringe. Unless the vaccine is provided in a pre-filled syringe, a new, sterile, disposable syringe and needle must be used for each injection.

Gloves and protective eyewear are not routinely recommended for immunisation service providers, unless the person administering the vaccine is at risk of coming into contact with body fluids or has open lesions on their hands.²

Equipment may include:

- medical waste (sharps) container that meets Australian standards (always keep sharps containers out of the reach of children)
- vaccine, plus diluent if reconstitution is required
- 2 or 3 mL syringe (unless vaccine is in pre-filled syringe)
- appropriate drawing-up needle (19 or 21 gauge needle if required, to draw up through rubber bung and for reconstitution of vaccine)
- appropriate injecting needle (refer to Table 2.2.2 Recommended needle size, length and angle for administering vaccines (http://www.immunise.health.gov.au/internet/immunise/publishing.nsf/Content/handbook10-home-handbook10part2-handbook10-2-2#table-2-2-2))
- clean cotton wool and hypoallergenic tape to apply to injection site after vaccination
- a rattle or noisy toy for distraction after the injection.

Preparing the vaccine

- Ensure that the minimum/maximum thermometer displays temperatures within the +2°C to +8°C range before removing vaccine from the refrigerator.
- Ensure that the correct vaccine is taken from the refrigerator and that it is within the expiry date.
- Ensure that the diluent container is not damaged and potentially contaminated.
- Shake vaccine (either vial/pre-filled syringe or reconstituted vaccine) to ensure a homogeneous suspension is obtained. Check for particulate matter or colour change in the vaccine. If either is apparent, refer to the vaccine product information.
- Wash hands with soap and water (if visibly soiled) or use a waterless alcohol-based hand rub.¹,³
- Prepare the appropriate injection equipment for the vaccine to be administered.

Injectable vaccines that do not require reconstitution

- If the vaccine is in a vial, remove the cap carefully to maintain sterility of the rubber bung. There is no need to wipe the rubber bung of single-dose vials with an alcohol swab if it is visibly clean. If there is visible contamination, the bung should be cleaned with a single-use swab, allowing time to dry before drawing up the contents.⁴
- Use a new, sterile, disposable 19 or 21 gauge needle to draw up the recommended dose through the bung (or through the top of the ampoule), if required.
- Change the needle after drawing up from a vial with a rubber bung or ampoule, before giving the injection. If using a safety needle system, once the vaccine has been drawn up, draw back on the syringe to ensure as much vaccine as possible is removed from the tip of the needle, and then eliminate any air into the syringe without re-priming the needle.

Injectable vaccines that require reconstitution

- Reconstitute the vaccine as needed immediately before administration.
- Use a new, sterile, disposable 21 gauge needle for reconstitution. Use a separate new, sterile, disposable 23 or 25 gauge needle, 25 mm in length, for administration of the vaccine in most circumstances.
- Use only the diluent supplied with the vaccine; do not use sterile water for injection instead of a supplied diluent. Ensure that the diluent and vaccine are completely mixed.⁵
- Check reconstituted vaccines for signs of deterioration, such as a change in colour or clarity, and if apparent refer to the vaccine product information.
- Administer reconstituted vaccines as soon as practicable after they have been reconstituted as they may deteriorate rapidly. Refer to individual vaccine product information for recommended times from vaccine reconstitution to administration.
- Never freeze a vaccine after it has been reconstituted.

For all injectable vaccines

- Do not extrude small air bubbles through the needle for injection. However, in the rare instance of a large air bubble in a pre-filled syringe, first draw back on the needle to ensure no air is expelled along with the air, and then expel the air through the needle, taking care not to prime the needle with any of the vaccine, as this can lead to increased local reaction.
- Never mix other vaccines together in the one syringe (unless that is the manufacturer’s registered recommendation, e.g. Infanrix hexa).⁵


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Intradermal

Oral

Distraction measures that may decrease discomfort following vaccination in young children include:

- shucking a noisy toy (for infants and very young children)
- swaddling and holding the infant securely (but not excessively)

The routine use of distraction, relaxation and other measures have been shown to reduce distress and pain following vaccination in young children.

2.2.3 Route of administration

Most vaccines available in Australia are given intramuscularly. Only a few vaccines are given subcutaneously, orally or intradermally.

Rotavirus vaccines are only available for oral administration and must never be injected.

Table 2.2.1 summarises the route of administration for vaccines used in Australia.

<table>
<thead>
<tr>
<th>Intramuscular (IM) injection*</th>
<th>Subcutaneous (SC) injection*</th>
<th>IM or SC injection</th>
<th>Intradermal</th>
<th>Oral</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diphtheria-tetanus vaccine (dT)</td>
<td>Inactivated poliomyelitis vaccine (IPV)†</td>
<td>Influenza§</td>
<td>Bacille Calmette-Guérin (BCG) vaccine</td>
<td>Rotavirus vaccine</td>
</tr>
<tr>
<td>Diphtheria-tetanus-acellular pertussis vaccine (dTPa and dTPa)</td>
<td>Quadrivalent meningococcal polysaccharide vaccine (4vMenPV)</td>
<td>Measles-mumps-rubella vaccine (MMR) (Priorix only)</td>
<td>Cholera vaccine</td>
<td></td>
</tr>
<tr>
<td>DTPa- and dTPa-combination vaccines</td>
<td>Varicella vaccine (VV)</td>
<td>Measles-mumps-rubella-varicella vaccine (MMRV) (Priorix only)</td>
<td>Typhoid vaccine</td>
<td></td>
</tr>
<tr>
<td>Hepatitis A vaccine and Hepatitis A combination vaccines</td>
<td>Japanese encephalitis vaccine (I-mojev)</td>
<td>Q fever vaccine§</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hepatitis B† vaccine and Hepatitis B combination vaccines</td>
<td>Q fever vaccine§</td>
<td>23-valent pneumococcal polysaccharide vaccine (23vPPV)§</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Haemophilus influenzae type b (Hib) vaccine</td>
<td>Measles-mumps-rubella vaccine (MMR) (M-M-R II only)‡</td>
<td>Measles-mumps-rubella-varicella vaccine (MMRV) (ProQuad only)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Human papillomavirus (HPV) vaccine</td>
<td>Zoster vaccine</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>IPV-containing combination vaccines§</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Japanese encephalitis vaccine (JE-expect)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>10-valent pneumococcal conjugate vaccine (10vPCV)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>13-valent pneumococcal conjugate vaccine (13vPCV)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Typhoid Vi polysaccharide vaccine</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Meningococcal B vaccine (MenBV)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Quadrivalent meningococcal conjugate vaccine (4vMenCV)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Rabies vaccine (PCEDV)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

* In the instance where a vaccine is inadvertently administered via an alternative route, refer to 2.2.5 Vaccine injection techniques below for advice on the need for revaccination.
† IPV-containing combination vaccines are administered by IM injection; IPV (IPOL) is administered by SC injection.
§ The IM route is preferred to the SC route because it causes fewer local adverse events.¶ However, if administered by SC injection, the vaccine does not need to be re-administered.
¶ Q fever skin testing and BCG vaccine should be administered only by specially trained immunisation service providers.
§ The intradermal route may be considered for the administration of additional doses of hepatitis B vaccine to HBsAg-negative healthcare workers who are non-responders to a primary course of vaccination and to subsequent additional IM doses (refer to 4.5 Hepatitis B).

2.2.4 Preparation for vaccine administration

Skin cleaning

Provided the skin is visibly clean, there is no need to wipe it with an antiseptic (e.g. alcohol wipe).[^1] If the immunisation service provider decides to clean the skin, or if the skin is visibly not clean, alcohol and other disinfecting agents must be allowed to dry before vaccine injection (to prevent inactivation of live vaccines and to reduce the likelihood of irritation at the injection site).[^2]

Distraction techniques

The routine use of distraction, relaxation and other measures have been shown to reduce distress and pain following vaccination in young children.[^1-4] Reducing children’s distress may enhance parents’ timely attendance for subsequent vaccinations.

Distraction measures that may decrease discomfort following vaccination in young children include:

- swaddling and holding the infant securely (but not excessively)
- shaking a noisy toy (for infants and very young children)
2.2.5 Vaccine injection techniques

Intramuscular injection technique

- For intramuscular (IM) injection, use a 25 mm needle in most cases (refer to Table 2.2.2 (http://www.immunise.health.gov.au/internet/immunise/publishing.nsf/Content/Handbook10-home-handbook10part2-handbook10-2-2#table-2-2-2)).

- Depending on the injection site, position the limb so as to relax the muscle into which the vaccine is to be injected.

- Pierce the skin at an angle of 90° to the skin, so the needle can be safely inserted to the hub. Provided an injection angle of >70° is used, the needle should reach the muscle layer.º²

- If using a 25 gauge needle for an IM vaccination, ensure the vaccine is injected slowly over a count of 5 seconds to avoid injection pain and muscle trauma (refer to Table 2.2.2 (http://www.immunise.health.gov.au/internet/immunise/publishing.nsf/Content/Handbook10-home-handbook10part2-handbook10-2-2#table-2-2-2)).

- If you have drawn back on the syringe plunger before injecting a vaccine (which is not considered necessary), then if inadvertently given SC. However, in special circumstances, for example, in persons with bleeding disorders, some hepatitis B vaccines may be given via the SC route (refer to 2.3.2 Adverse events following immunisation).

Studies have demonstrated that, for most vaccines, local adverse events are minimised and immunogenicity is enhanced by ensuring vaccine is into the muscle and not into the subcutaneous layer.¹¹,º²-ºº However, some vaccines (e.g. inactivated poliomyelitis, varicella and meningococcal polysaccharide vaccines) are only registered for SC administration (refer to Table 2.2.1 (http://www.immunise.health.gov.au/internet/immunise/publishing.nsf/Content/Handbook10-home-handbook10part2-handbook10-2-2#table-2-2-1)).

In the instance where a vaccine that is registered for administration only via the IM route (refer to Table 2.2.1 (http://www.immunise.health.gov.au/internet/immunise/publishing.nsf/Content/Handbook10-home-handbook10part2-handbook10-2-2#table-2-2-1)) is inadvertently administered via the SC route, check the vaccine product information and the ‘Vaccines’ section in relevant disease-specific chapters in Part 4 for additional information. Some vaccines may still be immunogenic when given via the SC route, and as such, would not need to be repeated. One vaccine that should be considered invalid and that therefore needs to be repeated is Rabipur Inactivated Rabies Virus Vaccine (PCECV) (refer to 4.16 Rabies and other lyssaviruses (including Australian bat lyssavirus (http://www.immunise.health.gov.au/internet/immunise/publishing.nsf/Content/Handbook10-home-handbook10part4-handbook10-4-16)). In general, hepatitis B vaccines should also be repeated if inadvertently given SC. However, in special circumstances, for example, in persons with bleeding disorders, some hepatitis B vaccines may be given via the SC route (refer to 3.3.5 Vaccination of persons with bleeding disorders(http://www.immunise.health.gov.au/internet/immunise/publishing.nsf/Content/Handbook10-home-handbook10part3-handbook10-3-3)).

A clinical trial demonstrated that for infant vaccination long (25 mm) needles (with the skin stretched flat and the needle inserted at 90°) were associated with significantly fewer local adverse events, while achieving comparable immunogenicity. Little difference in local adverse events or immune response was found between needles of the same length but with different gauges.¹⁹

Subcutaneous injection technique

For subcutaneous (SC) injection, administer the injection at a 45° angle to the skin. The standard needle for administering vaccines by SC injection is a 25 or 26 gauge needle, 16 mm in length.

In the instance where a vaccine that is registered for administration only via the SC route (refer to Table 2.2.1) is inadvertently administered via the IM route, the immune response to vaccines is unlikely to be affected. Therefore it is usually not necessary to repeat doses.

Intradermal injection technique

For intradermal injection of BCG vaccine, Q fever skin test or, if indicated, hepatitisB vaccine, a 26 or 27 gauge, 10 mm needle is recommended. The intradermal injection technique requires special training, and should be performed only by a trained provider (refer to 4.20 Tuberculosis (http://www.immunise.health.gov.au/internet/immunise/publishing.nsf/Content/Handbook10-home-handbook10part4-handbook10-4-20) and 4.15 Q fever (http://www.immunise.health.gov.au/internet/immunise/publishing.nsf/Content/Handbook10-home-handbook10part4-handbook10-4-15)).

Two influenza vaccines from the same manufacturer, presented in a purpose-designed syringe for intradermal administration, were registered for use in Australia in 2009 but are no longer available.

### Table 2.2.2: Recommended needle size, length and angle for administering vaccines¹¹,¹⁷,¹⁹,²²,²⁶

<table>
<thead>
<tr>
<th>Age or size of child/adult</th>
<th>Needle type</th>
<th>Angle of needle insertion</th>
</tr>
</thead>
<tbody>
<tr>
<td>Infant, child or adult for IM vaccines</td>
<td>23 or 25 gauge,* 25 mm in length†</td>
<td>90° to skin plane</td>
</tr>
<tr>
<td>Preterm babies (&lt;37 weeks gestation) up to 2 months of age; and/or very small infants</td>
<td>23 or 25 gauge,* 16 mm in length</td>
<td>90° to skin plane</td>
</tr>
<tr>
<td>Very large or obese patient</td>
<td>23 or 25 gauge, 38 mm in length</td>
<td>90° to skin plane</td>
</tr>
<tr>
<td>Subcutaneous injection in all persons</td>
<td>25 or 26 gauge, 16 mm in length</td>
<td>45° to skin plane</td>
</tr>
</tbody>
</table>

* If using a narrow 25 gauge needle for an IM vaccination, ensure vaccine is injected slowly over a count of 5 seconds to avoid injection pain and muscle trauma.
† The use of short needles for administering IM vaccines may lead to inadvertent SC injection and increase the risk of significant local adverse events, particularly with aluminium-adjuvanted vaccines (e.g. hepatitis B, DTPa, DTPa-combination or dT vaccines).

** Interruption to a vaccination **

If the process of administration of a vaccine given parenterally (IM or SC) is interrupted (e.g. by syringe–needle disconnection) and most of the dose has not been administered, the whole dose should be repeated as soon as practicable.

If most of an oral rotavirus vaccine dose has been spat out or vomited within minutes of administration, a single repeat dose can be administered during the same visit. If an infant regurgitates or vomits only a small part of a dose of oral rotavirus vaccine, it is not necessary to repeat the dose. Therefore, the regurgitated (and incomplete volume) dose is still considered part of a dose of oral rotavirus vaccine, and would not need to be repeated.
The choice of injection site depends primarily on the age of the person to be vaccinated. The two anatomical sites recommended as routine injection sites are the anterolateral thigh (Figures 2.2.5) and the deltoid muscle (Figure 2.2.6). Immunisation service providers should ensure that they are familiar with the landmarks used to identify any anatomical sites used for vaccination. Photographs and diagrams are provided in this section, but are not a substitute for training. Further detail on identifying the recommended injection sites is provided in 2.2.8 Identifying the injection site (http://www.immunise.health.gov.au/internet/immunise/publishing.nsf/Content/Handbook10-home~handbook10part2~handbook10-2-92~2-8).

Infants <12 months of age

The vastus lateralis muscle in the anterolateral thigh is the recommended site for IM vaccination in infants <12 months of age, due to its larger muscle size (refer to Figures 2.2.5 and 2.2.6) and the ventrogluteal area (refer to Figure 2.2.7). However, vaccine providers should be familiar with the landmarks used to identify this site. The reactogenicity and immunogenicity of vaccines given in this site are comparable to those of vaccines given in the anterolateral thigh.27-29

The deltoid muscle is not recommended for IM vaccination of infants <12 months of age.

Children ≥12 months of age

The deltoid muscle is the recommended site for IM vaccination in children ≥12 months of age (refer to Figure 2.2.8) and the ventrogluteal area is an alternative site for IM vaccination of infants. It is important that vaccine providers who choose to use this site are familiar with the landmarks used to identify it. The reactogenicity and immunogenicity of vaccines given in this site are comparable to those of vaccines given in the anterolateral thigh.27-29

The ventrogluteal area is an alternative injection site (refer to Figure 2.2.7) in 2.2.8 Identifying the injection site (http://www.immunise.health.gov.au/internet/immunise/publishing.nsf/Content/Handbook10-home~handbook10part2~handbook10-2-92~2-8). However, vaccine providers should be familiar with the landmarks used to identify this site. The vastus lateralis in the anterolateral thigh may also be used in children ≥12 months of age (refer to Figures 2.2.5 and 2.2.6) and the ventrogluteal area can also be considered (refer to Figure 2.2.7).

Children with congenital limb malformation or children in spica casts

Children with congenital limb malformation(s) should receive their vaccines in an unaffected limb where possible. The ventrogluteal area can also be considered (refer to Figure 2.2.7) in 2.2.8 Identifying the injection site (http://www.immunise.health.gov.au/internet/immunise/publishing.nsf/Content/Handbook10-home~handbook10part2~handbook10-2-92~2-8), but, if this site is used, the less locally reactogenic vaccines (e.g. MMR) should be given in the thigh.

Adolescents and adults

The deltoid muscle is the recommended site for IM vaccination in adolescents and adults (refer to Figure 2.2.8) and the anterolateral thigh can also be used in older children and adults (refer to Figure 2.2.5). The ventrogluteal area can also be considered as an alternative injection site (refer to Figure 2.2.7). However, it is important to administer the least reactogenic vaccine in this muscle to decrease the likelihood of local injection site reactions.

Patients undergoing treatment for breast cancer or patients with lymphoedema

It has been routine practice for many years to avoid giving injections, including vaccination, into a person’s arm(s) affected by lymphoedema.31,32 This recommendation is based on the potential for arm swelling related to vaccination to lead to, or exacerbate, lymphoedema, although there is limited evidence to support this. Where possible, use an alternative site, such as the other arm or thigh.33,34 For further information about vaccination of persons undergoing cancer treatment, refer to 3.3 Groups with special vaccination requirements (http://www.immunise.health.gov.au/internet/immunise/publishing.nsf/Content/Handbook10-home~handbook10part2~handbook10-2-93~3).

2.2.7 Positioning for vaccination

It is important that infants and children do not move during injection of vaccines. However, excessive restraint can increase their fear and result in increased muscle tension. The following section describes a variety of positions that may be used for vaccinating different age groups.

Infants <12 months of age

Cuddle position for infants

This section describes a variety of positions that may be used for vaccinating different age groups. It is important that infants and children do not move during injection of vaccines. However, excessive restraint can increase their fear and result in increased muscle tension. The following positions are recommended:

- **Infants <12 months of age**
  - **Cuddle position**: The infant is held securely against the mother's or father's chest, with the infant's head facing the caregiver's chest. The infant's arm and hand should be relaxed, and the injection should be given in the vastus lateralis muscle in the anterolateral thigh. Photographs and diagrams are provided in this section, but are not a substitute for training. Further detail on identifying the recommended injection sites is provided in 2.2.8 Identifying the injection site (http://www.immunise.health.gov.au/internet/immunise/publishing.nsf/Content/Handbook10-home~handbook10part2~handbook10-2-92~2-8).
Position the infant in a semi-recumbent cuddle position on the lap of the parent/carer (refer to Figure 2.2.1). The infant’s inside arm adjacent to the parent/carer should be restrained underneath the parent/carer’s arm or against the parent/carer’s chest. The infant’s outside arm must also be held securely. The parent/carer’s hand should restrain the infant’s outside leg and the knee should be flexed to encourage relaxation of the vastus lateralis for IM vaccinations. This position can also be used for young children.

Figure 2.2.1: Positioning a child <12 months of age in the cuddle position

An alternative is to lay an infant on his/her back on an examination table, with the infant’s feet towards the immunisation service provider, and the parent/carer beside the provider to immobilise and distract the baby (refer to Figure 2.2.2).

Keep the infant’s hip and knee flexed by cupping the patella in the non-injecting hand.

Although the exact mechanism is unclear, recent studies have shown that placing a child in the supine position may result in more pain than if the child is held in an upright position.16

Figure 2.2.2: Positioning an infant on an examination table for vaccination

For ventrogluteal injection, position the child face-down across the parent/carer’s lap (refer to Figure 2.2.7 below). This allows the hips to be flexed and provides access to the ventrogluteal area.

Children ≥12 months of age

Cuddle position for an older child

Sit the child sideways on the lap of the parent/carer, with the arm to be injected held close to the child’s body while the other arm is tucked under the armpit and behind the back of the parent/carer.

The child’s exposed arm should be secured at the elbow by the parent/carer, and the child’s legs should also be secured by the parent/carer (refer to Figure 2.2.3).

Figure 2.2.3: Positioning an older child in the cuddle position

Straddle position

An older child may be positioned facing the parent/carer with the legs straddled over the parent/carer’s lap. The child’s arms should be folded in front, with the parent/carer hugging the child’s body to the parent/carer’s chest. Alternatively the child may be positioned to ‘hug’ the parent/carer with the parent/carer’s arms holding the child’s arms in a reciprocal hug (refer to Figure 2.2.4). This position allows access to both deltoids and both anterolateral thighs.

Figure 2.2.4: Positioning a child in the straddle position
Prone position across the lap for ventrogluteal vaccination

For ventrogluteal injection, position the child face-down across the parent/carer’s lap (refer to Figure 2.2.7 below).

Older children, adolescents and adults

Solo sitting position for deltoid injections

Most vaccines can be administered into the deltoid area. Adults should sit in a straight-backed chair, feet resting flat on the floor with forearms and hands in a relaxed position on the upper thighs. Keep the arms flexed at the elbow to encourage the deltoid muscle to relax.

Encourage the shoulders to drop by asking the person to raise the shoulders up while taking a deep breath in and to drop them while breathing out fairly forcefully. Use distraction to keep muscles relaxed during the procedure, for example, have an interesting poster or similar for the person to concentrate on during the procedure and ask him/her to give you a detailed description of what can be seen.

The ventrogluteal and vastus lateralis are alternative sites if needed (adapting guidance provided in 2.2.6 Recommended injection sites and 2.2.8 Identifying the injection site).

2.2.8 Identifying the injection site

The choice of injection site depends on the age of the person to be vaccinated, and is discussed in 2.2.6 Recommended injection sites.

The anterolateral thigh (vastus lateralis)

- Make sure the infant’s nappy is undone to ensure the injection site is completely exposed and the anatomical markers can be easily identified by sight and palpation.
- Position the leg so that the hip and knee are flexed and the vastus lateralis is relaxed (refer to Figure 2.2.6).
- Identify the following anatomical markers: the upper marker is the midpoint between the anterior superior iliac spine and the pubic tubercle, and the lower marker is the upper part of the patella.
- Draw an imaginary line between the two markers down the front of the thigh. The correct site for IM vaccination is lateral to the midpoint of this line, in the outer (anterolateral) aspect (refer to Figures 2.2.5 and 2.2.6).
- Do not inject into the anterior aspect of the thigh where neurovascular structures can be damaged.

Figure 2.2.5 Anatomical markers used to identify the vastus lateralis injection site (X) on the anterolateral thigh

Figure 2.2.6: The vastus lateralis injection site (X) on the anterolateral thigh

The ventrogluteal area

Note: This area should not be confused with the dorsogluteal area (buttock).

The ventrogluteal area provides an alternative site for administering vaccines to a child of any age (as well as older children, adolescents and adults, adapting the guidance provided below), especially when multiple injections at the same visit are required. The ventrogluteal area is relatively free of major nerves and blood vessels, and the area provides the greatest thickness of gluteal muscle.36,37 There is a relatively consistent thinness of subcutaneous tissue over the injection site.37,38

- Make sure the child’s nappy is undone to ensure the injection site is completely exposed and the anatomical markers can be easily identified by sight and palpation. Anatomical markers are the anterior superior iliac spine (ASIS), the greater trochanter of the femur and the iliac crest (refer to Figure 2.2.7).
- Place the child in a prone position (face-down) on the parent/carer’s lap or on the clinic table/bed, with the child’s arms tucked against their chest. Allow the child’s legs to dangle towards the floor (refer to Figure 2.2.7).
- Ensure the knee and hip are turned inwards to encourage muscle relaxation at the injection site.
- Use the injection site that is closest to you.

Place the palm over the greater trochanter (the uppermost bony prominence of the thigh bone), with the thumb pointing towards the umbilicus. Point the index finger towards the anterior superior iliac spine, and spread the middle finger so it aims at the iliac crest, thus creating a ‘V’ outlining the ventrogluteal triangular area. The injection site is at the centre of this area as shown in the diagram in Figure 2.2.7. Note: In small children and infants, the placement of the hand in relation to these anatomical markers may vary, as shown in the photograph in Figure 2.2.7.

Figure 2.2.7: Anatomical markers used to identify the ventrogluteal injection site (X)

The deltoid area

To locate the deltoid site for injection:
- Expose the arm completely, from the top of the shoulder to the elbow; roll up the sleeve or remove the shirt if needed.
- Locate the shoulder tip (acromion) and the muscle insertion at the middle of the humerus (deltoid tuberosity).
- Draw an imaginary inverted triangle below the shoulder tip, using the identified anatomical markers (refer to Figure 2.2.8).

The deltoid site for injection is halfway between the acromion and the deltoid tuberosity, in the middle of the muscle (triangle).

Figure 2.2.8: Anatomical markers used to identify the deltoid injection site

Subcutaneous injection sites

Subcutaneous injections should be administered either over the deltoid muscle or over the anterolateral thigh. There are no studies that describe any specific differences in the technique used for an ‘SC injection’ compared with a ‘deep SC injection’. Figure 2.2.9 demonstrates the recommended technique for any SC injection.

Figure 2.2.9: A subcutaneous injection into the deltoid area of the upper arm using a 25 gauge, 16 mm needle, inserted at a 45° angle

Photo courtesy Jane Jelfs NCIRS

2.2.9 Administering multiple vaccine injections at the same visit

When sequentially administering multiple vaccines to children, give the most painful vaccine last (e.g. pneumococcal conjugate vaccine). Evidence suggests that this may decrease the overall pain response.

The location of each separate injection given should be recorded, so that if a local adverse event occurs, the implicated vaccine(s) can be identified.

Infants <12 months of age

The suitable sites for this age group are the anterolateral thighs (preferred) and the ventrogluteal areas. For the routine schedule where only two vaccines are required, one can be given in each thigh.

When three or four injectable vaccines are to be given at the same visit, the options are:
- two injections in the same anterolateral thigh, separated by at least 2.5 cm (refer to Figure 2.2.10, injection numbers 1 and 2); further IM vaccines can be given in this way in the other thigh (injection number 3), or
- one injection into each anterolateral thigh and one injection into each ventrogluteal area (only one injection should be given into each ventrogluteal area).

Figure 2.2.10: Recommended technique for giving multiple vaccine injections into the anterolateral thigh in an infant <12 months of age
Two studies were unable to demonstrate a difference in pain response in the child between simultaneous administration and sequential administration.

For younger children, the cuddle or straddle positions (Figures 2.2.3 and 2.2.4) are suitable for accessing multiple limbs during the one vaccination encounter.

Simultaneous injections by two immunisation providers

Currently there is insufficient evidence for or against having two immunisation providers administer vaccines at the same time rather than one vaccine after the other. Two studies were unable to demonstrate a difference in pain response in the child between simultaneous administration and sequential administration.

References

A full reference list is available on the electronic Handbook or www.immunise.health.gov.au.


Anaphylaxis is a severe adverse event of rapid onset, characterised by sudden respiratory compromise and/or circulatory collapse.

Anaphylaxis and vasovagal episodes

Anaphylaxis is classified as a severe reaction with rapid onset. Symptoms include:

- Hypotension
- Weak or absent pulses
- Loss of consciousness
- Marked respiratory compromise from upper airway oedema or bronchospasm
- Generalised erythema, urticaria and/or angioedema
- Gastrointestinal tract symptoms such as diarrhoea, vomiting

In severe cases, there is circulatory collapse with alteration in the level of consciousness.

Management of an immediate adverse event following immunisation

The vaccinated person should remain under observation for a short interval to ensure that they do not experience an immediate adverse event. It is recommended that vaccinated persons

It is important to consider two important factors in the management of adverse events:

1. Recognition and rapid referral
2. Management

An important factor in reducing the likelihood of an adverse event occurring is to screen each person to be vaccinated (using the pre-vaccination screening checklists in Part 2.2).

Expected common AEFI are described in the table Comparison of the effects of diseases and the side effects of NIP vaccines inside the back cover of this Handbook. Detailed information on the adverse events that are known to occur after vaccination is contained in the ‘Adverse events’ section of each disease-specific chapter in Part 4. This information should be used for medical consultation and management of adverse events.

Before departure, inform the vaccinated person or parent/carer, preferably in writing, of any expected adverse events following immunisation, and of the date of the next scheduled vaccination(s).

Take the opportunity to check the vaccination status of other family members (as appropriate) and discuss any catch-up vaccination requirements and options available (this can also be done earlier in the visit).

2.3.2 Adverse events following immunisation

What are adverse events following immunisation?

An adverse event following immunisation (AEFI) is any untoward medical occurrence that follows immunisation and does not necessarily have a causal relationship with the usage of the vaccine. The adverse event may be any unfavourable or unintended sign, abnormal laboratory finding, symptom or disease. Such an event may be caused by the vaccine(s) or may occur by chance (i.e. it would have occurred regardless of vaccination). Most vaccine adverse events are minor, such as low-grade fever, and pain or redness at the injection site; these should be anticipated. The frequency of adverse events has been classified by regulatory agencies, and is often reported in clinical trials as follows: very common (>10% of persons vaccinated), common (1–10%), uncommon (0.1–<1%), rare (0.01–<0.1%) and very rare (<0.01%).

Detailed information on types of expected common and rare adverse events is provided below.

An important factor in reducing the likelihood of an adverse event occurring is to screen each person to be vaccinated (using the pre-vaccination screening checklists in Tables 2.1.1 and 2.1.2) to ensure that the person does not have a condition that either increases the risk of an AEFI or is a contraindication to vaccination. Immunisation service providers should also check the relevant chapters of this Handbook, including the variations from product information, and any other relevant sources, such as state/territory guidelines. The use of correct injection procedures is also important (refer to 2.2 Administration of vaccines (handbook10-home-handbook10part2-handbook10-2-2)).

Expected common AEFI are described in the table Comparison of the effects of diseases and the side effects of NIP vaccines inside the back cover of this Handbook. Detailed information on the adverse events that are known to occur after vaccination is contained in the ‘Adverse events’ section of each disease-specific chapter in Part 4. Persons to be vaccinated and/or their parents/carers should be given advice (preferably written) as part of the consent procedure on what common or expected adverse events are likely and what they should do about them. The table inside the front cover of this Handbook, Side effects following immunisation for vaccines used in the National Immunisation Program (NIP) schedule, can be used for this purpose.

Parents/patients should be encouraged to contact their healthcare provider if they are concerned about an adverse event occurring after vaccination, particularly if it is an unexpected, uncommon and/or serious adverse suspected reaction to vaccination. Healthcare providers and parents/carers are encouraged to report any untoward medical occurrence that follows immunisation, particularly events that are serious and/or unexpected, and/or relate to a new vaccine or condition of interest. For more detailed information on reporting AEFI, refer to ‘Reporting adverse events following immunisation’ below and Table 2.3.3 Contact information for notification of adverse events following immunisation. In addition to reporting AEFI, immunisation providers should provide the patient/parents with information and a plan of management regarding the adverse event experienced, including the implications for subsequent vaccination. This is discussed more in the next three sections on management of immediate, common and rare adverse events, and also in 3.3.1 Vaccination of persons who have had an adverse event following immunisation.

Management of an immediate adverse event following immunisation

The vaccinated person should remain under observation for a short interval to ensure that they do not experience an immediate adverse event. It is recommended that vaccinated persons remain in the vicinity of the place of vaccination for at least 15 minutes. Driving or operating machinery should not occur in this immediate post-vaccination period.

The most serious immediate AEFI is anaphylaxis. Severe anaphylactic reactions usually have a rapid onset; life-threatening adverse events are most likely to begin within 15 minutes of vaccination. However, in adults and older children, the most common immediate adverse event is a vasovagal episode (fainting), either immediately or soon after vaccination. Because fainting after vaccination can lead to serious consequences, anyone who complains of giddiness or light-headedness before or after vaccination should be advised to lie down until free of symptoms.

Anaphylaxis and vasovagal episodes

Anaphylaxis following routine vaccination is very rare, but can be fatal. All immunisation service providers must be able to recognise all the symptoms and signs of anaphylaxis and distinguish between anaphylaxis, convulsions and fainting. The features listed in Table 2.3.1 may be useful in differentiating between fainting (vasovagal episode) and anaphylaxis.

Anaphylaxis is a severe adverse event of rapid onset, characterised by sudden respiratory compromise and/or circulatory collapse. Early signs include involvement of the skin (e.g. generalised erythema, urticaria and/or angioedema) and/or gastrointestinal tract (e.g. diarrhoea, vomiting). In severe cases, there is circulatory collapse with alteration in the level of consciousness, hypotension and weak or absent pulses, and/or marked respiratory compromise from upper airway oedema or bronchospasm.

Fainting (vasovagal episode) is relatively common after vaccination of adults and adolescents, but infants and children rarely faint. Sudden loss of consciousness in young children should be presumed to be anaphylaxis, particularly if a strong central pulse is absent. A strong central pulse (e.g. carotid) persists during a faint or convulsion.
Anaphylaxis occurs without warning, usually within 15 minutes of giving a vaccine. A protocol for the management of anaphylaxis, adrenaline and 1 mL syringes must always be immediately at hand whenever vaccines are given.

Rapid IM administration of adrenaline is the cornerstone of treatment of anaphylaxis. Adrenaline is life-saving and must be used promptly.

Anaphylaxis occurs within minutes of, or during, vaccine administration. Under-treatment of anaphylaxis is more harmful, and potentially life-threatening, than over-treatment of a mild or moderate allergic reaction.

Table 2.3.1: Clinical features that may assist differentiation between a vasovagal episode and anaphylaxis

<table>
<thead>
<tr>
<th>Vasovagal episode</th>
<th>Anaphylaxis*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Onset</td>
<td>Usually within 15 minutes, but can occur within hours of vaccine administration</td>
</tr>
<tr>
<td>Respiratory</td>
<td>Cough, wheeze, hoarseness, stridor, or signs of respiratory distress (e.g. tachypnoea, cyanosis, rib recession)</td>
</tr>
<tr>
<td>Symptoms/Signs</td>
<td>Upper airway swelling (lip, tongue, throat, uvula or larynx)</td>
</tr>
<tr>
<td>Cardiovascular</td>
<td>Bradycardia, weak/absent peripheral pulse, strong carotid pulse Hypotension – usually transient and corrects in supine position Loss of consciousness – improves once supine or in head-down position</td>
</tr>
<tr>
<td>Symptoms/Signs</td>
<td>Tachycardia, weak/absent carotid pulse Hypotension – sustained and no improvement without specific treatment (Note: in infants and young children, limpness and pallor are signs of hypotension) Loss of consciousness – no improvement once supine or in head-down position</td>
</tr>
<tr>
<td>Skin Symptoms/Signs</td>
<td>Generalised pallor, cool, clammy skin</td>
</tr>
<tr>
<td>Gastrointestinal Symptoms/Signs</td>
<td>Pruritus (skin itchiness), generalised skin erythema (redness), urticaria (weals) or angioedema (localised or general swelling of the deeper layers of the skin or subcutaneous tissues)</td>
</tr>
<tr>
<td>Neurological† Symptoms/Signs</td>
<td>Abdominal cramps, diarrhoea, nausea and/or vomiting</td>
</tr>
</tbody>
</table>

* Modified from The Brighton Collaboration Case Definition Criteria for Anaphylaxis.†

† Neurological symptoms are not listed in the Brighton case definition criteria for anaphylaxis; however, symptoms of anxiety and distress, including feelings of impending doom, are reported in persons experiencing anaphylaxis.

Management of anaphylaxis

Use of adrenaline

The use of 1:1000 adrenaline is recommended because it is universally available. Adrenaline 1:1000 (one in one thousand) contains 1 mg of adrenaline per mL of solution in a 1 mL glass vial. Adrenaline 1 in 10,000 is no longer recommended for the treatment of anaphylaxis. A 1 mL syringe should always be used to improve the accuracy of measurement when drawing up small doses of adrenaline.

The recommended dose of 1:1000 adrenaline is 0.01 mL/kg body weight (equivalent to 0.01 mg/kg or 10 µg/kg) up to a maximum of 0.5 mL, given by deep IM injection preferably in the anterolateral (upper outer) thigh. The anterolateral thigh is the preferred site because there is a more predictable dispersal of adrenaline from this site. Administration of adrenaline in the anterolateral thigh is also in accordance with recommendations from various emergency medicine, anaesthetic and immunology professional bodies.

Adrenaline 1:1000 must not be administered intravenously.

Table 2.3.2 lists the dose of 1:1000 adrenaline to be used if the exact weight of the person is not known.

The dose of 1:1000 (one in one thousand) adrenaline may be repeated every 5 minutes, as necessary, until there is clinical improvement.
Adrenaline dose

<table>
<thead>
<tr>
<th>Age Group</th>
<th>Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>4–6 years (approx. 20 kg)</td>
<td>0.2 mL</td>
</tr>
<tr>
<td>7–10 years (approx. 30 kg)</td>
<td>0.3 mL</td>
</tr>
<tr>
<td>10–12 years (approx. 40 kg)</td>
<td>0.4 mL</td>
</tr>
<tr>
<td>&gt;12 years and adult (over 50 kg)</td>
<td>0.5 mL</td>
</tr>
</tbody>
</table>


Uncommon/rare adverse events following immunisation

Some vaccines have been shown to cause uncommon or rare serious adverse events, although the rate of vaccine adverse events is usually hundreds to thousands times less frequent than the disease complications. Information on the benefits compared with risks of immunisation is always taken into account when making recommendations for vaccine use. It is important to provide persons to be vaccinated or their parent/carer with advice regarding known, but rare, adverse events following immunisation, and to place the advice in the context of the benefits of vaccination (refer to 3.3.1 Vaccination of persons who have had an adverse event following immunisation (Handbook10-home-handbook10part3-handbook10-3-3)).

If a patient has experienced a serious or uncommon/rare AEFI, it is important that they or their immunisation service provider seek advice from a specialist immunisation clinic or contact state/territory health authorities for more information regarding the need for further investigation and management (refer to Appendix 1 Contact details for Australian, state and territory government health authorities and communicable disease control). This will enable an assessment to determine the relationship to vaccination, consideration of the benefits and risks of further vaccination, and planning for receiving additional doses of that or other vaccines, as appropriate. Persons who have had a serious adverse event following immunisation (other than a contraindication, such as the confirmed identity of the vaccine component that triggered anaphylaxis) can usually subsequently be vaccinated under close medical supervision. For more detailed information refer to 3.3.1 Vaccination of persons who have had an adverse event following immunisation (Handbook10-home-handbook10part3-handbook10-3-3).

Examples of uncommon and rare adverse events are given below. It is important to remember that, although these events are uncommon or rare, they are still not necessarily causally related to vaccination, even if they occur following vaccination.

- **Febrile convulsions** are a relatively common response to fever of any cause in young children, particularly in those aged <3 years, with a peak incidence at 14–18 months of age. Overall, by the age of 5 years, approximately 3% of all children will have experienced a febrile convolution, irrespective of vaccination. Febrile convulsions are rare following immunisation. They do, however, occur more commonly, but still at a low rate, after some vaccines. For example, MMR and MMRV vaccines are associated with an increased risk of febrile convulsions approximately 7 to 12 days after the 1st vaccine dose (refer to 4.9 Measles (Handbook10-home-handbook10part4-handbook10-4-9f) for more information). Co-administration of trivalent influenza vaccine and 13-valent pneumococcal conjugate vaccine may also be associated with an increased risk of febrile convulsions (refer to 4.7 Influenza (Handbook10-home-handbook10part4-handbook10-4-7) and 4.13 Pneumococcal disease (Handbook10-home-handbook10part4-handbook10-4-13)). In 2010, there was an increased incidence of high fevers and febrile convulsions (estimated at 4.4 per 1000 doses in Western Australia) following administration of one brand of seasonal influenza vaccine (bioCSL Fluvax and Fluvax Junior) in children aged <5 years in Australia. This vaccine is no longer registered for use in this age group. An excess risk of fever and febrile convulsions was not observed with the other influenza vaccines given to children.\(^{15,16}\)

- **Brachial neuritis** (inflammation of a nerve in the arm, causing weakness or numbness) has been described following the administration of tetanus toxoid-containing vaccines, with an estimated excess risk of approximately 0.5–1 in 100 000 doses in adults.\(^{5,17}\) Case reports of brachial neuritis following administration of other vaccines, including HPV vaccines, are rare and a causal relationship has not been established.\(^{19}\)

- **Oral rotavirus vaccines** are associated with a small increased risk of intussusception (IS), a rare form of bowel blockage caused by telescoping of the intestine into itself. This risk appears to be particularly in the 7 days following the 1st vaccine dose; however, a smaller increased risk in the week following the 2nd dose has also been reported.\(^{20,22}\) It is not currently clear whether there is any overall increase in the risk of IS above that which would be expected in the 1st year of infancy without vaccine use. The increased risk represents approximately 1 in

Common adverse events following immunisation and their management

- **Autoinjectors are not recommended for use in children weighing less than 10 kg.**

- **Adrenaline autoinjectors, EpiPen or Anapen, are devices that administer a single, pre-measured dose of adrenaline. They are designed for use by any person, whether medically trained or not. Clear instructions on correct use are provided on the barrel and in the packaging of these devices. They are designed to be administered in the mid-outter thigh.**

- **Autoinjectors are usually recommended or prescribed for an individual who is at risk of anaphylaxis due to an existing allergy or where skin testing indicates a high risk of an allergic reaction on exposure to an allergen. If a patient who carries an autoinjector device develops anaphylaxis post vaccination, it is appropriate to use their autoinjector to administer adrenaline.**

- **Autoinjectors are generally not appropriate for inclusion in first aid kits for general use, due to several limitations:**
  - They are single-use only
  - They are dose-specific
  - EpiPen Jr or Anapen Jr containing 150 µg of adrenaline are recommended for children weighing between 10 kg and 20 kg
  - EpiPen or Anapen containing 300 µg of adrenaline are recommended for children and adults weighing over 20 kg
  - Multiple pens would be required to allow for repeat dosing and varying ages/weights of patients, and shelf-life is limited to 1 to 2 years maximum.

- **Autoinjectors are not recommended for use in children weighing less than 10 kg.**

- **Low-grade fever and tiredness (malaise), lasting a few days, are also common after many vaccines. These responses are usually mild and self-limiting, and generally do not require specific treatment.**

- **Prophylactic administration of paracetamol at the time of, or immediately after, vaccination to reduce the risk of fever is not recommended, with the exception of specific recommendations for prophylactic administration of paracetamol with meningococcal B vaccine in infants <2 years of age (refer to 4.10 Meningococcal disease (Handbook10-home-handbook10part4-handbook10-4-10)). However, if an infant, child or adult has a fever of >38.5°C following vaccination or has pain at the injection site, paracetamol can be given. The dose of paracetamol for an infant or child up to 12 years of age is 15 mg/kg/dose, up to a maximum dose of 60 mg/kg per day in four divided doses. Adults and children aged ≥12 years can receive 500 to 1000 mg every 4 to 6 hours; dosage must not exceed 4 g in 24 hours. Paracetamol should not be given for more than 48 hours without seeking medical advice.**\(^{14}\)

If patients exhibit unexpected, serious or prolonged adverse symptoms or signs following immunisation, medical advice should be sought. The symptoms and signs from medical illness unrelated to vaccination can sometimes be attributed to a recent immunisation and should be investigated and managed accordingly.

Vaccination of persons who have had an adverse event following immunisation (Handbook10-home-handbook10part3-handbook10-3-3))

Contact details for Australian, state and territory government health authorities and communicable disease control (available at [www.australianprescriber.com/magazine/34/4/article/1210.pdf](http://www.australianprescriber.com/magazine/34/4/article/1210.pdf)). Endorsed by the Australasian Society of Clinical Immunology and Allergy, the Royal Australasian College of Physicians, the Australasian College for Emergency Medicine, the Royal Australian and New Zealand College of Radiologists, the Internal Medicine Society of Australia and New Zealand, and the Australian Dental Association.

- **Examples of uncommon and rare adverse events are given below. It is important to remember that, although these events are uncommon or rare, they are still not necessarily causally related to vaccination, even if they occur following vaccination.**
Events where evidence demonstrates no causal link with immunisation

Since vaccines are mainly given to healthy people, a range of conditions that occur after a vaccine dose may be attributed to vaccination. This is particularly so for illnesses that are complex and have an unknown or uncertain cause. As many of these illnesses are rare and/or manifest months to years after vaccination, they are difficult to study in randomised controlled clinical trials, which are typically conducted before vaccines are registered for use. Therefore, there is strong epidemiological evidence, usually derived from multiple well-conducted post-marketing studies, that indicates there is no causal association between immunisation and many diseases/conditions in which vaccines were suggested to have been involved.

Examples of events unrelated to vaccination include:

- sudden infant death syndrome (SIDS) and any vaccine
- autism and MMR vaccine
- multiple sclerosis and hepatitis B vaccine
- inflammatory bowel disease and MMR vaccine
- diabetes and Hib vaccine
- asthma and any vaccine

Despite this evidence, patients/parents seeking further advice should discuss this with their immunisation provider or could be referred to a specialist immunisation clinic for further reassurance (refer to Appendix 1 Contact details for Australian, state and territory government health authorities and communicable disease control). For details on how to report AEFI, refer to the next section below.

No time limit has been set to report AEFI; however, timely notification of adverse events, particularly rapid reporting of serious events, is important to identify any potential concerns. Notification does not necessarily imply a causal association with vaccination, as some events may occur coincidentally following vaccination. Any event that is suspected of being related to vaccination can be reported. All reported AEFI are included in the Adverse Drug Reactions System (ADRS) database of the Therapeutic Goods Administration (TGA). For details on how to report AEFI, refer to the next section below.

How to report adverse events following immunisation

AEFI are reportable via different routes; immunisation service providers should be aware of the method of reporting for their location. In most jurisdictions (the Australian Capital Territory, New South Wales, the Northern Territory, Queensland, South Australia, Victoria and Western Australia), AEFI should be reported directly to the relevant state/territory health authority (refer to Table 2.3.3). AEFI notified to these state and territory health departments are then forwarded to the TGA, who manage the ADRS database, which includes all adverse reaction reports related to drugs and vaccines. Reporting can also be done directly to the TGA as described below.

Table 2.3.3: Contact information for notification of adverse events following immunisation

<table>
<thead>
<tr>
<th>State/Territory</th>
<th>Report adverse events to</th>
<th>Contact information</th>
</tr>
</thead>
<tbody>
<tr>
<td>Australian Capital Territory</td>
<td>ACT Health Department</td>
<td>02 6205 2300</td>
</tr>
<tr>
<td>New South Wales</td>
<td>NSW Public Health Units</td>
<td>1300 066 055 (for connection to Public Health Unit)</td>
</tr>
<tr>
<td>Northern Territory</td>
<td>NT Department of Health</td>
<td>08 8922 8044</td>
</tr>
</tbody>
</table>

2.3.4 Immunisation registers

In 2016, expansion of Australia’s immunisation registers began with the aim of improving data capture and vaccine coverage rates across the entire Australian community. Historically, there have been two national immunisation registers in place in Australia: the Australian Childhood Immunisation Register (ACIR) and the National Human Papillomavirus Vaccination Program Register (the HPV Register). The ACIR, administered by the Australian Government Department of Human Services, commenced on 1 January 1996 and recorded details of vaccinations given to children <7 years of age who live in Australia. The HPV Register, currently operated by the Victorian Cytology Service on behalf of the Australian Government Department of Health, was established in 2007 to record information about HPV vaccine doses administered in Australia, supporting the implementation and monitoring of the National HPV Vaccination Program funded by the Australian Government the same year.

The Australian Immunisation Register Act 2015 came into effect on 1 January 2016 and provides the legal authority for the expansion and ongoing administration and keeping of the registers. From 1 January 2016, the ACIR began accepting vaccination information from all children, adolescents and young adults <20 years of age (expanded from <7 years of age). From September 2016, the ACIR will further expand to become the Australian Immunisation Register (AIR), capturing vaccinations given throughout a person’s life through general practice and community clinics (refer to ‘Australian Childhood Immunisation Register and Australian Immunisation Register’ below).

From the 2017 school year, the HPV Register will become the Australian School Vaccination Register (ASVR) which will capture certain adolescent vaccinations which are given through community clinics (refer to ‘Australian Childhood Immunisation Register and Australian Immunisation Register’ below).

Australian Childhood Immunisation Register and Australian Immunisation Register

Children, adolescents and young adults <20 years of age who are enrolled in Medicare are automatically included on the ACIR. Adults ≥20 years of age enrolled in Medicare will automatically be included on the register once the register is expanded from September 2016. Individuals not enrolled in Medicare will be included when an immunisation service provider submits details of a vaccination to the register. Immunisation providers other than general practitioners need to register with the ACIR before they can send data to the register.
Immunise - The Australian Immunisation Handbook 10th Edition

Since 1998, data held on the ACIR have been used to determine a family’s entitlement to government family assistance payments including the Child Care Benefit and Child Care Rebate and, from July 2012, the Family Tax Benefit Part A supplement. From January 2016, immunisation requirements for eligibility for these payments were expanded to include children, adolescents and young adults up to 20 years of age. It is, therefore, important that immunisation service providers submit vaccination data to the ACIR promptly. More information on immunisation requirements for family assistance payments can be found on the Australian Government Department of Human Services website (www.humanservices.gov.au/customer/subjects/immunising-your-children).

Reporting to the Australian Childhood Immunisation Register

Immunisation service providers should send to the ACIR details of all NIP and private vaccinations given to all children, adolescents and young adults <20 years of age. Vaccination details can be submitted by sending data electronically via Medicare Online or the ACIR secure Internet site (refer to ‘Resources on the Australian Childhood Immunisation Register website’ below), or by using a paper form (either an Immunisation Encounter form or an Immunisation History form). An individual’s vaccination record can also be updated with vaccination details where there is documentation that the vaccination was performed by another immunisation service provider (including vaccines given while the child, adolescent or young adult was overseas) by completing and sending an Immunisation History form. Immunisation service providers in Queensland and the Northern Territory who currently send data to the ACIR via their state/territory health department should continue to do so.

When required, exemptions to immunisation due to medical contraindications or natural immunity to certain diseases (refer to 2.1.5 Catch-up, ‘Use of laboratory testing to guide catch-up vaccination’) can be submitted to the ACIR via the approved ACIR Immunisation Medical Exemption form. This form can only be completed by general practitioners. The form includes guidance for general practitioners on what is, and is not, considered a valid reason for a medical exemption. As of January 2016, vaccine objection on non-medical grounds is not accepted as a valid exemption from immunisation requirements. The medical exemption form for general practitioners to complete is available on the Australian Government Department of Human Services website (https://www.humanservices.gov.au/health-professionals/forms/im011) (www.humanservices.gov.au/health-professionals/forms/im011).

For further information about the ACIR and reporting vaccination information, refer to ‘Resources on the Australian Childhood Immunisation Register website’ below.

Resources on the Australian Childhood Immunisation Register website

The Australian Government Department of Human Services website (http://www.humanservices.gov.au/) houses ACIR information and resources. The website has a general information area for individuals and families, a general information area for health professionals and a secure area for immunisation service providers only. Immunisation-related forms, such as the Immunisation History form and the Immunisation Medical Exemption form, can be found in the health professionals area of the website.

The ACIR secure site, which is within Health Professionals Online Services (HPOS) (https://www.humanservices.gov.au/health-professionals/services/medicare/hpos) (www.humanservices.gov.au/hpos), allows immunisation service providers to obtain a range of statistical and identified reports. Depending on the access level granted to the provider, these reports enable approved providers to view a child, adolescent or young adult’s vaccination details, record vaccination information and access a range of other reports. All general practitioners with access to HPOS can access the ACIR secure site through this platform. Other immunisation service providers can register for access to the ACIR secure site by completing the online request form, available from the Department of Human Services website.

Further information or assistance on any reporting issues can be obtained by calling the ACIR Internet Helpline on 1300 650 039.

Immunisation History Statement

Immunisation History Statements contain details of all vaccines administered to a child, adolescent or young adult <20 years of age that are recorded on the ACIR and list the vaccines that are due next. These statements are automatically generated on completion of the childhood vaccination schedule (usually around 4 years of age). These statements will be mailed to the address most recently recorded by Medicare for that individual.

Parents/careers of children <14 years of age, and adolescents and young adults ≥14 years of age, can get a copy of their immunisation history at any time:

- via their Medicare online account through myGov
- through the Express Plus Medicare mobile app
- by calling 1800 653 809 (free call).

Immunisation History Statements can be used to assist in recalling vaccination history when required. For example:

- for school enrolment
- to determine eligibility for the Child Care Benefit, the Child Care Rebate and the Family Tax Benefit Part A supplement – this requires that children are assessed as fully immunised.

Recording details of a deceased child

The ACIR receives notification of the death of a child or young individual <20 years of age via Medicare. This information no longer needs to be provided to the ACIR by an immunisation service provider.

Children who have moved to live overseas

If a child, adolescent or young adult <20 years of age has moved overseas, their immunisation service provider can inform the ACIR by phone or secure site email. This prevents their name continuing to appear on ACIR reports of overdue individuals.

Children born overseas who have moved to live in Australia permanently

A child, adolescent or young adult <20 years of age born overseas who has moved permanently to Australia will be automatically added to the ACIR upon enrolment with Medicare. Individuals residing temporarily in Australia are not included on the ACIR until an immunisation service provider notifies the register of a vaccination administered to that individual.

School vaccination program registers

Since its introduction in 2007, the HPV Register has played an essential role in monitoring and evaluating the HPV Vaccination Program by recording information about HPV vaccine doses administered in Australia. From the 2017 school year, vaccinations given through school programs, including HPV and varicella vaccines and the diphtheria-tetanus-pertussis booster, will be captured in the Australian School Vaccination Register (ASVR), replacing the HPV Register. Until this date, the HPV Register will continue to record information about HPV vaccine doses administered in Australia (refer to ‘National Human Papillomavirus Vaccination Program Register’ below).

Some states and territories also maintain records of vaccinations delivered through school-based programs. Information on how to obtain such records can be obtained from state and territory government health departments (refer to Appendix 1 Contact details for Australian, state and territory government health authorities and communicable disease control).

National Human Papillomavirus Vaccination Program Register (the HPV Register)

Reporting to the HPV Register

Details on HPV vaccinations given in the community are provided to the HPV Register by the immunisation service provider who administers the vaccine. Vaccination details may be submitted electronically, via data uploads or direct entry using the secure website, or in hard copy, using one of the approved notification forms. Immunisation service providers in Queensland and the Northern Territory report data to the HPV Register via their state/territory health authority. Immunisation service providers wishing to submit vaccination data electronically need to be
HPV vaccination coverage and other reports

For immunisation service providers, the HPV Register has developed overdue HPV vaccine dose reports for their patients, which are available online via the secure website. De-identified HPV vaccination coverage data and other reports have also been developed to inform policy making, and support program delivery and approved research. National coverage data are made publicly available via the Immunise Australia website(http://www.immunise.health.gov.au).

HPV Register statements

The HPV Register sends Completion Statements and History/Reminder Statements. Immunisation History Statements, containing details of the vaccinations recorded on the HPV Register, are sent to persons who are overdue for HPV vaccination within the school-based program. Completion Statements are sent to persons who have completed the 3-dose HPV vaccination course. Vaccinated persons and parents/guardians can request a statement at any time by phoning 1800 478 734 (1800 HPV REG). In the event that booster doses are required in future, all eligible persons will be notified by the HPV Register.

HPV vaccination status

Vaccinated persons and parents/guardians can phone the HPV Register on 1800 478 734 (1800 HPV REG) to obtain their or their child’s HPV vaccination status. Immunisation service providers can also request a patient’s vaccination status by phone or can view these online if they are registered with the HPV Register. The HPV Register initially only recorded vaccinations for females, but since 2013 also records vaccinations given to males.

HPV Register secure website

The HPV Register secure website allows registered and approved immunisation service providers to view a patient’s vaccination history as well as to access overdue dose reports. Further information on how to request access to the HPV Register secure website can be found on the health professionals page of the HPV Register website(http://www.hpvregister.org.au) or by phoning 1800 478 734 (1800 HPV REG).

Other immunisation registers

The Australian Q Fever Register(http://www.qfever.org), established by Meat and Livestock Australia (MLA), has records of receipt of Q fever vaccination for some individuals, which can be accessed by registered users (refer also to 4.15 Q fever(Handbook10-home-handbook10part4-handbook10-14-15)).

Some state/territory governments operate a jurisdictional immunisation register, though the scope of these varies.

Queensland

The Vaccine Information and Vaccine Administration System (VIVAS) is a database of vaccination events for all children up to 10 years of age, adolescents and (some) adults in Queensland who are vaccinated with nationally- or state-funded vaccines.

Immunisation service providers in Queensland are encouraged to report all vaccinations, either directly to VIVAS via the Queensland Health Vaccination Record form or using practice software to electronically transfer data (via the ACIR) to Queensland Health. Vaccination Record forms can be posted reply paid to VIVAS or faxed directly. Providers reporting to VIVAS should do so at least once a week to ensure the supply of data is not delayed and is available for the purposes of calculating parental and provider incentive payments using ACIR data.


The Northern Territory

The NT Immunisation Register records details of all vaccines administered to anyone in the Northern Territory (NT). Immunisation service providers in the NT are encouraged to report all administered vaccines to the NT Immunisation Register. This can be done by direct electronic transfer from some services or via printed lists from clinical software programs and/or by completing the NT childhood or adult vaccination recording form(http://www.health.nt.gov.au/Centre_for_Disease_Control/Immunisation/Recording_and_Reporting_Forms/index.aspx) (www.health.nt.gov.au/Centre_for_Disease_Control/Immunisation/Recording_and_Reporting_Forms/index.aspx).

The Northern Territory Immunisation Register routinely provides relevant data on vaccination encounters to the ACIR and the HPV Register.

The NT Immunisation Register(http://www.health.nt.gov.au/Centre_for_Disease_Control/Immunisation/NT_Immunisation_Register/index.aspx) provides a number of services, such as recall lists for childhood immunisations in remote areas, individual vaccination records, and web-based access for NT immunisation service providers for immunisation histories for children <15 years of age.

References


Part 3 Vaccination for Special Risk Groups

- 3.1 Vaccination for Aboriginal and Torres Strait Islander people
- 3.2 Vaccination for international travel
- 3.3 Groups with special vaccination requirements
Recommendation for Indigenous persons

Children resident in the Northern Territory, Queensland, South Australia and Western Australia

All persons aged ≥ 6 months

Children resident in the Northern Territory, Queensland, South Australia and Western Australia

Since October 2009, only one type of Haemophilus influenzae

Influenza

Hepatitis B

Pneumococcal conjugate (13vPCV (pneumococcal conjugate vaccine))

Pneumococcal polysaccharide (23vPPV (23-valent pneumococcal polysaccharide vaccine))

Table 3.1.1: Additional* vaccines recommended for Indigenous persons, due to their higher risk of disease

Vaccine

BCG (bacille Calmette-Guérin)

Hepatitis A

Hepatitis B

Influenza

Pneumococcal conjugate (13vPCV (pneumococcal conjugate vaccine))

Pneumococcal polysaccharide (23vPPV (23-valent pneumococcal polysaccharide vaccine))

Recommendation for Indigenous persons

Neonates living in areas of high TB (tuberculosis) incidence

Children resident in the Northern Territory, Queensland, South Australia and Western Australia

2 doses in the 2nd year of life

Adults who have not previously been vaccinated against hepatitis B and are non-immune

All persons aged ≥ 6 months

Children resident in the Northern Territory, Queensland, South Australia and Western Australia

Booster dose in 2nd year of life in addition to primary course

Persons aged 15-49 years with underlying conditions increasing the risk of IPD (invasive pneumococcal disease)

All persons aged ≥50 years

* In addition to those vaccines recommended for all Australians or those in particular medical, occupational, behavioural or other risk groups.
† Northern Territory, Queensland, northern South Australia
‡ Exact ages may differ between jurisdictions.
§ Refer to 4.7 Influenza. (Handbook10-home~handbook10part4~handbook10-4-7#4-7)
¶ Refer to 4.13 Pneumococcal disease for recommendations on revaccination. (Handbook10-home~handbook10part4~handbook10-4-13#4-13)

3.1.1 Children

BCG (bacille Calmette-Guérin) vaccine and tuberculosis

BCG (bacille Calmette-Guérin) vaccine is recommended for Indigenous neonates in regions of high tuberculosis (TB (tuberculosis)) incidence, where infants are at higher risk of acquiring this serious condition. BCG (bacille Calmette-Guérin) vaccine is provided for Indigenous neonates in the Northern Territory, Queensland and parts of northern South Australia, but not longer in Western Australia. State/territory health authorities should be consulted to determine the recommendations for particular areas, including where BCG (bacille Calmette-Guérin) vaccine is provided for Indigenous neonates in the Northern Territory, Queensland and parts of northern South Australia, but not longer in Western Australia. State/territory health authorities should be consulted to determine the recommendations for particular areas, including where BCG (bacille Calmette-Guérin) vaccination is being considered for neonates <2.5 kg in weight. (Refer also to 4.20 Handbook10-home~handbook10part4~handbook10-4-20#4-20) Tuberculosis was most likely introduced to the Indigenous population in the early years of European settlement. It became the largest single cause of death for Indigenous persons in the last quarter of the 19th century and the first quarter of the 20th century, coinciding with large-scale movement from nomadic life to settlements. In some communities tuberculosis was responsible for more than 20% of deaths. Control measures in the second half of the 20th century were effective for both Indigenous and non-Indigenous populations, but disparities have persisted. In southern states the notification rate for tuberculosis in Indigenous persons is comparable to that of Australian-born non-Indigenous persons, but there is considerable geographic variation. The Northern Territory has consistently had the highest rates of any jurisdiction, and, in 2007, TB (tuberculosis) incidence was 13-fold higher among Indigenous persons than non-Indigenous persons. Very high rates among Indigenous persons have been documented in Far North Queensland and northern South Australia, but not in New South Wales in recent years. BCG (bacille Calmette-Guérin) vaccine reduces pulmonary tuberculosis and provides substantial protection against disseminated forms of the disease in young children. Nevertheless, as the incidence of pulmonary tuberculosis in adults and the risk of disseminated tuberculosis in infants decreases, the risk of severe complications of BCG (bacille Calmette-Guérin) vaccination, documented in indigenous persons of other countries, becomes a significant consideration. BCG (bacille Calmette-Guérin) vaccine is usually administered to eligible infants by hospital staff (i.e. midwives or nurses who have been specially trained) soon after delivery. Injection technique is particularly important for BCG (bacille Calmette-Guérin) vaccination, which must be administered intradermally. Adverse events, such as regional lymphadenitis, are less common when vaccination is performed by trained staff.

Haemophilus influenzae type b

Haemophilus influenzae type b (Hib) (Haemophilus influenzae type b) vaccine (PPV7 (PPV conjugated to tetanus toxoid)) has been used in Australian population. Since October 2009, only one type of Haemophilus influenzae type b (Hib) (Haemophilus influenzae type b) vaccine (PPV7 (PPV conjugated to tetanus toxoid)) has been used in Australian population.
and recorded hospitalisation rates are more than 50 times higher in Indigenous persons, particularly in remote areas. In addition, it also occurred at a younger age than in non-Indigenous children. Thus, a vaccine to prevent Hib (Haemophilus influenzae type b) infection in Indigenous children needed to be immunogenic as early as possible in infancy. The previously used Hib (Haemophilus influenzae type b)-containing vaccine, known by the abbreviation PRP-OMP (PRP conjugated to the outer membrane protein of Neisseria meningitidis), was more immunogenic at 2 months of age than the other conjugate Hib (Haemophilus influenzae type b) vaccines, and so were the preferred Hib (Haemophilus influenzae type b) vaccine type for Indigenous children in the first Hib vaccination programs beginning in 1993. Since then, there has been a dramatic decline in Hib disease in Indigenous children.33 New combination vaccines that include a Hib (Haemophilus influenzae type b) (PRP-T, PRP conjugated to tetanus toxoid) component, and have the advantage of reducing the number of injections, were introduced in some jurisdictions from November 2005. Initially PRP-T (PRP conjugated to tetanus toxoid) vaccines were not recommended for Indigenous children in jurisdictions with higher disease incidence, but other PRP-OMP (PRP conjugated to the outer membrane protein of Neisseria meningitidis) or PRP-T (PRP conjugated to tetanus toxoid) vaccine could be given to other children. Following an international shortage of PRP-OMP (PRP conjugated to the outer membrane protein of Neisseria meningitidis) vaccine, it was progressively replaced by PRP-T (PRP conjugated to tetanus toxoid) containing vaccines for all children. Invasive Hib (Haemophilus influenzae type b) disease and nasopharyngeal colonisation with Hib (Haemophilus influenzae type b) are being closely monitored in high-incidence settings such as the Northern Territory and Western Australia following this change. To date, there has been no change in Hib (Haemophilus influenzae type b) epidemiology found in association with the change to PRP-T (PRP conjugated to tetanus toxoid)-containing vaccines for Indigenous children.

**Hepatitis A**

Hepatitis A vaccination is recommended for Indigenous children in those jurisdictions with high disease incidence: the Northern Territory, Queensland, South Australia, and Western Australia (Refer to 4.4/Handbook10-home-handbook10part4-handbook10-4-484-4 Hepatitis A). Two doses should be given, commencing in the 2nd year of life. The recommended ages of administration vary between states and territories, so jurisdictional health authorities should be contacted for further details about local vaccination schedules.

Hepatitis A infection was common during the 1990s in Indigenous children across northern and central Australia. Most children acquired the virus in the first 5 years of life, which is a typical finding in populations with disadvantaged living conditions. Although the symptoms of infection in early childhood are usually mild or absent, cases complicated by liver failure and death have been reported among Indigenous children in Far North Queensland, and the Kimberley, and recorded hospitalisation rates are more than 50 times higher in Indigenous children than in non-Indigenous children. A vaccination program for Indigenous children was introduced in north Queensland in 1999 and resulted in a 92% decrease in the number of reported cases, from 787 cases in all children during the year 1996–1999 to 66 cases in the period 2000–2003. This decrease in hepatitis A disease was observed in both Indigenous and non-Indigenous children, suggesting a substantial herd immunity effect. From 2005, the hepatitis A vaccination program was extended to include all Indigenous children aged 2-15 years resident in the Northern Territory, Queensland, South Australia and Western Australia. Notifications have fallen by over 90%, from more than 50 per 100,000 in 2005 to less than 5 per 100,000 in 2009.

**Hepatitis B**

Refer to ‘Hepatitis B’ under ‘Adults’ below.

**Influenza**

Annual influenza vaccination is recommended for all Aboriginal and Torres Strait Islander children. In particular, Aboriginal and Torres Strait Islander children 6 months to <5 years and ≥15 years of age are at greater risk of influenza and its complications than non-Indigenous children of the same age. (Refer also to ‘Influenza’ in 3.1.2 Adults below). The risk of influenza complications is not as high in children aged 5-14 years. However, annual influenza vaccination of children in this age group can still offer individual protection against influenza as well as potential indirect protection to other members of their household (refer to 4.7 Influenza). Indigenous adults are also recommended to receive annual influenza vaccine (refer to 3.1.2 Adults below).

**Pneumococcal disease**

The 13-valent pneumococcal conjugate vaccine (13vPCV (pneumococcal conjugate vaccine)) is recommended for all children in a 3-dose infant vaccination schedule, replacing the 7-valent pneumococcal conjugate vaccine (7vPCV (pneumococcal conjugate vaccine)) in all jurisdictions except the Northern Territory, where it replaced the 4-dose schedule of the 10-valent pneumococcal conjugate vaccine (10vPCV (pneumococcal conjugate vaccine)). In addition to a primary course of 3 doses of 13vPCV (pneumococcal conjugate vaccine), at 2.4 and 6 months of age, a booster dose of 13vPCV (pneumococcal conjugate vaccine) is also recommended at 12–18 months of age for Indigenous children in areas of high incidence (i.e. the Northern Territory, Queensland, South Australia and Western Australia). This 13vPCV (pneumococcal conjugate vaccine) booster dose replaces the 23-valent pneumococcal polysaccharide booster or 4th dose of 10vPCV (pneumococcal conjugate vaccine) (which was used at this schedule point for a short time in the Northern Territory) (Refer to 4.13/Handbook10-home-handbook10part4-handbook10-4-1384-13 Pneumococcal disease).

Prior to the availability of conjugate pneumococcal vaccines, Central Australian Indigenous children had rates of IPD (invasive pneumococcal disease) that were among the highest ever reported in the world. Very high rates were also reported in Indigenous children in other parts of northern Australia. High rates of pneumococcal pneumonia have also been documented in Central Australian Aboriginal children, and Streptococcus pneumoniae has been implicated in the high rates of otitis media in Indigenous children. 7vPCV (pneumococcal conjugate vaccine) was made available for Indigenous children, and non-Indigenous children with medical risk factors, from 2001, 4 years prior to the universal program for all children in Australia. The initial program was highly successful, resulting in a rapid decline in invasive pneumococcal disease due to the serotypes contained in the 7vPCV (pneumococcal conjugate vaccine) among Indigenous and non-Indigenous children. However, a wider range of serotypes is responsible for disease in Indigenous children, and therefore a smaller proportion of cases is vaccine preventable. While an initial reduction in IPD (invasive pneumococcal disease) was observed, IPD (invasive pneumococcal disease) incidence still remains higher in Indigenous children than in non-Indigenous children.

**3.1.2 Adults**

**Hepatitis B**

Indigenous persons should have their risks and vaccination status for hepatitis B reviewed, be offered testing for previous hepatitis B infection, and be offered vaccination if non-immune. (Refer also to also 4.5/Handbook10-home-handbook10part4-handbook10-4-584-5 Hepatitis B.) High rates of mortality and morbidity from hepatitis B among Indigenous persons have been recognised ever since the original identification of the ‘Australia antigen’ in 1965. Prior to vaccination, estimates of the prevalence of markers of previous infection in Indigenous communities ranged from 20 to 100%. In the Northern Territory, the incidence of primary hepatocellular carcinoma was 10 times higher among Indigenous persons than in non-Indigenous persons, and comparable to high-incidence countries such as China. Vaccination programs have had substantial impacts on infection and carriage rates in both Indigenous and non-Indigenous Australians. However, there is evidence that new infections continue to occur at a higher rate in Indigenous persons. Probably due to a combination of pre-existing high carriage rates, susceptible persons in older age groups (who were not eligible for vaccination programs), a high rate of hepatitis B infection and death due to hepatitis B were observed, particularly in younger age groups who were not eligible for vaccination programs.

**Influenza**

Annual influenza vaccination is recommended for all Indigenous (refer to 3.1.1 Children above and Refer to 4.7/Handbook10-home-handbook10part4-handbook10-4-784-7 Influenza) individuals. It has been hypothesized that certain serotypes may have a higher prevalence in the community than in the population studied. Influenza disease incidence is greatest in young children and the elderly. Hospitalisation rates due to influenza and pneumonia are highest in young children and lowest in older children. Hospitalisation and death rates increase with age in all adults, but increase much earlier in Indigenous adults than in non-Indigenous adults. The vast majority of these hospitalisations and deaths are due to pneumonia, but it is not clear what http://www.immunise.health.gov.au/internet/immunise/publishing.nsf/Content/Handbook10-home

69/278
Pneumococcal disease

Pneumococcal polysaccharide vaccine is recommended for all Indigenous adults aged ≥50 years, and those aged 15–49 years who have conditions associated with an increased risk of IPD (invasive pneumococcal disease). The broader age-based recommendation for Indigenous persons is due to the high rates of pneumococcal disease and higher prevalence of risk factors (certain medical conditions and tobacco smoking) in Indigenous adults, compared to non-Indigenous adults. Revaccination is recommended 5 years after the 1st dose for those first vaccinated at ≥50 years of age, and a further revaccination is recommended in some circumstances (Refer to 4.13). For those aged 14 years and younger, and for those aged ≥15 years who have not previously been vaccinated, a 1st dose of PCV7 or PCV13 is provided as part of the Indigenous child vaccination schedule, commencing at 12 months of age. Immunisation coverage in Indigenous adults ≥25 years is generally lower than in non-Indigenous adults.41 Studies in Far North Queensland and the Kimberley have demonstrated a favourable impact of PCV7/PCV13 on rates of invasive pneumococcal disease in Indigenous adults.42,43 In some other regions there has been no decrease in disease, perhaps due to low vaccination coverage and/or non-vaccine serotype replacement.44-46 At a national level, disparities remain in disease rates between Indigenous and non-Indigenous adults. As is the case for influenza and pneumonia, rates of invasive pneumococcal disease are highest in older Indigenous adults, with rates around 4 times higher in Indigenous than non-Indigenous adults aged ≥50 years.47 Rates in younger adults are slightly lower, but the relative difference between Indigenous and non-Indigenous persons is much greater, around 12 times higher in Indigenous than in non-Indigenous adults aged 25–49 years. Vaccination coverage has been low in younger Indigenous adults, an issue that requires attention if the full benefits of vaccination are to be realised.8 Other diseases

Japanese encephalitis

The first ever outbreak of Japanese encephalitis (JE) in Australia occurred in the remote outer islands of the Torres Strait in 1995, with 3 cases, 2 of them fatal. There have been 5 cases to date acquired in Australia. Since then, JE virus has been detected frequently in sentinel animal surveillance in the outer islands. However, the sentinel pig surveillance system has been gradually disbanded since 2006, with surveillance of the last remaining herd on Cape York ceasing from the 2011–2012 wet season.

A JE vaccine (JE-Vax) was first offered to the residents of the Torres Strait Islands in late 1995 and the vaccine was integrated into the vaccination schedule for children resident in the Torres Strait Islands, commencing at 12 months of age.44,45

There has not been a case of JE in the Torres Strait since 1998 and the risk of JE has diminished considerably in the outer islands since the mid-1990s. Most communities have relocated pigs well away from homes, and major drainage works on most islands have markedly reduced potential breeding sites for vector mosquitoes. In 2007, the supply of JE-Vax vaccine into Australia ceased as the manufacturer stopped production. Because of this shortage of vaccine, for a short period from September 2007 to mid 2008,JE-Vax was restricted to use on the six outer Torres Strait Islands: Badu, Boigu, Dauan, Mabuiag, Moa and Sabal. Two new Japanese encephalitis vaccines, Imojev and JEspect, are now available for use in those at risk in the Torres Strait (Refer to 4.8).

Rubella

Although evidence suggests that endemic rubella is well controlled in Australia, Indigenous women living in rural and remote regions are more likely to be non-immune to rubella than non-Indigenous non-oversese-resident Australians.48,49 Every effort should be made to identify non-pregnant seronegative Indigenous women of child-bearing age and provide measles-mumps-rubella (MMR) vaccine, in order to prevent congenital rubella syndrome (Refer to 4.18).

Vaccination with MMR (Measles, Mumps and Rubella) vaccine also ensures adequate protection against measles (Refer to 4.9).

3.1.3 Service delivery

General practitioners, Aboriginal Community Controlled Health Services, Community Health Services, the Royal Flying Doctor Service and state/territory corrective services all provide vaccination services to Indigenous persons and are important to the success of programs to vaccinate Indigenous persons. While vaccination coverage estimates vary over time and between communities, a relatively consistent finding has been higher coverage in Indigenous persons in remote areas than in urban areas.47,48 More recently, however, this has not been the case for Indigenous children, where coverage has been high in both remote and urban areas;49 coverage in remote areas is lower for adults than for children.5 For vaccines recommended for both Indigenous and non-Indigenous persons, coverage is as high, or higher, in Indigenous persons as in non-Indigenous persons, but vaccination is more frequently delayed.50-53 For example, one study reported that at 7 months of age only 45.2% of Indigenous infants in the Northern Territory had completed the recommended schedule for that age point (Refer to 4.8).

Vaccination with MMR (Measles, Mumps and Rubella) vaccine also ensures adequate protection against measles (Refer to 4.9).

These disparities point to the importance of Indigenous status, particularly in mainstream health services, and particularly in urban areas. The use of patient information systems to record Indigenous status and schedule preventive health services has the potential to increase opportunistic vaccination and enable the provision of patient reminders, with resultant improvements in coverage and timeliness.54 Culturally appropriate service delivery and communication strategies, as well as use of Indigenous-specific Medicare items, will also assist in improving access to health services for Indigenous Australians.55-58

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3.2 Vaccination for international travel

This chapter has been amended on July 2016.

- 3.2.1 - Introduction
- 3.2.2 - Infections acquired by travellers
- 3.2.3 - Practical aspects of recommending vaccinations for travellers
- 3.2.4 - Vaccines
- 3.2.5 - Vaccinating the traveller with special risk factors
- 3.2.6 - Further information
- References

3.2.1 Introduction

The number of Australians who travel overseas has increased over recent years. Data available through the Australian Bureau of Statistics suggest that there were about 6.7 million short-term departures in 2010, with more than half travelling to destinations other than New Zealand or countries in North America and Europe. There are various risks to health associated with international travel, including exposures to infectious agents, extremes of altitude and temperature, and other physical, psychological, and environmental hazards. There could also be poor quality or limited access to clean water, shelter, hygiene and sanitation facilities, and health and medical care. The level of health risks will vary with individual factors, including the travellers’ underlying health and physiological state, the itinerary and activities undertaken, and the duration of exposure to various hazards during travel.

Travellers with increased risks to their health include young children and infants; pregnant women; people with underlying medical conditions, especially immunocompromising conditions due to disease or medical treatment; travellers spending extended periods in multiple regions with poor resources or in remote regions; those participating in mass gatherings (major sporting, cultural, social or religious events involving large numbers of people); and migrant families travelling back to their country/region of origin to visit friends and relatives (VFHR). Those undertaking VFHR travel are more likely to have closer contact with local populations, stay in remote or rural areas, and consume higher-risk food and beverages. They are also less likely to adequately perceive health risks associated with travelling, specifically seek pre-travel health advice, or be adequately vaccinated or prophylaxed.

3.2.2 Infections acquired by travellers

Exposure to infectious diseases, some of which are vaccine preventable, is one of the many health hazards of international travel. Although some of these diseases are present in Australia, the risk of acquiring them overseas may be higher because of higher incidence in other countries and/or increased risk of exposure resulting from activities undertaken during the travel period.

Common infections acquired by travellers include those that follow ingestion of contaminated food or beverages. Most of these are diarrhoeal diseases due to enteric pathogens, but infections with extra-intestinal manifestations, such as hepatitis A and typhoid, are also acquired this way. Vaccines against hepatitis A, typhoid and cholera are available. Insect-borne (particularly mosquito-borne) infections, such as malaria and dengue, are important causes of fever in Australian travellers returning from endemic areas, particularly Southeast Asia and Oceania. Japanese encephalitis occurs throughout a large part of Asia and the Western Pacific region, including eastern Indonesia and Papua New Guinea. Yellow fever occurs only in parts of Africa and South America, while tick-borne encephalitis occurs in parts of Europe and Asia. Vaccines are available for protection against Japanese encephalitis, yellow fever and tick-borne encephalitis.

Vaccine-preventable infections transmitted via aerosols and/or droplets include influenza, meningococcal disease, measles, mumps and varicella (chickenpox). Influenza is typically the most frequent vaccine-preventable infection among travellers. Incidences of measles and mumps are higher in many overseas countries, including some developed countries, than in Australia. Tuberculosis is a rare infection in travellers, and is more likely to be acquired by expatriates who live in endemic areas for long periods than by short-term visitors.

Blood-borne and sexually transmitted infections, such as hepatitis B, hepatitis C and human immunodeficiency virus (HIV), may pose a threat to some Australian travellers. In some areas, there is the possibility that these viruses and other blood-borne agents may be transmitted by healthcare workers using non-sterile medical equipment or other poor infection control practices. Hepatitis B vaccine is relevant to many travellers.

Travellers may be exposed to a variety of other exotic infectious agents, such as rashes (from bites or scratches from rabid dogs and other mammals in many countries), schistosomiasis (from exposure to water infested with the parasites, in Africa in particular), and leptospirosis (through activities like rafting or wading in contaminated streams). Of these, only rashes can be prevented by vaccination.

Some other vector-borne diseases and parasitic (including protozoal and helminthic) diseases are also important for international travellers, some of which are preventable through appropriate barrier precautions and chemoprophylaxis (e.g. malaria).

3.2.3 Practical aspects of recommending vaccinations for travellers

Although important, recommending appropriate vaccinations is not the only component of a pre-travel medical consultation, and vaccines relevant for travelling are not restricted to those for prevention of diseases that occur most commonly overseas (‘travel vaccines’). Recommendation of a vaccine for travelling only on the basis of the destination country is undesirable. There is no single ‘correct’ list of vaccines for travelling to any single country.

In a pre-travel medical consultation, it is prudent to also acquire adequate information regarding:

- relevant personal information of the traveller, including age, pregnancy or planning of pregnancy, or even possible financial constraints
- underlying medical conditions of the traveller, particularly immunocompromising conditions, and current medications
- vaccination history (including adverse events following immunisation) and allergy history of the traveller
- detailed intended itinerary, including date of departure (and time period available for vaccinations), specific localities and routes, rural versus urban stay, duration of stay, likely access to healthcare and other services, and probability of deviation from planned itinerary
- purpose(s) of travel and intended activities, especially those susceptible to various environmental risks and hazards
- plans for travel insurance.

This information will not only facilitate recommendations of preventive exposures and/or chemoprophylaxis that are commensurate with exposure risks and tailored to the proposed trip, but also provision of other important preventive health advice (e.g. food and water precautions, avoidance of bites from mosquitoes or other arthropods) and advice regarding management of possible health conditions during travel.

Some overseas organisations, such as schools, colleges and universities, have policies requiring evidence of vaccination and/or immunity against some vaccine-preventable diseases, for example, measles and meningococcal disease. These requirements should be taken into account while planning and scheduling immunisation prior to departure.

The vaccination needs for a traveller may be conveniently considered in several categories.

Routinely recommended vaccines (not specifically related to travelling overseas)

All travellers should be up to date with current standard vaccination recommendations. Consideration should also be given to any other vaccines that may be relevant to the individual’s health status or underlying medical conditions, occupation or lifestyle (e.g. pneumococcal polysaccharide vaccine for an elderly person or person otherwise recommended to have had pneumococcal vaccine, hepatitis B vaccine for a first aid officer). The probability of exposure to some of these diseases may be greater while travelling overseas, even to ‘developed’ countries (e.g. measles and mumps). For some itineraries, it may be appropriate for some booster doses to be received sooner (i.e. before travel) than at the routine recommended time (e.g. diphtheria-tetanus booster).
A risk assessment approach should be adopted in recommending some selective vaccines based on travel itineraries ('travel vaccines'). Potential risks of disease exposure and protective benefits from vaccinations should be weighed against potential adverse effects and both non-financial and financial costs arising from vaccinations. Priority should be given to vaccines for diseases that are common and of significant impact (e.g. influenza and hepatitis A), and to those diseases that, although less common, have severe potential adverse outcomes (e.g. Japanese encephalitis and rabies). Booster doses should be considered where appropriate (refer to Table 3.2.1). Because of the imminence of departure, sometimes an 'accelerated schedule' may be considered appropriate (e.g. for hepatitis B or the combined hepatitis A/hepatitis B vaccine – refer to the relevant disease-specific chapters in Part 4).

**Vaccines required by International Health Regulations or for entry into specific countries**

Yellow fever vaccination is required by the International Health Regulations (2005) for travelling in certain circumstances, for the purpose of individual protection if a traveller is likely to be exposed to yellow fever and/or for protection of vulnerable populations (in countries with relevant vectors) from importation of the disease (refer to 4.23).

Yellow fever vaccine is recommended for all travellers to countries in West and Central Africa where there is endemic yellow fever, and should be considered even for short stays in urban areas or in transit. It is highly recommended for travellers to countries in the Amazon Basin in South America. Yellow fever vaccine is not necessary in other developed countries, or countries where yellow fever is not endemic.

Influenza and pneumococcal disease

Influenza vaccine is recommended for all travellers, especially if travelling during the influenza season. Pneumococcal polysaccharide vaccine is recommended for all travellers aged 65 years or over, and also for those with underlying medical conditions, such as chronic lung disease, heart failure, diabetes, liver disease, kidney disease, or are on long-term corticosteroid therapy.

**Gastroenteritis**

Travel-related gastroenteritis is a common and significant cause of morbidity in travellers. Prevention includes ensuring adequate food hygiene, particularly when eating out, and avoiding uncooked and undercooked food and drinking water that may be contaminated.

**Hepatitis A**

Hepatitis A should be considered for all travellers to countries with intermediate or high endemicity of hepatitis A, or high endemicity of hepatitis A among the child population. In exceptional circumstances, when travelling to countries with intermediate endemicity of hepatitis A and no or low vaccination coverage in children, hepatitis A vaccination may be considered for travellers.

**Hepatitis B**

Most Australian children born since 2000, and a high proportion of adolescents, will have been vaccinated against hepatitis B under the NIP schedule. In exceptional circumstances, the NIP schedule may be considered appropriate (e.g. for hepatitis B or the combined hepatitis A/hepatitis B vaccine – refer to the relevant disease-specific chapters in Part 4). Because of the imminence of departure, sometimes an 'accelerated schedule' may be considered appropriate (e.g. for hepatitis B or the combined hepatitis A/hepatitis B vaccine – refer to the relevant disease-specific chapters in Part 4).

**Diphtheria, tetanus and pertussis**

All prospective travellers should have been vaccinated according to the recommended vaccination schedule appropriate for the traveller's age and underlying health conditions. All children should be vaccinated according to the NIP schedule. In exceptional circumstances, the NIP schedule may be administered at the minimum age rather than the recommended age (refer to 2.1.5).

**Pneumococcal disease**

Pneumococcal polysaccharide vaccine is recommended for all travellers aged 65 years or over, and also for those with underlying medical conditions, such as chronic lung disease, heart failure, diabetes, liver disease, kidney disease, or are on long-term corticosteroid therapy.

**Routinely recommended vaccines**

Routinely recommended vaccines (not specifically related to travelling overseas)

Diphtheria, tetanus and pertussis

Adult travellers should be adequately protected against tetanus before departure, particularly if their risk of sustaining tetanus-prone wounds is high or there could be delays in accessing health services where they can receive tetanus toxoid boosters safely if required. Protection against pertussis should also be offered at this opportunity (as dTpa) if no previous dose of dTpa has been given (refer to 4.12).

**Hepatitis B**

Most Australian children born since 2000, and a high proportion of adolescents, will have been vaccinated against hepatitis B under the NIP or jurisdictional school-based vaccination programs. Long-term or frequent travellers to regions of intermediate or high endemicity of hepatitis B, including Central and South America, Africa, Asia or Oceania, are recommended to be vaccinated against hepatitis B, due to the potential for inadvertent exposure to hepatitis B virus through blood-borne or sexual routes, including unplanned medical or dental procedures. A survey has shown that about half of Australian travellers who spent at least 3 nights in Southeast or East Asia had participated in at least one activity with a risk of acquiring hepatitis B.

**Influenza and pneumococcal disease**

Older travellers (usually those aged ≥65 years) and those with any relevant underlying medical or behavioural risk factors (refer to 4.7).

**Measles, mumps, rubella and varicella**

Measles outbreaks in Australia now result from an infection imported by inadequately vaccinated young travellers. Incidences of measles and mumps are higher in some overseas countries, regions or communities, including developed countries, than in Australia. Australians born during or since 1966 who have not received 2 doses of measles, mumps- and rubella-containing vaccines should be vaccinated with the MMR vaccine before travelling (no entry requirements) (refer to 4.9).

Meningococcal disease

A single dose of MenCCV-containing vaccine is recommended for all children at the age of 12 months (refer to 4.10 Meningococcal disease). This can be provided as either the combination vaccine Hib-MenCCV or MenCCV. Vaccination against meningococcal serogroup B is recommended for certain age groups who are at increased risk of meningococcal disease (refer to 4.10 Meningococcal disease).

Polioymelitis

All travellers should be age-appropriately immunised against polio (refer to 4.14(Handbook10-home-handbook10part4-handbook10-4-1444-14) Poliomyelitis). If travelling to countries where wild poliovirus transmission still occurs, inactivated poliomyelitis vaccine (IPV) should be offered to those who have not completed a 3-dose primary course of any polio vaccine, and a single booster dose should be given to those who have previously completed the primary course. An up-to-date list of polio-affected countries is available from the World Health Organization (WHO) Global Polio Eradication Initiative website(http://www.polioeradication.org). Documented evidence of polio vaccination is not routinely required for travellers under International Health Regulations but may be temporarily recommended in accordance with WHO recommendations in response to new evidence of the spread of wild poliovirus (refer to ‘Vaccine administration and documentation’ in 3.2.3 Practical aspects of recommending vaccinations for travellers above). As international polio epidemiology and any associated travel requirements are changing, current recommendations for Australian travellers should be sought from the Australian Government Department of Health website (http://www.health.gov.au/internet/main/publishing.nsf/Content/ohp-polioymelitis.htm).

Selected vaccines based on travel itinerary, activities and likely risk of disease exposure

Cholera

Cholera vaccine is rarely indicated for most travellers, as the risk of acquiring cholera for travellers in general is very low, provided that general precautions to avoid contaminated food and water are taken. The protective efficacy against V. cholerae O1 is high (>80%) among children aged 2–5 years for the initial 4–6 months after 3 doses, but wanes to become insignificant afterwards. For those aged >5 years, protective efficacy is about 78% and 63% for the 1st and 2nd year, respectively, and wanes to become insignificant beyond 2 years after vaccination. The vaccine does not protect against the V. cholerae O139 serogroup. It is only indicated for those travellers at considerable risk, such as those working in humanitarian disaster situations. However, since cholera and enterotoxigenic Escherichia coli (ETEC) share the same toxin, cholera vaccination does afford some partial short-term protection against ETEC-caused travellers’ diarrhoea. The effect lasts only 3 months, and the overall reduction of travellers’ diarrhoea risk would be less than 15%. However, there may be some travellers who would benefit from improved protection against travellers’ diarrhoea, including those with achlorhydria and those at increased risk of severe or complicated diarrhoeal disease (refer to 4.1 (Handbook10-home-handbook10part4-handbook10-4-184-1) Cholera).

Certification of cholera vaccination has been abandoned globally, and no countries have official entry requirements for cholera vaccination.

Hepatitis A

Hepatitis A vaccine should be recommended to all travellers ≥1 year of age travelling to moderately or highly endemic countries (including all developing countries), except those who are likely to have acquired natural immunity following previous infection (refer to 4.4(Handbook10-home-handbook10part4-handbook10-4-484-4) Hepatitis A). There is no longer any place for the routine use of normal human immunoglobulin to prevent hepatitis A in travellers (refer to 4.4(Handbook10-home-handbook10part4-handbook10-4-484-4) Hepatitis A).

Japanese encephalitis

Vaccination is recommended for travellers spending a month or more in endemic areas in Asia and Papua New Guinea during the JE virus transmission season and should be considered for shorter-term travellers, particularly if travel is during the wet season or anticipated to be repeated, and/or there is considerable outdoor activity and/or staying in accommodation without air conditioning, screens or bed nets (refer to 4.8(Handbook10-home-handbook10part4-handbook10-4-484-8) Japanese encephalitis).

Updated information regarding JE virus activity should be sought from a reputable source prior to travel (for example, Health information for international travel[http://www.cdc.gov/travel] [the ‘Yellow book’] published by the US Centers for Disease Control and Prevention, available at [www.cdc.gov/travel/yellowbook]). While the overall risk of JE in travellers to JE endemic countries is likely to be low (<1 per 1 million travellers), the risk is determined by the season of travel, the regions visited, the duration of travel, the extent of outdoor activity and the extent to which mosquito avoidance measures are taken.

Meningococcal disease

Up-to-date epidemiological information should be sought to determine the need for meningococcal vaccination in travellers. Quadrivalent meningococcal vaccine (which includes serogroups A, C, W135 and Y antigens) is recommended for those who intend travelling to parts of the world where epidemics of meningococcal disease occur, in particular the ‘meningitis belt’ of sub-Saharan Africa. The Saudi Arabian authorities require that all pilgrims travelling to Mecca (for the Hajj or Umra) have evidence of recent vaccination with the quadrivalent meningococcal vaccine[refer to 3.2.6(Handbook10-home-handbook10part3-handbook10-3-283-2.6) Further information below]. The quadrivalent meningococcal conjugate vaccine (4vMenCV) should be used in preference to the quadrivalent meningococcal polysaccharide vaccine (4vMenPV) (refer to 4.10(Handbook10-home-handbook10part4-handbook10-4-1084-10) Meningococcal disease).

Rabies

Travellers to rabies-endemic regions should be advised of the risk of rabies infection, and to avoid close contact with either wild, stray or domestic animals, in particular dogs, cats, monkeys and bats. Travellers should also be aware of the importance of appropriate immediate wound care of all animal bites and scratches (refer to 4.16 (Handbook10-home-handbook10part4-handbook10-4-1684-16) Rabies and other lyssaviruses (including Australian bat lyssavirus)).

Recommendation for pre-travel (i.e. pre-exposure prophylaxis) rabies vaccination (or, where indicated, booster doses) is based on an assessment of the likelihood of contact and risk of exposure to potentially rabid animals, the access to appropriate healthcare and availability of post-exposure prophylaxis, including rabies immunoglobulin, should there be an at-risk exposure, and the timeliness of such access after exposure. The previous recommendation for pre-exposure prophylaxis based on duration of stay in rabies-endemic areas (i.e. for more than a month) is arbitrary, and most Australian travellers who have required post-exposure prophylaxis have undertaken shorter periods of travel. A lower threshold for recommending rabies pre-exposure prophylaxis should be adopted for children travelling to endemic areas (refer to 4.16(Handbook10-home-handbook10part4-handbook10-4-1684-16) Rabies and other lyssaviruses (including Australian bat lyssavirus)). Vaccination against rabies before travel ensures that a safe and efficacious vaccine has been used and simplifies the management of a subsequent exposure because fewer doses of vaccine are needed. It also means that rabies immunoglobulin, which is often extremely expensive, difficult or even impossible to obtain in many developing countries, is not required, and reduces the urgency of post-exposure prophylaxis.

Tick-borne encephalitis

Tick-borne encephalitis (TBE) is caused by a tick-borne RNA flavivirus and may involve the central nervous system. The disease is prevalent in parts of temperate regions of central and northern Europe and across northern Asia. Travellers are at particular risk when hiking or camping in forested areas in endemic regions during the summer months. Safe and effective vaccines are available. Vaccination is recommended only for individuals with a high risk of exposure. Two inactivated TBE vaccine formulations (from Austria and Germany) are available in Europe (based on the European subtype), and two other formulations, based on the Far Eastern subtypes, are available in Russia. There is limited evidence that suggests the Austrian and German vaccines induce cross-protecting immunity against the Far Eastern and Siberian subtypes. While the conventional schedule for completing the primary vaccination course takes 9 to 12 months, accelerated schedules are available (refer to 3.2.6(Handbook10-home-handbook10part3-handbook10-3-283-2.6) Further information below). While no TBE vaccine is registered in Australia, a small stock of vaccine may be available in Australia for use under the Special Access Scheme.

Tuberculosis

Duration of immunity and/or booster recommendations

A primary course is 3 doses of dT-containing vaccine, 1.0 mL. As different strains circulate from year to year, annual single dose, for older adults, and younger adults with underlying medical conditions – please refer to the product information.

For unvaccinated adults, 3 doses with minimum interval 0, 1, 6 months or 0.5 mL as appropriate if more than 5 years have elapsed since their last dose of dT-containing vaccine.

Reactivity to tuberculin may be depressed for as long as 4 weeks following viral infections or live viral vaccines, particularly measles infection and measles-containing vaccines.

Tuberculin skin tests and BCG vaccine are available from state/territory tuberculosis services.

Reactivity to tuberculin may be depressed for as long as 4 weeks following viral infections or live viral vaccines, particularly measles infection and measles-containing vaccines.

Typhoid vaccine may be recommended to travellers ≥2 years of age travelling to endemic regions, including the Indian subcontinent, most Southeast Asian countries and several South Pacific nations, including Papua New Guinea. This advice is also relevant for those travelling (back) to endemic regions to visit friends and relatives (VFR travel). Inactivated parenteral or live oral typhoid vaccine formulations are available (refer to 4.23(Handbook10-home-handbook10part4-handbook10-4-21#4-21) Typhoid).

The yellow fever vaccine is recommended for all persons ≥9 months of age travelling to, or living in, an area with a risk of yellow fever virus transmission (refer to 4.23(Handbook10-home-handbook10part4-handbook10-4-23#4-23) Yellow fever). To minimise the risk of yellow fever introduction, some countries require documented evidence of yellow fever vaccination for entry, in accordance with the International Health Regulations (refer to 3.2.3(Handbook10-home-handbook10part3-handbook10-3-2#3-2-3) Practical aspects of recommending vaccinations for travellers).

The risk of being infected with the yellow fever virus, country entry requirements, and individual factors like age, pregnancy and underlying medical conditions must be taken into account when considering yellow fever vaccination. Vaccination is generally not recommended when travelling to areas where there is low potential for yellow fever virus exposure (i.e. no human yellow fever cases ever reported and evidence to suggest only low levels of yellow fever virus transmission in the past). However, vaccination might be considered for a small subset of travellers to these areas who are at increased risk of exposure to mosquitoes or unable to avoid mosquito bites. People aged ≥60 years or at increased risk of severe adverse events after primary yellow fever vaccination. Vaccination of persons in this age group should be weighed against the potential for yellow fever virus exposure and, in turn, the benefits of vaccination (refer to 4.23(Handbook10-home-handbook10part4-handbook10-4-23#4-23) Yellow fever).

In most individuals, a booster dose is not required as a single dose of yellow fever vaccine induces protective antibody levels that persist for many decades. However, there are certain individuals for whom a booster is recommended if 10 years have passed since their last dose and they are at ongoing risk of yellow fever infection (refer to 4.23(Handbook10-home-handbook10part4-handbook10-4-23#4-23) Yellow fever).

"Table 3.2.1: Dose and routes of administration of commonly used vaccines in adult travellers (the lower age limit for the adult dosage varies with individual vaccines – please refer to the product information)"

<table>
<thead>
<tr>
<th>Vaccine (adults)</th>
<th>Brand name</th>
<th>Dose (adults)</th>
<th>Route</th>
<th>Dosing intervals</th>
<th>Duration of immunity and/or booster recommendations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diphtheria-tetanus (dT)</td>
<td>ADT Booster</td>
<td>0.5 mL</td>
<td>IM</td>
<td>A primary course is 3 doses of dT-containing vaccine, given a minimum of 4 weeks apart; followed by booster doses 10 and 20 years after.</td>
<td>Prior to travel, adults should receive a booster dose of dT (or dTpa if not given previously), if more than 10 years have elapsed since their last dose of dT-containing vaccine. For persons undertaking high-risk travel, consider giving a booster dose of either dTpa or dT (as appropriate) if more than 5 years have elapsed since their last dose of dT-containing vaccine.</td>
</tr>
<tr>
<td>Diphtheria-tetanus-pertussis (dTpa)</td>
<td>Boostrix or Adacel</td>
<td>0.5 mL</td>
<td>IM</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Diphtheria-tetanus-pertussis-inactivated poliomyelitis (dTpa-IPV)</td>
<td>Boostrix-IPV or Adacel Polio</td>
<td>0.5 mL</td>
<td>IM</td>
<td>A completed series probably gives life-long immunity.</td>
<td></td>
</tr>
<tr>
<td>Hepatitis B</td>
<td>Engerix-B</td>
<td>1.0 mL</td>
<td>IM</td>
<td>0, 1, 6 months or 0, 1, 2, 12 months or 0, 7, 21 days and 12 months*</td>
<td>A completed series probably gives life-long immunity.</td>
</tr>
<tr>
<td>Influenza (seasonal)</td>
<td>H-B-Vax II</td>
<td>1.0 mL</td>
<td>IM</td>
<td>0, 1, 6 months</td>
<td>As different strains circulate from year to year, annual vaccination with the current formulation is necessary.</td>
</tr>
<tr>
<td>Measles-mumps-rubella</td>
<td>Various</td>
<td>0.5 mL</td>
<td>IM</td>
<td>Single dose</td>
<td>A 2-dose schedule provides long-lasting immunity.</td>
</tr>
<tr>
<td></td>
<td>Priorix</td>
<td>0.5 mL</td>
<td>SC/IM</td>
<td>Australians born during or since 1966 who do not have documented evidence of having received 2 doses of measles-, mumps- and rubella-containing vaccine should receive at least 1 dose of MMR vaccine before travel</td>
<td>Recommendations vary according to age, Indigenous status and predisposing medical conditions – refer to 4.13(Handbook10-home-handbook10part4-handbook10-4-13#4-13) Pneumococcal disease.</td>
</tr>
<tr>
<td></td>
<td>M-M-R II</td>
<td>0.5 mL</td>
<td>SC</td>
<td>Single dose, for older adults, and younger adults with predisposing medical conditions – refer to 4.13(Handbook10-home-handbook10part4-handbook10-4-13#4-13) Pneumococcal disease.</td>
<td>Recommendations vary according to age, Indigenous status and predisposing medical conditions – refer to 4.13(Handbook10-home-handbook10part4-handbook10-4-13#4-13) Pneumococcal disease.</td>
</tr>
<tr>
<td>Pneumococcal</td>
<td>Prevenar 13 or Pneumovax 23</td>
<td>0.5 mL</td>
<td>IM</td>
<td>Single dose, for older adults, and younger adults with predisposing medical conditions – refer to 4.13(Handbook10-home-handbook10part4-handbook10-4-13#4-13) Pneumococcal disease.</td>
<td>Recommendations vary according to age, Indigenous status and predisposing medical conditions – refer to 4.13(Handbook10-home-handbook10part4-handbook10-4-13#4-13) Pneumococcal disease.</td>
</tr>
<tr>
<td>Poliomyelitis</td>
<td>IPOL</td>
<td>0.5 mL</td>
<td>SC</td>
<td>For unvaccinated adults, doses with minimum interval of 1 to 2 months between doses</td>
<td>A booster dose 10-yearly is only necessary if travelling to a poliomyelitis endemic country.</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Vaccine (adults)</th>
<th>Brand name</th>
<th>Dose (adults)</th>
<th>Route</th>
<th>Dosing intervals</th>
<th>Duration of immunity and/or booster recommendations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Combination vaccines (dTpa-IPV)</td>
<td>Refer to Diphtheria-tetanus-pertussis-inactivated poliomyelitis (dTpa-IPV) above and 4.14 (Handbook10-home-handbook10part4-handbook10-4-144-14) Poliomyelitis.</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Varicella (chickenpox)</td>
<td>Varilrix or Varivax Refrigerated</td>
<td>0.5 mL SC</td>
<td>If there is a lack of reliable history of chickenpox or the person is non-immune, and has not been vaccinated in childhood 0, 4 weeks if aged ≥14 years</td>
<td>A 2-dose schedule provides long-lasting immunity.</td>
<td></td>
</tr>
<tr>
<td>Combined vaccines</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Varicella (chickenpox)</td>
<td>Varilrix or Varivax Refrigerated</td>
<td>0.5 mL SC</td>
<td>If there is a lack of reliable history of chickenpox or the person is non-immune, and has not been vaccinated in childhood 0, 4 weeks if aged ≥14 years</td>
<td>A 2-dose schedule provides long-lasting immunity.</td>
<td></td>
</tr>
<tr>
<td>Typhoid</td>
<td>Typherix or Typhim Vi</td>
<td>0.5 mL IM</td>
<td>Single dose</td>
<td>Give 3-yearly boosters if the person is at ongoing risk.</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Typhoid</td>
<td>Typherix or Typhim Vi</td>
<td>0.5 mL IM</td>
<td>Single dose</td>
<td>A 10-yearly booster dose is only recommended for: – certain persons (i.e. those who received their initial dose while pregnant or when infected with HIV, and those at high risk of infection due to travel or occupation) if they are at ongoing risk of yellow fever virus infection – travellers who need to meet country-specific vaccination entry requirements. Refer to 4.23 (Handbook10-home-handbook10part4-handbook10-4-234-23) Yellow fever.</td>
<td></td>
</tr>
</tbody>
</table>

3.2.5 Vaccinating the traveller with special risk factors

Children should receive relevant travel vaccines, according to age-specific dosage and schedules as shown in Table 3.2.2 (Handbook10-home-handbook10part3-handbook10-3-2#table-3-2-2); further information relating to administration is provided in the relevant disease-specific chapters in Part 4 (Handbook10-home-handbook10part4).

Particular effort should be made to encourage the families of recent migrants to Australia to seek health advice before travelling to their country of origin to visit relatives and friends.

### Table 3.2.2: Recommended lower age limits of travel vaccines for children

<table>
<thead>
<tr>
<th>Vaccine</th>
<th>Lower age limit</th>
<th>Dose/route</th>
<th>Dosing intervals</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Hepatitis A</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Aveaix</td>
<td>2 years</td>
<td>0.5 mL IM</td>
<td>2 doses: 0 and 6–12 months</td>
</tr>
<tr>
<td>Havrix Junior</td>
<td>2 years</td>
<td>0.5 mL IM</td>
<td>2 doses: 0 and 6–12 months</td>
</tr>
<tr>
<td>Vaqta</td>
<td>1 year</td>
<td>0.5 mL IM</td>
<td>2 doses: 0 and 6–18 months</td>
</tr>
<tr>
<td>Paediatric/Adolescent formulation</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Hepatitis A/B combined</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Twinrix (360/10)</td>
<td>1 year</td>
<td>0.5 mL IM</td>
<td>3 doses: 0, 1 and 6 months</td>
</tr>
<tr>
<td>Twinrix (72/20)</td>
<td>1 year</td>
<td>1.0 mL IM</td>
<td>2 doses: 0 and 6–12 months</td>
</tr>
<tr>
<td><strong>Japanese encephalitis</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>JEspect</td>
<td>2 months (to &lt;3 years)</td>
<td>0.25 mL IM</td>
<td>2 doses: 0 and 28 days</td>
</tr>
<tr>
<td>Imojev</td>
<td>3 years</td>
<td>0.5 mL SC</td>
<td>Single dose</td>
</tr>
</tbody>
</table>
|                               | 9 months        | 0.5 mL IM  | Varies by age at time of vaccination and vaccine brand. Refer to Table 4.10.3 in refer to 4.10
| **Meningococcal ACW135**       |                 |            |                                   |
| (quadrivalent conjugate 4vMenCV) |             |            |                                   |
| Menevor                        | 2 months        | 0.5 mL IM  |                                   |
| Menastra                       | 0.5 mL IM       | Varies by age at time of vaccination and vaccine brand. Refer to Table 4.10.4 in refer to 4.10
| Nimengrux                      | 12 months       | 0.5 mL IM  | (Handbook10-home-handbook10part4-handbook10-4-10#4-10) Meningococcal disease
| **Meningococcal ACW135**       |                 |            |                                   |
| (quadrivalent polysaccharide 4vMenPV) |         |            |                                   |
| Mencevax ACWY                  | 7 years         | 0.5 mL SC  | Single dose                       |
| Menevrum                       | 7 years         | 0.5 mL SC  | Single dose                       |
| Rabies                         |                 |            |                                   |
| Mérieux Inactivated Rabies     | No lower age    | 1.0 mL IM  | 3 doses: 0, 7, 21–28 days         |
| Vaccine limit                  | IM/SC           | 3 doses: 0, 7, 21–28 days         |
| Rabipur Inactivated Rabies     | No lower age    | 1.0 mL IM  | 3 doses: 0, 7, 21–28 days         |
| Virus Vaccine                  | limit           | 3 doses: 0, 7, 21–28 days         |
| **Typhoid**                    |                 |            |                                   |
| Vivotif Oral                   | 6 years         | Oral       | One capsule each on days 1, 3, 5 (3-dose course), and preferably also day 7(4-dose course) |
| Typhrix                        | 2 years         | capsule    | Single dose                       |
| Typhrim Vi                     | 2 years         | 0.5 mL IM  | Single dose                       |
|                               |                 | 0.5 mL IM  |                                   |
| **Yellow fever**               |                 |            |                                   |
| Stamaril                       | 9 months        | 0.5 mL IM  | Single dose                       |
|                               |                 | IM/SC      |                                   |

* Refer also to minimum ages in Table 2.1.5 (Handbook10-home-handbook10part2-handbook10-2-1#table-2-1-5) Minimum acceptable age for the 1st dose of scheduled vaccines in infants in special circumstances.
† This schedule is not recommended if prompt protection against hepatitis B is required (refer to 4.5 (Handbook10-home-handbook10part4-handbook10-4-5#4-5) Hepatitis B).
‡ JEspect can be administered to children aged ≥2 months to ≤18 years in circumstances where an alternative is not available or is contraindicated (refer to 4.8 (Handbook10-home-handbook10part4-handbook10-4-8#4-8) Japanese encephalitis).
§ Imojev can be administered to persons aged ≥9 months (refer to 4.8 (Handbook10-home-handbook10part4-handbook10-4-8#4-8) Japanese encephalitis).
¶ 4vMenCV is preferred. However, 4vMenPV is a suitable alternative for travellers aged ≥7 years when the need for repeat doses is not anticipated (refer to 4.10 (Handbook10-home-handbook10part4-handbook10-4-10#4-10) Meningococcal disease).
¶ A 4th capsule of oral typhoid vaccine on day 7 is preferred (refer to 4.21 (Handbook10-home-handbook10part4-handbook10-4-21#4-21) Typhoid).
** Yellow fever vaccine is contraindicated in infants <9 months of age. (Vaccination may be considered in outbreak control situations for infants from 6 months of age.) (Refer to 4.23 (Handbook10-home-handbook10part4-handbook10-4-23#4-23) Yellow fever.)

3.2.6 Further information

International travellers’ health risks are changing constantly. Up-to-date information and knowledge of the changing epidemiology and occurrence of outbreaks of a variety of infectious and emerging diseases is essential. Useful online information sources include:

- the World Health Organization (WHO)[http://www.who.int] for disease outbreak news (www.who.int), and its Travel and health[http://www.who.int/topics/travel/en] section (www.who.int/topics/travel/en) for more specific advice on travel and health, including travel vaccination recommendations

Comprehensive technical advice on international travel and health, including but not limited to vaccinations, is available in the latest editions of the WHO publication International travel and health (http://www.who.int/ith/en) and the US Centers for Disease Control and Prevention (CDC) publication Health information for international travel (http://www.cdc.gov/travel) (the ’Yellow book’) (available at www.cdc.gov/travel).

The Ministry of Health of Saudi Arabia’s requirements and recommendations for travellers on pilgrimage to Mecca (Hajj and Umra) are published annually in the Weekly Epidemiological Record of the WHO (http://www.who.int/wer).

References

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vaccine's ovalbumin content prior to vaccine administration.

residual egg ovalbumin may vary from year to year due to manufacturing processes, vaccine batches and country of origin. The PI of the vaccine to be given should be checked for the

to manufacturing changes, the quantity of egg ovalbumin present in the majority of influenza vaccines used in Australia is less than 1 μg of ovalbumin per dose.

of studies indicating that the majority of persons with egg allergy, including anaphylaxis, can be safely vaccinated with influenza vaccines that contain less than 1 μg of ovalbumin per dose.

Vaccination of persons who have had an adverse event following immunisation

serious reaction associated with a vaccine dose is usually not possible to predict which individuals may have a mild or a rare, serious reaction to a vaccine. However, by following guidelines regarding when vaccines should and should not be used, the risk of adverse effects can be minimised. The term ‘adverse event following immunisation’ (AEFI) refers to any untoward medical occurrence that follows immunisation, whether expected or unexpected, and whether triggered by the vaccine or only coincidentally occurring after receipt of a vaccine dose. For more information on AEFI, refer to 2.3.2 (Handbook10-home-handbook10part4) Adverse events following immunisation.

Serious adverse events occur rarely after immunisation. Recognised rare and serious AEFI are described in 2.3.2 (Handbook10-home-handbook10part2-handbook10-2-382-3-2) Adverse events following immunisation. Pre-vaccination screening should identify persons who have experienced an AEFI and also identify persons with conditions that are precautions and/or contraindications to vaccines (refer to Table 2.1.1 (Handbook10-home-handbook10part1-handbook10-2-1-1) Pre-vaccination screening checklist). The relevant disease-specific chapter(s) in Part 4 (Handbook10-home-handbook10part4) of this Handbook should be consulted for each vaccine regarding contraindications and precautions that are relevant. In general, persons who have had a non-serious adverse event can be safely revaccinated by their usual immunisation service provider. Determining whether revaccination should be provided after a serious event has occurred following vaccination can be more challenging. At the individual patient level, an assessment should be made as to whether the vaccine(s) was causally related to the adverse event. This includes a thorough medical assessment, including determining the need for, or availability of, specific tests to predict whether the AEFI is likely to recur with subsequent doses. Persons who have experienced a serious adverse event following immunisation (other than a contraindication, such as anaphylaxis confirmed as triggered by a vaccine or one of its components) can usually subsequently be vaccinated under close medical supervision. However, further advice should be sought where appropriate, by referral to a specialist clinic for the management of persons with special vaccination requirements (including persons who have had a previous AEFI).

Information about specialist immunisation clinics, or the contact details for paediatricians or medical specialists with experience in management of persons with AEFI, are usually available from state and territory health authorities (refer to Appendix 1 Contact details for Australian, state and territory government health authorities and communicable disease control) and from the Immunise Australia website (http://www.immunise.health.gov.au) (www.immunise.health.gov.au).

Allergies

Vaccines rarely produce allergy or anaphylaxis (a rapid and life-threatening form of allergic reaction). Overall, the risk of anaphylaxis after a single vaccine dose has been estimated as less than 1 case per 1 million; however, this risk varies depending on the vaccine type. Antibiotics, gelatin and egg proteins are the components most often implicated in allergic reactions. Yeast has only rarely been associated with vaccine-related allergic reaction. Persons allergic to latex may be at risk from some vaccines. This is usually not from the vaccine formulation itself, but from the presence of latex in the equipment used to hold the vaccine, such as vaccine vial stoppers (bungs) and syringe plungers. However, very few vaccine bungs contain natural latex.

Before administering the vaccine, consult the product information (PI) of each vaccine to check for the presence of latex or, where not listed on the PI, contact the vaccine manufacturer for specific details.

It is important that immunisation service providers assess each individual for a history of allergies and previous reactions to vaccines prior to giving any dose of vaccine. Depending on the allergy identified, there often may not be a contraindication to vaccination. For example, a history of allergy to antibiotics most commonly relates to β-lactam or related antibiotics and is not a contraindication to vaccines that contain other classes of antibiotics like neomycin, polymyxin B or gentamicin. Previous reactions to neomycin that only involved the skin are not considered a risk factor for a severe allergic reaction or anaphylaxis to vaccines manufactured with neomycin because there are only trace amounts of this antibiotic in the final product. Similarly, the measles and mumps components of measles-mumps-rubella (MMR) vaccine contain only a negligible quantity of egg ovalbumin and do not contraindicate MMR vaccination of persons with egg allergy (even anaphylaxis) (refer to ‘Vaccination of persons with a known egg allergy’ below). It is important that persons who experience an allergic reaction associated with a vaccine dose are fully investigated appropriately to ascertain the possible causal relationship to vaccination, and determine if, and under what circumstances, repeat doses of vaccine can be provided. Specialist advice should be sought where appropriate (refer above).

Vaccination of persons with a known egg allergy

Influenza vaccines

A history of anaphylaxis or a serious allergic reaction to eggs has previously been considered an absolute contraindication to influenza vaccination. However, there have now been a number of studies indicating that the majority of persons with egg allergy, including anaphylaxis, can be safely vaccinated with influenza vaccines that contain less than 1 μg of ovalbumin per dose (refer to 4.7 (Handbook10-home-handbook10part4-handbook10-4-784-7) Influenza).

The majority of vaccine-associated anaphylaxis cases reported as likely due to egg allergy occurred following administration of one of the older formulations of influenza vaccine. Today, due to manufacturing changes, the quantity of egg ovalbumin present in the majority of influenza vaccines used in Australia is less than 1 μg of ovalbumin per dose. Note that the amount of residual egg ovalbumin may vary from year to year due to manufacturing processes, vaccine batches and country of origin. The PI of the vaccine to be given should be checked for the vaccine's ovalbumin content prior to vaccine administration.
Recommendation reports of vaccines administered during pregnancy; for example, the registry for VZV-containing vaccines in place in the United States from March 1995 to October 2013 (refer to Inadvertent receipt of a vaccine contraindicated in pregnancy can be reported to the Therapeutic Goods Administration (TGA). For mechanisms for reporting to the TGA, benefits of yellow fever vaccination, and other strategies to mitigate the risk of acquiring yellow fever, should be discussed (inadvertently given. The live attenuated yellow fever vaccine is not recommended in pregnant women; however, where travel to a yellow fever risk country is unavoidable, the risks and vaccine is inadvertently given to a pregnant woman, or if a woman becomes pregnant within 28 days of vaccination, she should be counselled about the potential for adverse effects, albeit Live attenuated viral vaccines are contraindicated in pregnant women because of the hypothetical risk of harm should vaccine virus replication occur in the fetus. If a live attenuated viral vaccine is inadvertently given to a pregnant woman, or if a woman becomes pregnant within 28 days of vaccination, she should be counselled about the potential for adverse effects, albeit extremely unlikely, to the fetus (refer also to 4.18(Handbook10-home–handbook10part4–handbook10-4-1884-18) Rubella and 4.22 (Handbook10-home–handbook10part4–handbook10-4-2284-22) Varicella). There is, however, no indication to consider termination of a pregnancy if a live attenuated vaccine has been inadvertently given. The live attenuated yellow fever vaccine is not recommended in pregnant women; however, where travel to a yellow fever risk country is unavoidable, the risks and benefits of yellow fever vaccination, and other strategies to mitigate the risk of acquiring yellow fever, should be discussed (refer to 4.23 (Handbook10-home–handbook10part4–handbook10-4-2384-23) Yellow fever).

Inadvertent receipt of a vaccine contraindicated in pregnancy can be reported to the Therapeutic Goods Administration (TGA). For mechanisms for reporting to the TGA, refer to 2.3.2 (Handbook10-home–handbook10part2–handbook10-2-03923-2) Adverse events following immunisation. Post-marketing studies of pregnancy outcomes following vaccine administration are important to understand the safety profile of vaccines in this setting. For this reason some vaccine manufacturers also operate pregnancy registries, specific for their products, that will accept reports of vaccines administered during pregnancy. For example, the registry for VZV-containing vaccines in place in the United States from March 1995 to October 2013 (refer to 4.22 (Handbook10-home–handbook10part4–handbook10-4-2284-22) Varicella).

### 3.3.2 Vaccination of women who are planning pregnancy, pregnant or breastfeeding, and preterm infants

#### Women planning pregnancy
The need for vaccination, particularly for hepatitis B, measles, mumps, rubella and varicella, should be assessed as part of any pre-conception health check. Where previous vaccination history or infection is uncertain, relevant serological testing can be undertaken to ascertain immunity to hepatitis B, measles, mumps and rubella. Routine serological testing for varicella does not provide a reliable measure of vaccine-induced immunity, although it can indicate whether previous natural infection has occurred (refer to 4.22 (Handbook10-home–handbook10part4–handbook10-4-2284-22) Varicella). Influenza vaccine is recommended for all women who wishes to be protected against influenza and is recommended for women planning pregnancy. Those with risk factors for pneumococcal disease, including smokers and Aboriginal and Torres Strait Islander women, should be assessed for pneumococcal vaccination. Women who receive live attenuated viral vaccines should be advised against falling pregnant within 28 days of vaccination.

Refer to the relevant disease-specific chapters in Part 4 (Handbook10-home–handbook10part4) for more information about vaccination requirements for these diseases.

It is also important that women of child-bearing age who present for immunisation should be questioned regarding the possibility of pregnancy as part of the routine pre-vaccination screening, to avoid inadvertent administration of a vaccine(s) not recommended in pregnancy (refer to 2.1.4(Handbook10-home–handbook10part2–handbook10-2-1392-1-4) Pre-vaccination screening).

### Pregnant women
Refer to Table 3.3.1 (Handbook10-home–handbook10part3–handbook10-3-39table–3-3-1) summarises the recommendations for vaccine use in pregnancy. More detailed information is also provided under the ‘Pregnancy and breastfeeding’ sections of each disease-specific chapter in Part 4 (Handbook10-home–handbook10part4) of this Handbook.

Seasonal influenza and dTpa are the only vaccines that are routinely recommended for pregnant women.

Many other inactivated vaccines are not routinely recommended during pregnancy on precautionary grounds; however, there is no convincing evidence that pregnancy should be an absolute contraindication to vaccination with these vaccines. There is some evidence that fever per se is teratogenic; however, in clinical studies most inactivated vaccines are not associated with increased rates of fever in adults (as compared with placebo). Recommendations regarding vaccine use in pregnancy are made where the benefits of protection from vaccination outweigh the risks. Eliminating the risk of exposure to vaccine-preventable diseases during pregnancy (e.g. by changing travel plans, avoiding high-risk behaviours or occupational exposures) is both an alternative and complementary strategy to vaccination.

Live attenuated viral vaccines are contraindicated in pregnant women because of the hypothetical risk of harm should vaccine virus replication occur in the fetus. If a live attenuated viral vaccine is inadvertently given to a pregnant woman, or if a woman becomes pregnant within 28 days of vaccination, she should be counselled about the potential for adverse effects, albeit extremely unlikely, to the fetus (refer also to 4.18(Handbook10-home–handbook10part4–handbook10-4-1884-18) Rubella and 4.22 (Handbook10-home–handbook10part4–handbook10-4-2284-22) Varicella). There is, however, no indication to consider termination of a pregnancy if a live attenuated vaccine has been inadvertently given. The live attenuated yellow fever vaccine is not recommended in pregnant women; however, where travel to a yellow fever risk country is unavoidable, the risks and benefits of yellow fever vaccination, and other strategies to mitigate the risk of acquiring yellow fever, should be discussed (refer to 4.23 (Handbook10-home–handbook10part4–handbook10-4-2384-23) Yellow fever).

### Table 3.3.1: Recommendations for vaccination in pregnancy (refer also to disease-specific chapters in Part 4 (Handbook10-home–handbook10part4))

<table>
<thead>
<tr>
<th>Vaccines routinely recommended in pregnancy</th>
<th>Recommendation</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Inactivated vaccines</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Influenza</strong></td>
<td>Recommended for all pregnant women at any stage of pregnancy, particularly those who will be in the second or third trimester during the influenza season.</td>
<td>There is evidence from clinical trial data and observational studies that there is no increased risk of congenital defects or adverse effects in the fetuses of women who are vaccinated against influenza in pregnancy. Influenza immunisation protects the mother, as pregnancy increases her risk of severe influenza, and also protects her newborn baby in the first few months after birth (refer to 4.7 Influenza).</td>
</tr>
<tr>
<td><strong>Diphtheria-, tetanus-, and pertussis-containing vaccines (dTpa)</strong></td>
<td>dTpa recommended as a single dose during the third trimester of each pregnancy (ideally at 28–32 weeks)</td>
<td>Pertussis vaccination during the third trimester of pregnancy has been shown to be more effective in reducing the risk of infant pertussis than maternal vaccination post partum. Studies have found no evidence of an increased risk of adverse pregnancy outcomes related to pertussis vaccination during pregnancy. (Refer to 4.12(Handbook10-home–handbook10part4–handbook10-4-1284-12) Pertussis for more details.)</td>
</tr>
</tbody>
</table>

### Inactivated bacterial vaccines

<table>
<thead>
<tr>
<th>Recommendation</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Diphtheria-tetanus vaccine (dT)</strong></td>
<td>Not routinely recommended. Can be given under certain circumstances, such as for management of a tetanus-prone wound. Tetanus- and diphtheria-containing vaccines have been used extensively in pregnant women, with no increased risk of congenital abnormalities in fetuses of women who were vaccinated during pregnancy. <a href="http://www.immunise.health.gov.au/internet/immunise/publishing.nsf/Content/Handbook10-home~handbook10part4~handbook10-4-2#4-2">23-25</a> Diphtheria and 4.19 Tetanus for more details.</td>
</tr>
<tr>
<td><strong>Cholera (oral) vaccine</strong></td>
<td>Not routinely recommended. There are limited data on the safety of oral cholera vaccine in pregnancy. [26]</td>
</tr>
<tr>
<td><strong>Haemophilus influenzae type b (Hib) vaccine</strong></td>
<td>Not routinely recommended. Can be given to pregnant women at increased risk of Hib disease (e.g. with asplenia). Limited available data suggest that it is unlikely that use of Hib vaccine in pregnant women has any deleterious effects on pregnancy outcomes. [27]</td>
</tr>
<tr>
<td><strong>Meningococcal conjugate vaccines (MenCCV, Hib-MenCCV or 4vMenCV)</strong></td>
<td>Not routinely recommended. Can be given to pregnant women at increased risk of meningococcal disease (refer to 4.10). Limited available data suggest that it is unlikely that use of meningococcal polysaccharide vaccine in pregnant women has any deleterious effects on pregnancy outcomes. [28,29] Where clinically indicated, meningococcal conjugate vaccine (MenCCV or 4vMenCV) can be given to pregnant women. [29] Hib-MenCCV is not indicated for use in adolescents or adults.</td>
</tr>
<tr>
<td><strong>Meningococcal polysaccharide vaccine (4vMenPV)</strong></td>
<td>Not routinely recommended. Can be given to pregnant women at increased risk of meningococcal disease (refer to 4.10). Limited available data suggest that it is unlikely that use of meningococcal polysaccharide vaccine in pregnant women has any deleterious effects on pregnancy outcomes. [28,29] Where clinically indicated, meningococcal polysaccharide vaccine can be given to pregnant women, although 4vMenCV is preferred. [29]</td>
</tr>
<tr>
<td><strong>Meningococcal B vaccine (MenBV)</strong></td>
<td>Not routinely recommended. Can be given to pregnant women at increased risk of meningococcal disease (refer to 4.10). No data are available. Vaccination during pregnancy has not been evaluated, although is unlikely to result in adverse effects.</td>
</tr>
<tr>
<td><strong>13-valent pneumococcal conjugate vaccine (13vPCV)</strong></td>
<td>Not routinely recommended. Can be given to pregnant women at the highest increased risk of invasive pneumococcal disease (IPD) (e.g. with asplenia, immunocompromise, cerebrospinal fluid leak) (refer to 4.13). (Handbook10-home-handbook10part4-handbook10-4-13#4-13) Pneumococcal disease. No data are available. Vaccination during pregnancy has not been evaluated, although is unlikely to result in adverse effects. Women of child-bearing age with known risk factors for IPD (including smokers) should ideally be vaccinated before pregnancy or as soon as practicable after delivery (refer to 4.13) (Handbook10-home-handbook10part4-handbook10-4-13#4-13) Pneumococcal disease.</td>
</tr>
<tr>
<td><strong>23-valent pneumococcal polysaccharide vaccine (23vPPV)</strong></td>
<td>Not routinely recommended. Can be given to pregnant women at the highest increased risk of invasive pneumococcal disease (IPD) (e.g. with asplenia, immunocompromise, cerebrospinal fluid leak) (refer to 4.13). (Handbook10-home-handbook10part4-handbook10-4-13#4-13) Pneumococcal disease. 23vPPV has been administered in pregnancy in the context of clinical trials [22] with no evidence of adverse effects; however, data are limited. Women of child-bearing age with known risk factors for IPD (including smokers) should ideally be vaccinated before pregnancy or as soon as practicable after delivery (refer to 4.13) (Handbook10-home-handbook10part4-handbook10-4-13#4-13) Pneumococcal disease.</td>
</tr>
<tr>
<td><strong>Q fever vaccine</strong></td>
<td>Not routinely recommended. Safe use in pregnancy has not been established.</td>
</tr>
<tr>
<td><strong>Typhoid Vi polysaccharide vaccine</strong></td>
<td>Not routinely recommended. Can be given to pregnant women travelling to endemic countries where water quality and sanitation is poor. No data are available. Vaccination during pregnancy has not been directly evaluated, although is unlikely to result in adverse effects.</td>
</tr>
</tbody>
</table>

### Inactivated viral vaccines

<table>
<thead>
<tr>
<th>Recommendation</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Hepatitis A vaccine</strong></td>
<td>Not routinely recommended. Can be given to susceptible pregnant women travelling to areas of moderate to high endemicity or those who are at increased risk of exposure through lifestyle factors, or where severe outcomes may be expected (e.g. pre-existing liver disease). Limited data are available. Hepatitis A vaccine should only be given to pregnant women who are non-immune and at increased risk for hepatitis A. [34]</td>
</tr>
</tbody>
</table>

### Vaccines not routinely recommended in pregnancy

- Vaccines not routinely recommended in pregnancy.
### Vaccines not recommended in pregnancy

<table>
<thead>
<tr>
<th>Vaccines not recommended in pregnancy</th>
<th>Recommendation</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Hepatitis B vaccine</strong></td>
<td>Not routinely recommended</td>
<td>Can be given to susceptible pregnant women for whom this vaccine would otherwise be recommended, for example, as post-exposure prophylaxis in a non-immune pregnant woman with a significant exposure to a HBsAg-positive source.</td>
</tr>
<tr>
<td><strong>Japanese encephalitis (JE) vaccine (JEspect)</strong></td>
<td>Not routinely recommended</td>
<td>Can be given to pregnant women at high risk of acquiring JE</td>
</tr>
<tr>
<td><strong>Rotavirus vaccines</strong></td>
<td>Not routinely recommended</td>
<td>Can be given to pregnant women at high risk of poliovirus exposure (e.g. travel to endemic countries)</td>
</tr>
<tr>
<td><strong>Yellow fever vaccine</strong></td>
<td>Not routinely recommended</td>
<td>Can be given to pregnant women for whom this vaccine would otherwise be recommended (e.g. post-exposure prophylaxis).</td>
</tr>
<tr>
<td><strong>Japanese encephalitis (JE) vaccine (Imojev)</strong></td>
<td>Contraindicated</td>
<td></td>
</tr>
<tr>
<td><strong>Live attenuated bacterial vaccines</strong></td>
<td>Contraindicated</td>
<td>BCG vaccine</td>
</tr>
<tr>
<td><strong>Live attenuated viral vaccines</strong></td>
<td>Contraindicated</td>
<td>Oral typhoid vaccine</td>
</tr>
<tr>
<td><strong>Japanese encephalitis (JE) vaccine (Imojev)</strong></td>
<td>Contraindicated</td>
<td></td>
</tr>
<tr>
<td><strong>Measles-mumps-rubella (MMR) vaccine or Measles-mumps-rubella-varicella (MMRV) vaccine</strong></td>
<td>Contraindicated</td>
<td></td>
</tr>
<tr>
<td><strong>Rotavirus vaccine</strong></td>
<td>Contraindicated</td>
<td></td>
</tr>
<tr>
<td><strong>Varicella vaccine</strong></td>
<td>Contraindicated</td>
<td></td>
</tr>
</tbody>
</table>

### Vaccines contraindicated in pregnancy

<table>
<thead>
<tr>
<th>Vaccines contraindicated in pregnancy</th>
<th>Recommendation</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Human papillomavirus (HPV) vaccine</strong></td>
<td>Not recommended</td>
<td>Although HPV vaccination is not recommended during pregnancy, evidence from clinical trials and limited data from observational studies where HPV vaccine was inadvertently administered during pregnancy, indicate that there is no increased risk of adverse effects on the fetus. In the event of pregnancy, completion of a 3-dose course of vaccination should be deferred until after delivery.</td>
</tr>
</tbody>
</table>

**Note:** Vaccination during pregnancy is contraindicated for certain vaccines due to theoretical or potential risks to the mother or fetus. However, many of these vaccines are crucial for protecting against serious diseases. Consult with healthcare providers for personalized advice.
Contact between pregnant women and persons who have recently received live vaccines

Household contacts of pregnant women should be age-appropriately vaccinated. It is safe to administer measles-, mumps-, rubella- and varicella-containing vaccines, zoster vaccine and rotavirus vaccine to the contacts of pregnant women. There is no risk of transmission of measles, mumps or rubella vaccine viruses from vaccinated household contacts. There is an almost negligible risk of transmission of varicella-zoster virus (from persons vaccinated with varicella or zoster vaccines); however, vaccine recipients with a varicella-like rash should be advised to cover the rash if in contact with a pregnant woman. Although there is a very small possibility of transmission of the rotavirus vaccine viruses to pregnant contacts, the benefit of immunising infants to protect against rotavirus disease and, in turn, reduce the risk of rotavirus in household contacts, far outweighs any theoretical risk (refer to 4.17 (Handbook10-home~handbook10part4~handbook10-4-1-1784-17) Rotavirus).

Use of immunosuppressive therapy during pregnancy

Women who are receiving immunosuppressive therapy during pregnancy can be given inactivated vaccines where indicated (refer to Table 3.3.1 (Handbook10-home~handbook10part3~handbook10-3-183-1) Recommendations for vaccination in pregnancy). (Refer also to 3.3.3 (Handbook10-home~handbook10part3~handbook10-3-383-3) Vaccination of immunocompromised persons for more detailed information.) This includes pregnant women who have received short-term antenatal corticosteroids, for example, in the context of preterm labour. Certain immunosuppressive medications given for management of a medical condition in a woman during pregnancy (e.g. biological disease modifying anti-rheumatic drugs [bDMARDs]) may cross the placenta and be detectable in the infant, particularly if given during the third trimester.50-52 In this setting, administration of live attenuated vaccines in the first few months of the infant’s life, particularly BCG vaccine, is not recommended.56 (Refer also to 4.20 (Handbook10-home~handbook10part4~handbook10-4-2084-20) Tuberculosis.) This is because of the risk that the infant’s immune response to vaccination may be reduced and potentially associated with increased vaccine virus/bacteria replication and related adverse effects. Although no specific time intervals are indicated, withholding BCG vaccine until the infant is 6 months of age is prudent.59 There are no data on the use of other live vaccines in infants born to women who have received immunosuppressive therapy in pregnancy. Due to the theoretical concern that a risk also applies to the administration of rotavirus vaccines, some experts recommend not giving rotavirus vaccine to infants born to mothers who received bDMARDs during pregnancy.58 Inactivated vaccines should be administered to these infants according to the recommended schedule. However, immune responses may be suboptimal. Additional inactivated vaccine doses may be required; expert advice should be sought regarding this.

Breastfeeding and vaccination

Vaccination is rarely contraindicated in breastfeeding women. The rubella vaccine virus may be secreted in human breast milk and there has been documented transmission to breastfed infants. However, where infection has occurred in an infant, the symptoms have been absent or mild.68-71 Infants born to mothers who are hepatitis B surface antigen (HBsAg)-positive can also be breastfed, provided the infant is appropriately immunised at birth. Although studies have indicated the presence of hepatitis B virus (HBV) in the breast milk of mothers with HBV infection, breastfeeding poses no additional risk of virus transmission, compared with formula feeding, in vaccinated infants.62 Administration of yellow fever vaccine to breastfeeding women should be avoided, except in situations where the risk of acquiring yellow fever is high, and/or travel cannot be avoided or postponed.63,64 While extremely rare, there have been several case reports of probable transmission of the yellow fever vaccine virus via breast milk.63,64 For most vaccines, the immune response to vaccination of infants in relationship to breastfeeding has been studied and taken into account. In general, breastfeeding does not adversely affect immunisation, and breastfeeding is not a contraindication to the administration of any vaccines recommended in infants.

Preterm infants

Preterm (premature) infants are defined as those born at <37 weeks gestational age. Prematurity, particularly extreme prematurity (<28 weeks gestational age) can place children at increased risk of vaccine-preventable diseases.65-67 However, despite their immunological immaturity, preterm infants generally respond satisfactorily to vaccines.68-70 Provided they are medically stable and there are no contraindications to vaccination, preterm infants should be vaccinated according to the recommended schedule at the usual chronological age, without correction for prematurity.71-73

Immunisation has been associated with an increased risk of apoeno in preterm infants vaccinated in hospital, particularly those still requiring complex medical care and/or with an existing history of apoeno. Although in this setting, apoeno is generally self-limiting, measures to manage this anticipated AEFI should be taken.74,75 Specifically, hospitalised preterm infants should be monitored for apoeno or bradycardia for up to 48 hours post vaccination.76,77 If there is a history of apoeno post vaccination, consideration should be given to administering future immunisations under medical supervision.78-80 Vaccination has not been associated with an increased risk of sudden infant death syndrome (SIDS).81,82 The following recommendations are specific for preterm infants. The child’s birth weight, precise gestational age and the presence of a chronic medical condition(s) need to be considered.

Pneumococcal vaccines

All preterm infants born at <28 weeks gestation are recommended to be given 4 doses of 13-valent pneumococcal conjugate vaccine, at 2, 4, 6 and 12 months of age. A single booster dose of 23-valent pneumococcal polysaccharide vaccine at 4–5 years of age is also recommended (refer to 4.13 (Handbook10-home~handbook10part4~handbook10-4-1384-13) Pneumococcal disease and Table 2.1.11 (Handbook10-home~handbook10part2~handbook10-2-184table-2-1-11) Catch-up schedule for 13vPCV (Prevenar 13) and 23vPPV (Pneumovax 23) in children with a medical condition(s) associated with an increased risk of IPD, presenting at age <2 years). Children who were born at <28 weeks gestation but who do not have a chronic medical condition(s) that places them at ongoing increased risk of invasive pneumococcal disease (IPD) (refer to 4.13 (Handbook10-home~handbook10part4~handbook10-4-1384-13) Pneumococcal disease, refer to List 4.13.1 (Handbook10-home~handbook10part4~handbook10-4-1384-13-1) Conditions associated with an increased risk of IPD in children and adults, by severity of risk), and who have received the additional pneumococcal vaccine doses to age 5 years recommended above, do not need further pneumococcal vaccine doses after age 5 years. However, all children and adults who have chronic lung disease, or certain other chronic medical conditions, whether related to preterm birth or not, should also receive additional pneumococcal vaccine doses up to and beyond the age of 5 years (refer to 4.13 (Handbook10-home~handbook10part4~handbook10-4-1384-13) Pneumococcal disease).

Hepatitis B vaccine

Low-weight preterm newborn infants do not respond as well to hepatitis B-containing vaccines as full-term infants.77,82,83 Thus, for low-birth-weight infants (<2000 g) and/or infants born at <32 weeks gestation (irrespective of weight), who are born to mothers who are HBsAg-negative, it is recommended to give hepatitis B vaccine at birth, followed by 3 doses of a hepatitis B-containing vaccine, at 2, 4 and 6 months of age, with a booster dose at 12 months of age. The booster dose can be administered without measuring the antibody titre following the primary series. Alternatively, if an anti-HBs titre is measured, this should be done a minimum of 1 month after the 6-month dose, and if the anti-HBs titre is <10 mIU/mL, a booster dose should be given (refer to 4.5 (Handbook10-home~handbook10part4~handbook10-4-568-5) Hepatitis B). Preterm infants born to HBsAg-positive mothers should be given hepatitis B vaccine and hepatitis B immunoglobulin (HBIG) after birth as specified in 4.5 Hepatitis B.

Influenza vaccine

A person can be immunocompromised due to congenital or acquired disorders, disease and/or medical treatment. The extent of immunocompromise can vary from insignificant to profound, and this, together with the risk of acquiring a vaccine-preventable disease, should be taken into account when considering the administration of any vaccine(s). Vaccination of immunocompromised persons presents numerous challenges. For example, the extent of immunocompromise can be difficult to determine in a given individual (depending on underlying disease, medical treatment and other factors); immune protection attained from previous immunisation may be diminished; the response to vaccines administered in the setting of immunocompromise may be reduced, with additional booster vaccine doses required; the risk of vaccine-preventable diseases and their complications may be increased; and the risk of adverse events, particularly from live vaccines, may be increased.

When considering vaccination of persons on immunosuppressive therapy, it is particularly important to consider a number of factors, including the biologic target of the medication being used (mechanism and duration of effect on the immune system) as well as the consequence of using combination therapies (e.g. corticosteroids and other immunosuppressive therapies such as disease modifying anti-rheumatic drugs (DMARDs)), which can contribute to the nature, extent and length of immunocompromise. (Refer also to ‘Immunocompromise associated with corticosteroid administration’ and ‘Persons with autoimmune diseases and other chronic conditions’ below.) It is also important to know the anticipated duration of immunocompromise, whether due to therapy or the underlying disease. In some instances, additional booster doses of vaccines may be required to optimise protection in immunocompromised persons (e.g. pneumococcal vaccines at diagnosis of haematological malignancy). To determine the need for booster doses, it may be useful to measure post-vaccination antibody titres in selected groups in some circumstances, such as for adults or children who have received haematopoietic stem cell transplants (refer to ‘Haematopoietic stem cell transplant recipients’ below). Reliable serological testing is not readily available and/or validated to measure vaccine-induced immunity for all vaccines, and, in addition, results should be interpreted using standardised serological correlates. (Refer also to 2.15 (Handbook10-home-handbook10part4-handbook10-2-192-1-5) Catch-up, ‘Use of serological testing to guide catch-up vaccination.’) Expert advice should be sought if required.

The recommendations in this section for the use of vaccines in immunocompromised persons have been divided where applicable into paediatric (0–18 years) and adult (≥19 years) recommendations. This distinction has been made on the basis of scientific evidence, where available, and to assist in vaccine delivery in paediatric and adult special risk settings.

### Routine vaccination of immunocompromised persons

Many vaccine-preventable diseases are associated with an increased risk of morbidity and mortality in immunocompromised persons. It is particularly important to assess the vaccination history and need for additional vaccines, or further vaccine doses, for all persons who are immunocompromised or for persons who are anticipating future immunocompromise due to disease or treatment.

Two important examples of vaccines routinely recommended for immunocompromised persons are influenza and pneumococcal vaccines. Annual influenza vaccination should be given to all immunocompromised persons 6 months of age and older (refer to 4.7 (Handbook10-home-handbook10part4-handbook10-4-7) Influenza). Immunocompromised persons may also require additional doses of pneumococcal vaccines; the timing, number of doses and type of vaccine(s) vary depending on age and the underlying risk for IPD (refer to 4.13 (Handbook10-home-handbook10part4-handbook10-4-13) Pneumococcal disease). These, and other specific vaccine recommendations, are discussed in more detail below.

Persons with certain specific immunocompromising conditions, haematopoietic stem cell transplant or solid organ transplant, who receive influenza vaccine for the first time are recommended to receive 2 vaccine doses, at least 4 weeks apart (irrespective of age), and 1 dose annually thereafter (refer to relevant sections below and 4.7 (Handbook10-home-handbook10part4-handbook10-4-7) Influenza). Where it is known that a new influenza vaccine strain is circulating in the community which cross-protective immunity in the population is low (such as in the setting of an influenza pandemic), it may be appropriate that immunocompromised persons receive 2 doses of inactivated influenza vaccine, a minimum of 4 weeks apart, to achieve an optimal immune response, irrespective of their previous influenza vaccination history. For example, in the 2009–2010 H1N1 global influenza pandemic it was shown that seroconversion to influenza vaccination in immunocompromised adolescents and adults was improved following receipt of 2 vaccine doses. Further information and annual influenza vaccine recommendations are available on the Immunise Australia website (http://www.immunise.health.gov.au).

### Household contacts of immunocompromised persons

To protect immunocompromised household persons, whether adults or children, their household and other close contacts should be fully vaccinated according to current recommendations. Annual influenza vaccination is recommended for all household contacts (6 months of age) of immunocompromised persons. Assessment of the need for household contacts of immunocompromised persons to receive pertussis-containing and/or varicella vaccines is also very important (refer to 4.12 (Handbook10-home-handbook10part4-handbook10-4-12) Pertussis and 4.22 (Handbook10-home-handbook10part4-handbook10-4-224) Varicella). The use of live attenuated viral vaccines in contacts of immunocompromised persons (MMR, MMRV, varicella and rotavirus vaccines, where indicated) is safe, and strongly recommended to reduce the likelihood of contacts infecting the immunocompromised person. Persons ≥50 years of age who are household contacts of an immunocompromised person are also recommended to receive zoster vaccine. Although there is no risk of transmission of the MMR vaccine viruses, and an almost negligible risk of transmission of varicella-zoster virus (from varicella or zoster vaccine), there is a small risk of transmission of the rotavirus vaccine virus. Hand washing and careful disposal of soiled nappies is recommended to minimise transmission.

Immunocompromised persons should avoid contact with persons with varicella and herpes zoster, where possible. (Refer also to 4.9 (Handbook10-home-handbook10part4-handbook10-4-9) Measles, 4.17 (Handbook10-home-handbook10part4-handbook10-4-17) Rotavirus, 4.22 (Handbook10-home-handbook10part4-handbook10-4-22) Varicella and 4.24 (Handbook10-home-handbook10part4-handbook10-4-24) Zoster).

### Use of live viral or live bacterial vaccines in immunocompromised persons

There is a risk that the administration of live vaccines in immunocompromised persons may result in adverse events or vaccine-related disease due to unchecked infection (replication) of the vaccine virus or bacteria. This is particularly so for measles-, mumps-, rubella- and VZV-containing (varicella and zoster) vaccines and for bacille Calmette-Guérin (BCG) vaccine. However, the risk of disease varies by vaccine and by individual. Caution is required for vaccination in the setting of immunocompromise, and in severely immunocompromised persons most live vaccines are contraindicated. If there is uncertainty around the level of immunocompromise and when vaccine administration may be safe, vaccination should be withheld and expert advice sought from the treating physician and/or an immunisation specialist.

Immunocompromised persons who have been inadvertently vaccinated with a live attenuated vaccine should be promptly assessed to establish the degree of immunocompromise and extent of risk of vaccine-associated adverse effects in order to inform appropriate management. Management may include rapid administration of immunoglobulin and/or antiviral or antibacterial therapy depending on the vaccine and clinical context. Specialist advice should be sought.

The following is a list of current recommendations for use of live vaccines in immunocompromised persons.

**Tuberculosis vaccine (BCG) is always contraindicated.**
Vaccination in pregnancy

Pregnant women who received short-term antenatal corticosteroids, for example, in the context of preterm labour, can receive inactivated vaccines where indicated (refer to Table 3.3.1). Changes in maternal corticosteroid dose are not a contraindication to vaccination. Patients who are receiving inhaled corticosteroids alone (and who have no other immunocompromising factors that would contraindicate vaccine use) can receive live attenuated vaccines.

Immunocompromise associated with corticosteroid administration

Administration of live attenuated vaccines (such as MMR, MRV, zoster, varicella and yellow fever) may be unsafe in persons receiving corticosteroid therapy. The dose and duration of therapy with corticosteroids, as well as their use in combination with other immunosuppressive therapies such as bDMARDs and tsDMARDs (refer to 'Persons with autoimmune diseases and other chronic conditions' below), determines the impact on the immune system. In general, the combination of corticosteroid therapy and other immunosuppressing treatments or conditions is a contraindication to vaccination. Refer to the relevant vaccine chapters for specific exceptions.

Depending on the dose and duration of corticosteroid therapy, live attenuated vaccines may be safe, for example, when corticosteroid therapy is in low doses and it is the only risk factor for immunosuppression. The recommended timing of live vaccine administration in patients on corticosteroids alone is shown in Table 3.3.8. There are a number of different formulations of systemic corticosteroids (e.g. prednisone, dexamethasone, cortisone, methylprednisolone); the table therefore refers to a prednisone equivalent dose.

It is also always important, once treatment with corticosteroids has ceased, to assess whether the person has other underlying immunocompromising disease or is receiving other immunosuppressive therapy that may influence decisions about whether vaccines, particularly live vaccines, can be given. In cases where there is uncertainty around the level of immunocompromise and when live attenuated vaccine administration may be safe, vaccination should be withheld and expert advice sought from the treating physician and/or an immunosuppression specialist.

Table 3.3.8: Recommended timing of administration of live attenuated vaccines in adults and children in relation to the use of corticosteroids (specifically the prednisone equivalent dose)

<table>
<thead>
<tr>
<th>Prednisone equivalent dose*</th>
<th>Duration of therapy</th>
<th>Potential timing of vaccination</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adolescents aged ≥16 years and adults</td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;20 mg per day</td>
<td>Any duration</td>
<td>Any time during therapy</td>
</tr>
<tr>
<td>≥20 mg per day</td>
<td>Less than 14 days</td>
<td>Immunise 1 month prior to corticosteroid initiation or any time after cessation of corticosteroids</td>
</tr>
<tr>
<td></td>
<td>14 days or longer</td>
<td>Immunise 1 month prior to corticosteroid initiation or at least 1 month after cessation of corticosteroids</td>
</tr>
</tbody>
</table>

| Children and adolescents aged <16 years |
| Weight ≤10 kg | Weight >10 kg |
| <1 mg/kg per day | <10 mg per day | Less than 28 days | Any time during therapy |
| <2 mg/kg per day | <20 mg per day | Less than 14 days* | Any time during therapy |
| ≥2 mg/kg per day | ≥20 mg per day | Between 14 days and 28 days | Immunise 1 month prior to corticosteroid initiation or at least 1 month after cessation of corticosteroids |
| Any dose for 28 days or longer | Immunise 1 month prior to corticosteroid initiation or at least 1 month after cessation of corticosteroids |

* Systemic doses of different formulations of systemic corticosteroids (such as dexamethasone, cortisone, methylprednisolone) should be converted to a prednisone equivalent dose for the purpose of assessing suitability to receive live viral vaccines.

† Children taking lower doses (eg <1 mg/kg per day or <10 mg in total per day) for 14 to <28 days may also be suitable to receive live attenuated vaccines any time during therapy, but only after expert advice is sought.

‡ Zoster vaccine can be given to patients receiving low-dose corticosteroids (<20 mg per day of prednisone equivalent dose as above) either on their own or in combination with certain csDMARDs in low doses (i.e. methotrexate ≤0.4 mg/kg per week, azathioprine ≤3.0 mg/kg per day or mercaptopurine ≤1.5 mg/kg per day). At these doses, it is likely that the level of immunocompromise is not severe (refer to 4.24 Zoster).

Patients who are receiving inhaled corticosteroids alone (and who have no other immunocompromising factors that would contraindicate vaccine use) can receive live attenuated vaccines. Persons who received short-term antenatal corticosteroids, for example, in the context of preterm labour, can receive inactivated vaccines where indicated (refer to Table 3.3.1 Recommendations for vaccination in pregnancy).
When indicated, inactivated vaccines should be administered to patients with autoimmune diseases and other chronic conditions to optimise protection against the respective vaccine-preventable disease. This is despite the potential for reduced immunogenicity of vaccines in these patients due to both immunosuppressive therapies and the underlying disease. Clinical and laboratory measures of disease activity, and the choice, duration and dose of immunosuppressive therapies, do not always predict who will respond poorly to vaccination.

Every effort should be made to administer all indicated live vaccines before initiation of immunosuppressive therapy, with an interval of at least 1 month between the administration of a live vaccine and the commencement of treatment with DMARDs. Live vaccines are generally contraindicated in individuals who are already receiving DMARDs. However, the administration of live vaccines may be considered in consultation with a specialist, with careful consideration of the patient’s level of immune function and current and/or future disease risk.

In general, immunocompromised persons who are receiving bDMARDs or tsDMARDs should not receive live attenuated vaccines until after therapy has been discontinued for at least 12 months; however, specialist advice should be sought on the most appropriate interval for the patient and their individual circumstances.

Live vaccines, particularly BCG, are not recommended for use in infants aged <6 months who were born to mothers who received bDMARDs, particularly in the third trimester. Persons with a history of Guillain-Barre syndrome (GBS) have an increased likelihood, in general, of developing GBS again, and the chance of them developing the syndrome following influenza vaccination may be higher than in persons with no history of GBS. A small increased risk of GBS was associated historically with one influenza vaccine in the United States in 1976, but, since then, close surveillance has shown that GBS has occurred at a very low rate of up to 1 in 1 million doses of influenza vaccine, if at all.

Hypopituitarism is not a contraindication to vaccination if the person is only receiving physiological corticosteroid replacement, as this is not considered immunosuppressive. If the person has been weaned and is on high-dose corticosteroids for more than 14 days, the use of live attenuated vaccines should be delayed for a minimum of 1 month (refer to Table 3.3.8).

Persons with metabolic diseases should be vaccinated using the routine schedule, as vaccinations are generally considered safe in these persons. Influenza and pneumococcal vaccines are recommended for those with metabolic disease. Any individual concerns should be discussed with the treating metabolic physician.

Oncology patients

Paediatric and adult patients undergoing cancer chemotherapy who have not completed a primary vaccination schedule before diagnosis

Live vaccines, including BCG, MMR, zoster and varicella vaccines, are contraindicated in cancer patients receiving immunosuppressive therapy and/or who have poorly controlled malignant disease. These vaccines are recommended to be administered to seronegative persons at least 3 months after completion of chemotherapy, provided the underlying malignancy is in remission.

Administration of live attenuated viral vaccines (MMR-containing or varicella-containing vaccines) should be deferred if blood products or immunoglobulins have been recently administered (refer to Table 3.3.6 Recommended intervals between either immunoglobulins or blood products and MMR, MMRV or varicella vaccination). Influenza vaccination is recommended annually in all cancer patients aged 6 months. Cancer patients who are immunocompromised who receive influenza vaccine for the first time are recommended to receive 2 vaccine doses at least 4 weeks apart (irrespective of age) and 1 dose annually thereafter.

Persons receiving chemotherapy may receive inactivated vaccines (e.g. 13vPCV, hepatitis B) according to a routine or catch-up vaccination schedule. The immune response may be suboptimal, but the vaccines are safe to administer.

Vaccines should not be administered during times of severe neutropenia (absolute neutrophil count <0.5 x 10^9/L), to avoid precipitating an acute febrile episode.

Persons with underlying haematological malignancies (such as multiple myeloma, Hodgkin’s lymphoma, non-Hodgkin’s lymphoma, chronic lymphocytic leukaemia) are recommended to receive pneumococcal vaccination, due to the increased risk of invasive pneumococcal disease (IPD). Newly diagnosed children or adults who have not previously received a dose of 13vPCV are recommended to receive at least one 13vPCV dose, depending on age, and should subsequently receive 23vPPV. These vaccines should be administered as early as possible after diagnosis, according to the person’s age and previous vaccination history.

Paediatric and adult patients with cancer who have completed cancer therapy and who completed a primary vaccination schedule before diagnosis

The majority of the following vaccines may be administered without checking antibody titres beforehand, and can be given at the same time.

The following schedule of booster vaccination is recommended if the person is well and in remission 6 months after chemotherapy:

- single dose of DTPa-containing vaccine if <10 years of age; use either dT or reduced antigen content dTpa if ≥10 years of age
- single dose of MMR, IPV, hepatitis B vaccines
- single dose of 13vPCV (if previous age-appropriate dose(s) not received; refer to 4.13 (Handbook10-home-handbook10part4-handbook10-4-13#4-13) Pneumococcal disease)
- 23vPPV dose(s) (following 13vPCV, and as per 4.13 (Handbook10-home-handbook10part4-handbook10-4-13#4-13) Pneumococcal disease)
- single dose of Hib vaccine (if <5 years of age or if ≥5 years of age with asplenia, refer to Table 3.3.5)
- 4vHPV vaccine: if 19 years of age, single dose if previously completed a primary course; 3-dose schedule if not previously received (schedule 0, 2 and 6 months) (refer to 4.6 (Handbook10-home-handbook10part4-handbook10-4-6#4-6) Human papillomavirus)
- varicella vaccine: persons who are seronegative to varicella-zoster virus (VZV) should receive a 2-dose schedule of varicella vaccine, at least 6 months after chemotherapy has ceased (refer to 4.22 (Handbook10-home-handbook10part4-handbook10-4-22#4-22) Varicella).

Measles and rubella antibody status should be checked 6 to 8 weeks after vaccination with MMR or MMRV vaccine. Persons who have not seroconverted should receive a further dose.

Administration of live attenuated viral vaccines (MMR-containing or varicella-containing vaccines) should be deferred if blood products or immunoglobulins have been recently administered (refer to Table 3.3.6 Recommended intervals between either immunoglobulins or blood products and MMR, MMRV or varicella vaccination).

Solid organ transplant recipients

For solid organ transplant (SOT) recipients, depending on the transplanted organ, and to prevent rejection, variable doses of immunosuppressive agents are required and may influence the effectiveness of vaccines. Where possible, children undergoing solid organ transplantation should be vaccinated well before transplantation. Inactivated vaccines can be administered safely after transplantation, but are usually administered from 6 months after transplantation to maximise the immune response. Live vaccines are contraindicated in most post-transplantation protocols due to concerns of disseminated infection, although data in this population are limited. Recommended vaccinations for child and adult SOT recipients are given in Table 3.3.2.

Table 3.3.2: Recommendations for vaccinations for solid organ transplant (SOT) recipients


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### Vaccines recommended before transplantation

<table>
<thead>
<tr>
<th>Vaccine</th>
<th>Child (0–18 years)</th>
<th>Adult (≥19 years)</th>
<th>Comment</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Streptococcus pneumoniae (pneumococcal disease)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>13-valent pneumococcal conjugate vaccine (13vPCV)</td>
<td>Yes (aged ≥6 weeks)</td>
<td>Yes</td>
<td>Recommendations depend on age. Refer to 4.13 Pneumococcal disease and Table 2.1.11 (Handbook10-home<del>handbook10part2</del>handbook10-2-1#table-2-1-11) Catch-up schedule for 13vPCV (Prevenar 13) and 23vPPV (Pneumovax 23) in children with a medical condition(s) associated with an increased risk of IPD, presenting at age &lt;2 years.</td>
</tr>
<tr>
<td>23-valent pneumococcal polysaccharide vaccine (23vPPV)</td>
<td>Yes (≥8 weeks after 13vPCV)</td>
<td>Yes (≥8 weeks after 13vPCV)</td>
<td>Recommendations depend on age. Refer to 4.13 Pneumococcal disease and Table 2.1.11 (Handbook10-home<del>handbook10part2</del>handbook10-2-1#table-2-1-11) Catch-up schedule for 13vPCV (Prevenar 13) and 23vPPV (Pneumovax 23) in children with a medical condition(s) associated with an increased risk of IPD, presenting at age &lt;2 years.</td>
</tr>
<tr>
<td><strong>Haemophilus influenzae type b</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hib vaccine</td>
<td>Yes</td>
<td>Not indicated</td>
<td>If possible, complete vaccination before transplantation.</td>
</tr>
<tr>
<td><strong>Diphtheria, tetanus, pertussis</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>DTPa-containing vaccine for children &lt;10 years of age</td>
<td>Yes, provided dTpa has not been given in the last 10 years</td>
<td>Yes, provided dTpa has not been given in the last 10 years</td>
<td>The primary schedule should be completed before transplantation. For recipients &lt;10 years of age, not previously vaccinated, give all 3 doses as DTPa-containing vaccine. For recipients ≥10 years of age, not previously vaccinated, give the 1st dose as dTpa, followed by 2 doses of dT. If dT is unavailable, complete vaccination course with dTpa. Refer also to catch-up tables for children and adults in refer to 2.1.5 (Handbook10-home<del>handbook10part2</del>handbook10-2-1#2-1-5) Catch-up.</td>
</tr>
<tr>
<td>dTpa for those ≥10 years of age</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Influenza</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Influenza vaccine</td>
<td>Yes (refer to comments)</td>
<td>Yes (refer to comments)</td>
<td>Adults who have received a routine course of polio vaccination in childhood are recommended to receive a booster every 10 years if they plan to travel to a polio-endemic area or have an occupational risk of polio exposure (e.g. laboratory workers).</td>
</tr>
<tr>
<td><strong>Poliomyelitis</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>IPV</td>
<td>Yes</td>
<td>Yes</td>
<td>Adults who have received a routine course of polio vaccination in childhood are recommended to receive a booster every 10 years if they plan to travel to a polio-endemic area or have an occupational risk of polio exposure (e.g. laboratory workers).</td>
</tr>
<tr>
<td><strong>Hepatitis B</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hepatitis B vaccine</td>
<td>Yes, depending on serological status</td>
<td>Yes, depending on serological status</td>
<td>Recommended for all seronegative SOT candidates. Immunogenicity is likely to be improved when vaccination is administered before transplantation. Accelerated schedules can be used (refer to Table 4.5.2 Accelerated hepatitis B vaccination schedules (for persons with imminent risk of exposure)).</td>
</tr>
<tr>
<td><strong>Hepatitis A</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hepatitis A vaccine*</td>
<td>Yes, if seronegative (refer to comments)</td>
<td>Yes, if seronegative (refer to comments)</td>
<td>Recommended for all liver SOT recipients, or transplant candidates or recipients with chronic liver disease, or those chronically infected with either hepatitis B or hepatitis C.</td>
</tr>
<tr>
<td><strong>Neisseria meningitidis (meningococcal disease)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Meningococcal C conjugate vaccine (MenCCV or Hib-MenCCV)</td>
<td>Yes</td>
<td>Not indicated</td>
<td>A single dose of meningococcal C conjugate vaccine is recommended at 12 months of age. 4vMenCV is recommended for persons with certain medical conditions or treatments that increase their risk of IMD (refer below).</td>
</tr>
</tbody>
</table>
A recommended schedule of vaccination is outlined in Table 3.3.3. Vaccination for international travel is recommended.

### Human papillomavirus

<table>
<thead>
<tr>
<th>HPV vaccine</th>
<th>Child (0–18 years)</th>
<th>Adult (≥19 years)</th>
<th>Comment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Yes</td>
<td>Yes</td>
<td>Yes, if no history of prior immunisation</td>
<td>3-dose schedule of 4vHPV is recommended for those aged &gt;9 years. The routine schedule is 1st dose on day 0 (day of vaccination), 2 months, and 6 months (after 1st dose).</td>
</tr>
</tbody>
</table>

### Mumps, measles, and rubella

<table>
<thead>
<tr>
<th>MMR vaccine</th>
<th>Child (0–18 years)</th>
<th>Adult (≥19 years)</th>
<th>Comment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Yes, unless 2 previous documented doses</td>
<td>Contraindicated</td>
<td>Contraindicated</td>
<td>The primary schedule should be completed before transplantation provided the transplant candidate is taking no immunosuppressive therapy and has no underlying cellular immunodeficiency.</td>
</tr>
</tbody>
</table>

### Varicella

<table>
<thead>
<tr>
<th>Varicella vaccine</th>
<th>Child (0–18 years)</th>
<th>Adult (≥19 years)</th>
<th>Comment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Yes, if non-immune (refer to comments)</td>
<td>Contraindicated</td>
<td>Contraindicated</td>
<td>Confirm immunity with reliable history of varicella disease and confident clinical diagnosis or serological testing. The primary vaccination schedule should be completed before transplantation, provided the transplant candidate is taking no immunosuppressive therapy and has no underlying cellular immunodeficiency.</td>
</tr>
</tbody>
</table>

* Any transplant recipient who anticipates travelling may require additional vaccination, such as for hepatitis A and meningococcal disease (refer also to 3.2 Vaccination for international travel).

### Haematopoietic stem cell transplant recipients

Haematopoietic stem cells are sourced from peripheral blood, bone marrow or umbilical cord blood. Protective immunity to vaccine-preventable diseases is partially or completely lost following either allogeneic or autologous stem cell transplantation. Immunocompromise following allogeneic transplantation is caused by a combination of the preparative chemotherapy given before transplantation, graft-versus-host disease (GVHD), and immunosuppressive therapy following transplantation. Persisting immunocompromise is common, particularly in persons with chronic GVHD. Immunity is also impaired in autologous HSCT recipients due to high-dose chemotherapy and radiotherapy, but GVHD is not a concern as donor stem cells are derived from the transplant recipient. In most cases, autologous HSCT recipients will recover their immunity more quickly than allogeneic transplant recipients.

Separate vaccination schedules for autologous or allogeneic HSCT recipients have not been supported in published guidelines because of limited data. For practical purposes, the same schedule is recommended for these two groups, regardless of donor source (peripheral blood, bone marrow or umbilical cord), preparative chemotherapy (ablative or reduced intensity), or transplant type (allogeneic or autologous). Live vaccines should by delayed until 24 months after cessation of HSCT, providing the individual does not have ongoing immunosuppression (refer to Table 3.3.3 Recommendations for revaccination following haematopoietic stem cell transplant (HSCT) in children and adults, irrespective of previous immunisation history). HSCT recipients with ongoing GVHD or remaining on immunosuppressive therapy should not be given live vaccines. Chronic GVHD (cGVHD) is associated with functional hyposplenism and therefore increases susceptibility to infections with encapsulated organisms, especially Streptococcus pneumoniae. For persons with cGVHD who remain on active immunosuppression, antibiotic prophylaxis is recommended. The immune response to inactivated vaccines is usually poor during the first 6 months after HSCT. Donor immunisation with hepatitis B, tetanus, Hib and meningococcal conjugate vaccines before stem cell harvesting has been shown to elicit improved early antibody responses in HSCT recipients vaccinated in the post-transplant period. However, practical and ethical considerations currently limit the use of donor immunisation.

Routine serological testing for several infectious agents and antibody levels conferring protective immunity are poorly defined. For those vaccines that are recommended for all HSCT recipients (tetanus, diphtheria, poliomyelitis, influenza, pneumococcal, Hib), pre-vaccination testing is not recommended as the response to a primary course of these vaccines is generally adequate. The serological response to pneumococcal vaccine is less predictable. Pneumococcal serology is only available in a few specialised laboratories and is not routinely recommended. Serology before and approximately 4 to 6 weeks after vaccination with the final dose of a hepatitis B vaccine course, and after MMR vaccine, is recommended as antibody levels will determine the need for revaccination.

Post-vaccination varicella serology using commercial assays is very insensitive for vaccine-induced immunity (as compared with natural infection) and is not recommended (refer to 4.22 Varicella).

A recommended schedule of vaccination is outlined in Table 3.3.3.

### Table 3.3.3: Recommendations for revaccination following haematopoietic stem cell transplant (HSCT) in children and adults, irrespective of previous immunisation history

<table>
<thead>
<tr>
<th>Vaccine</th>
<th>Months after HSCT</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vaccine</td>
<td>Months after HSCT</td>
<td>24</td>
</tr>
<tr>
<td>---------------------------------------------</td>
<td>-------------------</td>
<td>------------------------------</td>
</tr>
<tr>
<td><strong>Streptococcus pneumoniae</strong> (pneumococcal disease)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>13-valent pneumococcal conjugate vaccine (13vPCV)</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>23-valent pneumococcal polysaccharide vaccine (23vPPV)</td>
<td>No</td>
<td>No</td>
</tr>
<tr>
<td><strong>Haemophilus influenzae type b</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hib</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td><strong>Diphtheria, tetanus, pertussis</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>DTPa-containing vaccine for children &lt;10 years of age</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>dTpa for those ≥10 years of age</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Poliomyelitis</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>IPV</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td><strong>Hepatitis B</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hepatitis B vaccine</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td><strong>Influenza</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Two doses of influenza vaccine at least 4 weeks apart are recommended for all HSCT recipients receiving influenza vaccine for the first time (irrespective of age), with the 1st dose given as early as 6 months after transplant (refer also to the introduction of 3.3.3 Vaccination of immunocompromised persons above), then a single dose annually thereafter.</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Neisseria meningitidis</strong> (meningococcal disease)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Meningococcal B vaccine (MenBV)</td>
<td>Yes</td>
<td>Not needed (refer to comments)</td>
</tr>
<tr>
<td>Quadrivalent meningococcal conjugate vaccine (4vMenCV)</td>
<td>Yes</td>
<td>Not needed (refer to comments)</td>
</tr>
</tbody>
</table>
HPV vaccine

A 3-dose course of 4vHPV is recommended at intervals of 0, 2 and 6 months. Specific immunogenicity data in this group are not available; better immune responses may be expected at ≥12 months post transplantation when a greater level of immune reconstitution has been achieved.

Individual recommendations for HPV vaccination in those ≥9 years of age should be determined by an individual risk assessment (refer to 4.6 Human papillomavirus).

Measles, mumps and rubella

Table 3.3.4: Categories of immunocompromise in HIV-infected persons, based on age-specific CD4+ counts and percentage of total lymphocytes

<table>
<thead>
<tr>
<th>Category</th>
<th>&lt;12 months</th>
<th>1–5 years</th>
<th>6–24 years</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>CD4 + per µL</td>
<td>%</td>
<td>CD4 + per µL</td>
</tr>
<tr>
<td>No evidence of immunocompromise</td>
<td>≥1500</td>
<td>≥25</td>
<td>≥1000</td>
</tr>
<tr>
<td>Severe immunocompromise</td>
<td>&lt;750</td>
<td>&lt;15</td>
<td>&lt;500</td>
</tr>
</tbody>
</table>

HIV-infected persons should be vaccinated as described below.

Live attenuated vaccines

- Rotavirus vaccines appear to be safe and immunogenic in HIV-infected but clinically stable children, although data on their use are limited. Vaccination can be given according to the routine schedule unless there is severe immunocompromise. (Refer also to 4.17: Meningococcal disease.)
- MMR vaccine should be routinely administered to HIV-infected children in a 2-dose schedule at 12 months and 18 months of age unless the child has a CD4+ count of <750 per µL. The serologic response is likely to be greatly improved after the 2nd dose of MMR vaccine in HIV-infected children and, therefore, normal human immunoglobulin (NHIG) should be given as post-exposure prophylaxis, regardless of vaccination status. (Refer to 4.18: Meningococcal disease.)
- The combination MMRV vaccine is not recommended for use in HIV-infected persons, due to a lack of data on its use. (Refer also to varicella text below.)

Varicella vaccine

† The recommended interval between doses is 12 weeks for children who commenced their 4vMenCV course between 7 and 23 months of age as outlined in Table 4.10.2 in 4.10 Meningococcal disease.

HIV-infected persons

Vaccination schedules for HIV-infected persons should be determined by the person’s age, degree of immunocompromise (CD4+ count) and the risk of infection (refer to Table 3.3.4 below). Children with perinatally acquired HIV differ substantially from adults, as immunisation and first exposure to vaccine antigens occurs after HIV infection, whereas in adults, most vaccines are inducing a secondary ‘boosted’ immune response. HIV-infected persons of any age whose disease is well controlled on combination antiretroviral therapy (undetected or low viral load with good preservation of CD4+ lymphocyte count) are likely to respond satisfactorily to vaccines.

* Any transplant recipient who anticipates travelling may require additional vaccination, such as for meningococcal and hepatitis A disease (refer also to 3.2: Vaccination for international travel).
† The recommended interval between doses is 12 weeks for children who commenced their 4vMenCV course between 7 and 23 months of age as outlined in Table 4.10.2 in 4.10 Meningococcal disease.

Table 3.3.4: Categories of immunocompromise in HIV-infected persons, based on age-specific CD4+ counts and percentage of total lymphocytes

<table>
<thead>
<tr>
<th>Category</th>
<th>Age</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>&lt;12 months</td>
</tr>
<tr>
<td></td>
<td>CD4 + per µL</td>
</tr>
<tr>
<td>No evidence of immunocompromise</td>
<td>≥1500</td>
</tr>
<tr>
<td>Severe immunocompromise</td>
<td>&lt;750</td>
</tr>
</tbody>
</table>

HIV-infected persons should be vaccinated as described below.

Live attenuated vaccines

- Rotavirus vaccines appear to be safe and immunogenic in HIV-infected but clinically stable children, although data on their use are limited. Vaccination can be given according to the routine schedule unless there is severe immunocompromise. (Refer also to 4.17: Meningococcal disease.)
- MMR vaccine should be routinely administered to HIV-infected children in a 2-dose schedule at 12 months and 18 months of age unless the child has a CD4+ count of <750 per µL. The serologic response is likely to be greatly improved after the 2nd dose of MMR vaccine in HIV-infected children and, therefore, normal human immunoglobulin (NHIG) should be given as post-exposure prophylaxis, regardless of vaccination status. (Refer to 4.18: Meningococcal disease.)
- The combination MMRV vaccine is not recommended for use in HIV-infected persons, due to a lack of data on its use. (Refer also to varicella text below.)
- Varicella vaccine may be given to HIV-infected adults or children ≥12 months of age who are asymptomatic, although data on efficacy and safety in HIV-infected persons is limited. Use of the monovalent varicella vaccine (VV) given in 2 doses, at least 3 months apart, in children ≥12 months of age with age-specific CD4+ count ≥15% is recommended. The same 2-dose SV vaccine strategy can be considered for HIV-infected adults who are varicella-seronegative and who have a CD4+ count ≥200 per µL. The combination MMRV vaccine is not recommended for use in HIV-infected persons. (Refer also to 4.19: Varicella.)
- Zoster vaccine is not recommended for adults with AIDS or symptomatic HIV infection. However, zoster vaccine can be administered to persons with asymptomatic HIV infection who are on antiretroviral therapy and who have a very low or undetectable viral load and CD4+ count of >350 per µL. Where there is a strong indication to vaccinate, some experts suggest a CD4+ count of >200 per µL is safe. Expert advice should be sought from the treating physician and/or an immunisation specialist. Serological confirmation of previous VZV infection is recommended prior to vaccination. Serological confirmation of previous VZV infection is recommended prior to vaccination. Zoster vaccine is only registered for use in adults ≥50 years of age. (Refer also to 4.24: BCG vaccine.)
- Yellow fever vaccine can be administered to HIV-infected persons who are not immunocompromised (i.e. with CD4+ counts >200 per µL) if they are at risk of yellow fever virus infection; however, vaccination of individuals with evidence of immunocompromise where risk of yellow fever virus exposure is unavoidable should be considered on a case-by-case basis with the person’s treating clinician. (Refer also to 4.23: Yellow fever and 3.2: Vaccination for international travel.)
- BCG vaccine should not be given to HIV-infected children or adults because of the risk of disseminated BCG infection. (Refer also to 4.20: BCG vaccine.)
Inactivated (non-live) vaccines

- Diphtheria-tetanus-pertussis (DTPa/DTa), Hib and IPV vaccines can be given according to routine recommendations \(^{154,155}\) (refer to relevant disease-specific chapters in Part 4 (Handbook10-home-handbook10part4-handbook10-4-148-4)).

- The 4vHPV vaccine can be given to children (29 years of age) and adults with HIV. It was safe and immunogenic in a small study of HIV-infected men. \(^{156}\) HIV-infected persons should receive the routine course of 3 doses of 4vHPV vaccine at times 0, 2, and 6 months. Vaccination is recommended for persons in the age range for which the vaccine is registered (females aged 9–45 years and males 9–26 years); use of HPV vaccine in males up to the age of 45 years is unlikely to be associated with immunogenicity or adverse events that differ from those observed in females. However, the benefit of HPV vaccination is optimal when delivered to children or young adolescents prior to sexual debut (refer to 4.6 (Handbook10-home-handbook10part4-handbook10-4-684-6) Human papillomavirus).

- Pneumococcal disease, both respiratory and invasive (IPD), is a frequent cause of morbidity in HIV-infected children and adults (refer to List 4.13.1 (Handbook10-home-handbook10part4-handbook10-4-1384-13-1)). \(^{157}\) Pneumococcal disease. \(^{158}\) Children should be vaccinated initially with pneumococcal conjugate vaccine (13vPCV); the number of doses depends on age at diagnosis and vaccination history (refer to Table 2.1.11 (Handbook10-home-handbook10part2-handbook10-2-1itable-2-1-11) Catch-up schedule for 13vPCV (Prevenar 13) and 23vPPV (Pneumovax 23) in children with a medical condition(s) associated with an increased risk of IPD, presenting at age <2 years). For children aged >5 years and adults, a single dose of 13vPCV is recommended, followed by 23vPPV; repeat doses of 23vPPV are also indicated. \(^{159}\) Refer to 4.13 (Handbook10-home-handbook10part4-handbook10-4-1384-13) Pneumococcal disease for details.

- Annual influenza vaccination is recommended in all HIV-infected adults and children (≥6 months of age). In all HIV-infected children <9 years of age, 2 doses, administered a minimum of 4 weeks apart, are recommended if the first time influenza vaccine is given. HIV viral load may increase after influenza vaccination, but CD4 counts are unaffected and the benefits exceed the risk. \(^{160,161}\) (Refer also to 4.7 (Handbook10-home-handbook10part4-handbook10-4-784-7) Influenza.)

- Hepatitis B is safe to use in HIV-infected persons, but the immunological response may be diminished. Serological testing for evidence of previous hepatitis B infection should be undertaken prior to commencing vaccination. Limited studies in HIV-positive adults have demonstrated an improved and accelerated serological response to a vaccination schedule that consists of 4 doses, comprising two injections of the standard adult dose (using Engerix-B) on each occasion, at times 0, 1, 2 and 6 months. \(^{162,163}\) HIV-positive children should receive 3 doses of hepatitis B vaccine using an adult formulation (i.e. double the standard recommended dose for children). \(^{164,165}\) Antibody level should be measured at the completion of the vaccination schedule, if the anti-HBs titre is <10 mIU/mL, further doses are required (refer to 4.5 (Handbook10-home-handbook10part4-handbook10-4-584-5) Hepatitis B.).

- Hepatitis A vaccines are immunogenic in most HIV-infected children, \(^{166}\) but are only recommended for use in non-immune HIV-infected persons if they have independent risk factors for acquisition of hepatitis A (refer to 4.4 (Handbook10-home-handbook10part4-handbook10-4-484-4) Hepatitis A.).

- Parenteral Vi polysaccharide typhoid, inactivated Japanese encephalitis and rabies vaccines are safe and can be used in HIV-infected persons, if indicated. \(^{167}\) (Refer to relevant disease-specific chapters in Part 4 (Handbook10-home-handbook10part4-handbook10-4-148-4)).

- 4vMenCV and MenBv are recommended (refer to 4.10 (Handbook10-home-handbook10part4-handbook10-4-1084-10) Meningococcal disease). A diminished immune response follow a single dose of 4vMenCV has been reported in HIV-infected persons. \(^{168,169}\) However, this improves for some serogroups following a 2nd dose. \(^{170}\) There is no clinical data on the use of MenBv in HIV-infected persons; however, vaccination is recommended based on the expected benefit in these individuals.

Persons with functional or anatomical asplenia

Persons with an absent or dysfunctional spleen are at a life-long increased risk of fulminating bacterial infection, most notably invasive pneumococcal disease (IPD). \(^{171}\) Pneumococcal, meningococcal, Hib and influenza vaccination are particularly recommended for all persons with asplenia, whether functional or anatomical (such as splenectomy). Other vaccinations should be up to date. Vaccines should be provided according to the person’s age and previous immunisation history, and immunisation status should be reviewed regularly. \(^{172}\) Specific vaccine recommendations for persons with asplenia are discussed below and shown in Table 3.3.5.

In persons undergoing an elective splenectomy, vaccination should be completed, where possible, 2 weeks before the scheduled operation date. In an unplanned splenectomy, vaccination should commence approximately 1 week after the splenectomy has occurred. \(^{173}\)

Children with splenic dysfunction should also be given antibiotic prophylaxis to prevent bacterial infection, until at least 5 years of age. \(^{174}\) Other asplenic persons and/or their parents/carers should also be educated about the importance of early investigation and treatment of febrile illnesses, including the use of emergency antibiotics. Asplenic persons are recommended to wear a medical alert. Vaccination cannot provide protection against all bacterial infections, or even all pneumococcal serotypes that cause IPD, hence it is particularly important that persons with asplenia are informed of the life-long increased risk of severe bacterial infection, even if they have been appropriately vaccinated.

Pneumococcal vaccination

Additional doses of pneumococcal vaccine are recommended for persons with asplenia, depending on their age and previous immunisation history, as shown in Table 3.3.5. Detailed information is provided in 4.13 (Handbook10-home-handbook10part4-handbook10-4-1384-13) Pneumococcal disease and in Table 2.1.11 (Handbook10-home-handbook10part2-handbook10-2-1itable-2-1-11) Catch-up schedule for 13vPCV (Prevenar 13) and 23vPPV (Pneumovax 23) in children with a medical condition(s) associated with an increased risk of IPD, presenting at age <2 years in 2.1.5 (Handbook10-home-handbook10part2-handbook10-2-182-1-5) Catch-up. A single dose of 13vPCV is recommended for asymptomatic splenic adults and children who have not previously received any previous 13vPCV dose. \(^{175}\) This should precede 23vPPV doses when possible. However, if more than 2 doses of 23vPPV have previously been given, 13vPCV should be given at the next available opportunity, and at least 1 year after the last 23vPPV dose. Subsequent doses of 23vPPV are recommended, with a maximum of 3 doses in adulthood (age ≥18 years). Age-specific recommendations are discussed in 4.13 (Handbook10-home-handbook10part4-handbook10-4-1384-13) Pneumococcal disease.

Meningococcal vaccination

4vMenCV is recommended from 2 months of age for persons with asplenia. The vaccine brand and doses required depend on the age at which the vaccine course is commenced (refer to Table 4.10.1 in 4.10 (Handbook10-home-handbook10part4-handbook10-4-1084-10) Meningococcal disease). MenBv is recommended from 2 months of age for persons with asplenia. The number of doses depends on the age at which the vaccine course is commenced (refer to Table 4.10.1 in 4.10 (Handbook10-home-handbook10part4-handbook10-4-1084-10) Meningococcal disease).

Hib vaccination

A single dose of Hib vaccine is recommended for asymptomatic persons who were not vaccinated in infancy or who are incompletely vaccinated (refer to 4.3 (Handbook10-home-handbook10part4-handbook10-4-384-3) Haemophilus influenzae type b and Table 2.1.8 (Handbook10-home-handbook10part2-handbook10-2-1itable-2-1-8) Catch-up schedule for Hib vaccination for children <5 years of age in 2.1.5 (Handbook10-home-handbook10part2-handbook10-2-182-1-5) Catch-up). Subsequent booster doses of Hib vaccine are not required. Persons who have received all scheduled doses of Hib vaccine do not require a booster dose before or after splenectomy. \(^{176}\)

Influenza vaccination

Annual influenza vaccine is recommended in all persons from 26 months of age (refer to 4.7 (Handbook10-home-handbook10part4-handbook10-4-784-7) Influenza), particularly those who are immunocompromised. Influenza infection can be complicated by secondary bacterial infections, such as IPD. The influenza vaccine dose is dependent on previous influenza vaccination history and age. (Refer also to Table 4.7.1 (Handbook10-home-handbook10part4-handbook10-4-748-7) Recommended doses of influenza vaccine in 4.7 (Handbook10-home-handbook10part4-handbook10-4-748-7) Influenza).

Table 3.3.5: Recommendations for vaccination in persons with functional or anatomical asplenia

<table>
<thead>
<tr>
<th>Vaccine</th>
<th>Age Group</th>
<th>Dose</th>
<th>Note</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hib</td>
<td>0-2 years</td>
<td>1</td>
<td>Booster if incompletely vaccinated.</td>
</tr>
<tr>
<td>MenBv</td>
<td>2-23 months</td>
<td>2</td>
<td>Booster if incompletely vaccinated.</td>
</tr>
<tr>
<td>MenBv</td>
<td>24 months-15 years</td>
<td>2-3</td>
<td>Booster if incompletely vaccinated.</td>
</tr>
<tr>
<td>MenBv</td>
<td>16 years+</td>
<td>3</td>
<td>Booster if incompletely vaccinated.</td>
</tr>
</tbody>
</table>

### Pneumococcal vaccines

#### 6 weeks to <2 years

Give a 3-dose primary course of 13vPCV, with an additional dose of 13vPCV at age ≥12 months. Refer to Table 4.13 (Handbook10-home-handbook10part4-handbook10-4-13#table-4-13) and Table 2.1.11 (Handbook10-home-handbook10part2-handbook10-2-1#table-2-1-11) for catch-up schedules.

#### 2 to 5 years

If the primary course of PCV is incomplete or if the recommended 13vPCV dose at age ≥12 months was not received, give 1 or 2 doses of 13vPCV as per Table 4.13.2 (Handbook10-home-handbook10part4-handbook10-4-13#table-4-13-2)

Give a single dose of 23vPPV at age 4–5 years.  

#### 5 to <18 years

If a 13vPCV dose has not previously been given, give a single dose of 13vPCV, preferably prior to 23vPPV.

If a dose of 23vPPV was received at age 4–5 years, give another dose of 23vPPV 5 years later (at age 9–10 years).

If asplenia is newly diagnosed, give 2 doses of 23vPPV, 5 years apart (after 13vPCV, refer to above).

#### ≥18 years

If a 13vPCV dose has not previously been given, give a single dose of 13vPCV, preferably prior to 23vPPV.

There is a maximum limit of 3 doses of 23vPPV during adulthood 1 (age ≥18 years). Give the 1st adult dose at diagnosis (after 13vPCV: refer to above), or at least 5 years after the last 23vPPV dose, whichever is later.

### Meningococcal vaccines

#### ≥2 years

4vMenCV is recommended according to the age at which the vaccine course commenced (refer to 4.10 (Handbook10-home-handbook10part4-handbook10-4-10#table-4-10-1)).

MenBV is recommended according to the age at which the vaccine course commenced (refer to 4.10 (Handbook10-home-handbook10part4-handbook10-4-10#table-4-10-2)).

#### 6 months–<5 years

Give the recommended course of Hib-containing vaccine, or catch-up vaccination, according to Table 2.1.8 Catch-up schedule for Hib vaccination for children <5 years of age.

Additional/repeat doses are not required.

#### ≥5 years

If a Hib vaccine has not previously been given, or if the primary course of Hib vaccine is incomplete, give a single dose of Hib-containing vaccine.

If Hib vaccination is complete (as per children <5 years above), additional/repeat doses are not required.

### Haemophilus influenzae type b (Hib) vaccine

#### 6 weeks–<5 years

Give 1 dose (0.25 mL) in subsequent years.

Additional/repeat doses are not required.

#### ≥5 years

Give 2 doses (0.25 mL each), 4 weeks apart, in the first year of vaccination.

Give 1 dose (0.25 mL) in subsequent years.

### Influenza vaccine

#### 6 months–<3 years

Give 2 doses (0.25 mL each), 4 weeks apart, in the first year of vaccination.

Give 1 dose (0.25 mL) in subsequent years.

#### 3–<9 years

Give 2 doses (0.5 mL each), 4 weeks apart, in the first year of vaccination.

Give 1 dose (0.5 mL) in subsequent years.

#### ≥9 years

Give 1 dose (0.5 mL) every year.  

* Whenever possible, 13vPCV dose(s) should precede the recommended 23vPPV dose(s). If 13vPCV follows 23vPPV, a minimum interval of 12 months between 13vPCV and the last previous 23vPPV dose is recommended. The recommended minimum interval between a 13vPCV dose and a subsequent 23vPPV dose is 2 months. Also note that the recommended minimum interval between any two 23vPPV doses is 5 years.

† If asplenia is diagnosed at age ≥65 years (age ≥50 years for Indigenous adults), only a single revaccination dose of 23vPPV is recommended.

‡ MenBV can be given from 6 weeks of age to align with the schedule for other routine infant vaccines. The co-administration of MenBV and 4vMenCV in persons who are at increased risk of meningococcal disease is acceptable based on first principles. (Refer also to 4.10 (Handbook10-home-handbook10part4-handbook10-4-10#table-4-10-1)).

§ Two doses of influenza vaccine in the first year influenza vaccine is given are required if the asplenic person has another underlying immunocompromising condition such as post SOT or HSCT.

### 3.3.4 Vaccination of recent recipients of normal human immunoglobulin and other blood products

The immune response to live parenteral viral vaccines (with the exception of yellow fever and zoster vaccine) may be inhibited by normal human immunoglobulin (NHIG). The interval recommended is dependent on the type and half-life of the immunoglobulin administered (refer to Table 3.3.6 Recommended intervals between either immunoglobulins or blood products and MMR, MMRV or varicella vaccination and 4.8 (Handbook10-home-handbook10part4-handbook10-4-8#table-4-8-4) Japanese encephalitis).

Rotavirus vaccine may be administered at any time before or after, or concurrently with, any blood product, including antibody-containing products, following the routinely recommended schedule for rotavirus vaccine among infants who are eligible for vaccination (refer to 4.17 (Handbook10-home-handbook10part4-handbook10-4-17#table-4-17-17)). Rotavirus. Minimal data are available on the impact of blood products on the immune response to the vaccine in these infants. Completing the full rotavirus vaccine series will optimise protection.  

Zoster vaccine can be given at any time before or after administration of immunoglobulin, or any antibody-containing blood product, because those for whom it is registered (persons ≥50 years of age) are assumed to have had a previous VZV infection and, therefore, already have serum antibody levels comparable to those found in blood products (refer to 4.24 (Handbook10-home-handbook10part4-handbook10-4-24#table-4-24-4) Zoster).

BCG vaccine can be given at any time before or after administration of immunoglobulin or any antibody-containing blood product (refer to 4.20 (Handbook10-home-handbook10part4-handbook10-4-20#table-4-20-4) Tuberculosis).

In persons with agammaglobulinaemia who are receiving monthly NHIG, the use of live vaccines is not recommended as the immune response may be inhibited. In addition, these people will have sufficient circulating antibody (e.g. measles, varicella) from the NHIG to protect them in the case of exposure. Inactivated vaccines are recommended as per the routine schedule; the response may be suboptimal, but these vaccines are safe to administer.

Persons, who have received a blood transfusion, including mass blood transfusions, do not require any past vaccinations to be repeated. However, following the receipt of any blood product, including plasma or platelets, an interval of 3 to 11 months should elapse, dependent on the blood product transfused, before vaccination with an MMR, MMRV or varicella vaccine (refer to Table 3.3.6 Recommended intervals between either immunoglobulins or blood products and MMR, MMRV or varicella vaccination). An interval is suggested because there may be low levels of antibodies present in the blood product that may impair the immune response to the live vaccine.
### Table 3.3.6: Recommended intervals between either immunoglobulins or blood products and measles-mumps-rubella (MMR), measles-mumps-rubella-varicella (MMRV) or varicella vaccination*<sup>177</sup>

<table>
<thead>
<tr>
<th>Immunoglobulin/blood product</th>
<th>Route</th>
<th>Dose Estimated mg IgG/kg</th>
<th>Dose IU or mL</th>
<th>Interval (months)</th>
</tr>
</thead>
<tbody>
<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>Cytomegalovirus immunoglobulin</td>
<td>IV</td>
<td>3 mL/kg</td>
<td>150</td>
<td>6</td>
</tr>
<tr>
<td>HBIG as hepatitis B prophylaxis</td>
<td>IM</td>
<td>100 IU</td>
<td>10</td>
<td>3</td>
</tr>
<tr>
<td>NHIG (intravenous) for ITP treatment</td>
<td>IV</td>
<td>400 IU</td>
<td>8</td>
<td></td>
</tr>
<tr>
<td>NHIG (intravenous) for ITP treatment</td>
<td>IV</td>
<td>1000 IU</td>
<td>10</td>
<td></td>
</tr>
<tr>
<td>NHIG (intravenous) for ITP or Kawasaki disease treatment</td>
<td>IV</td>
<td>1600–2000 IU</td>
<td>11</td>
<td></td>
</tr>
<tr>
<td>NHIG as hepatitis A prophylaxis</td>
<td>IM</td>
<td>0.5 mL (&lt;25 kg)</td>
<td>3</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>1.0 mL (25–50 kg)</td>
<td>5</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>2.0 mL (&gt;50 kg)</td>
<td>6</td>
<td></td>
</tr>
<tr>
<td>NHIG as measles prophylaxis:</td>
<td>IM</td>
<td>(max. dose 15 mL)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Standard</td>
<td></td>
<td>0.2 mL/kg</td>
<td>5</td>
<td></td>
</tr>
<tr>
<td>Immunocompromised</td>
<td></td>
<td>0.5 mL/kg</td>
<td>6</td>
<td></td>
</tr>
<tr>
<td>Plasma or platelet products</td>
<td>IV</td>
<td>10 mL/kg</td>
<td>160</td>
<td>7</td>
</tr>
<tr>
<td>HRIG as rabies prophylaxis</td>
<td>IM</td>
<td>20 IU/kg</td>
<td>22</td>
<td>4</td>
</tr>
<tr>
<td>Replacement (or therapy) of immune deficiencies (as NHIG [intravenous], various doses)</td>
<td>IV</td>
<td>300–400 IU</td>
<td>9</td>
<td></td>
</tr>
<tr>
<td>Rh (D) IG (anti-D)</td>
<td>IM</td>
<td></td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>TIG (IM use) for tetanus prophylaxis</td>
<td>IM</td>
<td>250 IU (given within 24 hours of injury)</td>
<td>10</td>
<td>3</td>
</tr>
<tr>
<td></td>
<td></td>
<td>500 IU (&gt;24 hours after injury)</td>
<td>20</td>
<td></td>
</tr>
<tr>
<td>ZIG as varicella prophylaxis</td>
<td>IM</td>
<td>200 IU (0–10 kg)</td>
<td></td>
<td>5</td>
</tr>
<tr>
<td></td>
<td></td>
<td>400 IU (11–30 kg)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>600 IU (&gt;30 kg)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

* Zoster vaccine can be given at any time before or after administration of immunoglobulin or any antibody-containing blood product.

### 3.3.5 Vaccination of persons with bleeding disorders

Persons who are receiving anticoagulant therapy may develop haematomas in IM injection sites. The length of anticoagulant therapy should be clarified and immunisation delayed if therapy is going to be of short-term duration. Unless warfarin or low molecular weight heparin (LMWH) doses are known to be stable, persons receiving anticoagulants should have appropriate levels checked before vaccine administration, if possible. Intramuscular injections should be deferred if the INR is >3.0 (warfarin) or the anti-Xa (LMWH) level 4 hours post dose is >0.5 Units/mL.

If a person has haemophilia and is receiving clotting factor replacement or similar therapy, IM vaccine administration should be conducted as soon as possible after the medication is received.<sup>177</sup> The site should not be rubbed post administration, but firm pressure applied for approximately 5–10 minutes. Vaccine recipients and/or carers should be informed about the possibility of haematoma formation. Ice and immobilisation may be used in the case of a small haematoma. The subcutaneous route could be considered as an alternative in a person with haemophilia or on anticoagulant therapy; however, the intramuscular route is preferred if that is the usual recommended mode of vaccine administration – seek expert advice. If a vaccine is administered subcutaneously, there may be diminished immune response (e.g. requirement to check anti-HBs antibodies) and additional vaccine doses may be required.<sup>178,179</sup>

### 3.3.6 Vaccination before or after anaesthesia/surgery

Recent or imminent surgery is not a contraindication to vaccinations, and recent vaccination is not a contraindication to surgery (refer to 2.1.4 (Handbook10-home–handbook10part2–handbook10-2-1#2-1-4) Pre-vaccination screening). There are no randomised controlled trials providing evidence of adverse outcomes with anaesthesia and surgery in recently vaccinated children. It is possible that the systemic effects from recent vaccination, such as fever and malaise, may cause confusion in the post-operative period. As the evidence is limited, it is possible to administer vaccines as per the routine schedule, or electively during a procedure for a person in a special risk group, if the appropriate vaccine delivery safety mechanisms are in place.<sup>180</sup>

If elective surgery and anaesthesia are to be postponed, some guidelines recommend postponing for 1 week after inactive vaccination and for 3 weeks after live attenuated viral vaccination in children. Routine vaccination may be deferred for 1 week after surgery.<sup>181</sup>

A person who receives any blood products during surgery will need to be informed of the need to delay some vaccinations (refer to Table 3.3.6 Recommended intervals between either immunoglobulins or blood products and MMR, MMRV or varicella vaccination).

### 3.3.7 Vaccination of persons at occupational risk

Certain occupations, particularly those associated with healthcare, are associated with an increased risk of some vaccine-preventable diseases. Furthermore, some infected workers, particularly healthcare workers and those working in early childhood education and care, may transmit infections such as influenza, rubella, measles, mumps, varicella and pertussis to susceptible contacts, with the potential for serious health outcomes. Many infectious diseases, measles in particular, are highly infectious several days before symptoms become apparent. Healthcare workers employed within the public health system should check local state or territory healthcare worker immunisation requirements and the necessary documentation required (refer to Appendix 1 Contact details for Australian, state and territory government health authorities and communicable disease control).

Where workers are at significant occupational risk of acquiring a vaccine-preventable disease, the employer should implement a comprehensive occupational vaccination program, which includes a vaccination policy, current staff vaccination records, provision of information about the relevant vaccine-preventable diseases, and the management of vaccine refusal (e.g. reducing the risk of a healthcare worker transmitting disease to vulnerable persons). Employers should take all reasonable steps to encourage non-immune workers to be vaccinated.

Current recommended vaccinations for persons at risk of occupationally acquired vaccine-preventable diseases are listed in Table 3.3.7. In addition to the vaccines specific to a person’s occupation and work-related activities recommended here, all adults should be up to date with routinely recommended vaccines, such as dT-containing and MMR vaccines. (Refer also to Table 2.1.12 (Handbook10-home-handbook10part2-handbook10-2-1#table-2-1-12) in 2.1.5 (Handbook10-home-handbook10part2-handbook10-2-1#2-1-5) Catch-up.)

Standard precautions should be adopted where there is risk of occupational exposure to blood and body fluids. Preventive measures include the appropriate handling and disposal of sharps, the donning of gloves when handling body fluids, and the use of goggles/face shields when splashes are likely.

If a non-immune person is exposed to a vaccine-preventable disease, post-exposure prophylaxis should be administered where indicated (refer to relevant disease-specific chapters in Part 4 (Handbook10-home-handbook10part4), and Part 5 (Handbook10-home-handbook10part5) Passive immunisation).

### Table 3.3.7: Recommended vaccinations for persons at increased risk of certain occupationally acquired vaccine-preventable diseases

<table>
<thead>
<tr>
<th>Occupation</th>
<th>Vaccine</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Healthcare workers (HCW)</strong></td>
<td></td>
</tr>
<tr>
<td><strong>All HCW</strong></td>
<td><strong>Hepatitis B</strong></td>
</tr>
<tr>
<td>Includes all workers and students directly involved in patient care or</td>
<td><strong>Influenza</strong></td>
</tr>
<tr>
<td>the handling of human tissue, blood or body fluids</td>
<td><strong>MMR (if non-immune)</strong></td>
</tr>
<tr>
<td>**HCW who work in remote Indigenous communities or with Indigenous</td>
<td><strong>Pertussis (dTpa)</strong></td>
</tr>
<tr>
<td>children in NT, Qld, SA and WA, and other specified healthcare workers</td>
<td><strong>Varicella (if non-immune)</strong></td>
</tr>
<tr>
<td>in some jurisdictions</td>
<td></td>
</tr>
<tr>
<td>**HCW who may be at high risk of exposure to drug-resistant cases of</td>
<td></td>
</tr>
<tr>
<td>tuberculosis (dependent on state or territory guidelines)</td>
<td></td>
</tr>
<tr>
<td><strong>Persons who work with children</strong></td>
<td></td>
</tr>
<tr>
<td>All persons working with children, including:</td>
<td></td>
</tr>
<tr>
<td>• staff and students working in early childhood education and care</td>
<td></td>
</tr>
<tr>
<td>• correctional staff working where infants/children cohabitate with</td>
<td></td>
</tr>
<tr>
<td>mothers</td>
<td></td>
</tr>
<tr>
<td>• school teachers (including student teachers)</td>
<td></td>
</tr>
<tr>
<td>• outside school carers</td>
<td></td>
</tr>
<tr>
<td>• child counselling services workers</td>
<td></td>
</tr>
<tr>
<td>• youth services workers</td>
<td></td>
</tr>
<tr>
<td><strong>Staff working in early childhood education and care</strong></td>
<td></td>
</tr>
<tr>
<td><strong>Carers</strong></td>
<td></td>
</tr>
<tr>
<td><strong>Carers of persons with developmental disabilities</strong></td>
<td></td>
</tr>
<tr>
<td>**Staff of nursing homes and long-term care facilities for persons of</td>
<td></td>
</tr>
<tr>
<td>any age**</td>
<td></td>
</tr>
<tr>
<td>**Providers of home care to persons at risk of high influenza</td>
<td></td>
</tr>
<tr>
<td>morbidity**</td>
<td></td>
</tr>
<tr>
<td><strong>Emergency and essential service workers</strong></td>
<td></td>
</tr>
<tr>
<td><strong>Police and emergency workers</strong></td>
<td></td>
</tr>
<tr>
<td><strong>Armed forces personnel</strong></td>
<td></td>
</tr>
<tr>
<td><strong>Staff of correctional facilities</strong></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Occupation</th>
<th>Vaccine</th>
</tr>
</thead>
<tbody>
<tr>
<td>Staff of detention and immigration centres</td>
<td>Hepatitis B</td>
</tr>
<tr>
<td></td>
<td>Influenza</td>
</tr>
<tr>
<td></td>
<td>MMR (if non-immune)</td>
</tr>
<tr>
<td></td>
<td>Tetanus (dT or dTpa)</td>
</tr>
<tr>
<td>Laboratory personnel</td>
<td></td>
</tr>
<tr>
<td>Laboratory personnel handling veterinary specimens or working with Q fever organism (Coxiella burnetii)</td>
<td>Q fever</td>
</tr>
<tr>
<td>Laboratory personnel handling either bat tissues or lyssaviruses (including rabies virus and Australian bat lyssavirus)</td>
<td>Rabies</td>
</tr>
<tr>
<td>Laboratory personnel routinely working with these organisms:</td>
<td></td>
</tr>
<tr>
<td>Bacillus anthracis</td>
<td></td>
</tr>
<tr>
<td>Corynebacterium diphtheria</td>
<td></td>
</tr>
<tr>
<td>Japanese encephalitis virus</td>
<td></td>
</tr>
<tr>
<td>Neisseria meningitidis</td>
<td></td>
</tr>
<tr>
<td>Poliomyelitis virus</td>
<td></td>
</tr>
<tr>
<td>Salmonella enterica subspecies enterica serovar Typhi (S. Typhi)</td>
<td></td>
</tr>
<tr>
<td>Vaccinia poxviruses</td>
<td></td>
</tr>
<tr>
<td>Yellow fever virus</td>
<td></td>
</tr>
<tr>
<td>Persons who work with specific communities</td>
<td></td>
</tr>
<tr>
<td>Workers who live with, or make frequent visits to, remote Indigenous communities in NT, Qld, SA and WA</td>
<td></td>
</tr>
<tr>
<td>Workers assigned to the outer Torres Strait Islands for a total of 30 days or more during the wet season</td>
<td></td>
</tr>
<tr>
<td>Persons who work with animals</td>
<td></td>
</tr>
<tr>
<td>Veterinarians, veterinary students, veterinary nurses</td>
<td></td>
</tr>
<tr>
<td>Agricultural college staff and students (aged &gt;15 years) exposed to high-risk animals</td>
<td></td>
</tr>
<tr>
<td>Abattoir workers and contract workers in abattoirs (excluding pig abattoirs)</td>
<td></td>
</tr>
<tr>
<td>Livestock transporters</td>
<td></td>
</tr>
<tr>
<td>Sheep shearers and cattle, sheep and dairy farmers</td>
<td></td>
</tr>
<tr>
<td>Those culling or processing kangaroos or camels</td>
<td></td>
</tr>
<tr>
<td>Tanning and hide workers</td>
<td></td>
</tr>
<tr>
<td>Goat farmers</td>
<td></td>
</tr>
<tr>
<td>Livestock saleyard workers</td>
<td></td>
</tr>
<tr>
<td>Those handling animal products of conception</td>
<td></td>
</tr>
<tr>
<td>Wildlife and zoo workers who have contact with at-risk animals, including kangaroos and bandicoots</td>
<td>Q fever</td>
</tr>
<tr>
<td>Persons who come into regular contact with bats (both ‘flying foxes’ and microbats), bat handlers, bat scientists, wildlife officers, zoo curators</td>
<td>Rabies</td>
</tr>
<tr>
<td>Poultry workers and others handling poultry, including those who may be involved in culling during an outbreak of avian influenza, and swine industry workers</td>
<td>Influenza</td>
</tr>
<tr>
<td>Other persons exposed to human tissue, blood, body fluids or sewage</td>
<td></td>
</tr>
<tr>
<td>Embalmers</td>
<td>Hepatitis B</td>
</tr>
<tr>
<td>Workers who perform skin penetration procedures (e.g. tattooists, body-piercers)</td>
<td>Hepatitis B</td>
</tr>
<tr>
<td>Funeral workers and other workers who have regular contact with human tissue, blood or body fluids and/or used needles or syringes</td>
<td>Hepatitis B</td>
</tr>
<tr>
<td>Plumbers or other workers in regular contact with untreated sewage</td>
<td>Hepatitis A</td>
</tr>
<tr>
<td></td>
<td>Tetanus (dT or dTpa)</td>
</tr>
</tbody>
</table>

* Work activities, rather than job title, should be considered on an individual basis to ensure an appropriate level of protection is afforded to each worker. In addition to providing protection against certain vaccine-preventable diseases that persons in these occupations may be at increased risk of acquiring, vaccination may also reduce the risk of transmission of diseases to others with whom these persons are in contact.

† In addition to the vaccines specific to a person's occupation and work-related activities recommended here, all adults should be up to date with routinely recommended vaccines, such as:

‡ Poliomyelitis (IPV)                                                     |
§ Typhoid                                                                |
¶ Smallpox                                                               |
** Yellow fever                                                          |

§§ Q fever

** Work activities, rather than job title, should be considered on an individual basis to ensure an appropriate level of protection is afforded to each worker. In addition to providing protection against certain vaccine-preventable diseases that persons in these occupations may be at increased risk of acquiring, vaccination may also reduce the risk of transmission of diseases to others with whom these persons are in contact.

‡‡ In addition to the vaccines specific to a person’s occupation and work-related activities recommended here, all adults should be up to date with routinely recommended vaccines, such as:

‡‡ Poliomyelitis (IPV)                                            |
¶¶ Typhoid                                                        |
** Yellow fever                                                   |
Inmates of correctional facilities should be up to date with routinely recommended vaccines for influenza, hepatitis A and hepatitis B, and should be vaccinated against these infections.185 Most states and territories provide migrant/refugee immunisation through hospital outpatient departments. Some clinics have also linked families with local general practitioners who are of a similar ethnic and cultural background to ensure ongoing follow-up and referral where required. In addition, some local councils also provide a similar service. Immunisation records, where available for refugees, are likely to have been given to the nominated head of the household at the refugee camp health centre. The Australian Government Department of Immigration and Citizenship (DIAC) may in some circumstances be able to provide further information regarding vaccine(s) administered to refugees before entering Australia, usually by accessing an electronic health manifest. The World Health Organization website lists immunisation schedules for most countries and may provide some information regarding vaccine schedules. (apps.who.int/immunization_monitoring/globalsummary)

If there is a valid record of vaccination from overseas, the history of previous doses should be taken into account when planning a catch-up vaccination schedule. However, some doses may be invalid, as the interval between doses may be too short. This is often the case with oral poliomyelitis vaccines and tetanus vaccines.

If a migrant/refugee has no valid documentation of vaccination, the standard ‘catch-up’ schedule should be commenced. Serological testing to determine the need for specific vaccinations is not routinely recommended in the absence of documented vaccination. However, serology should be offered to migrants from hepatitis B endemic countries to detect past (or current) infection. (Refer also to 4.5(Handbook10-home-handbook10part4-handbook10-4-5#4-5) Hepatitis B). Serology is not routinely recommended in the absence of documentation of MMR-containing vaccines; however, testing for rubella immunity can be performed in migrant women of child-bearing age to identify women who are seronegative and require vaccination (refer to 4.18(Handbook10-home-handbook10part4-handbook10-4-18H4-18) Rubella).

If a child is 212 months of age, the 1st doses of DTPa, hepatitis B, IPV, MMR, MenCCV, 13vPCV and Hib vaccines can be given at the same visit. For details, refer to 2.1.5 (Handbook10-home-handbook10part2-handbook10-2-1#2-1-5) Catch-up. Migrant/refugee adults also need to be targeted for vaccination, especially against rubella, using MMR vaccine. This is particularly important for women of child-bearing age. Some refugees aged between 9 months and 54 years may have been offered MMR as part of a pre-departure screening, but may require a subsequent dose on arrival in Australia.184 It is important to take into account any live attenuated viral vaccines that may have been administered as part of a pre-departure screening, such as measles-containing vaccines or yellow fever vaccine (especially in those persons arriving from central and northern African nations). It is important to allow a minimum 4-week interval before administering any other live attenuated viral vaccines.

All vaccines administered to children <7 years of age should be reported to the Australian Childhood Immunisation Register (ACIR), including vaccinations documented pre-arrival and those for children not enrolled with Medicare. ACIR History Statements can be issued after documented overseas vaccination(s) have been recorded on the ACIR. In addition, vaccinations provided to adolescents via school-based programs are recorded by state/territory health authorities and HPV vaccines should be recorded on the National HPV Vaccination Program Register (NHVPR, or the ‘HPV register’) (refer to 2.3.4(Handbook10-home-handbook10part2-handbook10-2-3R2-3-4) Immunisation registers). It is particularly important to ensure that families are provided with a written record of all vaccines administered, and that all sources of vaccination record checks are checked prior to vaccination, as multiple immunisation providers may have been consulted after arrival.185 186

3.3.9 Vaccination of inmates of correctional facilities

Inmates of correctional facilities are at risk of acquiring influenza, hepatitis A and hepatitis B, and should be vaccinated against these infections (refer to 4.4 (Handbook10-home-handbook10part4-handbook10-4-4#4-4) Hepatitis A, and 4.5(Handbook10-home-handbook10part4-handbook10-4-5#4-5) Hepatitis B and refer to 4.7 (Handbook10-home-handbook10part4-handbook10-4-7#4-7) Influenza).186 In addition, inmates of correctional facilities should be up to date with routinely recommended vaccines for adults, such as dT-containing and MMR vaccines. (Refer also to Table 2.1.12 (Handbook10-home-handbook10part2-handbook10-2-1#2-1-2) Catch-up.)

3.3.10 Vaccination of men who have sex with men

Men who have sex with men are at risk of acquiring hepatitis A and hepatitis B, and should be vaccinated against these infections (refer to 4.4 (Handbook10-home-handbook10part4-handbook10-4-4#4-4) Hepatitis A, and 4.5(Handbook10-home-handbook10part4-handbook10-4-5#4-5) Hepatitis B). Human papillomavirus vaccine may also be indicated (refer to 4.6 Human papillomavirus). In addition, men who have sex with men should be up to date with routinely recommended vaccines for adults, such as dT-containing and MMR vaccines. (Refer also to Table 2.1.2 (Handbook10-home-handbook10part2-handbook10-2-1#2-1-2) in 2.1.5 (Handbook10-home-handbook10part2-handbook10-2-1#2-1-5) Catch-up.)

3.3.11 Vaccination of persons who inject drugs

Persons who inject drugs are at risk of acquiring hepatitis A and hepatitis B, and should be vaccinated against these infections (refer to 4.4 Hepatitis A and 4.5 Hepatitis B). In addition, persons who inject drugs should be up to date with routinely recommended vaccines for adults, such as dT-containing and MMR vaccines. (Refer also to Table 2.1.12 (Handbook10-home-handbook10part2-handbook10-2-1#2-1-2) in 2.1.5 (Handbook10-home-handbook10part2-handbook10-2-1#2-1-5) Catch-up.)

3.3.12 Vaccination of sex industry workers

Sex industry workers are at risk of acquiring hepatitis A and hepatitis B, and should be vaccinated against these infections (refer to 4.4 (Handbook10-home-handbook10part4-handbook10-4-4#4-4) Hepatitis A, and 4.5(Handbook10-home-handbook10part4-handbook10-4-5#4-5) Hepatitis B). Human papillomavirus vaccine may also be indicated (refer to 4.6 Human papillomavirus). In addition, sex industry workers should be up to date with routinely recommended vaccines for adults, such as dT-containing and MMR vaccines. (Refer also to Table 2.1.12 (Handbook10-home-handbook10part2-handbook10-2-1#2-1-2) in 2.1.5 (Handbook10-home-handbook10part2-handbook10-2-1#2-1-5) Catch-up.)

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Part 4 Vaccine-Preventable Diseases

- 4.1 Cholera
- 4.2 Diphtheria
- 4.3 Haemophilus influenzae type b
- 4.4 Hepatitis A
- 4.5 Hepatitis B
- 4.6 Human papillomavirus
- 4.7 Influenza
- 4.8 Japanese encephalitis
- 4.9 Measles
- 4.10 Meningococcal disease
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- 4.13 Pneumococcal disease
- 4.14 Poliomyelitis
- 4.15 Q fever
- 4.16 Rabies and other lyssaviruses (including Australian bat lyssavirus)
- 4.17 Rotavirus
- 4.18 Rubella
- 4.19 Tetanus
- 4.20 Tuberculosis
- 4.21 Typhoid
- 4.22 Varicella
- 4.23 Yellow fever
- 4.24 Zoster (herpes zoster)
4.1.1 Bacteriology

Vibrio cholerae is a motile, curved Gram-negative bacillus. Differences in the O antigens have led to the description of more than 150 serogroups, only two of which have been found to cause cholera. Cholera is caused by enterotoxin-producing V. cholerae of serogroups O1 and O139 (sometimes referred to as the ‘Bengal’ strain). Serogroup O1 includes two biotypes (classical and El Tor), each of which includes organisms of Inaba, Ogawa and Hikojima serotypes. The ability of V. cholerae to persist in water is determined by the temperature, pH, salinity and availability of nutrients; it can survive under unfavourable conditions in a viable dormant state.\(^1\) Transmission predominantly occurs when people ingest faecally contaminated food or water.\(^1\)

4.1.2 Clinical features

Cholera is an acute bacterial infection that is generally characterised by the sudden onset of painless, profuse, watery diarrhoea. In rare situations more than half the severe cases will die. Mild cases also occur, as does subclinical infection.\(^1\)

The cholera toxin does not produce intestinal inflammation. The cholera toxin induces secretion of increased amounts of electrolytes into the intestinal lumen, resulting in mild to severe dehydration and, in some cases, metabolic acidosis.

4.1.3 Epidemiology

The disease is usually transmitted via food and water contaminated with human excreta. Seafood such as shellfish obtained from contaminated waters have also been responsible for outbreaks.\(^1\) Cholera is a substantial health burden in developing countries and is considered to be endemic in Africa, Asia, South America and Central America.\(^2\) Cholera epidemics are common in circumstances where food and water supplies can become contaminated, such as after natural disasters and civil unrest.\(^2\) Cases of cholera in Australia (about 2 to 6 cases a year) almost always occur in individuals who have been infected in endemic areas overseas.\(^3\) However, the overall risk of cholera to travellers with access to a safe water source and hygienic food preparation is considered to be low, even when visiting countries where cholera is endemic. The risk of infection has been estimated at 0.2 cases per 100 000 travellers from western countries, and the risk of severe disease is considerably lower,\(^4\) although under-detection and under-reporting of cholera among travellers is likely.\(^2,4,5\)

In 1977, a locally acquired case led to the discovery of V. cholerae in some rivers of the Queensland coast.\(^6\) Because of this, health workers should be aware that sporadic cases of cholera may, on rare occasions, follow contact with estuarine waters. All cases of cholera reported since the commencement of the National Notifiable Diseases Surveillance System in 1991 have been acquired outside Australia, except for 1 case of laboratory-acquired cholera in 1996 and 3 cases in 2006.\(^7,9\) The 3 cases in 2006, reported in Sydney, were linked and associated with consumption of raw imported whitebait.\(^7\) These patients had no history of recent travel to known cholera-endemic areas.\(^7\)

4.1.4 Vaccines

- **Dukoral – CSL Limited and Crucell Sweden AB (inactivated whole-cell V. cholerae O1, in combination with a recombinant cholera toxin B subunit [rCTB]).** Each 3.0 mL liquid vaccine dose vial contains heat and formalin-inactivated Inaba, Ogawa, classic and El Tor strains of V. cholerae O1, 31.25 x 10^8 vibrios of each, combined with 1.0 mg rCTB.

The buffer consists of a sachet of effervescent granules of anhydrous sodium carbonate, sodium bicarbonate, anhydrous citric acid, sodium citrate, saccharin sodium and raspberry flavour. This formulation does not contain aspartame.

Trials of the oral cholera vaccine that contained inactivated whole-cell V. cholerae O1 combined with rCTB have been performed mainly in Bangladesh and Peru.\(^5,14\) The large randomised controlled trial in Bangladesh included over 120 000 children (aged 2–15 years) and women (aged >15 years), with up to 5 years follow-up. About 13 000 children and 8 000 women received 3 doses of the study vaccine. When cholera cases in all age groups were aggregated, the protective efficacy of this vaccine (in a 3-dose regimen with inactivated Escherichia coli as control) was 85%, 6 months after the 3rd dose. The protective efficacy decreased to 62% after 1 year, and to 57% after 2 years.\(^8,10\) On long-term follow-up (up to 5 years) no significant protective efficacy was observed beyond 2 years.\(^8,14\) The efficacy of the vaccine was lower and waned more rapidly in children aged 2–5 years.\(^14\) In this age group, the efficacy was 100% during the first 4–6 months after vaccination, it became non-significant in the latter half of the 1st year of follow-up (during a cholera epidemic), resulting in an overall efficacy of 38% after 1 year; efficacy after 2 years was comparable.\(^8,14\) In contrast, for those aged >5 years, the efficacy estimates were 76%, 78% and 63%, respectively, at these three time points.\(^8,9,14\) The protective efficacy of the vaccine, over a 3-year follow-up period, was not significantly different among those who received a total of 2 doses versus those who received 3 doses (including all ages).\(^8,9\)

A randomised controlled trial in Peru among military recruits aged 16–45 years found a vaccine efficacy of 86% against symptomatic cholera after 2 vaccine doses.\(^12\) Another Peruvian household study showed an overall efficacy of 61% among 2–65-year-olds,\(^12\) after a booster dose given 10 months after a 2-dose primary series.\(^12\) A field effectiveness case-control study in Mozambique, during a mass oral cholera vaccination program in an endemic population aged 22 years, found that 1 or more doses of the inactivated oral cholera vaccine was 78% protective (1–6 months after the 1st dose). The per-protocol effectiveness of 2 doses was 84% (0.5–4.5 months after the 2nd dose).\(^15\)

There is structural similarity and immunologic cross-reactivity between the cholera toxin and the heat-labile toxin of E. coli, which is often associated with ‘travellers’ diarrhoea’. Therefore, it had been suggested that the rCTB-containing vaccine may also provide protection against heat-labile toxin producing enterotoxigenic E. coli (LT-ETEC). A study in short-term Finnish tourists\(^16\) showed that the inactivated oral cholera vaccine also provided a 60% reduction in diarrhoea caused by LT-ETEC. A study in Bangladesh, an endemic area, showed 67% protection against LT-ETEC for 3 months.\(^17\) It can be expected that the inactivated vaccine will reduce the proportion of travellers’ diarrhoea that is caused by LT-ETEC. Approximately 30 to 40% of travellers to developing countries contract travellers’ diarrhoea, with an average of 20% of cases caused by LT-ETEC; hence, the 60% efficacy of the oral inactivated vaccine against LT-ETEC could be expected to prevent up to 15% of travellers’ diarrhoea.\(^18–20\) However, in Australia this vaccine is only registered for the prevention of cholera.

To date, there is no vaccine marketed in Australia to protect against V. cholerae O139. An oral killed whole-cell bivalent cholera vaccine (against both serogroups O1 and O139) has been evaluated in Vietnam.\(^21,22\) More recently, in India, an interim analysis of a cluster-randomised controlled trial reported a protective efficacy of 67% against V. cholerae O1 after 2 years. Specific efficacy against V. cholerae O139 could not be assessed in this study, as cholera episodes caused by this serogroup were not detected.\(^23\)

4.1.5 Transport, storage and handling

Transport according to National vaccine storage guidelines: Store for 5\(^\circ\)C to 8\(^\circ\)C. Do not freeze. Protect from light.

Because the person to be vaccinated will be responsible for looking after the vaccine following purchase, details of how it should be transported (from pharmacy to home) and stored in the...
4.1.6 Dosage and administration

Dukoral is an oral vaccine.

Food and drink should be avoided for 1 hour before and 1 hour after administration of the inactivated cholera vaccine, as the vaccine is acid labile.

Children aged 2–6 years

Three doses are required, given a minimum of 1 week and up to 6 weeks apart. If an interval of more than 6 weeks occurs between any of the doses, re-start the vaccination course.

Dukoral is administered orally. After dissolving the buffer granules in 150 mL of water, half the solution is then poured away and the entire contents of the vaccine vial are mixed with the remaining 75 mL for administration.

Adults and children aged >6 years

Two doses are required, given a minimum of 1 week and up to 6 weeks apart. If the 2nd dose is not administered within 6 weeks, re-start the vaccination course.

Dukoral is administered orally. After dissolving the buffer granules in 150 mL of water, the contents of the vaccine vial are then added to the solution for administration.

Co-administration with other vaccines

The inactivated oral cholera vaccine can be given with, or at any time before or after, other travel vaccines, such as yellow fever or parenteral Vi polysaccharide typhoid vaccines.

However, there should be an interval of at least 8 hours between the administration of the inactivated oral cholera vaccine and oral live attenuated typhoid vaccine (see 4.1.10 Precautions below).

4.1.7 Recommendations

Vaccination against cholera is not an official requirement for entry into any foreign country.

Routine cholera vaccination is not recommended as the risk to travellers is very low, despite the endemicity of cholera in some countries often visited by Australians. Careful and sensible selection of food and water is of far greater importance to the traveller than cholera vaccination.

Cholera vaccination should be considered for travellers at increased risk of acquiring diarrhoeal disease, such as those with achlorhydria, and for travellers at increased risk of severe or complicated diarrhoeal disease, such as those with poorly controlled or otherwise complicated diabetes, inflammatory bowel disease, HIV/AIDS or other conditions resulting in immunocompromise, or significant cardiovascular disease.

Cholera vaccination should also be considered for travellers with considerable risk of exposure to, or acquiring, cholera, such as humanitarian disaster workers deployed to regions with endemic or epidemic cholera.

Dukoral is not registered for use in children aged <2 years and is not recommended for use in this age group.

Booster doses

Booster doses are recommended for those who are at ongoing risk of exposure to cholera.

Children aged 2–6 years who are at ongoing risk should receive a single booster dose 6 months after completion of the primary course. If the interval between primary immunisation and the booster dose is more than 6 months, primary immunisation must be repeated.

Adults and children aged >6 years who are at ongoing risk should receive a single booster dose up to 2 years after completion of the primary course. If the interval between primary immunisation and the booster dose is more than 2 years, primary immunisation must be repeated.

4.1.8 Pregnancy and breastfeeding

Cholera vaccine is not routinely recommended for pregnant or breastfeeding women.

There is limited information on the use of inactivated oral cholera vaccines during pregnancy and breastfeeding.25

Refer to 3.3 Groups with special vaccination requirements, Table 3.3.1 Recommendations for vaccination in pregnancy(Handbook10-home~handbook10part3~handbook10-3-3#table-3-3-1) for more information.

4.1.9 Contraindications

The only absolute contraindications to cholera vaccine are:

- anaphylaxis following a previous dose of the vaccine
- anaphylaxis following any vaccine component.

4.1.10 Precautions

Postpone administration of cholera vaccine during either an acute febrile illness or acute gastrointestinal illness with persistent diarrhoea or vomiting, until recovered.

Although the vaccine is not contraindicated in people who are immunocompromised, including those with HIV infection, data on effectiveness in this population are limited.

There should be an interval of at least 8 hours between the administration of the inactivated oral cholera vaccine and oral live attenuated typhoid vaccine, as the buffer in the cholera vaccine may affect the transit of the capsules of oral typhoid vaccine through the gastrointestinal tract.

4.1.11 Adverse events

The inactivated oral cholera vaccine has a good safety profile, with similar rates of adverse events reported among vaccine and placebo clinical trial participants.12,16,25 Mild abdominal pain, discomfort and diarrhoea were reported in post-marketing surveillance at a frequency of 0.1–1%.25

4.1.12 Public health management of cholera

Cholera is a notifiable and quarantinable disease in all states and territories in Australia.

Further instructions about the public health management of cholera, including management of cases of cholera and their contacts, should be obtained from state/territory public health authorities (see Appendix 1 (Handbook10-home~handbook10-tools~handbook10-appendices~handbook10-appendix1)Contact details for Australian, state and territory government health authorities and communicable disease control).

4.1.13 Variations from product information

The production information for Dukoral states that a booster dose is recommended for adults 2 years after the completion of the primary vaccine course if there is an ongoing risk of cholera.

The ATAGI recommends that a booster dose is also recommended 2 years after the completion of the vaccine course for children >6 years of age if there is an ongoing risk of cholera.

References


4.2.1 Bacteriology
Diphtheria is an acute illness caused by toxigenic strains of Corynebacterium diphtheriae, a Gram-positive, non-sporing, non-capsulate bacillus. The exotoxin produced by C. diphtheriae acts locally on the mucous membranes of the respiratory tract or, less commonly, on damaged skin, to produce an adherent pseudomembrane. Systemically, the toxin acts on cells of the myocardium, nervous system and adrenals.

4.2.2 Clinical features
The incubation period is 2 to 5 days. The disease is communicable for up to 4 weeks, but carriers may shed organisms for longer. Spread is by aerosol transmission or by direct contact with skin lesions or articles soiled by infected persons. The disease can involve almost any mucous membrane. Pharyngeal diphtheria, by far the commonest form of disease in the unimmunised, is characterised by an inflammatory exudate that forms a greyish or green membrane in the upper respiratory tract, which can cause acute severe respiratory obstruction. Life-threatening complications from diphtheria toxin include myocarditis and neuritis (usually affecting motor nerves). The case-fatality rate in the last three decades has been reported as up to 16%.1 Diphtheria antitoxin, which neutralises unbound toxin, was first used in the 1890s. Together with antibiotics, antitoxin is the mainstay of treatment for diphtheria, but this may not always be successful. The first death from diphtheria in Australia for over 20 years occurred in 2011 in an unvaccinated person.2 Effective protection against diphtheria is only achieved by active immunisation with diphtheria toxoid-containing vaccines.1,3

4.2.3 Epidemiology
In the early 1900s, diphtheria caused more deaths in Australia than any other infectious disease, but increasing use of diphtheria vaccines since World War II has led to its virtual elimination.4 The current epidemiology of diphtheria in Australia is similar to that in other developed countries. Almost all recent cases in the United Kingdom and the United States have been associated with imported infections.5 In Australia, there have been two imported infections identified, one case in 2001 and one imported infection in 2011, resulting in two additional cases, including one death.6,7 The 2011 fatal case of pharyngeal diphtheria occurred in an unvaccinated person infected by a friend who acquired diphtheria in a less developed country.2

4.2.4 Vaccines
Diphtheria toxoid is available in Australia only in combination with tetanus, with or without other antigens such as pertussis, inactivated poliomyelitis, hepatitis B and Haemophilus influenzae type b.

The acronym DTPa, using capital letters, signifies child formulations of diphtheria, tetanus and acellular pertussis-containing vaccines. The acronym dTpa is used for formulations that contain substantially lesser amounts of diphtheria toxoid and pertussis antigens than child (DTPa-containing) formulations; dTpa vaccines are usually used in adolescents and adults.

Diphtheria vaccination stimulates the production of antitoxin, which protects against the toxin produced by the organism. The immunogen is prepared by treating a cell-free preparation of C. diphtheriae with formalin. The toxoid (diphtheria antitoxin) is purified from horses and precipitated with aluminium hydroxide.

The circulating levels of antitoxin required for protection from diphtheria are well described. Antitoxin levels of <0.01 IU/mL are poorly protective, 0.01 to 0.1 IU/mL are usually protective, and ≥0.1 IU/mL are associated with more certain and prolonged protection.9 Complete immunisation induces protective levels of antitoxin lasting throughout childhood, but, by middle age, at least 50% of persons not vaccinated since childhood have levels <0.1 IU/mL.8,10 This has been confirmed in Australia by a national serosurvey.11 Single low doses of toxoid in previously immunised adults induce protective levels within 6 weeks.12

Formulations for children aged <10 years

- **Hexaxim** – Sanofi-Aventis Australia Pty Ltd (DTPa-hepB-IPV-Hib; diphtheria-tetanus-acellular pertussis-hepatitis B-inactivated poliovirus-Haemophilus influenzae type b). Each 0.5 mL pre-filled syringe contains ≥20 IU diphtheria toxoid, ≥40 IU tetanus toxoid, 25 µg pertussis toxin (PT), 25 µg filamentous haemagglutinin (FHA), 10 µg recombinant HibSAg, 40 D-antigen units inactivated poliovirus type 1 (Mahoney), 8 D-antigen units type 2 (MEF-1), 32 D-antigen units type 3 (Saukett) and 12 µg purified Hib capsular polysaccharide (PRP) conjugated to 22–36 µg tetanus toxoid, adsorbed onto 0.6 mg aluminium as aluminium hydroxide. May contain traces of glutaraldehyde, formaldehyde, neomycin, streptomycin and polymyxin B.

- **Infanrix** – GlaxoSmithKline Australia Pty Ltd (DTPa; diphtheria-tetanus-acellular pertussis). Each 0.5 mL monodose vial or pre-filled syringe contains ≥30 U diphtheria toxoid, ≥40 IU tetanus toxoid, 25 µg PT, 25 µg FHA, 8 µg pertactin (PRN), adsorbed onto 0.5 mg aluminium as aluminium hydroxide. May contain traces of glutaraldehyde, formaldehyde, neomycin, streptomycin and polymyxin B.

- **Infanrix hexa** – GlaxoSmithKline Australia Pty Ltd (DTPa-hepB-IPV-Hib; diphtheria-tetanus-acellular pertussis-hepatitis B-inactivated poliovirus-Haemophilus influenzae type b). The vaccine consists of both a 0.5 mL pre-filled syringe containing ≥30 IU diphtheria toxoid, ≥40 IU tetanus toxoid, 25 µg PT, 25 µg FHA, 8 µg PRN, 10 recombinant HibSAg, 40 D-antigen units inactivated poliovirus type 1 (Mahoney), 8 D-antigen units type 2 (MEF-1) and 32 D-antigen units type 3 (Saukett), adsorbed onto aluminium hydroxide/phosphate; traces of formaldehyde, polysorbate 80, polysorbate 20, polyoxymethylene and a vial containing a lyophilised pellet of 10 µg purified Hib capsular polysaccharide (PRP) conjugated to 20–40 µg tetanus toxoid. May contain yeast proteins.

- **Infanrix IPV** – GlaxoSmithKline Australia Pty Ltd (DTPa-IPV; diphtheria-tetanus-acellular pertussis-inactivated poliovirus). Each 0.5 mL pre-filled syringe contains ≥30 IU diphtheria toxoid, ≥40 IU tetanus toxoid, 25 µg PT, 25 µg FHA, 8 µg PRN, 40 D-antigen units inactivated poliovirus type 1 (Mahoney), 8 D-antigen units type 2 (MEF-1) and 32 D-antigen units type 3 (Saukett), adsorbed onto aluminium hydroxide; traces of formaldehyde, polysorbate 80, polyoxymethylene and a vial containing a lyophilised pellet of 10 µg purified Hib capsular polysaccharide (PRP) conjugated to 20–40 µg tetanus toxoid. May contain yeast proteins.

- **Quadracel** – Sanofi Aventis Australia Pty Ltd (DTPa; diphtheria-tetanus-acellular pertussis-inactivated poliovirus). Each 0.5 mL monodose vial contains ≥30 IU diphtheria toxoid, ≥40 IU tetanus toxoid, 20 µg PT, 20 µg FHA, 3 µg PRN, 5 µg FIM 2+3, 40 D-antigen units inactivated poliovirus type 1 (Mahoney), 8 D-antigen units type 2 (MEF-1) and 32 D-antigen units type 3 (Saukett); 1.5 mg aluminium phosphate; ≤50 ng bovine serum albumin; phenoxethanol as preservative; traces of formaldehyde, glutaraldehyde, polysorbate 80, polyoxymethylen and neomycin.

- **Tripacel** – Sanofi Aventis Australia Pty Ltd (DTPa; diphtheria-tetanus-acellular pertussis). Each 0.5 mL monodose vial contains ≥30 IU diphtheria toxoid, ≥40 IU tetanus toxoid, 10 µg PT, 5 µg FHA, 3 µg PRN, 5 µg FIM 2+3; 1.5 mg aluminium phosphate; 3.4 mg phenoxethanol.

Reduced antigen formulations for adults, adolescents and children aged ≥10 years


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4.2.5 Transport, storage, and handling
Transport according to National vaccine storage guidelines: Strive for 5.\textsuperscript{15} Store at +2°C to +8°C. Do not freeze. Protect from light.

Infanrix hexa must be reconstituted by adding the entire contents of the syringe to the vial and shaking until the pellet is completely dissolved. Reconstituted vaccine should be used as soon as practicable. If storage is necessary, hold at room temperature for not more than 8 hours.

4.2.6 Dosage and administration
The dose of all diphtheria-containing vaccines is 0.5 mL, to be given by IM injection.

Do not mix DTPa- or dTPa-containing vaccines or DT vaccine with any other vaccine in the same syringe, unless specifically registered for use in this way.

4.2.7 Recommendations
Infants and children

Primary doses
Diphtheria toxoid is given in combination with tetanus toxoid and acellular pertussis as DTPa-containing vaccines. The recommended 3-dose primary schedule is at 2, 4 and 6 months of age. The 1st dose can be given as early as 6 weeks of age, due to the high morbidity and occasional mortality associated with pertussis in very young infants. If the 1st dose is given at 6 weeks of age, the next scheduled doses should still be given at 4 months and 6 months of age (refer to 4.12 Pertussis(Handbook10-home-handbook10part4-handbook10-4-12)).

Booster doses
Two booster doses of DTPa-containing vaccine are recommended during childhood (at 18 months and 4 years of age) to provide ongoing protection against pertussis through to early adolescence (refer to 4.12 Pertussis(Handbook10-home-handbook10part4-handbook10-4-12)).

For details on the management of children who require catch-up vaccination for diphtheria, including minimum acceptable intervals between vaccine doses, refer to 2.1.5 Catch-up (Handbook10-home-handbook10part2-handbook10-2-1#2-1-5).

Older children and adolescents
An additional booster dose (i.e. in addition to those recommended for young children, refer above) is recommended for adolescents between 10 and 17 years of age, using the reduced antigen content dTpa. The optimal age for administering this dose is 11–13 years, particularly due to waning of the pertussis antibody response following the booster dose recommended at 4 years of age. (refer to 4.12 Pertussis(Handbook10-home-handbook10part4-handbook10-4-12)) This adolescent booster dose of diphtheria-containing vaccine is essential for maintaining immunity to diphtheria (and tetanus and pertussis) into adulthood.

It is recommended to use the reduced antigen content of dTpa for booster doses. However, when necessary, dT can also be used for the booster dose or, if necessary, for the primary dT course, in persons aged ≥10 years (refer to 4.2.12 Variations from product information below).

For details on the management of children and adolescents who require catch-up vaccination for diphtheria, refer to 2.1.5 Catch-up (Handbook10-home-handbook10part2-handbook10-2-1#2-1-5).

Adults

Booster doses
All adults who reach the age of 50 years without having received a booster dose of dT in the previous 10 years should receive a further diphtheria booster dose. This should be given as dTpa, to also provide protection against pertussis (refer to 4.12 Pertussis(Handbook10-home-handbook10part4-handbook10-4-12)). This stimulates further production of circulating diphtheria antibodies at an age when waning of diphtheria and tetanus immunity is commencing in the Australian population.\textsuperscript{11}

A single booster dose of dTpa is also recommended for adults aged ≥65 years (if not received in the previous 10 years), for protection against pertussis (refer to 4.12 Pertussis (Handbook10-home-handbook10part4-handbook10-4-12)).

Diphtheria can be a significant risk for travellers to some countries (particularly Southeast Asia, New Guinea, the states of the former Soviet Union, Baltic countries or eastern European countries). Travellers to countries where health services are difficult to access may require additional protection against diphtheria before departure. They should receive a booster dose of dT (or dTpa if not given previously) if more than 10 years have elapsed since the last dose of dT-containing vaccine.

For persons undertaking travel to a country in which there is a high risk of diphtheria, consider giving a booster dose of either dTpa or dT (as appropriate) if more than 5 years have elapsed since the last dose of dT-containing vaccine.

Persons who may be occupationally exposed to toxigenic Corynebacterium diphtheriae should consider a booster dose of either dTpa or dT (as appropriate) if more than 10 years have elapsed since the last dose of dT-containing vaccine. Serology should be conducted at an interval of not less than 10-yearly.

Primary doses
Persons who have not received any diphtheria vaccines are also likely to have missed tetanus vaccination. Therefore, 3 doses of dT should be given at minimum intervals of 4 weeks, followed by booster doses at 10 and 20 years after the primary course. One of these 3 doses (preferably the 1st) should be given as dTpa, to also provide additional protection against pertussis. In the event that dT vaccine is not available, dTpa can be used for all primary doses.\textsuperscript{14}

For additional information on adults with no history of a primary course of dT vaccine requiring catch-up, refer to 2.1.5 Catch-up (Handbook10-home-handbook10part2-handbook10-2-1#2-1-5)
In some circumstances where protection against pertussis is required as soon as possible, a single dose of dTpa vaccine can be administered at any time after a dose of tetanus- and diphtheria-containing vaccine (refer to 4.12 Pertussis(Handbook10-home-handbook10part4-handbook10-4-12)). If providing dT or dTpa vaccine as part of a dT catch-up schedule in adults or children aged ≥10 years, the recommended minimum intervals between doses should be met (refer to 2.2(Handbook10-home-handbook10part2-handbook10-4-2) Administration of vaccines).

4.2.8 Pregnancy and breastfeeding

Although dT vaccines are not routinely recommended for pregnant women, they can be given under certain circumstances, such as for management of a tetanus-prone wound (refer to 4.19 Tetanus(Handbook10-home-handbook10part4-handbook10-4-19)).

dTpa vaccine is recommended for pregnant women (in the third trimester of each pregnancy) to prevent pertussis in pregnant women and their newborns (refer to 4.12 Pertussis (Handbook10-home-handbook10part4-handbook10-4-12)).

dT or dTpa vaccines can be given to breastfeeding women.

Refer to 3.3 Groups with special vaccination requirements, Table 3.3.1(Handbook10-home-handbook10part3-handbook10-3-3#table-3-3-1) Recommendations for vaccination in pregnancy for more information.

4.2.9 Contraindications

The only absolute contraindications to diphtheria-containing vaccines are:

- anaphylaxis following a previous dose of any diphtheria-containing vaccine
- anaphylaxis following any vaccine component.

4.2.10 Adverse events

Mild discomfort or pain at the injection site persisting for up to a few days is common. Administration of more than one dose of a dT-containing vaccine in a 5-year period in previously immunised adults had previously been thought to be associated with an increased risk of injection site reactions. However, recent studies indicate that, in adults and adolescents, the adverse reactions to a single dose of dTpa are similar whether administered shortly (18 months) or at a longer interval after a previous dose of a vaccine containing tetanus/diphtheria toxoids.16-19 (Refer also to 4.12 Pertussis(Handbook10-home-handbook10part4-handbook10-4-12).)

Uncommon general adverse events following dT vaccine include headache, lethargy, malaise, myalgia and fever. Anaphylaxis, urticaria and peripheral neuropathy occur very rarely. Brachial neuritis (inflammation of a nerve in the arm, causing weakness or numbness) has been described following the administration of tetanus toxoid-containing vaccines, with an estimated excess risk of approximately 0.5–1 in 100 000 doses in adults.20-21 For specific adverse events following combination vaccines containing both diphtheria and pertussis antigens, refer to 4.12 Pertussis(Handbook10-home-handbook10part4-handbook10-4-12).

4.2.11 Public health management of diphtheria

Diphtheria is a notified disease in all states and territories in Australia.

Further instructions about the public health management of diphtheria, including management of cases of diphtheria and their contacts, should be obtained from state/territory health authorities (refer to Appendix 1(Handbook10-home-handbook10-tools-handbook10 appendices-handbook10-appendix1) Contact details for Australian, state and territory government health authorities and communicable disease control).

Confirmed or suspected diphtheria is of considerable public health importance and should be notified immediately to state/territory public health authorities. In general, contacts of a proven or presumptive diphtheria case will require vaccination (either primary or booster, depending on vaccination status), and appropriate prophylactic antibiotics22 (refer to 4.12 Pertussis (Handbook10-home-handbook10part4-handbook10-4-12)).

Advice should be sought with respect to diphtheria antitoxin access and dosage, and special arrangements made if hypersensitivity is suspected; this can be coordinated through the relevant state/territory health authority (refer to Appendix 1(Handbook10-home-handbook10-tools-handbook10 appendices-handbook10-appendix1) Contact details for Australian, state and territory government health authorities and communicable disease control and Part 5 Passive immunisation).

4.2.12 Variations from product information

The product information for Infanrix states that this vaccine is indicated for primary immunisation of infants from the age of 2 months to 12 months and as a booster dose for children from 15 months to 6 years of age who have previously been vaccinated against diphtheria, tetanus and pertussis. The ATAGI recommends that this vaccine may also be used for catch-up of the primary schedule or as a booster in children <10 years of age. The ATAGI also recommends that the primary schedule may be commenced at 6 weeks of age, if required.

The product information for Infanrix hexa states that this vaccine is indicated for primary immunisation of infants from the age of 6 weeks and as a booster dose for children 18 months of age if boosting is required for all antigens. The ATAGI recommends that this vaccine may also be used for catch-up of the primary schedule or as a booster in children <10 years of age.

The product information for Infanrix IPV states that this vaccine is indicated for use in a 3-dose primary schedule for immunisation of infants from the age of 6 weeks and as a single booster dose for children ≤6 years of age who have previously been vaccinated against diphtheria, tetanus, pertussis and poliomyelitis. In addition, the ATAGI recommends that this product may also be used for catch-up of the primary schedule or as a booster in children <10 years of age.

The product information for Quadracel states that this vaccine is indicated for use in a 3-dose primary schedule from the age of 2 months to 12 months and may also be used as a booster dose for children from 15 months to 6 years of age who have previously been vaccinated against diphtheria, tetanus, pertussis and poliomyelitis. The ATAGI recommends that, when appropriate, this product may also be used for either catch-up of the primary schedule or as a booster dose in children aged <10 years. The ATAGI also recommends that the primary schedule may be commenced at 6 weeks of age, if required.

The product information for Tripacel states that this vaccine is indicated for use in a 3-dose primary schedule from the age of 2 months to 12 months and may also be used as a booster dose for children from 15 months to 6 years of age who have previously been vaccinated against diphtheria, tetanus and pertussis. The ATAGI recommends that, when appropriate, this product may also be used for either catch-up of the primary schedule or as a booster dose in children aged <10 years. The ATAGI also recommends that the primary schedule may be commenced at 6 weeks of age, if required.

The product information for ADT Booster states that this vaccine is indicated for use as a booster dose only in children aged ≤5 years and adults who have previously received at least 3 doses of diphtheria and tetanus vaccines. The ATAGI recommends instead that, where a dT vaccine is required, ADT Booster can be used, including for primary immunisation against diphtheria and tetanus (for any person ≥10 years of age).

The product information for Adacel and Boostrix (reduced antigen content dTpa) states that these vaccines are indicated for booster doses only. The ATAGI recommends instead that, when a 3-dose primary course of diphtheria/tetanus toxoids is given to an adolescent/adult, dTpa should replace the 1st dose of dT, with 2 subsequent doses of dT. If dT is not available, dTpa can be used for all 3 primary doses.

The product information for Adacel states that vaccination in pregnancy is not recommended unless there is a definite risk of acquiring pertussis. The product information for Boostrix states that the vaccine should be used during pregnancy only when clearly needed, and the possible advantages outweigh the possible risks for the fetus. The ATAGI recommends that pregnant women receive a dose with every pregnancy.
The product information for Adacel, Boostrix-IPV and Adacel states that these vaccines are contraindicated in children and adults with encephalopathy of unknown aetiology or with neurologic complications occurring within 7 days following a vaccine dose. The ATAGI recommends instead that, if protection against pertussis is required, dTpa-containing vaccines can be administered at any time following receipt of a dT-containing vaccine.

The product information for Adacel Polio states that dTpa-containing vaccine should not be given within 3 years of a tetanus toxoid-containing vaccine. The ATAGI recommends instead that, if protection against pertussis is required, dTpa-containing vaccines can be administered at any time following receipt of a dT-containing vaccine.

The product information for Boostrix, Boostrix-IPV and Adacel states that dTpa-containing vaccine should not be given within 5 years of a tetanus toxoid-containing vaccine. The ATAGI recommends instead that, if protection against pertussis is required, dTpa-containing vaccines can be administered at any time following receipt of a dT-containing vaccine.

The ATAGI recommends that pregnant women receive a booster dose every pregnancy and that other adults in contact with infants and/or at increased risk from pertussis can receive a booster dose every 10 years.

The product information for Boostrix-IPV and Adacel states that dTpa-containing vaccine should not be given within 3 years of a tetanus toxoid-containing vaccine. The ATAGI recommends instead that, if protection against pertussis is required, dTpa-containing vaccines can be administered at any time following receipt of a dT-containing vaccine.

The ATAGI recommends that the only contraindication is a history of anaphylaxis to a previous dose or to any of the vaccine components.

References

4.3 Haemophilus influenzae type b

4.3.1 Bacteriology

Haemophilus influenzae is a Gram-negative coccobacillus that is a normal part of upper respiratory tract flora. It can be isolated in two forms: capsular and non-capsular. Strains isolated from respiratory tract specimens, such as sputum and middle ear or sinus fluid, usually do not have a capsule, and are known as non-typeable Haemophilus influenzae (NTHi). Six capsular types (a to f) have been described and, before the introduction of vaccination against Haemophilus influenzae type b (Hib), almost all H. influenzae isolates from sterile sites (blood, cerebrospinal fluid, joint or pleural fluid) were of the b capsular type.1

Before Hib immunisation, invasive disease caused by Hib rarely occurred after the age of 5 years. This was because the prevalence of antibody to Hib progressively increased from the age of 2 years, thought to be related to exposure to Hib (or cross-reacting organisms) colonising the nasopharynx or other sites. Children <2 years of age are usually unable to mount an antibody response to the b capsular polysaccharide, even after invasive disease.2

4.3.2 Clinical features

Clinical categories of invasive disease caused by Hib include meningitis, epiglottitis and a range of other infections such as septic arthritis, cellulitis and pneumonia.3 Hib is rarely isolated from the blood without a focal infection such as the above being evident or developing subsequently. The classical clinical signs of meningitis – neck stiffness and photophobia – are often not detected in infants, who present with drowsiness, poor feeding and high fever. Epiglottitis (inflammation of the epiglottis) presents with respiratory obstruction, associated with soft stridor and often drooling in a pale, febrile, anxious child who remains upright to maximise his or her airway. Meningitis and epiglottitis are almost invariably fatal without appropriate treatment. The case-fatality rate for Hib meningitis in developed countries is at least 3% even with treatment, and 15 to 30% of survivors have permanent neurological sequelae.3 There are no specific clinical features of any of the focal infections due to Hib that enable them to be differentiated from those due to other organisms. However, before the introduction of Hib vaccines, epiglottitis was due to Hib in over 95% of cases.4 Non-typeable Haemophilus influenzae strains may occasionally cause invasive disease, but are a common cause of otitis media in children and bronchitis in adults.2 Hib vaccines are not effective in preventing NTHi infections.

4.3.3 Epidemiology

Since Hib vaccines were included in the routine vaccination schedule in 1993, there has been a reduction of more than 95% in notified cases of Hib disease. In 1992 alone, 549 Hib cases were reported; in contrast, during the 2 years from January 2006 to December 2007, a total of 39 Hib infections were notified in Australia, giving an average annual notification rate of 0.09 per 100,000 population.2,5-7 The reduction in the incidence of Hib disease following routine vaccination has been particularly marked in Indigenous children, although absolute rates remain substantially higher than those in the non-Indigenous population.6,8-10 Similar impressive reductions in Hib disease have been seen in other countries with routine childhood vaccination.11,12 Since Hib disease has become relatively rare, cases of epiglottitis can no longer be assumed to be due to H. influenzae type b and, moreover, even when H. influenzae is isolated from a normally sterile site, it may not be type b. Thus, laboratory confirmation of H. influenzae infection and serotype should always be sought before vaccine failure is assumed.13,14

4.3.4 Vaccines

Four types of conjugate Hib vaccines have been developed, each containing the Hib capsular polysaccharide polylbutosylribitol-phosphate (PRP) conjugated to a different carrier protein. Of these, PRP-OMP (conjugated to the outer membrane protein of Neisseria meningitidis), PRP-T (conjugated to tetanus toxoid) and Haemophilus MenCCV (conjugated to diphtheria toxoid); MenCCV (Hib-MenCCV (which contains meningococcal serogroup C and Haemophilus influenzae type b antigens) has been used under the NIP since July 2013. The Hib PRP-T component in Hib-MenCCV has similar immunogenicity and safety to monovalent PRP-T Hib vaccine.16-21 PRP-OMP vaccines have not been used routinely in Australia since 2009 and were discontinued in 2017. In Australia, the differing epidemiology of invasive Hib disease by ethnicity and region has determined the recommendations for Hib vaccine choice (refer to Handbook10-part3-handbook10-3-1). There are four distinct eras of implementation of the Hib vaccination program for Australian children, which are described in detail elsewhere.10

Some Hib combination vaccines containing acellular pertussis are known to produce lower Hib antibody responses than similar formulations containing whole-cell pertussis.22 When administered according to the United Kingdom’s schedule as 3 primary doses at 2, 3 and 4 months of age without a booster, their use has been associated with an increased risk of vaccine failure.23 In other European countries that routinely give a 4th dose around the time of the 1st birthday, as Australia does, no loss of effectiveness has been observed.24,25
4.3.5 Transport, storage, and handling
Transport according to National vaccine storage guidelines: Strive for 5°C to +8°C. Do not freeze. Protect from light.

Act-HIB must be reconstituted by adding the entire contents of the diluent syringe to the vial and shaking until the powder is completely dissolved. Reconstituted vaccine must be used immediately.

Hiberix must be reconstituted by adding the entire contents of the diluent container to the vial and shaking until the pellet is completely dissolved. Reconstituted vaccine should be used as soon as practicable. If storage is necessary, hold at +2°C to +8°C for not more than 24 hours.

Infanrix hexa must be reconstituted by adding the entire contents of the syringe to the vial and shaking until the pellet is completely dissolved. Reconstituted vaccine should be used as soon as practicable. If storage is necessary, hold at room temperature for not more than 6 hours.

Meritorix must be reconstituted by adding the entire contents of the diluent syringe to the vial and shaking until the powder is completely dissolved. Reconstituted vaccine should be used as soon as practicable. If storage is necessary, hold at +2°C to +8°C for not more than 24 hours.

4.3.6 Dosage and administration
The dose of all Hib-containing vaccines is 0.5 mL to be given by IM injection.

Co-administration with other vaccines
All Hib-containing vaccines may be administered in separate sites on the same day as any of the other childhood vaccines, such as pneumococcal conjugate, hepatitis B, DTPa-containing, inactivated poliomyelitis (IPV or IPV-containing) and monovalent meningococcal C (MenCCV) vaccines. General catch-up vaccination principles outlined in 2.1.5 Catch-up should be followed when planning catch-up schedules for Hib that require the use of Hib-MenCCV.

No or minimal immunologic interference has been observed when children are vaccinated with pneumococcal conjugate vaccines (7vPCV – Prevenar; 13vPCV – Prevenar 13; or 10vPCV – Synflorix) and PRP-T-containing hexavalent vaccine (Infanrix hexa) at the same immunisation visit.37-39

Interchangeability of Hib vaccines
Where possible, the same brand of Hib-containing vaccine should be used for all primary doses. If different Hib-containing vaccines (i.e. PRP-OMP and PRP-T vaccines) are used in the primary series, for example, in a child born overseas, then 3 doses (of any Hib-containing vaccine) are required at 2, 4 and 6 months of age, with a booster of a Hib-containing vaccine at 12 months of age.

For booster doses and in children >16 months of age, regardless of previous Hib vaccinations, a single dose of any Hib-containing vaccine is sufficient for protection.

4.3.7 Recommendations
Infants
A Hib-containing vaccine is recommended in a 3-dose primary schedule for infants at 2, 4 and 6 months of age, followed by a booster dose at 12 months of age (refer to ‘Booster doses’ below).

The 1st dose of a Hib-containing vaccine can be given as early as 6 weeks of age. If the 1st dose is given at 6 weeks of age, the next scheduled doses should still be given at 4 months and 6 months of age.

Booster doses
A single booster dose of Hib-containing vaccine is recommended at 12 months of age (refer to ‘Infants’ above). This can be provided as either the monovalent Hib vaccine or the combination vaccine Hib-MenCCV (refer to 4.10) (Handbook10-home-handbook10part4-handbook10-4-10H4-10) Meningococcal disease).

Children aged >15 months and up to 59 months of age at presentation who have not received a primary course of a Hib or Hib-containing vaccine will only require 1 dose of vaccine as catch-up, irrespective of the number of previous doses administered. There should be a minimum 2-month interval between their last dose and the catch-up dose. Catch-up for Hib vaccination for children up to 59 months of age is outlined in Table 2.1.8 Catch-up schedule for Hib vaccination for children <5 years of age (Handbook10-home-handbook10part2-handbook10-2-1table-2-1-8) in 2.1.5 Catch-up.

Preterm infants
Preterm infants can be immunised according to their chronological age, without correction for prematurity (refer to 3.3.2 Vaccination of women who are planning pregnancy, pregnant or breastfeeding, and preterm infants (Handbook10-home-handbook10part3-handbook10-3-3W-3-3-2)). For PRP-T-containing Hib vaccines, including Infanrix hexa, no change in the usual schedule is required. Preterm infants have been shown to produce good antibody responses to all the antigens in Infanrix hexa following administration at 2, 4 and 6 months of age, although the responses to hepatitis B and Hib are not quite as high as in full-term infants.31

If a PRP-OMP-containing Hib vaccine is used for the primary doses in an extremely preterm and/or low-birth-weight baby (<28 weeks gestation or <1500 g birth weight), an additional dose should be given at 6 months of age; that is, doses should be given at 2, 4, 6 and 12 months of age.

Persons with functional or anatomical asplenia
Hib is an uncommon cause of post-splenectomy sepsis in adults and children. A single dose of Hib vaccine is recommended for persons with functional or anatomical asplenia who were not fully vaccinated in early childhood according to the recommendations above and Table 2.1.8 Catch-up schedule for Hib vaccination for children <5 years of age (Handbook10-home-handbook10part2-handbook10-2-1table-2-1-8). If vaccination is required, the dose should, where possible, be given 2 weeks before a planned splenectomy or at approximately 1 week following an emergency splenectomy. Subsequent booster doses of Hib vaccine are not required.32 For all recommendations for persons with functional or anatomical asplenia, refer to 3.3.3 Vaccination of immunocompromised persons (Handbook10-home-handbook10part3-handbook10-3-3W-3-3-3), Table 3.3.5 Recommendations for vaccination in persons with functional or anatomical asplenia (Handbook10-home-handbook10part3-handbook10-3-3table-3-3-5).

4.3.8 Pregnancy and breastfeeding
Hib vaccine is not routinely recommended for pregnant or breastfeeding women. However, for women who have functional or anatomical asplenia refer to ‘Persons with functional or anatomical asplenia’ above.
4.3.9 Contraindications
The only absolute contraindications to Hib-containing vaccines are:
- anaphylaxis following a previous dose of any Hib-containing vaccine
- anaphylaxis following any vaccine component.

4.3.10 Adverse events
Swelling and redness at the injection site after the 1st dose are common and have been reported in up to 5% of vaccinated children. Fever in up to 2% has also been reported. These adverse events usually appear within 3 to 4 hours of vaccination and resolve completely within 24 hours. The incidence of these adverse events declines with subsequent doses, so it is recommended that the course of vaccination be completed regardless.

4.3.11 Public health management of invasive Hib disease
Haemophilus influenzae type b is a notifiable disease in all states and territories in Australia.

Further instructions about the public health management of Hib, including management of cases of invasive Hib disease and their contacts, should be obtained from state/territory public health authorities (refer to Appendix 1 [Handbook10-home-handbook10-tools-handbook10-appendices-handbook10-appendix1]) Contact details for Australian, state and territory government health authorities and communicable disease control).

4.3.12 Variations from product information
The product information for Infanrix hexa states that this vaccine is indicated for primary immunisation of infants from the age of 6 weeks and as a booster dose for children 18 months of age if boosting is required for all antigens. The ATAGI recommends that this vaccine may also be used for catch-up of the primary schedule in children <10 years of age.

The product information for Hib vaccines indicates that this vaccine is contraindicated in children with encephalopathy of unknown aetiology or with neurologic complications occurring within 7 days following a vaccine dose. The ATAGI recommends instead that the only contraindication is a history of anaphylaxis to a previous dose or to any of the vaccine components.

The product information for Act-Hib and Hiberox states that these vaccines are indicated for use in children aged 2 months to 5 years. The ATAGI also recommends administration of Hib vaccine to older people with asplenia or following either allogeneic or autologous haematopoetic stem cell transplantation.

References


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Hepatitis A is an acute infection of the liver caused by the hepatitis A virus (HAV), a picornavirus (a small single-stranded RNA virus). The virus survives well in the environment outside of the human host. It persists on hands for several hours and in food kept at room temperature for considerably longer, and is relatively resistant to heat and freezing.

4.4.1 Virology

Hepatitis A is an infection of humans; there is no animal reservoir. HAV is predominantly transmitted by the faecal–oral route. The infecting dose is unknown, but it is presumed to be low. The incubation period of hepatitis A is 15 to 50 days, with a mean of about 28 days. HAV is excreted in faeces for up to 2 weeks before the onset of illness and for at least 1 week afterwards.

In young children, HAV usually causes either an asymptomatic infection or a very mild illness without jaundice; adults are more likely to have symptomatic infection (over 70%). Patients with symptomatic illness typically have a 4- to 10-day pro Bradref 1071em of systemic (fever, malaise, weakness and anorexia) and gastrointestinal (nausea and vomiting) symptoms. Dark urine is usually the first specific manifestation of acute hepatitis A infection, followed a day or two later by jaundice and pale faeces. The prodromal symptoms tend to wane with the onset of jaundice, although the anorexia and malaise may persist; pruritus and localised hepatic discomfort or pain may follow. The duration of illness varies, but most patients feel better and have normal, or near normal, liver function tests within a month of the onset of illness. Complications of hepatitis A are uncommon but include, on rare occasions, fulminating hepatitis. The case-fatality rate of hepatitis A increases with age. Hepatitis A does not cause chronic liver disease. Relapse has been found in up to 10% of cases, but recovery is universal. HAV does not cause chronic infection and immunity after infection is lifelong. Diagnosis of hepatitis A is made by detecting anti-HAV IgM in serum during the acute illness. Anti-HAV IgM is invariably present by the time the patient presents and persists for 3 to 6 months after the acute illness. Serum anti-HAV IgG alone indicates past infection (or possibly immunisation) and therefore immunity; it probably persists for life.

4.4.2 Clinical features

Hepatitis A is an infection of humans; there is no animal reservoir. HAV is predominantly transmitted by the faecal–oral route. The infecting dose is unknown, but it is presumed to be low. The incubation period of hepatitis A is 15 to 50 days, with a mean of about 28 days. HAV is excreted in faeces for up to 2 weeks before the onset of illness and for at least 1 week afterwards.

In young children, HAV usually causes either an asymptomatic infection or a very mild illness without jaundice; adults are more likely to have symptomatic infection (over 70%). Patients with symptomatic illness typically have a 4- to 10-day pro Bradref 1071em of systemic (fever, malaise, weakness and anorexia) and gastrointestinal (nausea and vomiting) symptoms. Dark urine is usually the first specific manifestation of acute hepatitis A infection, followed a day or two later by jaundice and pale faeces. The prodromal symptoms tend to wane with the onset of jaundice, although the anorexia and malaise may persist; pruritus and localised hepatic discomfort or pain may follow. The duration of illness varies, but most patients feel better and have normal, or near normal, liver function tests within a month of the onset of illness. Complications of hepatitis A are uncommon but include, on rare occasions, fulminating hepatitis. The case-fatality rate of hepatitis A increases with age. Hepatitis A does not cause chronic liver disease. Relapse has been found in up to 10% of cases, but recovery is universal. HAV does not cause chronic infection and immunity after infection is lifelong. Diagnosis of hepatitis A is made by detecting anti-HAV IgM in serum during the acute illness. Anti-HAV IgM is invariably present by the time the patient presents and persists for 3 to 6 months after the acute illness. Serum anti-HAV IgG alone indicates past infection (or possibly immunisation) and therefore immunity; it probably persists for life.

4.4.3 Epidemiology

Hepatitis A was a considerable public health problem in Australia in the 1990s. During this time, numerous outbreaks occurred in child day-care centres and preschools, Indigenous communities, communities of men who have sex with men, schools and residential facilities for the disabled, and communities of persons who inject drugs. A very large outbreak of hepatitis A associated with the consumption of raw oysters, occurred in New South Wales in 1997 and there was a large outbreak associated with semired tomatoes during 2009, 2010.

In recent years, hepatitis A notifications and hospitalisations have been low with a downward trend. This has been accompanied by an increasing proportion of cases related to travel to countries where hepatitis A is endemic. Advocacy for hepatitis A vaccination of travellers and those at increased risk because of lifestyle or occupation remains a priority, as does the hepatitis A vaccination program for Aboriginal and Torres Strait Islander children. Established initially in north Queensland in 1999 for Indigenous children aged 18 months, the hepatitis A vaccination program was expanded in 2005 to include all Indigenous children aged ≤2 years in the Northern Territory, Queensland, South Australia and Western Australia, contributing substantially to the decline in notifications. In north Queensland, most Indigenous children >2 years of age have now been immunised against hepatitis A. However, it is important to note that Indigenous children remain at considerably greater risk – not only of acquiring hepatitis A, but also for being hospitalised with the infection – than non-Indigenous children. This is particularly true for Indigenous children residing in other regions of Queensland, the Northern Territory, South Australia and Western Australia. (Refer to 3.1 Vaccination for Aboriginal and Torres Strait Islander people.)

4.4.4 Vaccines

Monovalent hepatitis A vaccines

- **Avasim** – Sanofi-Aventis Australia Pty Ltd (formaldehyde-inactivated hepatitis A virus [GBM strain]). Each 0.5 mL pre-filled syringe contains 160 antigen units of hepatitis A virus (HAV) antigens inactivated by formaldehyde; 0.3 mg aluminium as aluminium hydroxide; 2.5 µL phenoxethanol; 12.5 µg formaldehyde; ≤5 µg neomycin; <10 ng bovine serum albumin; traces of polysorbate 80.

- **Havrix Junior** – GlaxoSmithKline (formaldehyde-inactivated hepatitis A virus [HM175 strain]). Each 0.5 mL monodose vial or pre-filled syringe contains 720 ELISA units of HAV antigens; 0.25 mg aluminium as aluminium hydroxide; traces of formaldehyde, neomycin and polysorbate 20.

- **Havrix 1440** – GlaxoSmithKline (formaldehyde-inactivated hepatitis A virus [HM175 strain]). Each 1.0 mL monodose vial or pre-filled syringe contains 1440 ELISA units of HAV antigens; 0.5 mg aluminium as aluminium hydroxide; traces of formaldehyde, neomycin and polysorbate 20.

- **Vaqta Paediatric/Adolescent formulation** – CSL Limited/Merck & Co Inc (formaldehyde-inactivated hepatitis A virus [CR326F strain]). Each 0.5 mL monodose vial or pre-filled syringe contains approximately 25 units (U) of hepatitis A virus protein; 0.25 mg aluminium as aluminium hydroxide; 35 µg borax; traces of formaldehyde, neomycin and bovine serum albumin.

- **Vaqta Adult formulation** – CSL Limited/Merck & Co Inc (formaldehyde-inactivated hepatitis A virus [CR326F strain]). Each 1.0 mL monodose vial or pre-filled syringe contains approximately 50 U of hepatitis A virus protein; 0.45 mg aluminium as aluminium hydroxide; 70 µg borax; traces of formaldehyde, neomycin and bovine serum albumin.

Combination vaccines that contain hepatitis A

- **Twixirix Junior (360/10)** – GlaxoSmithKline (formaldehyde-inactivated hepatitis A virus [HM175 strain] and recombinant hepatitis B vaccine). Each 0.5 mL monodose vial or pre-filled syringe contains 360 ELISA units of HAV antigens, 10 µg recombinant DNA hepatitis B surface antigen protein; 0.225 mg aluminium as aluminium phosphate/hydroxide; traces of formaldehyde, neomycin, trometamol and polysorbate 20. May contain yeast proteins.

- **Twixirix (720/20)** – GlaxoSmithKline (formaldehyde-inactivated hepatitis A virus [HM175 strain] and recombinant hepatitis B vaccine). Each 1.0 mL monodose vial or pre-filled syringe contains 720 ELISA units of HAV antigens, 20 µg recombinant DNA hepatitis B surface antigen protein; 0.45 mg aluminium as aluminium phosphate/hydroxide; traces of formaldehyde, neomycin, trometamol and polysorbate 20. May contain yeast proteins.

- **Vivaxim** – Sanofi-Aventis Australia Pty Ltd (formaldehyde-inactivated hepatitis A virus [GBM strain] and typhoid Vi capsular polysaccharide). Supplied in a dual-chamber syringe which enables the two vaccines to be mixed just before administration. Each 1.0 mL dose of mixed vaccine contains 160 antigen units of inactivated hepatitis A virus antigen, 25 µg purified typhoid Vi capsular polysaccharide strain Ty2; 0.3 mg aluminium as aluminium hydroxide; 2.5 µL phenoxethanol; 12.5 µg formaldehyde; ≤5 µg neomycin; <10 ng bovine serum albumin; traces of polysorbate 80.
Inactivated hepatitis A vaccines are prepared from HAV harvested from human cell cultures, purified by chromatography, inactivated by formaldehyde, and adsorbed onto aluminium hydroxide adjuvant. Although the vaccines are prepared from differing strains of HAV, there is only one known serotype; immunity induced by a particular strain probably provides protection against all strains.\(^1\)

Inactivated hepatitis A vaccines induce HAV antibodies (anti-HAV) at titles many-fold greater than are provided by the recommended dose of normal human immunoglobulin. Although the vaccines are highly immunogenic (refer to below), antibody titres are usually below the detection limits of the routinely available commercial tests for anti-HAV.\(^1\) Therefore, serological testing to assess immunity after vaccination against hepatitis A is neither necessary nor appropriate. Likewise, it is also inappropriate to undertake testing if an individual cannot recall if he/she has been vaccinated against hepatitis A in the past; if no vaccination records are available, vaccination should be advised. However, certain groups of people should be screened for natural immunity to hepatitis A to avoid unnecessary vaccination: those born before 1950; those who spent their early childhood in endemic areas; and those with an unexplained previous episode of hepatitis or jaundice. In addition, it is necessary to test for other causes of hepatitis, in particular hepatitis B, in those with unexplained jaundice.

Hepatitis A vaccines are highly immunogenic in both children and adults, with virtually universal seroconversion 4 weeks after vaccination.\(^1\) The duration of immunity, and therefore protection, following vaccination is not certain. However, vaccine-induced anti-HAV probably persists for many years. There is no current evidence that booster doses are required; in healthy individuals, it is quite possible that they will never be required.\(^2\)

### 4.4.5 Transport, storage and handling

Transport according to National vaccine storage guidelines: Strive for 5.\(^{22}\) Store at +2°C to +8°C. Do not freeze.

### 4.4.6 Dosage and administration

Inactivated hepatitis A vaccines are to be given by IM injection. The recommended doses and schedules are shown in Table 4.4.1.

#### Table 4.4.1: Recommended doses and schedules for use of inactivated hepatitis A and hepatitis A combination vaccines

<table>
<thead>
<tr>
<th>Vaccine</th>
<th>Age of vaccine recipient (years)</th>
<th>Dose (HAV antigen)</th>
<th>Volume per dose (mL)</th>
<th>Number of doses</th>
<th>Vaccination schedule</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Monovalent hepatitis A vaccines</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Avaxim</td>
<td>≥2</td>
<td>160 antigen U</td>
<td>0.5</td>
<td>2</td>
<td>1st dose: day 0 (day of vaccination) 2nd dose: 6 to 36 months after 1st dose</td>
</tr>
<tr>
<td>Havrix Junior</td>
<td>2–&lt;16</td>
<td>720 ELISA U</td>
<td>0.5</td>
<td>2</td>
<td>1st dose: day 0 (day of vaccination) 2nd dose: 6 to 12 months after 1st dose</td>
</tr>
<tr>
<td>Havrix 1440</td>
<td>≥16</td>
<td>1440 ELISA U</td>
<td>1.0</td>
<td>2</td>
<td>1st dose: day 0 (day of vaccination) 2nd dose: 6 to 12 months after 1st dose</td>
</tr>
<tr>
<td>Vaqta Paediatric/Adolescent</td>
<td>1–&lt;18</td>
<td>25 U</td>
<td>0.5</td>
<td>2</td>
<td>1st dose: day 0 (day of vaccination) 2nd dose: 6 to 18 months after 1st dose</td>
</tr>
<tr>
<td>Vaqta Adult</td>
<td>≥18</td>
<td>50 U</td>
<td>1.0</td>
<td>2</td>
<td>1st dose: day 0 (day of vaccination) 2nd dose: 6 to 18 months after 1st dose</td>
</tr>
<tr>
<td><strong>Combination hepatitis A/hepatitis B vaccines</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Twinrix Junior (360/10)  (^†)</td>
<td>1–&lt;16</td>
<td>360 ELISA U</td>
<td>0.5</td>
<td>3</td>
<td>1st dose: day 0 (day of vaccination) 2nd dose: 1 month after 1st dose 3rd dose: 6 months after 1st dose</td>
</tr>
<tr>
<td>Twinrix (720/20)  (^†)</td>
<td>1–&lt;16</td>
<td>720 ELISA U</td>
<td>1.0</td>
<td>2</td>
<td>1st dose: day 0 (day of vaccination) 2nd dose: 6 to 12 months after 1st dose</td>
</tr>
<tr>
<td>Twinrix (720/20)  (^†)</td>
<td>≥16</td>
<td>720 ELISA U</td>
<td>1.0</td>
<td>3</td>
<td>1st dose: day 0 (day of vaccination) 2nd dose: 1 month after 1st dose 3rd dose: 6 months after 1st dose</td>
</tr>
<tr>
<td>Twinrix (720/20)  (^†)</td>
<td>≥16</td>
<td>720 ELISA U</td>
<td>1.0</td>
<td>4</td>
<td>1st dose: day 0 (day of vaccination) 2nd dose: 7 days after 1st dose 3rd dose: 21 days after 1st dose 4th dose: 12 months after 1st dose Note: This accelerated schedule is not suitable for all circumstances. (^2)</td>
</tr>
<tr>
<td><strong>Combination hepatitis A/typhoid vaccine</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Vivaxim</td>
<td>≥16</td>
<td>160 antigen U</td>
<td>1.0</td>
<td>1</td>
<td>1st dose: single dose of Vivaxim (mixed vaccine) on day 0 (day of vaccination) 2nd dose: for long-term protection against hepatitis A, a 2nd dose of hepatitis A-containing vaccine (monovalent hepatitis A vaccine) should be given between 6 and 36 months after the dose of Vivaxim</td>
</tr>
</tbody>
</table>

\(^*\) For more information on combination hepatitis A/hepatitis B vaccines and schedules, refer to 4.5 Hepatitis B (Handbook10-home~handbook10part4~handbook10-4-5).

\(^†\) This schedule should not be used for persons who require prompt protection against hepatitis B, for example, if there is close contact with a person known to be chronically infected with hepatitis B.
Those with chronic liver disease of mild to moderate severity mount a satisfactory immune response following vaccination, but those with end-stage liver disease do not respond as well, and liver transplant recipients may not respond at all.

Hepatitis A vaccination is recommended for persons with chronic liver disease of any aetiology. Persons with chronic liver disease, liver solid organ transplant recipients and/or those chronically infected with either hepatitis B or hepatitis C should be vaccinated, preferably as early in the course of the disease as possible.

Persons whose lifestyle puts them at increased risk of acquiring hepatitis A

Persons whose occupation puts them at increased risk of acquiring hepatitis A include: persons who live or work in rural and remote Indigenous communities and/or persons who regularly provide care for Aboriginal and Torres Strait Islander children in the Northern Territory, Queensland, South Australia and Western Australia; staff working in early childhood education and care; carers of persons with developmental disabilities; and plumbers or sewage workers. Refer to 3.3 Groups with special vaccination requirements, (Handbook10-home-handbook10part3-handbook10-3-3#table3-3-2) Table 3.3.2 Recommended vaccinations for persons at increased risk of certain occupationally acquired vaccine-preventable diseases.

Persons whose occupation puts them at increased risk of acquiring hepatitis A

Persons who engage in certain sexual practices such as anal intercourse (including men who have sex with men and sex industry workers) and persons who inject drugs (including inmates of correctional facilities) may be at increased risk of acquiring hepatitis A. Refer also to 4.4.3 Epidemiology above and 3.3 Groups with special vaccination requirements (Handbook10-home-handbook10part3-handbook10-3-3). Persons with occupational risks of exposure to both hepatitis A and hepatitis B

Persons whose occupation puts them at increased risk of acquiring hepatitis A

Persons whose occupation puts them at increased risk of acquiring hepatitis A include: persons who live or work in rural and remote Indigenous communities and/or persons who regularly provide care for Aboriginal and Torres Strait Islander children in the Northern Territory, Queensland, South Australia and Western Australia; staff working in early childhood education and care; carers of persons with developmental disabilities; and plumbers or sewage workers. Refer to 3.3 Groups with special vaccination requirements, (Handbook10-home-handbook10part3-handbook10-3-3#table3-3-2) Table 3.3.2 Recommended vaccinations for persons at increased risk of certain occupationally acquired vaccine-preventable diseases.

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Persons whose occupation puts them at increased risk of acquiring hepatitis A include: persons who live or work in rural and remote Indigenous communities and/or persons who regularly provide care for Aboriginal and Torres Strait Islander children in the Northern Territory, Queensland, South Australia and Western Australia; staff working in early childhood education and care; carers of persons with developmental disabilities; and plumbers or sewage workers. Refer to 3.3 Groups with special vaccination requirements, (Handbook10-home-handbook10part3-handbook10-3-3). Persons with occupational risks of exposure to both hepatitis A and hepatitis B

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Persons whose occupation puts them at increased risk of acquiring hepatitis A include: persons who live or work in rural and remote Indigenous communities and/or persons who regularly provide care for Aboriginal and Torres Strait Islander children in the Northern Territory, Queensland, South Australia and Western Australia; staff working in early childhood education and care; carers of persons with developmental disabilities; and plumbers or sewage workers. Refer to 3.3 Groups with special vaccination requirements, (Handbook10-home-handbook10part3-handbook10-3-3). Persons with chronic liver disease, liver solid organ transplant recipients and/or those chronically infected with either hepatitis B or hepatitis C

Hepatitis A vaccination is recommended for persons with chronic liver disease of any aetiology. Those with chronic liver disease of mild to moderate severity mount a satisfactory immune response following vaccination, but those with end-stage liver disease do not respond as well, and liver transplant recipients may not respond at all.

Hepatitis A vaccination is recommended for persons who engage in certain sexual practices such as anal intercourse (including men who have sex with men and sex industry workers) and persons who inject drugs (including inmates of correctional facilities) may be at increased risk of acquiring hepatitis A. Refer also to 4.4.3 Epidemiology above and 3.3 Groups with special vaccination requirements (Handbook10-home-handbook10part3-handbook10-3-3). Persons with occupational risks of exposure to both hepatitis A and hepatitis B

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Recommendations for the use of combination hepatitis A/typhoid vaccine

The combination hepatitis A/typhoid vaccine (refer to Table 4.4.1) is recommended as an option for all persons ≥16 years of age who intend travelling to developing countries where there is an increased risk of acquiring hepatitis A and typhoid fever. This combination is particularly useful for those already immunised against hepatitis B.

To provide longer-term protection against hepatitis A, a single dose of a monovalent adult formulation hepatitis A vaccine administered between 6 and 36 months after the single dose of combination hepatitis A/typhoid vaccine is required (refer to Table 4.4.1). If there is a continued risk of typhoid infection, a booster dose of parenteral typhoid Vi polysaccharide vaccine is required 3 years after the single dose of combination hepatitis A/typhoid vaccine. The combination hepatitis A/typhoid vaccine may be used as ‘a booster’ vaccine for hepatitis A if a person received a previous dose of a monovalent adult formulation hepatitis A vaccine; this should be given at a minimum interval of 6 months after the 1st dose of hepatitis A vaccine.

Serological testing for hepatitis A immunity from infection and/or vaccination

Serological testing for immunity to hepatitis A is not recommended before routine administration of hepatitis A vaccine to those in most of the categories above, for example, Aboriginal and Torres Strait Islander children or travellers. However, previous infection with hepatitis A is more likely to have occurred in persons born before 1950, those who spent their early childhood in an endemic area, and those with an unexplained previous episode of hepatitis or jaundice. In such persons, testing for total hepatitis A antibodies or anti-HAV IgG may be indicated, and, if positive, indicates immunity to hepatitis A. Such persons do not need hepatitis A vaccination.

Interpretation of the results of serological testing may be enhanced by discussion with the laboratory that performed the test, ensuring that relevant clinical information is provided.

Serological testing following vaccination is not routinely required.

4.4.8 Pregnancy and breastfeeding

Hepatitis A vaccine is not routinely recommended for pregnant or breastfeeding women, but can be given where vaccination is considered necessary (refer to 4.4.7 Recommendations above).

Refer to 3.3 Groups with special vaccination requirements, Table 3.3.1 Recommendations for vaccination in pregnancy (Handbook10-home-handbook10part3-handbook10-3-3#table-3-3-1) for more information.

4.4.9 Contraindications

The only absolute contraindications to hepatitis A vaccines are:

- anaphylaxis following a previous dose of any hepatitis A vaccine
- anaphylaxis following any vaccine component.

Combination vaccines containing the hepatitis B component are contraindicated in persons with a history of anaphylaxis to yeast.

4.4.10 Adverse events

The most common adverse events following administration of hepatitis A vaccines are mild local events of a short duration, probably caused by the aluminium hydroxide adjuvant. About 15% of adults report headache and approximately 5% report malaise or fatigue following vaccination.26 Up to 20% of children who receive either Havrix or Vaqta experience soreness at the injection site. In both adults and children, systemic adverse events such as headache and fever are much less common than local adverse events.26

Hepatitis A vaccines do not affect liver enzyme levels. They can be safely given to persons with HIV infection, and do not adversely affect either the HIV load or CD4+ cell count.30

4.4.11 Public health management of hepatitis A

Hepatitis A is a notifiable disease in all states and territories in Australia. Detailed information regarding the management of hepatitis A cases and contacts can be found in the national guidelines for control of hepatitis A (http://www.health.gov.au/cdnasongs)31 (www.health.gov.au/cdnasongs).

Further instructions can also be obtained from state/territory public health authorities (refer to Appendix 1 Contact details for Australian, state and territory government health authorities and communicable disease control (Handbook10-home-handbook10tools-handbook10-appendices-handbook10-appendix1)).

Post-exposure prophylaxis using hepatitis A vaccine or normal human immunoglobulin (NHIG) can be used to prevent secondary cases in close contacts of hepatitis A cases. However, vaccination is recommended in preference to NHIG for use in post-exposure prophylaxis in persons ≥12 months of age who are immunocompetent (refer to 5 Passive immunisation (Handbook10-home-handbook10part5)).31

4.4.12 Variations from product information

None.

References

A full reference list is available on the electronic handbook or Immunise Australia website (http://wcmpro01.central.health/internet/immunise/publishing.nsf/Content/home).


4.5.1 Virology

Hepatitis B virus (HBV) contains circular, partially double-stranded DNA. The outer surface of the virus is glycoprotein, which contains the hepatitis B surface antigen (HBsAg). Other important antigenic components are the hepatitis B core antigen (HBeAg) and hepatitis B e antigen (HBeAg). HBsAg is not detectable in serum, but can be detected in liver tissue in persons with acute or chronic hepatitis B infection. HBeAg, and antibodies against HBeAg (anti-HBe) or the HBcAg (anti-HBc), are serological markers of HBV infection. Antibodies against HBsAg (anti-HBs) indicate immunity, which may result from either natural infection or immunisation (in which case there would not be any markers of HBV infection). Persistence of HBeAg denotes infectivity, which is greater if HBeAg and/or HBsAg DNA are also positive. Occult hepatitis B infection is characterised by the presence of HBV DNA in the liver (with or without detectable HBsAg DNA in the serum) and negative HBeAg.

4.5.2 Clinical features

In approximately 30 to 50% of adults, infection causes symptomatic acute hepatitis, but in neonates and young children, particularly those <1 year of age, initial infection is usually asymptomatic. The incubation period is usually 45 to 180 days and the period of communicability extends from several weeks before the onset of acute illness usually to the end of the period of acute illness. Acute illness is clinically indistinguishable from other forms of hepatitis, and symptoms include fever, jaundice, malaise, anorexia, nausea and vomiting, abdominal pain (especially in the right upper quadrant), myalgia, and the passage of dark-coloured urine and light-coloured stools. Jaundice may be preceded by an acute febrile illness with arthralgia or arthritis and rash, most typical of hepatitis B. During recovery, malaise and fatigue may persist for many weeks. Fulminant hepatitis occurs in up to 1% of acute cases.

Following acute infection, approximately 1 to 10% of persons infected in adulthood, but up to 90% of those infected in early infancy, become chronically infected with hepatitis B. Persons chronically infected with HBV are identified by the long-term presence (longer than 6 months) of circulating HBsAg. Those with occult infection may reactivate HBV infection if they become immunocompromised.

Persons with chronic HBV infection are capable of transmitting the disease, including mother-to-child peripartum transmission, though they often remain asymptomatic and may not be aware that they are infected. Most of the serious complications associated with hepatitis B occur in the context of chronic HBV infection, which is associated in up to 25% of cases with premature mortality due to cirrhosis and/or hepatocellular carcinoma.

4.5.3 Epidemiology

The prevalence of chronic HBV infection differs in different parts of the world, and may be quite variable within countries. The prevalence of chronic HBV infection varies from less than 0.5% among Caucasians in the United States, northern Europe and Australia, 1 to 5% in the Mediterranean countries, parts of eastern Europe, Africa, Central and South America, up to greater than 10% in many sub-Saharan African, East and Southeast Asian and Pacific island populations. In regions of moderate to high prevalence of HBsAg (where >2% of the population is HBsAg-positive), infections are mainly acquired perinatally or in early childhood.

Chronic infection and its sequelae, including cirrhosis and hepatocellular carcinoma, contribute to the majority of HBV disease burden in Australia. In recent decades, the burden of such disease has been increasing, concurrent with the increasing number of immigrants from regions of high HBV prevalence. Aboriginal and Torres Strait Islander people, and migrants born in Asia and Pacific islands, North Africa, Middle Eastern and Mediterranean countries, have a significantly increased prevalence of chronic HBV infection compared with the rest of the Australian-born population. First-generation immigrants of culturally and linguistically diverse background, who are mostly from countries of high HBV endemicity, usually retain the prevalence of chronic HBV infection of their country of origin. Other population groups with an increased prevalence of markers of HBV infection include patients with HIV infection, persons who used injected drugs between 1980 and 1990, and household contacts of persons diagnosed with hepatitis B between 1980 and 1990. Notification of chronic HBV infection depends on levels of hepatitis B testing and reporting, and a substantial proportion of persons with chronic HBV infection remain undiagnosed. It has been estimated by mathematical modelling that, in 2010, about 100 000 people were living with HBV infection in Australia, with about 335 deaths due to HBV infection in that year.

Newly acquired cases of HBV infection in Australia mostly occur in young adults, through injecting drug use, skin penetration procedures or sexual contact. Between 2006 and 2010, the notification rate of newly acquired hepatitis B in Australia ranged from 1.0 to 1.4 per 100 000 population. Since 2001, the rate of diagnosis of newly acquired infections has declined substantially among people aged 15–19 years and has remained relatively stable among people aged ≥30 years.

Similar to chronic infection, higher rates of notified cases of newly acquired hepatitis B, or hospitalisation due to acute hepatitis B, have been reported among Aboriginal and Torres Strait Islander people compared with the general Australian population. In one United States study, adults with diabetes mellitus had a greater chance of developing acute hepatitis B disease than the general population.

Transmission of HBV may result from inoculation through broken or penetrated skin, or by mucosal contact with blood or other body fluids (mainly vaginal fluids and semen) from an infectious person. There are four major routes of HBV transmission:

1. perinatal transmission from infected mother to neonate (vertical transmission), usually occurring at or around the time of birth
2. parenteral or mucosal exposure to infected blood and other bodily fluids; common scenarios include:
   - sharing of contaminated equipment that penetrates the skin, such as needles (among persons who inject drugs), tattoo equipment, body-piercing equipment, acupuncture equipment and razor blades
   - needle-stick injury, for example, in a healthcare setting
   - contact between infective body fluids and mucous membranes
   - sexual contact (including vaginal or anal intercourse, although the latter is associated with a higher risk)
3. non-sexual contact with an infected person (horizontal transmission), including household transmission, for example, child-to-child transmission through contact between open sores or wounds.

In Australia, screening of blood and organ donors using serological, and subsequently nucleic acid amplification testing, has virtually eliminated the risk of transmission of hepatitis B through blood transfusion and organ transplants. Saliva may contain levels of virus that are likely to be infective only if inoculated directly into tissue (ocular or mucous membranes). The risk of transmission by inadvertent inoculation by other means, such as by toothbrush, razor etc., or through close personal contact in households in which one or more infected persons reside, is minimal.
4.5.4 Vaccines

Monovalent hepatitis B vaccines

- **Engerix-B** – GlaxoSmithKline Australia Pty Ltd (recombinant DNA hepatitis B vaccine). Adult formulation – Each 1.0 mL monodose vial or pre-filled syringe contains 20 µg recombinant hepatitis B surface antigen (HBsAg) protein, adsorbed onto 0.5 mg aluminum as aluminum hydroxide. Paediatric formulation – Each 0.5 mL monodose vial or pre-filled syringe contains 10 µg HBsAg protein, adsorbed onto 0.25 mg aluminum as aluminum hydroxide. Both formulations may contain yeast proteins.

- **H-B-Vax II** – bioCSL Pty Ltd/Merck Sharp & Dohme (Australia) Pty Ltd (recombinant DNA hepatitis B vaccine). Adult formulation – Each 1.0 mL monodose vial or pre-filled syringe contains 10 µg recombinant HBsAg protein, adsorbed onto 0.5 mg aluminum hydroxide. Paediatric formulation – Each 0.5 mL monodose vial or pre-filled syringe contains 5 µg recombinant HBsAg protein, adsorbed onto 0.25 mg aluminum hydroxide. Dialysis formulation – Each 1.0 mL monodose vial contains 40 µg recombinant HBsAg protein, adsorbed onto 0.5 mg aluminum hydroxide. All formulations may contain yeast proteins.

Combination vaccines that contain hepatitis B

- **Hexaxim** – Sanofi-Aventis Australia Pty Ltd (DTPa-hepB-IPV-Hib; diphtheria-tetanus-acellular pertussis-hepatitis B-inactivated poliovirus-Haemophilus influenzae type b). Each 0.5 mL pre-filled syringe contains ≥20 IU diphtheria toxoid, 240 IU tetanus toxoid, 25 µg pertussis toxoid (PT), 25 µg filamentous haemagglutinin (FHA), 10 µg recombinant HBsAg, 40 D-antigen units inactivated poliovirus type 1 (Mahoney), 8 D-antigen units type 2 (MEF-1), 32 D-antigen units type 3 (Saukett) and 12 µg purified Hib capsular polysaccharide (PRP) conjugated to 22–36 µg tetanus toxoid, adsorbed onto 0.6 mg aluminum as aluminum hydroxide. May contain traces of glutraldehyde, formaldehyde, neomycin, streptomycin and polysorbate 80.

- **Infanrix hexa** – GlaxoSmithKline Australia Pty Ltd (DTPa-hepB-IPV-Hib; diphtheria-tetanus-acellular pertussis-hepatitis B-inactivated poliovirus-Haemophilus influenzae type b). The vaccine consists of both a 0.5 mL pre-filled syringe containing ≥30 IU diphtheria toxoid, 240 U tetanus toxoid, 25 µg PT, 25 µg FHA, 8 µg pertactin, 10 µg recombinant HBsAg, 40 D-antigen units inactivated poliovirus type 1 (Mahoney), 8 D-antigen units type 2 (MEF-1) and 32 D-antigen units type 3 (Saukett), adsorbed onto aluminum hydroxide/phosphate; traces of formaldehyde, polysorbate 80, polysorbate 20, polymyxin and neomycin; and a vial containing a lyophilised pellet of 10 µg purified capsular polysaccharide (PRP) conjugated to 20–40 µg tetanus toxoid. May contain yeast proteins.

- **Twining Junior (360/10)** – GlaxoSmithKline (formaldehyde-inactivated hepatitis A virus [HM175 strain] and recombinant hepatitis B vaccine). Each 0.5 mL monodose vial or pre-filled syringe contains 360 ELISA units of HAV antigens, 10 µg recombinant DNA hepatitis B surface antigen protein; 0.225 mg aluminum as aluminum phosphate/hydroxide; traces of formaldehyde, neomycin, trometamol and polysorbate 20. May contain yeast proteins.

- **Twining (720/20)** – GlaxoSmithKline (formaldehyde-inactivated hepatitis A virus [HM175 strain] and recombinant hepatitis B vaccine). Each 1.0 mL monodose vial or pre-filled syringe contains 720 ELISA units of HAV antigens, 20 µg recombinant DNA hepatitis B surface antigen protein, 0.45 µg aluminum as aluminum phosphate/hydroxide; traces of formaldehyde, neomycin, trometamol and polysorbate 20. May contain yeast proteins.

Hepatitis B vaccines are prepared using recombinant technology. After purification, the HBsAg protein is adsorbed onto elemental aluminium (as hydroxide and/or phosphate). Hepatitis B vaccines may contain up to 1% yeast proteins (but no yeast DNA).

The Engerix-B and the H-B-Vax II vaccines are manufactured by different processes, and the HBsAg content of 'equivalent' doses of these two vaccines is different. The HBsAg content of the paediatric formulations of these two vaccines is half that of the corresponding manufacturer’s adult formulation. Studies of hepatitis B vaccines have been conducted using different schedules and intervals for different age groups. Acceptable schedules are shown in Table 4.5.1 and are described below.

The standard 3-dose schedule and variations

Neonates, children and young adults aged <20 years

The recommended Australian infant schedule consists of a dose of monovalent hepatitis B vaccine given at birth, followed by 3 doses of a hepatitis B-containing combination vaccine, given at 2, 4 and 6 months of age (refer to ‘Infants and young children’ in 4.5.7) (http://www.immunise.health.gov.au/internet/immunise/publishing.nsf/Content/Handbook10-home~handbook10part4~handbook10-4-5#4-5-7) Recommendations below). If an infant did not receive the birth dose within the 1st 7 days of life, catch-up of that dose is not necessary. Such infants then only require 3 doses of a hepatitis B-containing vaccine, given at 2, 4 and 6 months of age.

A 3-dose schedule at birth, 1–2 months and 6–18 months of age has been shown to be equally as immunogenic as the recommended Australian schedule above; such schedules are often used overseas.30,32 Births born overseas who have received hepatitis B vaccine in such a 3-dose schedule can also be considered to have completed the primary vaccination course.

For infants, the final dose of the primary hepatitis B vaccine course should preferably be administered at ≥24 weeks of age. However, if the final dose is given at <24 weeks but ≥16 weeks of age, it is not necessary to repeat the dose, provided the minimum intervals between doses in Table 2.1.7 (in 2.1.5 Catch-up (http://www.immunise.health.gov.au/internet/immunise/publishing.nsf/Content/Handbook10-home~handbook10part2~handbook10-2-1)) have been met.

For older children and young adults aged <20 years (who have not received hepatitis B vaccination earlier in life) a 3-dose schedule of the paediatric formulation (0.5 µL) of monovalent hepatitis B vaccine can be used (at times 0, 1 and 6 months), as per Table 4.5.1. Immunogenicity studies suggest there can be some flexibility of the vaccination schedule intervals for monovalent hepatitis B vaccines. The use of longer time intervals between doses does not impair the immunogenicity of hepatitis B vaccine.31,34 The minimum interval between the 1st and 3rd doses of a 3-dose primary schedule is 4 months. This means that a shortened 3-dose schedule provided at either 0, 1, 4 months or 0, 2, 4 months is acceptable.35 More compressed 3-dose schedules (e.g. 0, 1, 3 months) are not recommended. Such compressed schedules are associated with lower peak levels of anti-HBs antibody,36,37 and hence likely shorter duration of antibody persistence (at levels ≥10 mIU/mL),38 although the clinical significance of this is uncertain.39 (Refer also to ‘Adults aged ≥20 years’ below.)

Adults aged ≥20 years

For adults, monovalent hepatitis B vaccine adult formulation (1.0 mL) is given in a 3-dose schedule at times 0, 1 and 6 months (refer to Table 4.5.1). There is some flexibility regarding the interval between the doses. The proportion of vaccine recipients achieving a seroprotective anti-HBs antibody level (≥10 mIU/mL), generally measured 1–2 months after vaccination, is comparable between adults who received their 3rd dose at 4–6 months after the 1st dose and those who received their 3rd dose 6 months or more after the 1st dose.68 Increasing the interval between the 1st and 2nd doses has little effect on the final antibody level attained, but a longer interval between the 2nd and 3rd doses is associated with a higher final antibody level.37,41,42 However, for those who may be exposed to hepatitis B, delaying the 3rd dose may increase the risk of acquiring HBV infection.

For a shortened 3-dose schedule to attain comparable antibody levels to the standard 3-dose schedule, all three of the following minimum interval requirements must be satisfied:

- the minimum interval between the 1st and 2nd doses is 1 month,
- the minimum interval between the 2nd and 3rd doses is 2 months, and
- the minimum interval between the 1st and 3rd doses is 4 months.

That is, either a 0, 1, 4 month or a 0, 2, 4 month interval schedule is an acceptable 3-dose schedule for adults.43

The minimum intervals outlined above should be met wherever possible. More compressed 3-dose schedules (e.g. 0, 1, 3 months) are not recommended. If a compressed 3-dose schedule that does not meet these minimum intervals has already been administered, it may not be necessary to repeat a dose. Although compressed schedules are associated with lower peak antibody levels, 30% of individuals with increased risk of HBV exposure, including infants at particular risk of infection at birth. Universal infant vaccination commenced in the Northern Territory in 1990. A universal hepatitis B vaccination program was recommended for infants and adolescents in 1997 and the universal infant program, which includes a dose given at birth, began nationally in 2000. The adolescent program commenced in some states and territories in 1997 and the universal infant program, which includes a dose given at birth, began nationally in 2000. The adolescent program will continue until those immunised for hepatitis B in the infant program reach adolescence.
Note that the interval between the 1st and 3rd doses has been shortened to less than 4 months in studies of 4-dose accelerated schedules, with the aim to achieve a higher seroprotective antibody level sooner. However, antibody levels are substantially lower after 3 accelerated doses than after the standard 3-dose schedule, so a 4th dose is required to achieve comparable antibody levels to the standard 3-dose schedule (refer to ‘Accelerated schedules’ below).

The standard 3-dose schedule induces protective levels of neutralising antibody against hepatitis B virus in more than 90% of adults. The frequency of seroconversion increases progressively from approximately 35% after the 1st dose to more than 90% after the 3rd dose. There is evidence of immunity in most vaccine recipients after administration of 2 doses of a 3-dose schedule. However, the 3rd dose is necessary to increase the percentage of responders and to provide long-term protection.

Alternative 2-dose schedule for adolescents

Several studies have demonstrated that adolescents 11–15 years of age who receive 2 doses of adult formulation monovalent hepatitis B vaccine 4 to 6 months apart develop similar protective antibody levels to those vaccinated using paediatric formulations in the standard 3-dose schedule.

Using a 2-dose schedule for the 11–15 years age group may improve compliance and will provide comparable immunogenicity to that of a 3-dose paediatric schedule. Adolescents (11–15 years of age) can be vaccinated with the adult formulation of either H-B-Vax II or Engerix-B in a 2-dose schedule (refer to Table 4.5.1).

Table 4.5.1: Recommended schedules for use of monovalent hepatitis B and hepatitis B combination vaccines

<table>
<thead>
<tr>
<th>Vaccine</th>
<th>Age of vaccine recipient</th>
<th>Dose (HBsAg protein)</th>
<th>Volume per dose (mL)</th>
<th>Number of doses</th>
<th>Recommended schedule intervals</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Recommended infant schedule</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Engerix-B (paediatric formulation) or H-B-Vax II (paediatric formulation)</td>
<td>birth</td>
<td>10 µg (Engerix-B) or 5 µg (H-B-Vax II)</td>
<td>0.5</td>
<td>1</td>
<td>Birth (if not given at birth, may be given up to 7 days of age)</td>
</tr>
<tr>
<td>Combination hepatitis B-containing vaccine (e.g. Infanrix hexa DTPa-hepB-IPV-Hib)</td>
<td>2, 4 and 6 months</td>
<td>10 µg</td>
<td>0.5</td>
<td>3</td>
<td>1st dose: 2 months of age; 2nd dose: 4 months of age; 3rd dose: 6 months of age</td>
</tr>
</tbody>
</table>

**Monovalent hepatitis B vaccines – standard 3-dose schedule**

<table>
<thead>
<tr>
<th>Vaccine</th>
<th>Age of vaccine recipient</th>
<th>Dose (HBsAg protein)</th>
<th>Volume per dose (mL)</th>
<th>Number of doses</th>
<th>Recommended schedule intervals</th>
</tr>
</thead>
<tbody>
<tr>
<td>Engerix-B (paediatric formulation)</td>
<td>&lt;20 years</td>
<td>10 µg</td>
<td>0.5</td>
<td>3</td>
<td>1st dose: day 0 (day of vaccination); 2nd dose: 1 month after 1st dose; 3rd dose: 6 months after 1st dose</td>
</tr>
<tr>
<td>Engerix-B (adult formulation)</td>
<td>≥20 years</td>
<td>20 µg</td>
<td>1.0</td>
<td>3</td>
<td>1st dose: day 0 (day of vaccination); 2nd dose: 1 month after 1st dose; 3rd dose: 6 months after 1st dose</td>
</tr>
<tr>
<td>H-B-Vax II (paediatric formulation)</td>
<td>&lt;20 years</td>
<td>5 µg</td>
<td>0.5</td>
<td>3</td>
<td>1st dose: day 0 (day of vaccination); 2nd dose: 1 month after 1st dose; 3rd dose: 6 months after 1st dose</td>
</tr>
<tr>
<td>H-B-Vax II (adult formulation)</td>
<td>≥20 years</td>
<td>10 µg</td>
<td>1.0</td>
<td>3</td>
<td>1st dose: day 0 (day of vaccination); 2nd dose: 1 month after 1st dose; 3rd dose: 6 months after 1st dose</td>
</tr>
<tr>
<td>H-B-Vax II (dialysis formulation)</td>
<td>≥20 years</td>
<td>40 µg</td>
<td>1.0</td>
<td>3</td>
<td>1st dose: day 0 (day of vaccination); 2nd dose: 1 month after 1st dose; 3rd dose: 6 months after 1st dose</td>
</tr>
</tbody>
</table>

**Monovalent hepatitis B vaccines – 2-dose schedule ONLY for adolescents aged 11–15 years**

<table>
<thead>
<tr>
<th>Vaccine</th>
<th>Age of vaccine recipient</th>
<th>Dose (HBsAg protein)</th>
<th>Volume per dose (mL)</th>
<th>Number of doses</th>
<th>Recommended schedule intervals</th>
</tr>
</thead>
<tbody>
<tr>
<td>Engerix-B (adult formulation)</td>
<td>11–15 years</td>
<td>20 µg</td>
<td>1.0</td>
<td>2</td>
<td>1st dose: day 0 (day of vaccination); 2nd dose: 6 months after 1st dose</td>
</tr>
<tr>
<td>H-B-Vax II (adult formulation)</td>
<td>11–15 years</td>
<td>10 µg</td>
<td>1.0</td>
<td>2</td>
<td>1st dose: day 0 (day of vaccination); 2nd dose: between 4 and 6 months after 1st dose</td>
</tr>
</tbody>
</table>

**Combination hepatitis A/hepatitis B vaccines**

<table>
<thead>
<tr>
<th>Vaccine</th>
<th>Age of vaccine recipient</th>
<th>Dose (HBsAg protein)</th>
<th>Volume per dose (mL)</th>
<th>Number of doses</th>
<th>Recommended schedule intervals</th>
</tr>
</thead>
<tbody>
<tr>
<td>Twinrix (720/20)</td>
<td>1–&lt;16 years</td>
<td>20 µg</td>
<td>1.0</td>
<td>2</td>
<td>1st dose: day 0 (day of vaccination); 2nd dose: between 6 and 12 months after 1st dose (2-dose schedule)</td>
</tr>
<tr>
<td>Twinrix Junior (360/10)</td>
<td>1–&lt;16 years</td>
<td>10 µg</td>
<td>0.5</td>
<td>3</td>
<td>1st dose: day 0 (day of vaccination); 2nd dose: 1 month after 1st dose; 3rd dose: 6 months after 1st dose</td>
</tr>
<tr>
<td>Twinrix (720/20)</td>
<td>≥16 years</td>
<td>20 µg</td>
<td>1.0</td>
<td>3</td>
<td>1st dose: day 0 (day of vaccination); 2nd dose: 1 month after 1st dose; 3rd dose: 6 months after 1st dose</td>
</tr>
</tbody>
</table>

Accelerated schedules

Engerix-B (monovalent hepatitis B vaccine, paediatric and adult) and Twinrix (720/20) (combination hepatitis A/hepatitis B vaccine) are also registered for use in accelerated schedules, which consist of 4 doses in total (refer to Table 4.5.2 below). Accelerated schedules result in a high proportion of vaccine recipients attaining a seroprotective anti-HBs antibody level (≥10 mIU/mL) in the early months following commencement of the schedule. However, multiple studies have consistently shown that antibody levels are substantially lower at month 7, after 3 accelerated doses, than after the standard 3-dose schedule (0, 1, 6 months).\(^4\) Also, some studies, in particular among persons who inject drugs and/or inmates of correctional facilities, have shown a lower proportion of subjects attaining the seroprotective antibody level after 3 doses of an accelerated schedule than after the standard 3-dose schedule.\(^4\) After the 4th dose of an accelerated schedule, administered at 12 months, anti-HBs antibody levels are higher or comparable to those after a standard 3-dose schedule. Hence, a 4th dose should be administered at 12 months to complete an accelerated schedule.

Accelerated schedules should only be used for those persons with an imminent risk of exposure, such as those intending to travel to hepatitis B endemic areas with a very limited time before departure. As higher seroprotective rates after the 3rd dose of an accelerated 4-dose schedule are seen after the 0, 1, 2, 12 months schedule than after the 0, 7, 21 days, 12 months schedule, it is recommended that the latter schedule only be used in exceptional circumstances.

<table>
<thead>
<tr>
<th>Vaccine</th>
<th>Age of vaccine recipient (years)</th>
<th>Dose (HBsAg protein)</th>
<th>Volume (mL)</th>
<th>Number of doses</th>
<th>Recommended schedule minimum interval</th>
</tr>
</thead>
<tbody>
<tr>
<td>Engerix-B (paediatric formulation)</td>
<td>&lt;20</td>
<td>10 µg</td>
<td>0.5</td>
<td>4</td>
<td>1st dose: day 0 (day of vaccination) 2nd dose: 1 month after 1st dose 3rd dose: 2 months after 1st dose 4th dose: 12 months after 1st dose</td>
</tr>
<tr>
<td>Engerix-B (adult formulation)</td>
<td>≥20</td>
<td>20 µg</td>
<td>1.0</td>
<td>4</td>
<td>1st dose: day 0 (day of vaccination) 2nd dose: 1 month after 1st dose 3rd dose: 2 months after 1st dose 4th dose: 12 months after 1st dose or 1st dose: day 0 (day of vaccination) 2nd dose: 7 days after 1st dose 3rd dose: 21 days after 1st dose 4th dose: 12 months after 1st dose</td>
</tr>
<tr>
<td>Twinrix (720/20)</td>
<td>≥16</td>
<td>20 µg</td>
<td>1.0</td>
<td>4</td>
<td>1st dose: day 0 (day of vaccination) 2nd dose: 7 days after 1st dose 3rd dose: 21 days after 1st dose 4th dose: 12 months after 1st dose</td>
</tr>
</tbody>
</table>

Combination hepatitis A/hepatitis B vaccine schedules

The schedules for combination hepatitis A/hepatitis B vaccines are shown in Table 4.5.1 and Table 4.5.2. Three-dose schedules for adults and children aged <16 years are acceptable; however, a 2-dose schedule in children 1—15 years of age, using Twinrix (720/20), also results in protective antibody levels for both hepatitis A and hepatitis B. An accelerated schedule for combination hepatitis A/hepatitis B vaccine in those aged ≥16 years is shown in Table 4.5.2. The appropriate use of accelerated schedules is discussed above.

The use of mixed vaccine schedules using both the combination hepatitis A/hepatitis B vaccine and monovalent hepatitis B vaccines is not routinely recommended. Generally, use of the same brand of vaccine is recommended. (Refer also to ‘Interchangeability of hepatitis B vaccines’ in 4.5.6 Dosage and administration below.)

4.5.5 Transport, storage and handling

Transport according to National vaccine storage guidelines: Store for 5\(^\circ\)C to 25\(^\circ\)C. Do not freeze.

Infanrix hexa must be reconstituted by adding the entire contents of the syringe to the vial and shaking until the pellet is completely dissolved. Reconstituted vaccine should be used as soon as practicable. If storage is necessary, hold at room temperature for not more than 8 hours.

4.5.6 Dosage and administration

The schedules for hepatitis B vaccines and for combination hepatitis A/hepatitis B vaccines are shown in Table 4.5.1 and Table 4.5.2. For combination hepatitis A/hepatitis B vaccines, refer also to 4.4 (Handbook10-home-handbook10part4-handbook10-4-4) Hepatitis A.

The dose of Engerix-B and H-B-Vax II (paediatric formulations) and Twinrix Junior (360/10) is 0.5 mL, to be given by IM injection.

The dose of Engerix-B and H-B-Vax II (adult formulations) and Twinrix (720/20) is 1.0 mL, to be given by IM injection.

The dose of Infanrix hexa is 0.5 mL, to be given by IM injection.

Hepatitis B and combination hepatitis A/hepatitis B vaccines can generally be co-administered simultaneously with, or at any time before or after, all other vaccines.

Interchangeability of hepatitis B vaccines

The Engerix-B and H-B-Vax II vaccines are manufactured by different processes, and the HBsAg content of an ‘equivalent’ dose is different. Although switching of vaccine brands is not recommended, in cases where the brand of vaccine used for previous doses is not known, another age-appropriate ‘equivalent’ dose brand (refer to Table 4.5.1) may be used. For example, a study in healthy neonates demonstrated comparable high levels of immunogenicity between two different mixed regimens that used two monovalent hepatitis B vaccines from different manufacturers.\(^6\) As there is only one brand of combination hepatitis A/hepatitis B vaccine, interchangeability is not relevant. (Refer also to ‘Combination hepatitis A/hepatitis B vaccines schedules’ in 4.5.4 Vaccines above.)
Infants and young children

The recommended hepatitis B vaccine schedule for infants from birth is shown in Table 4.5.1. A birth dose of monovalent paediatric formulation hepatitis B vaccine is recommended for all newborn infants. Following this birth dose, 3 doses of a hepatitis B-containing vaccine (usually provided as DTaP-hepB-IPV-Hib) are recommended for all children, at 2, 4 and 6 months of age. Thus, a total of 4 doses of hepatitis B vaccine are provided in the 1st year of life. The 1st dose of a hepatitis B-containing vaccine can be given as early as 6 weeks of age. If the 1st dose is given at 6 weeks of age, the next scheduled doses should still be given at 4 months and 6 months of age.

If an infant has not received a birth dose within the 1st 7 days of life, a primary 3-dose course of a hepatitis B-containing combination vaccine should be given, at 2, 4 and 6 months of age; catch-up of the birth dose is not necessary.

For hepatitis B vaccination of classroom contacts of hepatitis B cases is seldom indicated. Nevertheless, vaccination of all children and adolescents should be encouraged. Routine antenatal screening of pregnant women for HBsAg is recommended to enable appropriate management to prevent newborn infants developing HBV infection (refer to 4.5.2 Clinical features and 4.5.3 Epidemiology above). It also enables appropriate follow-up and management of mothers who have chronic HBV infection, identification of the HBV immune status of other household members, and protection of those who are susceptible to HBV infection.

Management of infants born to mothers who are HBsAg-positive

Routine hepatitis B vaccination of infants born to HBsAg-positive mothers is recommended. The dose of hepatitis B vaccine should be given to the infant preferably within 24 hours of birth, and definitely within 7 days. This regimen results in seroconversion rates of more than 90% in neonates, even with concurrent administration of HBIG. Vaccination should not be delayed beyond 7 days after birth, as vaccination alone has been shown to be reasonably effective in preventing infection, provided it is given early. Three subsequent doses of a hepatitis B-containing vaccine should be given, at 2, 4 and 6 months of age, so that the infant receives a total of 4 doses of hepatitis B-containing vaccines.

Preterm and low-birth-weight infants

Low-birth-weight preterm newborn infants do not respond as well to hepatitis B-containing vaccines as full-term infants. Therefore, for low-birth-weight infants (&lt;2000 g) and/or infants born at &lt;32 weeks gestation (irrespective of weight), it is recommended to give the vaccine in a 4-dose schedule at 0 (birth), 2, 4 and 6 months of age, followed by either:

- measuring the anti-HBs antibody level at 7 months of age, and if the antibody titre is &lt;10 mIU/mL, giving a booster at 12 months of age (due to a better immunogenic response at this age compared with a younger age); or
- giving a booster of a hepatitis B-containing vaccine at 12 months of age (without measuring the antibody titre).

HIV-positive and immunocompromised children

All HIV-positive and immunocompromised children should be age-appropriately vaccinated against hepatitis B. HIV-positive children should receive 3 doses of hepatitis B vaccine using an adult formulation (i.e. double the standard recommended dose for children). In a limited number of studies, paediatric haemodialysis patients have demonstrated improved response when given higher doses in a 3-dose schedule.

For specific hepatitis B recommendations for immunocompromised children, refer to 3.3.3 Vaccination of immunocompromised persons.

Adolescents

Vaccination of adolescents 10–13 years of age is recommended for all those in this age group who have not already received a primary course of hepatitis B vaccine. Refer to your state/territory health authority for further information about hepatitis B vaccine for this age group (refer to Appendix 1 Contact details for Australian, state and territory government health authorities and communicable disease control). The rationale for recommending the birth dose for all newborn infants is not only to prevent vertical transmission from a mother with chronic hepatitis B infection (recognising that there may be errors or delays in maternal testing, reporting, communication or appropriate response), but also to prevent horizontal transmission to the infant in the first months of life from persons with chronic hepatitis B infection who are household or other close contacts.

The birth dose should be given as soon as the baby is medically stable, and preferably within 24 hours of birth. Every effort should be made to administer the vaccine before discharge from the obstetric hospital or delivery unit. All newborns of mothers known to have chronic hepatitis B infection must be given a birth dose of hepatitis B vaccine and hepatitis B immunoglobulin (HBIG) (refer to 'Management of infants born to mothers who are HBsAg-positive' below).

Although it is not routinely recommended in Australia, infants or toddlers who have received a 3-dose schedule of hepatitis B vaccine (often given overseas) with doses at birth, 1–2 months of age and 26 months of age can also be considered fully vaccinated (refer to 4.5.4 Vaccines, 'The standard 3-dose schedule and variations' above).

For hepatitis B vaccine in infants who have been infected with HIV, refer to 4.5.6, 'HIV-positive and immunocompromised children'. A 2-dose schedule increases compliance and thus protection in this age group.

Adolescents who did not receive an age-appropriate completed course of vaccination should be identified and offered catch-up vaccination, particularly if they fall into one of the risk categories for hepatitis B infection, discussed under 'Adults' below.

Adolescents

Vaccination of adolescents 10–13 years of age is recommended for all those in this age group who have not already received a primary course of hepatitis B vaccine. Refer to your state/territory health authority for further information about hepatitis B vaccine for this age group (refer to Appendix 1 Contact details for Australian, state and territory government health authorities and communicable disease control).

As the risk in Australian schools is very low, vaccination of classroom contacts of hepatitis B cases is seldom indicated. Nevertheless, vaccination of all children and adolescents should be encouraged.

A 2-dose schedule of hepatitis B vaccine using the adult formulation of either of the available monovalent vaccines should be considered for adolescents aged 11–15 years who are to receive hepatitis B vaccination (refer to Table 4.5.1 and 4.5.4 Vaccines above). A 2-dose schedule increases compliance and thus protection in this age group.

Adolescents who did not receive an age-appropriate completed course of vaccination should be identified and offered catch-up vaccination, particularly if they fall into one of the risk categories for hepatitis B infection, discussed under 'Adults' below.

Household or other close (household-like) contacts of persons with hepatitis B

When vaccination against both hepatitis B and hepatitis A is indicated, the combination hepatitis A/hepatitis B vaccines may be used. Refer to Tables 4.5.1 and 4.5.2 above and 'Recommendations for the use of combination hepatitis A/hepatitis B vaccines' below.
Sexual contacts of persons with hepatitis B
Susceptible sexual partners of persons who are HBsAg-positive should be offered post-exposure HBIG and hepatitis B vaccination; both should be initiated within 14 days of the last sexual contact (refer to 4.5.11 Public health management of hepatitis B below and Table 4.5.3).

Hepatitis B is relatively common in clients of sexual health services and vaccination should be offered to susceptible persons at the time of first attendance.

Susceptible, sexually active men who have sex with men should be vaccinated. The combination hepatitis A/hepatitis B vaccine may be appropriate for men who have sex with men, if they are not immune to either disease, as they are at increased risk of both conditions (refer to ‘Recommendations for the use of combination hepatitis A/hepatitis B vaccines’ below).

Migrants from hepatitis B endemic countries

Migrants from hepatitis B endemic countries have a higher likelihood of having been infected with hepatitis B and of having a close household contact with chronic hepatitis B infection. Such persons should be offered testing for hepatitis B, and vaccination if appropriate. (Refer also to 3.3.8 Vaccination of migrants to Australia (Handbook10-home-handbook10part3-handbook10-3-3#3-7-1) Areas of high endemicity, indicated by high seroprevalence of HBsAg, include most of East and Southeast Asia (except Japan), Pacific island groups, parts of central Asia and the Middle East, the Amazon Basin, and sub-Saharan Africa.62

Aboriginal and Torres Strait Islander people

There is an increased risk of acquiring new HBV infection among Aboriginal and Torres Strait Islander people compared with other Australians.17,18 Although many younger Aboriginal and Torres Strait Islander people, especially children and adolescents, would have been eligible for, and have received, hepatitis B vaccination through population-wide vaccination programs, it is recommended that Aboriginal and Torres Strait Islander people have their risks and vaccination status for hepatitis B reviewed, be offered testing for previous hepatitis B infection, and be offered vaccination if non-immune. (Refer also to 3.1 Vaccination for Aboriginal and Torres Strait Islander people (Handbook10-home-handbook10part3-handbook10-3-1-1))

Adult haemodialysis patients and patients with severely impaired renal function in whom dialysis is anticipated

Dialysis patients, and patients with severely impaired renal function in whom dialysis is anticipated, may be at increased risk of acquiring hepatitis B infection and also respond less well to vaccination. These patients should be given a larger than usual dose of hepatitis B vaccine.

Adult haemodialysis or pre-dialysis patients should be given either:

- 1.0 mL of Engerix-B adult formulation (20 μg) in each arm at each schedule point (i.e. effectively giving a double dose on each occasion) in a 4-dose schedule at 0, 1, 2 and 6 months;63 or

- a single dose of H-B-Vax II dialysis formulation (40 μg) on each occasion in a 3-dose schedule at 0, 1 and 6 months.

Solid organ and haematopoietic stem cell transplant recipients

If seronegative for hepatitis B, solid organ transplant recipients should be vaccinated before transplantation as they may be at increased risk of infection from the transplanted organ.64 Haematopoietic stem cell transplant recipients should be revaccinated following transplantation, due to the loss of immune memory that often follows the transplant procedure. (Refer also to 3.3.3 Vaccination of immunocompromised persons (Handbook10-home-handbook10part3-handbook10-3-3#3-3-3))

HIV-positive adults and other immunocompromised adults

HIV-positive adults, and other immunocompromised adults, may be at increased risk of acquiring hepatitis B infection and also respond less well to vaccination. Limited studies in HIV1-positive adults have demonstrated an improved and accelerated serological response to a schedule that consists of 4 double doses, comprising two injections of the standard adult dose (using Engerix-B) on each occasion, at times 0, 1, 2 and 6 months.65,66

Persons with chronic liver disease and/or hepatitis C

Hepatitis B vaccination is recommended for those in this category who are seronegative for hepatitis B, because of the risk of severe liver disease following infection with hepatitis B.67

Persons who inject drugs

Persons who inject drugs should be tested, and be vaccinated if they have not previously been infected with HBV.

Recipients of certain blood products

Screening of all blood donors for HBV using HBsAg and nucleic acid amplification tests has greatly decreased the incidence of transfusion-related hepatitis B virus infection. Since 2010, nucleic acid testing has been introduced nationally to improve detection of hepatitis B infection in donated blood, mainly through reduction of the infectious window period when acute hepatitis B infection may not be detected using HBsAg, but also through detecting persons with occult hepatitis B infection. This further reduces the residual risk of hepatitis B transmission through transfusion in Australia, to approximately 1 in 882 000 per unit transfused.67 However, persons with clotting disorders who receive blood product concentrates, persons with recurrent transfusion requirements, and persons with underlying immunocompromise68 have an elevated risk of hepatitis B virus infection, and should therefore be vaccinated.

Persons with developmental disabilities

Vaccination is recommended for persons who attend either residential or non-residential day-care facilities for persons with developmental disabilities. This is due to the high prevalence of markers indicating past or current infection in persons in these settings, including an HBsAg prevalence of >10%,69-71

Inmates of correctional facilities

Inmates are at increased risk of hepatitis B infection because of the prevalence of chronic hepatitis B among inmates, and the potential for unprotected sexual intercourse, injecting drug use and amateur tattooing in correctional facilities. Therefore, they should be offered the opportunity to be screened for hepatitis B upon incarceration, as part of the preventive health program for blood-borne viruses, and vaccinated if susceptible.

Sex industry workers

Sex industry workers are one of the population groups at higher risk of HBV infection. They have been specifically identified as an important population on which to focus for the prevention of hepatitis B transmission.72 They are at a particularly high risk if they engage in unprotected sex.

Persons at occupational risk

The risk to persons in certain occupations differs considerably from setting to setting in different parts of Australia. However, it is recommended that all staff directly involved in patient care and/or the handling of human tissue, blood or body fluids should be vaccinated. In addition, standard precautions against exposure to human tissue, blood or body fluids should be used as a matter of routine.73

Other occupations where the risk of acquiring hepatitis B is increased include:


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Staff of child day-care centres will normally be at minimal risk of hepatitis B. If advice on risk is sought, the enquiry should be directed to the local public health authority.

Contact sports generally carry a low risk of hepatitis B infection. However, age-appropriate hepatitis B vaccination is recommended.

**Travellers to hepatitis B endemic areas**

Persons travelling to regions of intermediate or high endemicity, either long-term or for frequent short terms, or who are likely to undertake activities that increase their risks of exposure to HBV during travel, should be vaccinated.62 (Refer also to 3.2 Vaccination for international travel (Handbook10-home~handbook10part3~handbook10-3-2).)

**Recommendations for the use of combination hepatitis A/hepatitis B vaccines**

Combination hepatitis A/hepatitis B vaccines should be considered for susceptible persons in whom both hepatitis A and hepatitis B vaccines are recommended, including:

- travelling to or expatriates living in, or to moderately to highly endemic areas for hepatitis A and B
- persons of lifestyle who put them at increased risk of hepatitis A and hepatitis B (sexually active men who have sex with men, sex industry workers, persons who inject drugs and inmates of correctional facilities)
- persons who attend or work at residential or non-residential facilities for people with developmental disabilities
- persons with occupational risks of exposure to both hepatitis A and hepatitis B
- persons with chronic liver disease and/or hepatitis C
- solid organ transplant recipients who have chronic liver disease (refer to 3.3.2 Recommendations for vaccinations for solid organ transplant (SOT) recipients (Handbook10-home~handbook10part3~handbook10-3-3#table-3-3-2)).

If a combination hepatitis A/hepatitis B vaccine is not available, monovalent hepatitis A and hepatitis B vaccines can be administered simultaneously (in separate syringes at separate sites) (refer to ‘Interchangeability of hepatitis B vaccines’ above).

Refer to 4.5.7 Recommendations above and 4.4 (Handbook10-home~handbook10part4~handbook10-4-4) Hepatitis A for more details. Refer also to 3.3 Groups with special vaccination requirements (Handbook10-home~handbook10part3~handbook10-3-3).

**Booster doses**

Booster doses of hepatitis B vaccine (after completion of a primary course by using recommended schedule) are not recommended for immunocompetent persons. This applies to children and adults, including healthcare workers and dentists.49-51 This is because there is good evidence that a completed primary course of hepatitis B vaccination provides long-lasting protection. Even though vaccine-induced antibody levels may decline with time and may become undetectable, immune memory persists and is thought to result in a protective immune response on re-exposure.81 However, booster doses are recommended for persons who are immunocompromised, in particular those with either HIV infection or renal failure. The time for boosting in such persons should be decided by regular monitoring of anti-HBs levels at 6- to 12-monthly intervals.74

**Serological testing prior to hepatitis B vaccination**

Routine antenatal screening of all pregnant women for HBsAg is recommended to allow appropriate measures to be implemented to prevent newborn infants developing chronic HBV infection.69-71 (Refer to ‘Management of infants born to mothers who are HBsAg-positive’ above).

Serological testing for evidence of past (or current) hepatitis B infection prior to vaccination may be warranted for certain older children, adolescents and adults. This is particularly so for those at increased risk of acquiring hepatitis B infection, such as persons who inject drugs, sex industry workers, immunocompromised persons, and those living in communities with higher prevalence of HBV, including migrant communities and Aboriginal and Torres Strait Islander people. Serological testing enables identification of persons who were infected by HBV, to facilitate timely appropriate clinical management and prevention of onward transmission, hence reducing population impact of HBV infection. Testing also identifies those who are susceptible to HBV infection and, as such, should be offered vaccine if they continue to have a high exposure risk (refer to 4.5.7 Recommendations above).72 Testing for immunity to hepatitis A infection (and vaccination of susceptible at-risk persons with combination hepatitis A/hepatitis B vaccines) may also be indicated for some population groups at increased risk of hepatitis A exposure (refer to 4.4 (Handbook10-home~handbook10part4~handbook10-4-4#Hepatitis A)).

Interpretation of the results of serological testing may be enhanced by discussion with the laboratory that performed the test, ensuring that relevant clinical information is provided.

**Serological testing following hepatitis B vaccination**

Anti-HBs antibody and HBsAg levels should be measured in infants born to mothers with chronic hepatitis B infection 3 to 12 months after completing the primary vaccine course (for more information refer to ‘Management of infants born to mothers who are HBsAg-positive’ above).

Other than for infants born to mothers with chronic hepatitis B infection, post-vaccination serological testing is recommended 4 to 8 weeks after completion of the primary course for persons in the following categories:

- those at significant occupational risk (e.g. healthcare workers whose work involves frequent exposure to human tissue, blood or body fluids)
- those at risk of severe or complicated HBV disease (e.g. persons who are immunocompromised, and persons with pre-existing liver disease not related to hepatitis B)
- those in whom a poor response to hepatitis B vaccination may occur (e.g. haemodialysis patients, persons with bleeding disorders vaccinated via the SC route)
- sexual partners and household, or other close household-like, contacts of persons who are infected with hepatitis B.25

For these individuals, if adequate anti-HBs levels (≥10 mIU/mL) are not reached on serological testing 4 to 8 weeks after the 3rd dose, the possibility of HBV infection, including chronic HBV infection, should be investigated by testing for serological markers, including HBsAg and anti-HBc antibodies. In select cases in which hepatitis B infection is suspected, HBV nucleic acid testing may also be indicated, and expert advice regarding further management should be sought. If there are no markers of HBV infection, the individual should be managed as a non-responder to hepatitis B vaccination (refer to ‘Non-responders to primary vaccination’ below).

If persons who are at significant risk of hepatitis B (such as healthcare workers) were not tested for anti-HBs within 4 to 8 weeks after completion of the documented primary course, they should still undergo serological testing to ensure immunity. If, on testing, they have an anti-HBs level of <10 mIU/mL, they should be given a single booster dose (4th dose) of vaccine. Persons with immune memory established from effective prior vaccination should respond to this booster dose. Anti-HBs should be checked 4 weeks later, and if the anti-HBs level remains <10 mIU/mL, the possibility of HBV infection should be investigated (and, if excluded, the person should be managed as a non-responder to vaccination, refer to below). If the anti-HBs level is ≥10 mIU/mL, the person can be regarded as immune.

**Non-responders to primary vaccination**

A non-responder is a person without HBV infection who has a documented history of an age-appropriate primary course of hepatitis B vaccine, but with a current anti-HBs level <10 mIU/mL. There are a number of potential options for non-responders. Persons who do not respond to the primary vaccine course, and in whom chronic HBV infection has been excluded, should be offered additional doses.

As discussed above, in Serological testing following hepatitis B vaccination, a single booster dose (4th dose) of vaccine can be given to confirm non-responder status. Persons who are non-responders after being given the booster/4th dose (and in whom HBV infection has been excluded) should have 2 further doses of hepatitis B vaccine at monthly intervals, and be re-tested 6 months after the final dose. If this regimen does not result in an anti-HBs level of ≥10 mIU/mL, or anti-HBs persists ≥10 mIU/mL for 1st of the 3 repeat doses, as recommended for non-responders.
Engerix-B (0.25 mL [5 μg] per dose) was used in these studies, giving up to 4 doses.

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Younger age and longer duration (≥6 months) since the last IM dose may be associated with greater probability of response.86 If an intradermal dose(s) is given, it is recommended that the

anti-HBs levels be measured before each subsequent dose to assess for seroconversion.

Persistent non-responders should be informed that they should be considered not protected against hepatitis B and should minimise exposures. They should also be informed about the need

for HBIG within 72 hours of parenteral or mucosal exposure to HBV (refer to Table 4.5.3).

4.5.8 Pregnancy and breastfeeding

Hepatitis B vaccine is not routinely recommended for pregnant or breastfeeding women. However, the WHO (World Health Organization) states that neither pregnancy nor breastfeeding is a

contraindication to the use of this vaccine.86

Refer to 3.3 Groups with special vaccination requirements, Table 3.3.1 Recommendations for vaccination in pregnancy for more information.

(Handbook10-home-handbook10part3-handbook10-3-3#table-3-3-1)

4.5.9 Contraindications

The only absolute contraindications to hepatitis B vaccines are:

• anaphylaxis following a previous dose of any hepatitis B vaccine

• anaphylaxis following any vaccine component.

In particular, hepatitis B vaccines are contraindicated in persons with a history of anaphylaxis to yeast.

4.5.10 Adverse events

Extensive experience indicates that the birth dose of hepatitis B vaccine is very well tolerated by newborn infants. It does not interfere with either the establishment or maintenance of

breastfeeding, and it is not associated with an increased risk of either fever, medical investigation for sepsis, or serious outcomes in newborns who were vaccinated compared with the

unvaccinated.85-91

Adverse events after hepatitis B vaccination are transient and minor, and include soreness at the injection site (5%), fever (usually low grade; 2–3%), nausea, dizziness, malaise, myalgia and

arthralgia. Fever can be expected in some neonates following immunisation with hepatitis B vaccine (0.6–3.7%).

Anaphylaxis has been reported very rarely in adults, notably in yeast-sensitive individuals.92 Although various adverse events such as demyelinating diseases, Guillain-Barré syndrome and

arthritis have been reported, there is no evidence of a causal relationship with hepatitis B vaccination.92,93

The World Health Organization Global Advisory Committee on Vaccine Safety states that ‘multiple studies and review panels have concluded that there is no link between MS [multiple

sclerosis] and hepatitis B vaccination’.94,95

The vaccine produces neither therapeutic effects nor adverse events in infants with chronic HBV infection. It is also safe, though of no additional benefit, in those already immune to

hepatitis B through past natural infection.

4.5.11 Public health management of hepatitis B

Acute hepatitis B and newly identified chronic hepatitis B are notifiable diseases in all states and territories in Australia.

Further instructions about the public health management of hepatitis B, including management of cases of acute hepatitis B and newly identified chronic hepatitis B, and their contacts, should be

obtained from state/territory public health authorities (refer to Appendix 1 Contact details for Australian, state and territory government health authorities and communicable disease control

(Handbook10-home-handbook10-tools-handbook10-appendices-handbook10-appendix1)).

Following significant exposure (percutaneous, ocular or mucous membrane) to blood or to potentially blood-contaminated secretions, where feasible, the source individual should be tested

for HBsAg as soon as possible.

If the person exposed has not been previously vaccinated against hepatitis B, their anti-HBs level, and anti-HBc and HBsAg status, should be determined immediately. If the person exposed

was a documented protective response (anti-HBs level ≥10 mIU/mL) at any time after vaccination. If the response to previous vaccination is unknown, the anti-HBs level should be

measured before each subsequent dose to assess for seroconversion.

Table 4.5.3: Post-exposure prophylaxis for non-immune persons exposed to a HBsAg-positive source

<table>
<thead>
<tr>
<th>Type of exposure</th>
<th>Hepatitis B immunoglobulin</th>
<th>Vaccine</th>
</tr>
</thead>
<tbody>
<tr>
<td>Perinatal (exposure of babies during and after birth)*</td>
<td>100 IU, by IM injection</td>
<td>Single dose immediately after birth (preferably within 12 hours of birth and certainly within 48 hours)</td>
</tr>
<tr>
<td>Percutaneous, ocular or mucous membrane</td>
<td>400 IU, by IM injection 100 IU, if body weight &lt;30 kg</td>
<td>Single dose within 72 hours of exposure</td>
</tr>
<tr>
<td>Sexual</td>
<td>400 IU, by IM injection 100 IU, if body weight &lt;30 kg</td>
<td>Single dose, preferably within 72 hours of last sexual contact‡</td>
</tr>
</tbody>
</table>

‡ Refer to 3.3.

† Refer to Table 4.5.3.

§ Refer to 3.3.

Any person with probable or confirmed acute or chronic hepatitis B should be investigated for possible occupational exposure. The source should be tested for HBsAg as soon as possible.

Acute hepatitis B and newly identified chronic hepatitis B are notifiable diseases in all states and territories in Australia.
Hepatitis B immunoglobulin (HBIG) is prepared from plasma donated through routine blood bank collection. Samples are selected on the basis that they contain high levels of anti-HBs antibodies. As stocks of HBIG are very limited, use should be strictly restricted for those who are at high risk, such as babies born to mothers with chronic HBV infection and non-immune persons who are exposed through occupational exposure to the blood of unidentified persons or to persons who are chronically infected with hepatitis B or whose hepatitis status cannot be ascertained in time. Requests should be directed to the Australian Red Cross Blood Service in your state/territory (refer to 5.1.1 Availability of immunoglobulins in Part 5 Passive immunisation/handbook10-home-handbook10part5-handbook10-5-1)).

4.5.12 Variations from product information

The product information for Infanrix hexa states that this vaccine is indicated for primary immunisation of infants from the age of 6 weeks and as a booster dose for children 18 months of age if boosting is required for all antigens. The ATAGI recommends that this vaccine may also be used for catch-up of the primary schedule in children <10 years of age.

The product information for Infanrix hexa states that this vaccine is contraindicated in children with encephalopathy of unknown aetiology or with neurologic complications occurring within 7 days following a vaccine dose. The ATAGI recommends instead that the only contraindication is a history of anaphylaxis to a previous dose or to any of the vaccine components.

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BMC Infectious Diseases 2010;10:357.


The incidence rate of penile cancer cancer incidence has been steadily increasing over the past few decades; however, the increase has been greater in males than in females. The proportion of cancers of other anogenital sites that is attributable to HPV ranges from approximately 40% for vulval cancers to approximately 85% for anal cancers. More than 85% of Australians in remote and very remote areas have 1.5 times higher cervical cancer incidence than those living in major cities.

Australians in remote and very remote areas also have 1.5 times higher cervical cancer incidence than those living in major cities. The prevalence of high-risk HPV types 16 and 18, detected when cervical samples collected for cytology were tested for HPV DNA, was similar between screened through the National Cervical Screening Program.

Persistent HPV infection is the necessary precursor for the development of all cervical cancers. Malignant transformation in the cervix usually occurs 10 to 20 years following infection with high-risk HPV types, but has been reported to occur in less than 2 years.

Transmission of anogenital HPV occurs primarily through sexual intercourse; however, virus transmission can less commonly occur following non-penetrative sexual contact. Transmission of HPV can cause laryngeal infection in infants, rarely resulting in recurrent respiratory papillomatosis. HPV infection is often subclinical, but, dependent upon the infection HPV genotypes, may result in lesions that include cutaneous warts, genital warts, respiratory papillomatisms (low-risk HPV types), and dysplasias and cancers of the cervix, vulva, vagina, penis, anus, and the oral cavity and oropharynx (high-risk HPV types). Most genital HPV infections are cleared (no longer detectable via HPV DNA testing) within 12 to 24 months. In about 3 to 10% of infections, the virus persists. Persons with persistent HPV infection constitute the at-risk group for development of HPV-associated cancers.

The causal link between persistent cervical HPV infection and cervical cancer is well established. The strength of association between HPV infection and other cancers varies by site and oncogenic HPV type.

Cellular changes that occur in the cervix as a result of HPV infection are referred to as cervical intraepithelial neoplasia (CIN). The majority of these changes regress, but a minority will progress to cervical cancer. Malignant transformation in the cervix usually occurs 10 to 20 years following infection with high-risk HPV types, but has been reported to occur in less than 2 years.

The clinical features of other HPV-associated cancers and their precursor lesions in the anogenital region and oropharynx vary, and also depend on the anatomical site. The process of progression of HPV-associated precursor lesions to cancers in these sites is less well understood than the process in the cervix. Anogenital warts may present as painless lumps, or with local tenderness, itching or bleeding. Recurrent respiratory papillomatosis is a potentially fatal condition that usually occurs in childhood, characterised by multiple warty exsiccences on the mucosal surface of the respiratory tract.

Infection with HPV is very common in both men and women, with initial infection occurring close to the time of sexual debut. It is estimated that up to 75% of the general population will be infected with at least one genital type of HPV at some time in their lives. A greater number of sexual partners is consistently found to be associated with an increased risk of HPV acquisition.

HPV infection rates differ between geographic regions, and estimated population prevalence of HPV also varies depending on the anatomical site and the lesions sampled. About two-thirds of Australian women aged 15–20 years participating in cervical screening had HPV DNA detected in cervical samples collected for cytology.

Certain population subgroups are identified to be at increased risk of HPV infection and HPV-associated diseases, compared with the general population. Infection with multiple HPV genotypes and longer time to clear infection are commonly observed in men who have sex with men (MSM). In addition, the prevalence of high-risk HPV types is significantly higher in HIV-positive MSM than in MSM who are HIV-negative. Persons who are immunocompromised (due to disease or medical treatment) are at increased risk of HPV-related disease.

In a serosurvey conducted in Australia in 2005, 24% of females and 18% of males aged 0–69 years were seropositive to at least one of the four HPV types 6, 11, 16 and 18 – noting that fewer than 60% of women, and an even lower proportion of men, who are infected with HPV develop antibodies. The onset age of seropositivity for HPV in this study was 10–14 years in females and 15–19 years in males. The average age of sexual debut for both males and females in Australia was 16 years, as reported in 2000–2002. A more recent national survey in 2008 reported that about 80% of senior secondary school children (aged approximately 15–19 years) acknowledged having engaged in sexual activity that may transmit HPV.

Persistent HPV infection is the necessary precursor for the development of all cervical cancers. Worldwide, approximately 70% of cervical cancers contain HPV-16 DNA and 16% contain HPV-18 DNA. Australian data indicate that HPV-16 and HPV-18 are responsible for approximately 60% and 20%, respectively, of cervical cancers, and 37% and 8%, respectively, of high-grade cervical abnormalities.

In Australia, cervical cancer ranked 22nd in the overall cancer disease burden in 2008 and now occurs predominantly in women unscreened or under-screened through the National Cervical Screening Program. In 2007, the age-standardised incidence rate of cervical cancer in Australia was 6.8 per 100 000, and the mortality rate was 1.8 deaths per 100 000 women. The prevalence of high-risk HPV types 16 and 18, detected when cervical samples collected for cytology were tested for HPV DNA, was similar between Indigenous and non-Indigenous women. However, the incidence rate of cervical cancer in Aboriginal and Torres Strait Islander women is almost 3 times higher than in non-Indigenous Australian women, an indication of lower participation rates in cervical screening programs by Indigenous Australians and greater prevalence of cofactors for cervical cancer such as smoking, earlier and more pregnancies, and lower socioeconomic status.

Indigenous women are 5 times more likely to die from cervical cancer than non-Indigenous women. Also, Australians in remote and very remote areas have 1.5 times higher cervical cancer incidence than those living in major cities.

The proportion of cancers of other anogenital sites that is attributable to HPV ranges from approximately 40% for vulval cancers to approximately 85% for anal cancers. More than 85% of these HPV-associated cancers have evidence of infection due to the high-risk HPV types 16 and 18.

In Australia in 2007, incidence rates of vulval and vaginal cancers in women were 2.6 per 100 000 (n=276) and 0.65 per 100 000 (n=69). The incidence rate of penile cancer was 0.8 per 100 000. The age-standardised incidence rate for anal cancer was 1.3 per 100 000; however, a slightly higher incidence was observed in females than in males. Overall, anal cancer incidence has been steadily increasing over the past few decades; however, the increase has been greater in males than in females. The mortality rates for vulval, vaginal, penile and anal cancers were all less than 0.6 per 100 000.
In clinical trials, vaccine efficacy has been demonstrated up to at least 5 years for 4vHPV vaccine and 9.4 years for 2vHPV vaccine in women, with efficacy of HPV vaccines in females or males <16 years of age was not assessed in pre-market trials due to the genital sampling requirements of such studies. However, the antibody response in females results in some herd immunity benefits to males, with a significant decline in the diagnosis of genital warts observed in unvaccinated males of the same age, 55,56,58. In addition to reduction in genital warts, Victorian data have demonstrated a 48% decline in the incidence of high-grade cervical abnormalities in girls aged <18 years in the years after the introduction of the HPV Vaccination Program. 57 National cervical screening data are also indicating a decline in high-grade lesions diagnosed in women aged <20 years.59

4.6.4 Vaccines

There are two HPV vaccines registered for use in Australia: the bivalent vaccine (2vHPV; Cervarix), which contains virus-like particles (VLPs) of HPV types 16 and 18; and the quadrivalent vaccine (4vHPV; Gardasil), which contains VLPs of HPV types 16, 18, 6 and 11. VLPs are not infectious and do not replicate or cause cellular abnormalities.60,61

- **Cervarix** – GlaxoSmithKline Pty Ltd (recombinant protein particle [VLP] vaccine containing the major capsid [L1] protein of HPV types 16 and 18; 2vHPV). Each 0.5 mL monodose vial or pre-filled syringe contains 20 µg HPV-16 L1 protein and 20 µg HPV-18 L1 protein, adjuvanted with AS04 (comprised of 0.5 mg aluminium hydroxide and 50 µg 3-O-desacyl-4′-monophosphoryl lipid A [MPL]).

- **Gardasil** – bioCSL Pty Ltd/Merck Sharp & Dohme (Australia) Pty Ltd (recombinant protein particle [VLP] vaccine containing the major capsid [L1] protein of HPV types 6, 11, 16 and 18; 4vHPV). Each 0.5 mL monodose vial or pre-filled syringe contains 20 µg HPV-6 L1 protein, 40 µg HPV-11 L1 protein, 40 µg HPV-16 L1 protein and 20 µg HPV-18 L1 protein, adsorbed onto 0.225 mg of aluminium as aluminium hydroxypophosphate sulphate; 0.780 mg L-histidine; 50 µg polysorbate 80; 35 µg sodium borate. May also contain yeast proteins.

The 2vHPV and 4vHPV vaccines have been assessed in females in a number of international clinical trials. When given as a 3-dose series, HPV vaccines elicit a neutralising antibody level many times higher than the level observed following natural infection.61,62 Overall, seroconversion occurs in 97% to 100% of those vaccinated 63,65 in women who are naïve to HPV types 16 and 18 prior to vaccination, both vaccines are highly effective at preventing type-specific persistent infection and related cervical disease (approximately 90 to 100%).55-57 The 4vHPV vaccine also has already established efficacy (100%; 95% CI: 94–100%) against external anogenital and vaginal lesions (genital warts, and vulval, vaginal, perineal and perianal dysplasias) associated with HPV types 6, 11, 16 or 18 in women.

In women who are vaccinated irrespective of their baseline HPV status (i.e. women who may have pre-existing HPV infection), vaccine efficacy is lower than observed in HPV-naïve women, indicating reduced vaccine effectiveness among women who are already sexually active. This is because both HPV vaccines are prophylactic vaccines (i.e. preventing primary HPV infection). Vaccination will not treat an existing HPV infection or prevent disease that may be caused by an existing HPV vaccine-type infection.63,72,73 However, vaccination may still provide benefit for sexually active women by protecting them against new infections with other vaccine-preventable HPV types.

The efficacy of 4vHPV in males aged 16–26 years has been demonstrated in one clinical trial.74 Vaccination was greater than 85% protective against persistent anogenital infection and external genital lesions due to vaccine HPV types in HPV-naïve participants. Among HPV-naïve MSM participants within the clinical trial, vaccine efficacy was 95% against intra-anal HPV infection and 75% against high-grade anal intraepithelial neoplasia from vaccine HPV types. Efficacy of 2vHPV vaccine in males has not been assessed to date; however, the vaccine has demonstrated safety and immunogenicity in males aged 10–18 years.75

There is some evidence of HPV vaccine providing some cross-protection to disease due to other HPV types in women: 4vHPV vaccine against cervical disease due to HPV types 31 and 45 and 2vHPV vaccine against cervical disease due to HPV types 31, 33, 45 and 51.76 However, the level of protection is less than for the vaccine HPV types and the durability of any such protection is unknown. Next generation HPV vaccines that protect against a greater number of HPV types are in development, for example, a 9-valent VLP vaccine.77 Efficacy of HPV vaccines in females or males <16 years of age was not assessed in pre-market trials due to the genital sampling requirements of such studies. However, the antibody responses observed in pre-adolescent and adolescent females and males (>9 years of age) were greater than those in adult women and men, in whom clinical efficacy has been demonstrated for both the 4vHPV and 2vHPV vaccines.

It is not certain how long immunity following HPV vaccination persists, or whether a booster dose after the primary course will ever be required. However, long-term population-based follow-up studies to assess this are underway.78 In clinical trials, vaccine efficacy has been demonstrated up to at least 5 years for 4vHPV vaccine and 9.4 years for 2vHPV vaccine in women, with no breakthrough disease due to vaccine HPV types.61,62,64

Although clinical studies of 2vHPV and 4vHPV have demonstrated that the immunogenicity of a 2-dose schedule (with a 6-month interval between doses) is non-inferior in healthy adolescent girls (approximately 9 – 14 years of age) that achieved in a 3-dose schedule in older females (approximately 15 – 26 years of age), schedules of fewer than 3 doses are not currently recommended in Australia. 52,83 Studies comparing different intervals between HPV vaccine dose administration that show immunogenicity of 3-dose schedules with intervals between doses of up to 12 months is non-inferior to standard 3-dose schedules.84-86

4.6.5 Transport, storage and handling

Transport according to National vaccine storage guidelines: **Strive for 5.** Store at +2°C to +8°C. Do not freeze. Protect from light.

4.6.6 Dosage and administration

The dose of both HPV vaccines is 0.5 mL to be given by IM injection.

The primary vaccination course for both HPV vaccines consists of 3 doses.

The recommended 3-dose schedule for the 2vHPV vaccine is at times 0 (the day the 1st dose is given), 1 and 6 months. The 2vHPV vaccine is registered for use in females aged 10–45 years. The 2vHPV vaccine is not registered for use in males of any age.

The recommended 3-dose schedule for the 4vHPV vaccine is at times 0 (the day the 1st dose is given), 2 and 6 months. The 4vHPV vaccine is registered for use in females aged 9–45 years and in males aged 9–26 years.

Where vaccines have been administered at less than the minimum intervals (refer to Table 2.1.12)(Handbook10-home-handbook10part2-handbook10-2-1#table-2-1-12) Catch-up schedule for persons ≥10 years of age (for vaccines recommended on a population level), contact your state or territory health department for guidance. Refer also to Chief Medical Officer Guidance (http://www.health.gov.au/internet/immunise/publishing.nsf/Content/cmofull-advice-hpv-cnt)

Co-administration with other vaccines
Both HPV vaccines can be given concomitantly with reduced antigen content diphtheria-tetanus-acellular pertussis (dTpa) or diphtheria-tetanus-acellular pertussis-inactivated poliomyelitis vaccine (dTpa-IPV), and hepatitis B vaccine (monovalent). There are no clinical data regarding concomitant administration of either HPV vaccine with varicella vaccine, but there are no theoretical concerns about safety or efficacy of the vaccines if they are given simultaneously, using different injection sites.

Interchangeability of human papillomavirus vaccines
There are currently no clinical data available on the interchangeability of the two HPV vaccines. However, from first principles, acceptable antibody levels and protection against HPV-16 and 18 (the types that are shared by both these vaccines and that are the dominant causes of cervical cancer) would be expected following a combination schedule.

It is recommended that an HPV vaccination course commenced with one vaccine should, wherever possible, be completed with that vaccine and according to its recommended schedule. Where the course includes a combination of the two HPV vaccines, either inadvertently or because of an adverse event following one vaccine, the person is considered to be fully immunised against HPV-16 and 18 disease if a total of 3 doses of HPV vaccine have been given, provided that the minimum interval requirements between the doses are satisfied. Every effort should be made to complete a 3-dose schedule for effective protection against disease due to each of the vaccine HPV types.

4.6.7 Recommendations

The two HPV vaccines, 2vHPV and 4vHPV, are registered to use in different age groups and genders (refer to 4.6.6 Dosage and administration above. Neither vaccine is registered or recommended for use in children <9 years of age.

Females
Both the 4vHPV and 2vHPV vaccines are recommended for use in females, in a 3-dose schedule, for prevention of persistent infection and anogenital disease caused by HPV types 16 and 18. The 4vHPV vaccine also provides protection against vaccine-type genital warts (which are mostly caused by HPV types 6 and 11). (Refer also to 4.6.4 Vaccines above.)

Children and adolescents aged 9–18 years
Three doses of HPV vaccine are recommended for females 9–18 years of age. The optimal age for administering the HPV vaccine is approximately 11–13 years, as most females in this age group would not have commenced sexual activity and so would be naïve to all HPV types. Vaccination only provides protection against vaccine-type disease if the vaccine is delivered prior to acquisition of that HPV type. Therefore, the decision to vaccinate older adolescent females, who may have already commenced sexual activities, should follow an assessment of the potential benefits, based on their likely previous HPV exposure and future risks of HPV exposure.

Adults aged ≥19 years
Vaccination of all women in this age group is not routinely recommended, as many are likely to have been exposed to one or more vaccine HPV types through sexual activity (refer to 4.6.3 Epidemiology above). However, some adult females may gain an individual benefit from HPV vaccination. The decision to vaccinate older females should take into account their likelihood of previous exposure to HPV and their future risks of HPV exposure.

Males
The 4vHPV vaccine is recommended, in a 3-dose schedule, for use in males for prevention of persistent infection and anogenital disease caused by HPV types 6, 11, 16 and 18. The 4vHPV vaccine also provides protection against vaccine-type genital warts (which are mostly caused by HPV types 6 and 11). (Refer also to 4.6.4 Vaccines above.)

Children and adolescents aged 9–18 years
Three doses of 4vHPV vaccine are recommended for males 9–18 years of age. The optimal age for administering the 4vHPV vaccine is approximately 11–13 years, as most males in this age group would not have commenced sexual activity and so would be naïve to all HPV types. Vaccination only provides protection against vaccine-type disease if the vaccine is delivered prior to acquisition of that HPV type. Therefore, the decision to vaccinate older adolescent males, who may have already commenced sexual activities, should follow an assessment of the potential benefits, based on their likely previous HPV exposure and future risks of HPV exposure.

Adults aged ≥19 years
Vaccination of all men in this age group is not routinely recommended as many are likely to have been exposed to one or more vaccine HPV types through sexual activity (refer to 4.6.3 Epidemiology above). However, some adult males may gain an individual benefit from HPV vaccination. The decision to vaccinate older males should take into account their likelihood of previous exposure to HPV and their future risks of HPV exposure. Although the 4vHPV vaccine is only registered for use in males 9–26 years of age, there are no theoretical concerns that the efficacy or safety of this vaccine in males up to the age of 45 years will differ significantly from that in younger males, or females of the same age.

Men who have sex with men
The 4vHPV vaccine is recommended for men who have sex with men (MSM) who have not previously been vaccinated with 3 doses of HPV vaccine. The decision to vaccinate males in this group should take into account their likelihood of previous exposure to HPV and their future risks of HPV exposure. Overall, MSM are at increased risk of persistent HPV infection and associated disease (independent of HIV status or the presence of other immunocompromising conditions). In addition, at the population level, MSM are less likely to benefit from herd immunity attained from HPV vaccination of females. The safety and efficacy of 4vHPV vaccine has been demonstrated in MSM participants in a randomised clinical trial (refer to 4.6.4 Vaccines above).

Persons who are immunocompromised
HPV vaccine, in a 3-dose schedule, is recommended for adult men and women who are immunocompromised due to medical conditions (including HIV infection) or treatment. The decision to vaccinate immunocompromised persons should take into account their likelihood of previous exposure to HPV, their future risks of HPV exposure, and the extent and duration of their immunocompromise (refer to 3.3.3 Vaccination of immunocompromised persons)(Handbook10-home-handbook10part3-handbook10-3-3#3-3-3-3)). Immunocompromised adolescents who have not yet been vaccinated with 3 doses of HPV vaccine should be offered catch-up vaccination. This is based on evidence that persons who are immunocompromised are more likely to develop a persistent HPV infection and to subsequently progress to HPV-related disease.

There are currently no clinical trial data demonstrating the efficacy of either of the HPV vaccines in immunocompromised participants. However, 4vHPV has been shown to be well tolerated and immunogenic in HIV-infected males and women with systemic lupus erythematosus. As HPV vaccines are not live viral vaccines, there are no specific safety concerns regarding administration to persons with additional medical conditions.
For all sexually active women, regular cervical screening remains an important preventive measure against cervical disease (refer to the National Cervical Screening Program (http://www.cancerscreening.gov.au) at (www.cancerscreening.gov.au)). Vaccination is not an alternative to cervical screening but is a complementary preventive measure, as HPV types other than those included in the current vaccines have the potential to cause cervical cancer. Likewise cervical screening is not an alternative to HPV vaccination. Both are recommended.

Cervical screening detects histopathological changes. It is not recommended to test for the presence of HPV virus or antibody routinely as a way of determining whether HPV vaccination is indicated.

For women who have recently been diagnosed with cervical dysplasia, or have been treated for this in the past, HPV vaccine will have no impact on current disease, but may prevent future dysplasia due to different HPV types included in the vaccine.

4.6.8 Pregnancy and breastfeeding

HPV vaccines are not recommended for pregnant women.

Women who become pregnant after starting the HPV vaccination course should withhold getting further doses of the HPV vaccine while pregnant, and receive the remaining doses of the course after pregnancy.

Females who inadvertently receive a dose of HPV vaccine around the time of conception or during pregnancy should be informed of the body of evidence supporting lack of harm from vaccine administration in this setting. Among women who became pregnant during the course of 4vHPV vaccine clinical trials (despite recommendations for participants to avoid pregnancy), the overall proportions of pregnancies that resulted in an adverse outcome (spontaneous abortion, late fetal death, infant with congenital anomalies) were similar among 4vHPV vaccine recipients and placebo or control vaccine recipients. Although one clinical trial raised the possibility of an association between 4vHPV vaccine administered within 30 days following the estimated date of conception and an increased incidence of congenital anomalies in the infant, those conditions were relatively common and unrelated. Pooled analyses from multiple clinical trials have not confirmed such an association.

Pooled analysis of women who became pregnant during clinical trials showed that, overall, there were no differences in pregnancy outcomes between 2vHPV vaccine and control vaccine recipients.

HPV vaccines can be given to breastfeeding women. Among breastfeeding mothers in the clinical studies of 4vHPV vaccine, the rates of adverse events in the mother and the breastfeeding infant were comparable between 4vHPV vaccine and control vaccination groups. The effect on breastfed infants of the administration of 2vHPV vaccine to their mothers has not been evaluated directly in clinical studies, but breastfeeding is not considered a contraindication for receiving the 2vHPV vaccine.

Refer to 3.3 Groups with special vaccination requirements, Table 3.3.1(Handbook10-home~handbook10part3~handbook10-3-3#table-3-3-1) Recommendations for vaccination in pregnancy for more information.

4.6.9 Contraindications

The only absolute contraindications to HPV vaccines are:

- anaphylaxis following a previous dose of either HPV vaccine
- anaphylaxis following any vaccine component.

In particular, the 4vHPV vaccine is contraindicated in persons with a history of anaphylaxis to yeast.

4.6.10 Adverse events

Both the 2vHPV and 4vHPV vaccines are generally safe and well tolerated.

For both vaccines, injection site pain was the most commonly reported adverse event (approximately 80% of recipients), followed by swelling and erythema (20–30% for each). Injection site reactions were more commonly reported in vaccine recipients than in recipients of aluminium-containing placebo or control vaccines in clinical trials. Systemic reactions were also very common following both vaccines, occurring in up to about 30% of recipients. The most common adverse events included headache, fatigue, fever and myalgia. In most of the clinical trials, the frequencies of most of these common systemic adverse events were comparable between the HPV vaccine and the control vaccine recipients. Meta-analyses on pooled data from multiple clinical trials on both the 2vHPV and 4vHPV vaccines have shown no increase in the risk of serious adverse events among vaccine recipients compared with control recipients.

For both vaccines, the safety profile and the spectrum of adverse events following immunisation in males were similar to those reported in females of corresponding age groups, although some of the studies were not direct comparison studies.

Post-marketing passive surveillance of HPV vaccine use in the United States has identified syncope (fainting) as one of the most common adverse events reported following 4vHPV vaccine in adolescent and young adult females. A small proportion (about 10%) of syncopal episodes resulted in a fall with head injury. Similar or higher rates of syncope have been reported in other countries, through different surveillance mechanisms.

However, a prospective adverse events surveillance study in the United States, based on over 600,000 records of vaccine doses administered, did not find any increased risk of syncope with 4vHPV vaccination compared to the expected rate following non-4vHPV vaccination in youths and adults. Symptomatic syncope (fainting) may follow any vaccination, especially in adolescents and young adults, but is preventable through appropriate precautions. (Refer also to 2.3.2(Handbook10-home~handbook10part2~handbook10-2-3#section-2-3) Adverse events following immunisation). In an Australian study, 22 subjects (including 14 with syncope and 8 with syncopal seizure following 4vHPV vaccination) were reviewed in a Victorian clinic and received further doses while supine; no recurrence of syncope occurred.

Anaphylaxis and other suspected hypersensitivity reactions, including skin rash, after 4vHPV vaccine have also been reported. The estimated incidence rate of anaphylaxis following 4vHPV vaccine in Australia, as at June 2010, was 2.6 anaphylaxis episodes per million doses of vaccine distributed, which was within the rate range for other vaccines given to children and adolescents in international studies. A prospective surveillance study in the United States did not find any increased risk of anaphylaxis or allergic reactions with 4vHPV vaccination compared to the expected rate following childhood vaccines.

4.6.11 Variations from product information

The product information for the 4vHPV vaccine, Gardasil, states that this vaccine is indicated for use in males up to 26 years of age and females up to 45 years of age. The product information for the 2vHPV vaccine, Cervarix, states that this vaccine is indicated for use in females up to 45 years of age and is not registered for use in males of any age. The ATAGI instead recommends that some males aged >26 years, such as MSM and those who are immunocompromised, who are likely to derive an individual benefit from HPV vaccination, can be vaccinated with 4vHPV. The ATAGI also recommends that some females aged >45 years, such as those who are immunocompromised, can be vaccinated with either 2vHPV or 4vHPV, based on their individual risk of future HPV exposure and disease.

The product information for the 2vHPV vaccine, Cervarix, states that this vaccine is registered for use in a 2-dose schedule in girls who receive their first vaccine dose between 10 and 14 years of age. The ATAGI instead currently recommends girls in this age group routinely receive 3 doses of HPV vaccine.

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A full reference list is available on the electronic Handbook or Immunise Australia website (http://www.immunise.health.gov.au).


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Influenza is transmitted from person to person by virus-containing respiratory aerosols produced during coughing or sneezing, or by direct contact with respiratory secretions.1,2 Influenza virus infection causes a wide spectrum of disease, from no or minimal symptoms, to respiratory illness with systemic features, to multisystem complications and death from primary viral or secondary bacterial pneumonia. Severe disease from seasonal influenza is more likely with advanced age; infancy; lack of previous exposure to antigenically related influenza virus; greater virulence of the viral strain; chronic conditions, such as heart or lung disease, renal failure, diabetes and chronic neurological conditions; immunocompromise; obesity (class III); pregnancy; and smoking. Severe disease may also occur in otherwise healthy children and young adults. Annual attack rates in the general community are typically 5 to 10%, but may be up to 20% in some years. In households and ‘closed’ populations, attack rates may be 2 to 3 times higher.3,4 However, as asymptomatic or mild influenza illness is common and symptoms are non-specific, a large proportion of influenza infections are not detected.

In adults, the onset of illness due to influenza is often abrupt, usually after an incubation period of 1 to 3 days, and includes systemic features such as malaise, fever, chills, headache, anorexia and myalgia. These may be accompanied by a cough, nasal discharge and sneezing. Fever is a prominent sign of infection and peaks at the height of the systemic illness. Complications of influenza include: acute bronchitis, croup, acute otitis media, pneumonia (both primary viral and secondary bacterial pneumonia), cardiovascular complications including cardiac decompensation.

Influenza activity varies from year to year and is dependent on the circulating virus and the susceptibility of the population.1-5 Infection in young infants may be associated with more non-specific symptoms.

The clinical features of influenza in infants and children are similar to those in adults. However, temperatures may be higher in children (and may result in febrile convulsions in this susceptible age group), and otitis media and gastrointestinal manifestations are more prominent.5 Infection in young infants may be associated with more non-specific symptoms.5,6 Complications of influenza include: acute bronchitis, croup, acute otitis media, pneumonia (both primary viral and secondary bacterial pneumonia), cardiovascular complications including myocarditis and pericarditis, post-infectious encephalitis, Reye syndrome, and various haematological abnormalities. Primary viral pneumonia occurs rarely, but secondary bacterial pneumonia is a frequent complication in persons whose medical condition makes them vulnerable to the disease. Such persons are at high risk in epidemics and may die of pneumonia or cardiac decompensation.

In most years, minor or major epidemics of type A or type B influenza occur, usually during the winter months in temperate regions. It has long been recognised that the impact of influenza is often substantially underestimated. On average each year in Australia, approximately 100 deaths and 5100 hospitalisations are recorded as being directly attributable to influenza.1,2 In the 2017 influenza season, the highest levels of activity since the 2009 pandemic year were recorded. Systematic introduction of rapid influenza testing in hospitals in New South Wales may have contributed in part to the increased number of laboratory-confirmed notifications of influenza. Approximately 750 deaths were reported nationally among notified cases of laboratory-confirmed influenza in 2017.9 A study using mathematical modelling estimated that there are over 3000 deaths and more than 13 500 hospitalisations due to influenza per year among Australians aged over 50 years.10 Another mathematical modelling study estimated the annual rate of seasonal influenza A mortality to be as high as 25.8 per 100 000 population in Australians aged ≥65 years.11 Influenza activity varies from year to year and is dependent on the circulating virus and the susceptibility of the population.10,12 Changes in influenza detection methods, such as an increase in the routine use of polymerase chain reaction (PCR)-based laboratory testing in recent years, has impacted influenza detection and notification patterns.13

In Australia, like other developed countries, the highest rates of influenza hospitalisations are seen in the elderly and in children <5 years of age (Figure 4.7.1).13,14,15 The disease burden from influenza is greater in Aboriginal and Torres Strait Islander people than in non-Indigenous Australians, across all age groups.13 During annual epidemics of influenza, a greater rise in morbidity and mortality is seen among pregnant women and people with chronic diseases compared with otherwise healthy individuals.13,15

References

1. Pandemic subtypes arise following antigenic shift, which is due to direct adaptation to humans of an avian or animal virus, or to this adaptation occurring by genetic reassortment (mixing) with a human virus.

2. Both influenza A and influenza B viruses undergo frequent changes in their surface antigens, involving stepwise mutations of genes coding for H and N glycoproteins. This results in cumulative changes in antigenic subtypes, or ‘antigenic drift’, which is responsible for the annual outbreaks and epidemics of influenza and is the reason that the composition of influenza vaccines requires annual review. ‘Antigenic shift’, defined as a dramatic change in influenza A H (and other) antigen(s), occurs occasionally and unpredictably and can cause pandemic influenza.5 Pandemic subtypes arise following antigenic shift, which is due to direct adaptation to humans of an avian or animal virus, or to this adaptation occurring by genetic reassortment (mixing) with a human virus.
There were 44,403 confirmed A(H1N1)pdm09 cases and 213 deaths in Australia between May 2009 and November 2010. A live attenuated intranasal influenza vaccine is registered in Australia but is not currently available. It is formulated with higher quantities of inactivated virus and adjuvant (i.e. 60 µg HA per included virus strain per dose); the other contains an adjuvant, MF59, and the standard 15 µg of HA per strain per dose. Both vaccines are formulated to induce a greater immune response than standard TIVs.

From the late 1970s, influenza vaccines contained three strains of influenza virus – two influenza A subtypes and one influenza B lineage (i.e. trivalent influenza vaccines or TIVs). Inactivated quadrivalent influenza vaccines (QIVs) containing four influenza virus strains; ≤100 ng ovalbumin; ≤0.01 mg formaldehyde; 0.02 mg cetrimonium bromide; 1 ng gentamicin sulfate. May contain traces of sodium taurodeoxycholate, neomycin, polymyxin B and β-propiolactone.

Three influenza pandemics were recognised in the 20th century, in 1918 (H1N1), 1957 (H2N2) and 1968 (H3N2). Each of these pandemic strains replaced the previously circulating influenza A subtype and went on to circulate as seasonal influenza. In 1977, the A (H1N1) re-emerged in the human population and, since then, A (H1N1) and A (H3N2) have co-circulated with influenza B. More recently, various avian influenza A virus subtypes, particularly H5N1, H7N9 and H9N2, have caused human infections, but sustained human-to-human transmission has not been reported.

In 2009, the World Health Organization (WHO) declared a pandemic of a novel subtype A (H1N1) influenza virus, A(H1N1)pdm09, which originated in swine. The pandemic started in Mexico and the United States before spreading globally. There were 44,403 confirmed A(H1N1)pdm09 cases and 213 deaths in Australia between May 2009 and November 2010. The predominant clinical presentation was mild to moderate illness; however, risk factors for severe disease included obesity, pregnancy, diabetes mellitus and, in Australia, being of Aboriginal or Torres Strait Islander descent. Young healthy adults and pregnant women were over-represented among severe A(H1N1)pdm09 cases compared with previous seasonal outbreaks. The A(H1N1)pdm09 virus rapidly established itself and has become the dominant influenza strain in most parts of the world. This strain has been included in all seasonal influenza vaccine formulations used in the southern hemisphere since 2010.

Since the early 2000s, two influenza B lineages, B/Victoria and B/Yamagata, have been co-circulating in Australia in varying proportions; in some years one B lineage predominates over the other, while in other years both B lineages co-circulate in similar proportions.

4.7.4 Vaccines

All the influenza vaccines currently available in Australia are either split virion or subunit vaccines prepared from purified inactivated influenza virus that has been cultivated in embryonated hens' eggs. Although these vaccines may contain traces of egg-derived protein (ovalbumin) they contain less than 1 µg of ovalbumin per dose (refer also to 4.7.10 Precautions below and to ‘Vaccination of persons with a known egg allergy’ in 3.3.1 Vaccination of persons who have had an adverse event following immunisation). The influenza virus composition of vaccines for use in Australia is determined annually by the Australian Influenza Vaccine Committee following recommendations by the World Health Organization based on global influenza epidemiology.

From the late 1970s, influenza vaccines contained three strains of influenza virus – two influenza A subtypes and one influenza B lineage (i.e. trivalent influenza vaccines or TIVs). Inactivated quadrivalent influenza vaccines (QIVs) containing four influenza virus strains (the same strains in TIV and an additional influenza B virus strain from the other B lineage) have been registered for use in Australia since 2014 and in widespread use since 2016. Quadrivalent vaccines currently registered for use in persons aged ≥3 years contain 15 µg of haemagglutinin (HA) from each of the four virus strains and they are not adjuvanted. The ‘junior’ quadrivalent influenza vaccine registered for use from 6 months to <3 years of age contains 7.5 µg of HA from each virus strain. From 2018, two trivalent vaccines are registered for use in adults aged ≥65 years: one is a ‘high-dose’ vaccine that contains four times the HA content of standard trivalent vaccines; ≤100 µg formaldehyde; ≤250 µg octoxinol 9; ≤0.5 µg ovalbumin.

A live attenuated intranasal influenza vaccine is registered in Australia but is not currently available. Influenza vaccines presented in a purpose-designed syringe for intradermal administration were registered for use in Australia in 2009 but are no longer available.


Children aged ≥6 months to <3 years only

FluQuadri Junior – Sanofi-Aventis Australia Pty Ltd (quadrivalent inactivated influenza virus). Each 0.25 mL pre-filled syringe contains 7.5 µg haemagglutinin of each of the four recommended influenza virus strains; ≤50 µg formaldehyde; ≤125 µg octoxinol 9; ≤0.5 µg ovalbumin.

All persons aged ≥3 years

Fluarix Tetra – GlaxoSmithKline Australia Pty Ltd (quadrivalent inactivated influenza virus). Each 0.5 mL pre-filled syringe contains 15 µg haemagglutinin of each of the four recommended influenza virus strains; ≤0.05 µg ovalbumin; ≤5 µg formaldehyde; polysorbate 80; octoxinol 10. May contain traces of gentamicin, hydrocortisone and sodium deoxycholate.

FluQuadri – Sanofi-Aventis Australia Pty Ltd (quadrivalent inactivated influenza virus). Each 0.5 mL pre-filled syringe contains 15 µg haemagglutinin of each of the four recommended influenza virus strains; ≤100 µg formaldehyde; ≤250 µg octoxinol 9; ≤1 µg ovalbumin.

All adults aged ≥18 years

Afluria Quad – Seqirus (quadrivalent inactivated influenza virus). Each 0.5 mL pre-filled syringe contains 15 µg haemagglutinin of each of the four recommended influenza virus strains; <1 µg ovalbumin. May contain traces of sodium taurodeoxycholate, neomycin, polymyxin B and β-propiolactone.

Influvac Tetra – Mylan Health Pty Ltd (quadrivalent inactivated influenza virus). Each 0.5 mL pre-filled syringe contains 15 µg haemagglutinin of each of the four recommended influenza virus strains; ≤100 ng ovalbumin; ≤0.01 mg formaldehyde; 0.02 mg cetrimium bromide; 1 ng gentamicin sulfate. May contain traces of tylosine tartrate, hydrocortisone deoxycholate.

**Figure 4.7.1:** Average annual influenza hospitalisation rates for 2010 to 2015, Hospitalisations (ICD-coded; principal diagnosis) where the month of admission was between January 2010 and December 2015. IRR = incidence rate ratio.
The administration of influenza vaccine is the single most important measure in preventing or attenuating influenza infection and preventing mortality. After vaccination, most recipients develop antibody levels that are likely to protect them against the strains of virus represented in the vaccine. In addition, there is likely to be protection against many related influenza variants.

The efficacy and effectiveness of influenza vaccines of similar composition depends primarily on the age and immunocompetence of the vaccine recipient, and the degree of similarity between the virus strains in the vaccine and those circulating in the community. The magnitude of the potential additional benefit from QIV over TIV (due to protection against the additional B strain) cannot be predicted for any influenza season as it depends on a number of factors. These include annual variation in the proportion of all circulating influenza viruses that are attributable to the influenza B lineage not in the TIV, antigenic mismatch between vaccine and circulating strains, cross-protection against non-vaccine B strains afforded by the strain in the TIV, and an individual's pre-existing immunity to the circulating strains of influenza. Recent evidence suggested QIV to be 54% effective against laboratory-confirmed influenza.38

In a clinical trial, the trivalent vaccine with greater HA content (Fluzone High-Dose) was estimated to be 24% more effective against laboratory-confirmed influenza compared to standard TIV,39 and to be 2 to 36% more effective than standard TIV in reducing influenza-related deaths.40 In a large post-licensure study of community-dwelling adults aged ≥65 years, the adjuvanted TIV (Fluad) was estimated to be 25% more effective against hospitalisation for influenza or pneumonia compared to standard TIV.41 However, compared with QIVs, the potential for improved protection from these two more immunogenic TIVs is counter-balanced by the potential loss of protection against the second B lineage (conferred by QIVs), and also by increased injection site reactions42,43 (refer to 4.7.11 Adverse events below). In persons aged ≥65 years, however, disease from the A/H3 influenza strain is more common and associated with greater severity. Therefore, in this age group, the potential additional protection provided by these two TIVs against the strains included in the vaccine is likely to offset the loss of protection for the alternative B strain not included in the vaccine. In a clinical trial among adults aged ≥65 years, the TIV with greater HA content (Fluzone High-Dose) was estimated to be 23% more effective against laboratory-confirmed A/H3 influenza compared to the standard TIV.40

A recent systematic review estimated the overall efficacy of standard TIV against laboratory-confirmed influenza in healthy adults <65 years of age to be 59%, although efficacy varied by influenza season.44 The efficacy of inactivated standard TIV against influenza-like illness in persons ≥65 years of age living in the community is estimated to be 43% when viral circulation is high, although there have been few randomised controlled trials of influenza vaccine in elderly people.45 In nursing home settings, TIV is approximately 45% effective against hospitalisations due to influenza and pneumonia, and 60% effective against all-cause mortality in persons aged ≥65 years.46

Vaccination of pregnant women with standard TIV has been shown to be approximately 50% effective in reducing PCR-confirmed influenza infection and 65% effective against hospital admissions for acute respiratory illness.47,48 Vaccinating pregnant women against influenza also provides protection against laboratory-confirmed influenza to their infants up to 6 months of age, due to transplacental transfer of high titre influenza-specific antibodies. A recent systematic review concluded that maternal influenza vaccination results in an estimated 48% reduction in laboratory-confirmed influenza in infants <6 months of age.49

Young children can be vaccinated from 6 months of age, but, because they are immunologically naive to influenza, they require 2 doses of influenza vaccine when immunised for the first time, to maximise the immune response to all vaccine strains.50,51 There is evidence demonstrating that similar levels of protection are achieved in young children as in older children and adults, with an estimated vaccine effectiveness of 65% against laboratory-confirmed influenza in those aged 6 to 59 months.52,53 Recent evidence suggests that protection following influenza vaccination may begin to wane after 3 to 4 months.52,55-60 Low levels of protection may persist for a further year for some strains, if the prevalent circulating strain remains the same or undergoes only minor antigenic drift.19,37

Protection against influenza requires annual vaccination with a vaccine containing the most recent strains. Studies of the impact of repeated annual vaccination on year-to-year vaccine effectiveness have produced conflicting results. A few studies, predominantly in the United States, suggest a reduction in vaccine effectiveness after repeated annual influenza vaccination.61 However, an Australian study has reported sustained or increased vaccine effectiveness in preventing both influenza A and B illness and hospitalisation, particularly among children aged 2–6 years who have received influenza vaccination in previous seasons.55 Benefit from annual influenza revaccination is also observed among community-dwelling elderly people. Data collected over six influenza seasons shows annual influenza revaccination among community-dwelling elderly people is associated with a 15% reduction in the risk of annual mortality compared to first-time vaccination.49 Overall, despite conflicting opinion regarding the impact of repeated annual vaccination on vaccine effectiveness, greater protection against influenza infection is still observed among individuals who received influenza vaccination compared to those who did not receive any influenza vaccination.

### 4.7.5 Transport, storage and handling

Transport according to National vaccine storage guidelines: Store for 5 to 27°C (equivalent to +2°C to +8°C). Do not freeze. Protect from light. Influenza vaccines should be appropriately discarded when they reach their expiry date to avoid inadvertently using a product with the incorrect formulation in the following year.

### 4.7.6 Dosage and administration

Vaccines registered by the TGA, and the ages for which they are indicated, can change from year to year. Always check annual seasonal influenza vaccine availability statements published by ATAGI on the Immunise Australia website (http://www.immunise.health.gov.au) (www.immunise.health.gov.au), and consult individual product information.

Refer to Table 4.7.1 for the recommended doses of influenza vaccine for different age groups. For adults aged ≥65 years who have already received either a high-dose or adjuvanted TIV in the current influenza season, a further dose of QIV in the same season is not recommended, although not contraindicated.

Influenza vaccines available in Australia are presented in pre-filled syringes, of either 0.5 mL or 0.25 mL. Some 0.5 mL syringes have a graduated mark to indicate where the plunger can be depressed to provide a 0.25 mL dose if indicated.

Children aged 6 months to <3 years require a 0.25 mL dose. If a child aged 6 months to <3 years inadvertently receives a 0.5 mL dose of influenza vaccine, no immediate action is necessary. There is some evidence that a 0.5 mL dose of inactivated influenza vaccine is immunogenic in children <3 years of age, and evidence that a 0.5 mL dose is safe in this age group (apart from Afluria Quad).65,66 Any additional dose(s) required in that season or in future seasons should be given following standard recommendations (refer to Table 4.7.1).

Shake the pre-filled syringe vigorously before injection. The preferred route of administration for influenza vaccines is by IM injection; however, they may also be given by the SC route (refer to Table 2.2.1 Route of administration for vaccines used in Australia).

#### Table 4.7.1: Recommended doses of influenza vaccine

<table>
<thead>
<tr>
<th>Age</th>
<th>Dose</th>
<th>Number of doses required in the first year of influenza vaccination</th>
<th>Number of doses required if previously received 1 or more doses of influenza vaccine</th>
</tr>
</thead>
<tbody>
<tr>
<td>6 months to &lt;3 years, 65 years only</td>
<td>0.25 mL¹</td>
<td>2</td>
<td>1</td>
</tr>
<tr>
<td>≥3 years to &lt;9 years</td>
<td>0.5 mL²</td>
<td>2</td>
<td>1</td>
</tr>
</tbody>
</table>
Influenza vaccination of pregnant women also protects their infants.

Clinical risk groups

Influenza vaccination is recommended for persons with certain immunocompromising conditions (i.e. haematopoietic stem cell transplant or solid organ transplant) receiving influenza vaccine for the first time post transplant (irrespective of their age) (refer to 4.7.7 Recommendations below and 3.3 Groups with special vaccination requirements).

Co-administration with other vaccines

All inactivated influenza vaccines can be administered concurrently with any other vaccine, including pneumococcal polysaccharide vaccine, zoster vaccine and all scheduled childhood vaccines. Parents/carers of infants or children who are recommended to receive both influenza vaccine and 13-valent pneumococcal conjugate vaccine (13vPCV) should be advised of a possible small increased risk of fever following concomitant administration of these vaccines (refer to 4.7.10 Precautions below and 4.13 Pneumococcal disease).

Interchangeability of influenza vaccines

Where 2 doses of influenza vaccine are indicated in a single season (refer to Table 4.7.1 Recommended doses of influenza vaccine), different brands are considered interchangeable (providing they are age-appropriate).

Timing of influenza vaccination

Influenza vaccination can be offered from the time the vaccine becomes available, typically in March or April, although the exact timing can vary from year to year. Annual influenza vaccination before the onset of each influenza season is recommended. The period of peak influenza circulation is typically between June and September for most parts of Australia, but influenza can still occur year round, particularly in tropical areas. Recent evidence suggests that while protection is generally expected to last for the whole season, optimal protection against influenza occurs within the first 3 to 4 months following vaccination. Although detecting vaccination to a time 3 to 4 months before the winter months may result in greater immunity later in the season, it may also result in missed opportunities for vaccination and lack of protection in the event of an early onset influenza season. Providers need to weigh up the above factors for each individual and, in balance, whether to consider vaccinating of all individuals within a constrained time period. Vaccination should be offered throughout the influenza season. In particular, pregnant women and travellers can benefit from vaccination at any time of the year. Children receiving their first lifetime dose should be vaccinated as soon as possible after the vaccine becomes available to ensure there is sufficient time to receive a second dose (recommended ≥4 weeks later) before the influenza season commences.

4.7.7 Recommendations

Annual influenza vaccination is recommended for all persons ≥6 months of age.6,7,10,11 A single annual dose of influenza vaccine is recommended for most individuals; revaccination later in the same season is not recommended, although not contraindicated. Two doses at least 4 weeks apart are recommended for children aged 6 months to <9 years receiving influenza vaccine for the first time and persons receiving influenza vaccine for the first time post haematopoietic stem cell or solid organ transplant (irrespective of their age).

Influenza vaccination is particularly strongly recommended for the following groups:

All children aged <5 years

Infants and children aged <5 years have a higher risk of hospitalisation and increased morbidity following influenza (Figure 4.7.1).12 This includes young children without pre-existing medical conditions who are at greater risk of hospitalisation compared with older children and adults.17,72,73 Specific brands of influenza vaccine are registered by the TGA for use in children from 6 months of age and these may change from year to year (refer to 4.7.4 Vaccines and 4.7.6 Dosage and administration above).

All adults aged ≥65 years

Influenza-associated mortality rates are highest among adults aged ≥65 years.6,8,13 Evidence shows that influenza vaccine reduces hospitalisations from influenza and pneumonia and all-cause mortality in adults ≥65 years of age.45 The high-dose (Fluzone High-Dose) and adjuvanted (Fluad) TIVs are preferentially recommended over QIVs for adults aged ≥65 years. However, there is no preference for use between these two TIVs. (Refer also to 4.7.4 Vaccines above.)

Aboriginal and Torres Strait Islander people

Annual influenza vaccination is recommended for all Aboriginal and Torres Strait Islander people. The disease burden from influenza is significantly higher among Aboriginal and Torres Strait Islander people than in non-Indigenous Australians, across all age groups (refer to 4.7.3 Epidemiology above and 3.1 Vaccination for Aboriginal and Torres Strait Islander people).8

Pregnant women

Influenza vaccination is recommended for pregnant women in every pregnancy due to the increased risk of morbidity and mortality from influenza during pregnancy.18 The risk to the mother of complications from influenza increases in the later stages of pregnancy as does the potential for pre-term delivery.74,83 Influenza vaccination of pregnant women also protects their infants from influenza in early infancy, due to transplacental transfer of high-titre antibodies from the vaccinated woman to the fetus.75,84,85 Influenza vaccine can be given during any stage of pregnancy; the timing of vaccination should be considered in relation to the influenza season and vaccine availability. Influenza vaccine should be given as early as practicable in each pregnancy. If not already given, influenza vaccine can be administered concurrently with the dTpa vaccine, recommended for administration early in the third trimester (refer to 4.12 Pertussis). Pregnant women who may have received the previous years’ seasonal influenza vaccine early in their pregnancy can receive the current seasonal influenza vaccine (when it becomes available) later in the same pregnancy.

Clinical risk groups

Influenza vaccination is recommended for persons aged ≥6 months with conditions predisposing them to severe influenza.9,7 such as:

Cardiac disease, including cyanotic congenital heart disease, coronary artery disease and congestive heart failure – Influenza causes increased morbidity and mortality in children with congenital heart disease and adults with coronary artery disease and congestive heart failure.71,86,89

Down syndrome – Persons with Down syndrome should receive annual seasonal influenza vaccine whether or not they have congenital heart disease. This is due to the presence of anatomical abnormalities, which put them at increased risk of upper respiratory tract infections, as well as a high prevalence of other medical conditions that put them at increased risk of severe influenza.98

Obesity – Persons with a BMI ≥24 kg/m2 (classified as class III obesity) should receive annual seasonal influenza vaccine due to their increased risk of severe outcomes, particularly observed following infection with the A(H1N1)pdm09 influenza strain.90-93 This increased risk is independent of the presence of underlying comorbidities.94 There is also some evidence that persons who have a BMI between 30 and <40 (class II obesity) are at increased risk of severe influenza and may benefit from annual influenza vaccine.92,94,95 Studies assessing the
They may also have a reduced immune response to influenza vaccine, although vaccination does afford some protection.

influenza is circulating in the destination region.

vaccinations for persons at increased risk of certain occupationally acquired vaccine-preventable diseases infections can place considerable pressure upon both public and Essential services providers strain, with the potential for spread from human to human (i.e. initiate a pandemic as was the case with swine influenza in 2009). is a possibility that a person who is infected at the same time with animal and human strains of influenza virus could act as a vessel for reassortment of the two strains to form a virulent infection; vaccination of these groups is therefore recommended to protect those at risk: Carers and household contacts of those in high-risk groups, including providers of home care to persons at risk of high influenza morbidity Homeless people – The living conditions and prevalence of underlying medical conditions among homeless people will predispose them to complications and transmission of influenza.

Groups with special vaccination requirements, Table 3.3.7 Recommended vaccinations for persons at increased risk of certain occupationally acquired vaccine-preventable diseases. 4.7.8 Pregnancy and breastfeeding

Influenza vaccination is recommended for pregnant women (refer to 4.7.7 Recommendations above) and is safe to administer during any stage of pregnancy or while breastfeeding, despite the product information for influenza vaccines listing pregnancy as a precaution (refer to 4.7.13 Variations from production information below).
4.7.9 Contraindications

The only absolute contraindications to influenza vaccines are:

- anaphylaxis following a previous dose of any influenza vaccine
- anaphylaxis following any vaccine component.

Refer to 4.7.10 Precautions below for persons with a known egg allergy.

4.7.10 Precautions

Persons with known egg allergy

Persons with egg allergy, including anaphylaxis, can be safely vaccinated with influenza vaccines. Several published reviews, guidelines and reports have indicated that the risk of anaphylaxis associated with influenza vaccination of egg-allergic patients is very low. A 2012 review of published studies, including 4172 egg-allergic patients (of whom 513 reported a history of severe allergic reaction to egg), reported no cases of anaphylaxis following administration of inactivated influenza vaccine. The largest study in the review included 830 egg-allergic patients (of whom 164 reported a history of severe allergic reaction to egg) and only 17 (2%) of these patients experienced any adverse event. All adverse events were mild; they included abdominal pain, hives and respiratory symptoms such as wheezing.

Persons with a history of egg allergy (non-anaphylaxis) can receive an age-appropriate full dose of vaccine in any immunisation setting. This includes children that are sensitised (i.e. skin prick or RAST test positive) but have not yet eaten egg. Persons with a history of anaphylaxis to egg should be vaccinated in medical facilities with staff experienced in recognising and treating anaphylaxis. The vaccinated person should remain under supervision in the clinic for at least 30 minutes after vaccination. A full age-appropriate vaccine dose should be used. There is no need to split the dose into multiple injections (e.g. a test and then remainder of the dose).

Recommendations for administration of influenza vaccine in egg-allergic individuals are summarised in Table 4.7.2.

Anaphylaxis following a previous dose of any influenza vaccine is a contraindication to future influenza vaccination.

Table 4.7.2: Recommended administration of influenza vaccine in egg-allergic individuals

<table>
<thead>
<tr>
<th>Allergy</th>
<th>Vaccine administration and setting</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sensitised but not yet eaten egg</td>
<td>Vaccinate with full age-appropriate dose in any immunisation setting</td>
</tr>
<tr>
<td>Non-anaphylaxis egg allergy</td>
<td>Vaccinate with full age-appropriate dose in any immunisation setting</td>
</tr>
<tr>
<td>Anaphylaxis egg allergy</td>
<td>Vaccinate with full age-appropriate dose in medical facility with staff experienced in recognising and treating anaphylaxis</td>
</tr>
</tbody>
</table>

Refer also to ‘Vaccination of persons with a known egg allergy’ in 3.3.1 Vaccination of persons who have had an adverse event following immunisation.

Persons with a history of Guillain-Barré syndrome

Persons with a history of Guillain-Barré syndrome (GBS) have an increased likelihood in general of developing GBS again, and the chance of them coincidentally developing the syndrome following influenza vaccination may be higher than in persons with no history of GBS. Diagnosis of GBS is complex and must be made by a physician (refer to 3.3.3 Vaccination of immunocompromised persons ‘Persons with autoimmune diseases and other chronic conditions’). Individual concerns should be discussed and expert advice sought from the treating physician and/or an immunisation specialist when considering influenza vaccination for a person with a history of GBS.

Children requiring both influenza and 13-valent pneumococcal conjugate vaccine

One study has demonstrated a slightly higher risk of fever and febrile convulsions in children aged 6 months to <5 years (especially those aged 12–24 months) with the concurrent administration of inactivated trivalent influenza vaccine and 13vPCV (compared with giving the vaccines separately). The risk was estimated to be about 18 excess cases per 100 000 doses in children aged 6–59 months, with a peak of 45 per 100 000 doses in those aged 16 months. Given that the reported increase in risk was relatively small, and a more recent study did not demonstrate the same association between febrile seizures and the concurrent administration of these two vaccines, 13vPCV administration of 13vPCV and inactivated trivalent influenza vaccine at the same visit is acceptable when both vaccines are indicated. (Refer also to 4.13 Pneumococcal disease.)

4.7.11 Adverse events

Fever, malaise and myalgia occur commonly, in 1 to 10% of persons who receive inactivated standard TIVs. These adverse events may commence within a few hours of vaccination and may last for 1 to 2 days. In children <5 years of age, these side effects may be more pronounced. In 2010, an excess of fever and febrile convulsions following influenza vaccination was reported in children aged <5 years, particularly children aged <3 years. This was associated only with one manufacturer’s vaccine (Seqirus (previously biCSL), Fluvax and Fluvax Junior). Following vaccination with this vaccine, febrile convulsions occurred at a rate of 4.4 per 1000 doses in children <5 years of age. This vaccine is no longer available in Australia.

Local adverse events (induration, swelling, redness and pain) occur in more than 10% of vaccine recipients, following IM administration of standard TIV. Studies directly comparing trivalent and quadrivalent inactivated influenza vaccine formulations in children and adults have demonstrated a similar safety profile.

A higher rate of injection site reactions has been observed in clinical trials with the high-dose and adjuvanted TIVs registered for use in adults aged ≥65 years, compared with standard TIVs. Approximately 30% of Fluzone High-Dose and FlucelvaxIAQ recipients reported injection site reactions, compared to approximately 20% of recipients of standard TIVs; both groups reported similar rates of systemic reactions (approximately 30%). More injection site reactions in the week after vaccination are also seen with the adjuvanted TIV when compared to non-adjuvanted TIV (approximately 35% versus 18%). However, severe or serious adverse events have not been observed at a higher frequency in clinical trials or post-licensure surveillance studies with either the high-dose or adjuvanted vaccine. (While high-dose and adjuvanted TIVs are only registered for use in persons aged ≥65 years and are not currently recommended in younger ages, clinical trials in some younger populations and post-licensure safety data following inadvertent administration to younger people suggest a similar safety profile to that observed in persons aged ≥65 years.)

Post-vaccination symptoms may mimic influenza infection. However, none of the influenza vaccines currently available in Australia contain live influenza viruses, so they cannot cause influenza.

Immediate adverse events (such as hives, angioedema or anaphylaxis) are very rare consequences of influenza vaccination and probably represent an allergic response to a residual component of the manufacturing process, most likely egg protein. However, persons with a history of anaphylaxis after eating eggs or a history of a severe allergic reaction following occupational exposure to egg protein may receive influenza vaccination after medical consultation (refer to ‘Persons with known egg allergy’ in 4.7.10 Precautions).

A small increased risk of GBS was associated historically with one influenza vaccine in the United States in 1976, but, since then, close surveillance has shown that GBS has occurred at a very low rate of up to 1 in 1 million doses of influenza vaccine, if at all. Diagnosis of GBS is complex and must be made by a physician (refer to ‘Uncommon/rare AEFI’ in 2.3.2 Adverse events following immunisation).
4.7.12 Public health management of influenza

Laboratory-confirmed cases of influenza are notifiable in all states and territories in Australia. Detailed information regarding the management of influenza cases and contacts can be found in the national guidelines for control of influenza[50] Series of National Guidelines (SoNGs) (http://www.health.gov.au/cdnasongs) (www.health.gov.au/cdnasongs).

Further instructions about the public health management of influenza, including in residential care facilities, can also be obtained from state/territory public health authorities (refer to Appendix 1 Contact details for Australian, state and territory government health authorities and communicable disease control).

4.7.13 Variations from product information

The product information for influenza vaccines lists allergy to egg as a contraindication. The ATAGI recommends instead that patients with egg allergies can be vaccinated with an age-appropriate influenza vaccine. Refer to 4.7.10 Precautions above.

The product information for influenza vaccines lists pregnancy as a precaution. The ATAGI instead recommends that inactivated influenza vaccine can be given during any stage of pregnancy. Refer to 4.7.7 Recommendations above.

References


Kelly H, Carcione D, Dowse G, Effler P. Quantifying benefits and risks of vaccinating Australian children aged six months to four years with trivalent inactivated seasonal influenza vaccine.


4.8 Japanese encephalitis

Japanese encephalitis (JE) is caused by a mosquito-borne RNA flavivirus.

4.8.1 Virology

Japanese encephalitis virus (JEV) is a single-stranded positive-sense RNA virus belonging to the family Flaviviridae and the genus Flavivirus. It is not a human pathogen, but rather an arbovirus that is maintained in an enzootic cycle involving pigs and wading birds. Susceptible individuals may still be at risk when visiting areas where there are wild birds and pigs.

4.8.2 Clinical features

The disease is typically an acute neurological illness, characterised by headache, fever, convulsions, focal neurological signs and depressed level of consciousness. It has a high case-fatality rate (approximately 30%) and there is a high prevalence of neurological sequelae (up to 50%) in those who survive the acute illness. Less commonly, the disease may present as an acute flaccid paralysis. Milder forms include febrile illness with headache, and aseptic meningitis. It is recognised, however, that most infections are asymptomatic; published estimates of the symptomatic to asymptomatic infection ratio vary in different populations from 1:2.5 to 1:1,000.

4.8.3 Epidemiology

JEV (Japanese Encephalitis) is a significant public health problem in many parts of Asia, including the Indian subcontinent, Southeast Asia and China. In recent decades the disease has extended beyond its traditionally recognised boundaries to eastern Indonesia (including Bali) and Papua New Guinea. Occasional outbreaks have also occurred in the Torres Strait, and 1 case in north Queensland.

The first ever outbreak of Japanese encephalitis (JE) in Australia occurred in the remote outer islands of the Torres Strait in 1995, with 3 cases, 2 of them fatal. There have been 5 cases to date acquired in Australia. JE virus has only been detected infrequently in sentinel animal surveillance in the outer islands. The sentinel pig surveillance system has been gradually disbanded since 2006, with surveillance of the last remaining herd on Cape York ceasing from the 2011–2012 wet season.

There has not been a case of JE in the Torres Strait since 1998 and the risk of JE has diminished considerably in the outer islands since the mid-1990s. Most communities have relocated pigs well away from homes, and major drainage works on most islands have markedly reduced potential breeding sites for vector mosquitoes. Between 2001 and 2014, only 9 cases of JE virus infection were notified in Australia, all having been acquired overseas.

The JE virus is essentially a zoonosis of pigs and wading birds, and is transmitted between these animals by culicine mosquitoes. The virus replicates, leading to a transient high-level viraemia, within these ‘amplifying’ hosts, but not within other large vertebrates such as horses and humans. Indeed, humans are an incidental host, infected when living in close proximity to the enzootic cycle; this usually occurs in rural areas where there is prolific breeding of the vectors in flooded rice fields.

Two epidemiological patterns of JE in endemic regions were recognised historically. In the temperate or subtropical regions of Asia (northern Thailand, northern Vietnam, Korea, Japan, Taiwan, China, Nepal and northern India), the disease principally occurred in epidemics during the summer or wet season months (April to May until September to October). In the tropical regions (most of Southeast Asia, Sri Lanka, southern India), the disease occurs throughout the year, but particularly during the wet season. A 2006 study confirmed that JE virus is endemic in Bali, that it causes substantial human illness, and that it circulates year round.

In some countries (Japan, Taiwan, South Korea and some provinces of China), the incidence of JE has declined considerably in recent decades, and it has been eradicated from Singapore. Immunisation, changes in pig husbandry, a reduction in land utilised for rice farming, and improved socioeconomic circumstances have all contributed to these changes. Because JE virus is maintained in an enzootic cycle, susceptible individuals may still be at risk when visiting areas where there are few human cases due to established immunisation programs.

Updated information regarding JE virus activity and/or risk in travel destinations should be sought from a reputable source prior to travel (for example, Health information for international travel (the ‘Yellow book’) (http://www.cdc.gov/travel) published by the US Centers for Disease Control and Prevention, available at (www.cdc.gov/travel/yellowbook)).

4.8.4 Vaccines

Two JE vaccines, each with different characteristics, are available for use in Australia. The inactivated mouse brain-derived JE vaccine formulation manufactured in Japan, JE-Vax, which was previously used in Australia, is no longer manufactured. Clinical and animal studies have provided evidence in support of an immunological correlate of immunity (established by the World Health Organization as a neutralising antibody titre of ≥1:10).

Imojev is a recombinant JE vaccine produced using recombinant technology. Two genes of the 170-204 yellow fever vaccine virus have been replaced with two genes, prM and E genes, from the Japanese encephalitis virus strain SA 14-14-2. About 94% of healthy adults aged 18–84 years seroconverted to a strain homologous to that in the Imojev vaccine 14 days after a single vaccine dose.

Several clinical trials have demonstrated that, 28 days following vaccination with a single dose of Imojev, protective levels of neutralising antibodies against the homologous vaccine virus strain are present in 89% of vaccine-naive children aged 12–24 months and 99% of adults.

Immunogenicity was non-inferior to that attained after a 3-dose primary course of the inactivated mouse brain-derived JE vaccine that was previously used in Australia. Subjects also seroconverted to various wild-type, non-homologous, JE virus strains (70 to 99% of children aged 12–24 months and 70 to 100% of adults). 85% of adults developed neutralising antibodies against all four wild-type strains used for testing. A clinical trial of a single dose of Imojev in children aged 9–18 months reported that a comparable proportion of participants aged 9–12 and 12–18 months had protective levels of neutralising antibodies at 12 months after vaccination.

In adults, a protective antibody level to the vaccine strain was maintained in 98% of adults at 1 year after vaccination, in 92% at 3 years and in 87% at 5 years. Protective antibody levels to at least three wild-type virus strains have been demonstrated in about 65% of adults 5 years after a single vaccine dose. Establishment of immunological memory in vaccinated adult subjects has also been demonstrated. In children vaccinated at 12–24 months of age with a single dose of Imojev, protective antibody levels to the vaccine strain have been demonstrated in 87% of children at 7 months after vaccination, and in 75% at 3 years.

These statements are supported by the findings in children and adults, and should not be extrapolated to groups not included in the relevant clinical trials. Immunogenicity has also been demonstrated based on studies in both younger children and adults.
Imojev is a Vero cell-derived, inactivated, aluminium-adjuncted vaccine based on the attenuated SA 14-14-2 JE virus strain. JEspect has non-inferior immunogenicity (after 2 doses, given 4 weeks apart) to 3 doses of the previously available mouse brain-derived vaccine, with seroconversion achieved in 98% of subjects. Post-vaccination geometric mean titres (GMT) in JEspect recipients were significantly higher than GMTs attained after a mouse brain-derived vaccine. After a standard 2-dose course, protective levels of neutralising antibodies have been found to persist for 6 months in 95%, for 12 months in 83% and for 24 months in 48% of JEspect-vaccinated subjects in central Europe. In 83%, 58% and 48%, respectively, at these three time points in subjects in western and northern Europe. A suggested plausible explanation for the discrepancy between these two studies is prior vaccination with the tick-borne encephalitis (TBE) vaccine in a large proportion of subjects in the central European study. In a further study, of JEspect-vaccinated subjects who completed 5 years of follow-up, the seroprotection rate at 5 years was 64% for TBE-naïve individuals and 92% for those who received TBE vaccine prior to or during the study, in an extension of the western and northern European study, those who did not have a seroprotective antibody level at either the 6- or 12-month follow-up point were given a booster dose at 11 and/or 23 months after first vaccination; seropositivity was attained in 100% of these subjects.

The key paediatric clinical trial of JEspect was a phase III study in children aged 2 months to 17 years in the Philippines. In subjects given age-appropriate doses of JEspect, the proportions with protective antibody titres were 99% to 100% at day 56 and 85 to 100% at month 7, with no obvious pattern by age. A phase II study in 60 Indian children aged 1–<3 years also showed JEspect to be safe and immunogenic in this age group. A phase III immunogenicity study involving 64 children from non-JE endemic countries aged 2 months to <18 years (mean age 11.6 years; range 11 months to 17.9 years) showed 100% seroconversion to protective levels, with the proportion seroprotected at 6 months after the 2nd dose being 100% in the <3 years age group (n=2) and 90.6% in the ≥3 years age group (n=32).

A small study among healthy military personnel observed that the immune response after 4 weeks to 1 dose of JEspect, among those who had previously received at least 3 doses of mouse brain-derived JE vaccine, was non-inferior to the response after 2 doses of JEspect in those who were naïve to JE vaccines. A phase III study in 60 Indian children aged 1–<3 years, who had previously received at least 3 doses of mouse brain-derived JE vaccine, was non-inferior to the response after 2 doses of JEspect in those who were naïve to JE vaccines. A small study among travellers who had received at least 2 doses of a mouse brain-derived JE vaccine 1 to 21 years previously observed that, 4 to 8 weeks after a single dose of JEspect, a high proportion attained protective antibody levels against the vaccine strain in 100%, and against all wild-type strains in 99%. Ninety-three per cent showed JEspect to be safe and immunogenic in this age group. A phase III immunogenicity study involving 64 children from non-JE endemic countries aged 2 months to <18 years (mean age 11.6 years; range 11 months to 17.9 years) showed 100% seroconversion to protective levels, with the proportion seroprotected at 6 months after the 2nd dose being 100% in the <3 years age group (n=2) and 90.6% in the ≥3 years age group (n=32).

A small study among healthy military personnel observed that the immune response after 4 weeks to 1 dose of JEspect, among those who had previously received at least 3 doses of mouse brain-derived JE vaccine, was non-inferior to the response after 2 doses of JEspect in those who were naïve to JE vaccines. A small study among travellers who had received at least 2 doses of a mouse brain-derived JE vaccine 1 to 21 years previously observed that, 4 to 8 weeks after a single dose of JEspect, a high proportion attained protective antibody levels against both homologous and heterologous strains (98% and 95%, respectively), and these proportions were non-inferior compared to those who received a booster of mouse brain-derived JE vaccine. Follow-up data from this study found seroprotection rates of 89 to 100% against wild-type strains 2 years after a single JEspect booster in individuals primed with a mouse brain-derived JE vaccine. A phase III study in healthy adults comparing accelerated (day 0 and 7) and conventional (day 0 and 28) JEspect courses suggested non-inferior immune response, for the accelerated course of JEspect compared to the conventional course, at 28 days and 1 year after the 2nd dose.

**4.8.5 Transport, storage and handling**

Transport according to National vaccine storage guidelines: Strive for 5. Store at +2°C to +8°C. Do not freeze. Protect from light.

Imojev must be reconstituted by adding the entire contents of the diluent container to the vial and shaking until the powder is completely dissolved. Reconstituted vaccine must be used within 1 hour.

**4.8.6 Dosage and administration**

JEspect can be administered to persons aged ≥ 9 months based on evidence from clinical studies (refer to 4.8.4 Vaccines above). The dose of Imojev for infants and children (aged ≥ 9 months) and adults is 0.5 mL, to be given by SC injection.

JEspect can be administered to persons aged ≥ 2 months. However, clinical studies of JEspect in children are limited (refer to 4.8.4 Vaccines above). The ATAGI recommends that JEspect should only be used in children aged ≥2 months to <18 years in circumstances where an alternative is not available (e.g. in infants aged ≥2 months to <9 months) or is contraindicated (refer to 4.8.13 Variations from product information below). JEspect should be given by IM injection. When using JEspect in infants and children aged ≥ 2 months and <3 years, primary vaccination consists of 2 doses, each of 0.25 mL, 28 days apart (refer to Table 4.8.1 Recommended doses of JE vaccines).

When using JEspect in children aged ≥3 years and adults, primary vaccination consists of 2 doses, each of 0.5 mL, 28 days apart (refer to Table 4.8.1 Recommended doses of JE vaccines). Do not mix either Japanese encephalitis vaccine with any other vaccine in the same syringe.

**Table 4.8.1: Recommended doses of JE vaccines**

<table>
<thead>
<tr>
<th>Age of vaccine recipient</th>
<th>Vaccine</th>
<th>Number of doses</th>
<th>Booster</th>
</tr>
</thead>
<tbody>
<tr>
<td>≥2 to &lt;9 months</td>
<td>JEspect</td>
<td>2 doses (28 days apart)</td>
<td>Not required</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>≥9 months to &lt;18 years</td>
<td>Imojev</td>
<td>1 dose</td>
<td>1–2 years after primary dose</td>
</tr>
<tr>
<td></td>
<td>JEspect</td>
<td>2 doses (28 days apart)</td>
<td>Not required</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>≥18 years</td>
<td>Imojev</td>
<td>1 dose</td>
<td>1–2 years after primary dose</td>
</tr>
<tr>
<td></td>
<td>JEspect</td>
<td>2 doses (28 days apart)</td>
<td>Not required</td>
</tr>
</tbody>
</table>

**Note 1:** JEspect can be administered to children in this age group in circumstances where an alternative is not available or is contraindicated (refer to 4.8.6 Dosage and administration above).

**Note 2:** Currently there is very limited evidence available to inform recommendations regarding the need and appropriate time interval for a booster of JEspect in children who received JEspect as primary immunisation.

* Each dose of JEspect in infants and children aged ≥2 months is 0.25 mL.
† An accelerated primary course of JEspect (2 doses, each of 0.5 mL, 7 days apart) may be considered for adults who are at imminent risk of exposure to JE virus.

**Co-administration with other vaccines**

Imojev can be given at the same time as the yellow fever vaccine and MMR vaccine using separate syringes and separate injection sites. Data on the co-administration with other vaccines is not available. If Imojev and the yellow fever vaccine or other live vaccines are not given simultaneously, they should be given at least 4 weeks apart.
JE vaccines are contraindicated in persons who have had:

- anaphylaxis following any vaccine component.
- anaphylaxis following a previous dose of any JE vaccine

If co-administration of either JE vaccine with other vaccines is indicated, injections should be given in separate limbs.

Interchangeability of Japanese encephalitis vaccines

The vaccine used for a booster dose should preferably be the same as that used for the primary course. No studies have been conducted to assess the immune response to an Imojev booster in individuals who have received a primary course of JEspect, or vice versa. However, as both vaccines are derived from the same virus strain, a booster using the alternative vaccine, based on first principles, should provide a satisfactory immune response.

For individuals previously vaccinated with the mouse brain-derived JE vaccine, either Imojev or JEspect can be used for revaccination if there is an ongoing risk of JE virus exposure.

4.8.7 Recommendations

JE vaccines are recommended for the following groups who are at greater risk of acquiring JE. The two available JE vaccines are registered for different age groups, and have different vaccination schedules, booster dose requirements, and contraindications for use. These factors should be taken into account when deciding the most appropriate vaccine to use (refer to 4.8.6 Dosage and administration above, and ‘Booster doses’ and 4.8.9 Contraindications below).

The dose of Imojev should be administered at least 14 days prior to potential JE virus exposure.

The JEspect vaccine (2-dose) schedule should be completed at least 1 week prior to potential JE virus exposure.

Travellers

The risk of JE to travellers is determined by the season of travel, the regions visited, the duration of travel, the extent of outdoor activity and the extent to which mosquito avoidance measures are taken. While the overall risk of JE infection in travellers to JE endemic countries is likely to be low (<1 case per 1 million travellers), the risk is greater during prolonged travel to endemic areas, particularly rural areas, during the wet season; it is probably negligible during short business trips to urban areas.

JE vaccination is recommended for travellers spending 1 month or more in endemic areas in Asia and Papua New Guinea during the JE virus transmission season, including persons who will be based in urban areas but are likely to visit endemic rural or agricultural areas (refer to 4.8.3 Epidemiology above). Up-to-date information regarding JE virus activity and/or risk in travel destinations should be sought from a reputable source prior to travel (for example, Health information for international travel (the “Yellow book”) [http://www.cdc.gov/travel] published by the US Centers for Disease Control and Prevention, available at www.cdc.gov/travel/yellowbook). It is important to note that, as JE has occurred in travellers after shorter periods of travel, JE vaccination should be considered for shorter-term travellers, particularly if the travel is during the wet season, or is anticipated to be repeated, and/or there is considerable outdoor activity, and/or staying in accommodation without air conditioning, screens or bed nets.

All travellers to Asia (and other tropical regions) must be fully aware of the need to take appropriate measures to avoid mosquito bites. Booster doses may be required for persons who are at continued risk of acquiring JE (refer to ‘Booster doses’ below).

Torres Strait Islands

JE vaccination is recommended for:

- residents of the outer islands in the Torres Strait
- non-residents who will be living or working on the outer islands of the Torres Strait for a cumulative total of 30 days or more during the wet season (December to May).

The period of greatest risk is from February to March and the vaccination course for non-residents should be completed before February. Those arriving in the outer islands late in the wet season (i.e. in May) will arrive after the risk period and do not require vaccination. Those visiting the outer islands in the dry season (June to November) do not require vaccination. Those visiting only the inner islands, including Thursday Island, do not require vaccination. Timing of vaccination in residents should take into account a range of factors including age, time of year, vaccine schedule and recent epidemiology.

Booster doses may be required for persons who are at continued risk of acquiring JE (refer to ‘Booster doses’ below).

Laboratory personnel

JE vaccination is recommended for all research laboratory personnel who will potentially be exposed to the virus.

Booster doses

The need for a booster dose of JE vaccine depends on the age at which the primary vaccine course was given and the vaccine used for the primary course (refer to Table 4.8.1 in 4.8.6 Dosage and administration above).

 JE vaccination should be considered for laboratory personnel who will potentially be exposed to the virus.

A booster dose of Imojev is recommended 1 to 2 years after the primary course for children aged ≥9 months and <18 years who are at continued risk of acquiring JE (refer to risk groups above). A booster dose of Imojev is not currently recommended for adults as seroprotective antibody levels have been shown to persist in a high proportion of adults 5 years following a single dose of Imojev (refer to 4.8.4 Vaccines above).

A booster dose of JEspect is recommended 1 to 2 years after the primary course for adults who are at continued risk of acquiring JE (refer to risk groups above). Currently there is very limited evidence available to inform recommendations regarding the need and appropriate time interval for a booster of JEspect in children who received JEspect as primary immunisation; however, recommendations will be updated when suitable evidence becomes available.

4.8.8 Pregnancy and breastfeeding

Imojev is a live attenuated viral vaccine and is contraindicated in pregnant women. Pregnancy should be avoided for 28 days after vaccination.

There are no data on whether the Imojev vaccine virus is excreted in breast milk; the vaccine should not be given to breastfeeding women.

JE vaccination is not routinely recommended for pregnant or breastfeeding women. However, as JE virus infection during the first and second trimesters has been associated with miscarriage, pregnant women at risk of acquiring JE should be offered JE vaccination. Although this inactivated JE vaccine might pose a theoretical risk to the developing fetus, no adverse outcomes of pregnancy have been attributed to vaccination against JE.

No specific data are available regarding the administration of JEspect to breastfeeding women. Breastfeeding women who are at increased risk of acquiring JE should be offered JE vaccination.

Refer to 3.3 Groups with special vaccination requirements, Table 3.3.1(Handbook10-home~handbook10part3~handbook10-3-3#table-3-3-1) Recommendations for vaccination in pregnancy for more information.

4.8.9 Contraindications

JE vaccines are contraindicated in persons who have had:

- anaphylaxis following any vaccine component.
4.8.10 Precautions
JE vaccines should not be administered during an acute febrile illness.

There are few data on the safety and efficacy of JE vaccines in persons who are immunocompromised. Such persons may not mount an adequate immune response, but, as JE vaccines are inactivated vaccines, safety and reactogenicity are not expected to be of concern in those who are immunocompromised.

Vaccination after immunoglobulin or blood product administration
Administration of live attenuated JE vaccine (Imojev) should be delayed after administration of immunoglobulin-containing products. Imojev should not be given within 6 weeks, and preferably not within 3 months, following administration of immunoglobulins or immunoglobulin-containing blood products.

4.8.11 Adverse events
Local reactions and minor systemic reactions are common to very common following vaccination against JE.

In adults, adverse events following Imojev were similar to those in placebo recipients,7,10 but occurred less often than in recipients of the mouse brain-derived JE vaccine.9 The most common adverse events in two key studies were injection site pain, headache, fatigue and malaise; most symptoms resolved within 3 days.9 Similarly, in children aged 12–24 months, the frequency of adverse events after Imojev was comparable to that after the hepatitis A vaccine. About 40% of these subjects reported injection site reactions, including pain (32%), myalgia (23%) and swelling (9%), and about 50% reported at least one systemic reaction, including fever (21%), appetite loss (26%), irritability (28%) and abnormal crying (23%). Frequencies of adverse events in children aged 2–5 years who received Imojev after having been previously vaccinated with the mouse brain-derived vaccine were similar to, or lower than, those seen in children aged 12–24 months not previously vaccinated. All reactions were transient and almost all were mild. Most systemic reactions were mild or moderate, appeared within 7 days of vaccination, and lasted up to 3 days.8

In a pooled analysis of over 4000 healthy adults who received at least one dose of JE vaccine, 54% reported injection site reactions, most commonly pain (33%), tenderness (33%) and redness (9%).34 Headache and myalgia were the most commonly reported systemic adverse events.17,18,24 An earlier analysis found a comparable rate of adverse events in those who received JE vaccine compared with aluminium-containing placebo.46 Post-marketing surveillance reported adverse events following JE vaccines at a rate of about 10 per 100 000 doses distributed; no serious allergic reactions were observed during the first 12 months after marketing approval.24 The frequencies of adverse events reported following a booster dose were similar to those reported after a primary course.17,10

4.8.12 Public health management of Japanese encephalitis
JE virus infection is a notifiable disease in all states and territories in Australia.

Further instructions about the public health management of JE, including management of cases of JE, should be obtained from state/territory public health authorities (refer to Appendix 1 (Handbook 10-home-handbook10-tools-handbook10-appendices-handbook10-appendix1) Contact details for Australian, state and territory government health authorities and communicable disease control).

4.8.13 Variations from product information
JE vaccine is registered for use in persons aged ≥18 years. The ATAGI recommends that JE vaccine can be administered to children aged ≥ 2 months to <18 years in circumstances where an alternative is not available or is contraindicated. The ATAGI also recommends that children aged ≥ 2 months to <3 years receive 0.25 mL doses of JE vaccine.

The product information for JE vaccines states that it can be given with inactivated hepatitis A vaccine. The ATAGI recommends that JE vaccines can also be given with quadrivalent meningococcal conjugate vaccine and rabies vaccine (refer to 4.8.6 Dosage and administration).

References
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150/278
4.9 Measles

4.9.1 Virology

Measles is a paramyxovirus, genus Morbillivirus. It is an RNA virus with six structural proteins, three complexed to the RNA (ribonucleic acid) and three associated with the viral envelope. Two of the envelope proteins, the F (fusion) protein and the H (haemagglutinin) protein, are the most important in pathogenesis. The measles virus can survive for up to 2 hours in air, but is rapidly inactivated by heat, light and extremes of pH.1,2

4.9.2 Clinical features

Measles is a highly infectious, acute viral illness spread by respiratory secretions, including aerosol transmission. It is infectious from the beginning of the prodromal period and for up to 4 days after the appearance of the rash. The incubation period is usually 10 to 14 days. The prodrôme, lasting 2 to 4 days, is characterised by fever and malaise, followed by a cough, coryza and conjunctivitis. The maculopapular rash typically begins on the face and upper neck, and then becomes generalised.

Measles is often a severe disease, frequently complicated by otitis media (in approximately 9%), pneumonia (in approximately 6%) and diarrhoea (in approximately 8%).1 Acute encephalitis occurs in 1 per 1000 cases, and has a mortality rate of 10 to 15%, with a high proportion of survivors suffering permanent brain damage.5 Subacute sclerosing panencephalitis (SSPE) is a late complication of measles, occurring on average 7 years after infection in approximately 0.5 to 1 per 100 000 measles cases.1 SSPE causes progressive brain damage and is always fatal. Complications from measles are more common and more severe in the chronically ill, in children <5 years of age, and in adults.7 Approximately 60% of deaths from measles are attributed to pneumonia, especially in the young, while complications from encephalitis are more frequently refer to in adults.5,8 Measles infection during pregnancy can result in miscarriage and premature delivery, but has not been associated with congenital malformation.9 There is no specific therapy for acute measles infection.

4.9.3 Epidemiology

In March 2014, the World Health Organization (WHO) declared that endemic measles has been eliminated from Australia, with the absence of a circulating endemic measles strain for several years.4 However, measles cases in Australia continue to occur, particularly in returning non-immune travellers and their contacts, with measles outbreaks of limited size and duration following importation.5 In 2005 and 2007, measles notifications and hospitalisations were the lowest recorded in Australia.6-8 However, there has been a recent increase in imported measles cases in Australia and subsequent outbreaks,9 highlighting the importance of continued high 2-dose vaccine coverage. To ensure herd immunity and maintenance of elimination, 2 dose vaccine coverage in each new birth cohort should optimally be >95%.10 A decline in vaccination rates has resulted in a resurgence in endemic transmission in a number of European countries, including the United Kingdom.11 In 2009, the Australian Childhood Immunisation Register recorded that 94.0% of children aged 2 years had received at least 1 dose of measles-containing vaccine and 80.3% of children aged 5 years had received 2 doses.12 However, improvements have occurred since that time, with 2-dose coverage at 92.2% in children aged 5 years in 2013.13

National serosurveys in early 1999 (evaluating the 1998 National Measles Control Campaign) and in 2000 showed that those most at risk of measles infection in Australia were infants <12 months of age, 1 to <2-year olds due to delayed vaccine uptake, and persons born in the late 1960s to mid-1980s (especially the 1978–1982 birth cohort).14-16 Young adults are recognised to be at a greater risk of measles infection as many missed being vaccinated as infants (when vaccine coverage was low), while during their childhood a 2nd dose was not yet recommended and disease exposure was decreasing. They may also have missed catch-up vaccinations during their school years as part of either the Measles Control Campaign (which only targeted school-aged children) or the Young Adult Measles Control Campaign (which did not result in high coverage).17 A high proportion of recent measles cases in Australia have been in unvaccinated young adults.9 Since the Measles Control Campaign, there have been no deaths recorded from measles, with the last measles death recorded in 1995.14,15 Since 1996, 2 deaths have been attributed to SSPE in Australia, 1 in 1999 and 1 in 2004.1,7,20

Global elimination of measles

The WHO is overseeing efforts to eliminate measles worldwide through immunisation and surveillance strategies.21 In 2000, measles was the fifth leading cause of childhood morbidity and mortality worldwide. There were an estimated 770 000 deaths, with more than half of these occurring in Africa.22 Following extensive vaccination campaigns, there was a 78% reduction to 184 000 deaths worldwide in 2008, with the majority of deaths reported in Southeast Asia.23 In 2003, measles elimination, defined as the absence of endemic measles virus transmission, was included as a regional goal under the Expanded Programme on Immunisation (EPI) for the WHO Western Pacific Region, with a target date set for 2012.24 Considerable progress has been made with an 86% decline in measles cases in the region.25 However, achieving elimination requires continued strengthening of immunisation and surveillance efforts, particularly identification of measles virus genotypes to confirm the absence of an enzootic strain. Globally, a number of countries have formally declared measles elimination, including Australia;6,8 with plans for achieving measles control and elimination across all WHO regions under continual development.26,27

4.9.4 Vaccines

Monovalent measles vaccine is not available in Australia. Measles vaccination is provided using either measles-mumps-rubella (MMR) or measles-mumps-rubella-varicella (MMRV) vaccines. Two combination vaccines containing live attenuated measles, mumps, rubella and varicella viruses (MMRV) are registered in Australia.

Measles immunity induced by 1-dose vaccination provides long-term immunity in most recipients.2,27 However, approximately 5% of recipients fail to develop immunity to measles after 1 dose.28 Following a 2nd vaccine dose, approximately 99% of subjects overall will be immune to measles. Measles vaccine effectiveness studies have found the measles-containing vaccines to be 90 to 95% effective in developed country settings with high vaccination coverage and low incidence of measles.2 A Cochrane review reported 1-dose vaccine effectiveness to be 95%,29 however, effectiveness has been demonstrated to vary, particularly by region (e.g. Asia, Africa) in 1-dose recipients.30

Combination MMRV vaccines have been shown in clinical trials, predominantly conducted in children 12 months to 6 years of age, to produce similar rates of seroconversion to all four vaccine components compared with MMR and monovalent varicella vaccines administered concomitantly at separate injection sites.31,32 In one comparative study assessing seroresponses to a single MMRV vaccine dose in 12–14-month-old children, the seroresponse rates to measles, mumps and rubella were similar, but varicella seroresponses were lower in Priorix-tetra recipients than in ProQuad recipients.33 However, the clinical significance of this is not clear, particularly for MMRV given after MMR vaccine.34

Information on adverse events related to MMR and MMRV vaccines is provided in 4.9.11 Adverse events below, and also in 4.22 Varicella (for MMRV).
4.9.5 Transport, storage and handling

Transport according to National vaccine storage guidelines: Store for 5.36 Store at +2°C to +8°C. Do not freeze. Protect from light.

Both MMR and MMRV vaccines must be reconstituted by adding the entire contents of the diluent container to the vial containing the pellet and shaking until the pellet is completely dissolved.

Reconstituted Priorix (MMR). M-M-R II (MMR) and Priorix-tetra (MMRV) vaccines should be used as soon as practicable. If storage is necessary, hold at +2°C to +8°C for not more than 8 hours.

Reconstituted ProQuad (MMRV) vaccine should be used immediately. If storage is necessary, hold at +20°C to +25°C for not more than 1 hour or at +2°C to +8°C for not more than 2.5 hours.

4.9.6 Dosage and administration

The dose of Priorix (MMR) vaccine for both children and adults is 0.5 mL, to be given by either SC or IM injection.

The dose of M-M-R II (MMR) vaccine for both children and adults is 0.5 mL, to be given by SC injection.

For children <14 years of age, the dose of MMRV vaccine is 0.5 mL, to be given by SC injection. Priorix-tetra may also be given by IM injection. 37

MMRV vaccines are not recommended for use in persons aged ≥14 years.

When 2 doses of MMR-containing vaccine are required, the minimum interval between doses is 4 weeks.

Co-administration with other vaccines

MMR or MMRV vaccines can be given at the same time as other live attenuated parenteral vaccines (e.g. varicella, BCG, yellow fever) or other inactivated vaccines (including DTPa, hepatitis B, Hib, IPV, MenCCV, hepatitis A and pneumococcal conjugate vaccine), 38 using separate syringes and injection sites. If MMR or MMRV vaccine is not given simultaneously with other live attenuated parenteral vaccines, they should be given at least 4 weeks apart. 39

If MMRV vaccine is given at the same time as monovalent varicella vaccine (VV), they should be given using separate syringes and injection sites. MMR vaccine and monovalent VV should not be mixed together prior to injection.

Separate administration of measles, mumps or rubella vaccine is not available as an alternative to MMR vaccine, although a monovalent varicella vaccine is available (refer to 4.22 Varicella).

Interchangeability of MMR-containing vaccines

In general, the two brands of MMR vaccine can be considered interchangeable, that is, the 2nd MMR dose does not have to be of the same brand as the 1st. The same principle applies to the two available MMRV vaccines, 36 although they are not routinely recommended in a 2-dose schedule.

4.9.7 Recommendations

For additional recommendations associated with MMRV administration to prevent varicella disease, refer to 4.22 Varicella.

Infants aged <12 months

MMR-containing vaccines are not routinely recommended for infants <12 months of age. However, MMR vaccine can be given to children from as early as 9 months of age in certain circumstances, including travel to highly endemic areas and during outbreaks (refer to "Travellers" below). This is because maternal antibodies to measles are known to persist in many infants until approximately 11 months of age and may interfere with active immunisation before 12 months of age. 2 However, there is some evidence that a dose provided at ≥11 months (but prior to 12 months) of age is sufficiently immunogenic; as such, doses given in this timeframe may not need to be repeated in all circumstances (refer to also Table 2.1.5 Minimum acceptable age for the 1st dose of scheduled vaccines in infants in special circumstances).

Children

Two doses of measles-containing vaccine are recommended for all children. The 1st dose should be given at 12 months of age as MMR vaccine. MMRV vaccines are not recommended for use as the 1st dose of MMR-containing vaccine in children >4 years of age, due to a small but increased risk of fever and febrile seizures when given as the 1st MMR-containing vaccine dose in this age group (refer to 4.9.11 Adverse events and Table 4.9.1 below).

The 2nd dose of measles-containing vaccine is recommended to be given routinely at 18 months of age as MMRV vaccine. This is to commence from July 2013 once MMRV vaccine(s) are available under the NIP (refer to Table 4.9.1 below). The recommended age for administration of the 2nd dose of measles-containing vaccine will be moved down from 4 years of age, to provide earlier 2-dose protection against measles, mumps and rubella, and to improve vaccine uptake (refer to 4.9.3 Epidemiology above).

Catch-up vaccination of children who did not receive the 2nd dose of MMR-containing vaccine at 18 months of age can occur at the 4-year-old schedule point, until all relevant children have reached 4 years of age. Use of MMRV vaccine at the 4-year-old schedule point is preferred when varicella vaccination is also indicated (refer to 4.22 Varicella).

Children >12 months of age who have received 1 dose of MMR vaccine can be offered their 2nd dose of MMR-containing vaccine early (if at least 4 weeks after the 1st dose has elapsed) if they are considered at risk of coming in contact with measles 40 (refer to 4.9.12 Public health management of measles below).
MMR and MMRV vaccines are contraindicated in persons who have had:

Refer also to

There is no risk to pregnant women from contact with recently vaccinated persons. The vaccine virus is not transmitted from vaccinated persons to susceptible contacts.

MMRV vaccines are not recommended for use in persons ≥14 years of age.

MMR vaccines can be given to breastfeeding women. (Refer also to

MMR-containing vaccines are contraindicated in pregnant women. Pregnancy should be avoided for 28 days after vaccination.

Table 4.9.1: Recommendations for measles vaccination with (a) measles-mumps-rubella (MMR) (currently available), and (b) once measles-mumps-rubella-varicella (MMRV) vaccines are available from July 2013.

<table>
<thead>
<tr>
<th>Vaccines</th>
<th>12 months</th>
<th>18 months</th>
<th>4 years</th>
</tr>
</thead>
<tbody>
<tr>
<td>(a) Only monovalent varicella vaccine available</td>
<td>MMR</td>
<td>VV</td>
<td>MMR *</td>
</tr>
<tr>
<td>(b) When MMRV vaccine available</td>
<td>MMR</td>
<td>MMRV</td>
<td>–</td>
</tr>
</tbody>
</table>

* The 2nd dose of MMR-containing vaccine is recommended to be provided at 18 months of age to improve 2-dose coverage and protection against measles in young children. However, until June 2013, the 2nd dose of MMR vaccine is included under the NIP schedule for administration at 4 years of age. From July 2013, the 2nd dose of MMR vaccine will move to the 18-month NIP schedule point and be provided as MMRV vaccine.

Adults and adolescents

Persons born before 1966

No vaccination is required for persons born before 1966 (unless serological evidence indicates otherwise), as circulating virus and disease were prevalent before this time, suggesting most persons would have acquired immunity from natural infection. However, confirmed cases of measles have occurred in persons born before 1966 and, if doubt exists, it may be more expedient to offer vaccination than serological testing. (Refer also to ‘Serological testing for immunity to measles’ below.)

Persons born during or since 1966

All persons born during or since 1966 who are ≥18 months of age (or, until catch-up following the move of the 2nd NIP dose of measles-containing vaccine to 18 months of age is completed, are ≥24 years of age) should have documented evidence of 2 doses of MMR-containing vaccine (administered at least 4 weeks apart and with both doses administered at ≥12 months of age; refer to ‘Children’ above) or have serological evidence of protection for measles, mumps and rubella.

It is recommended that all adolescents and young adults have their vaccination records reviewed to ensure they have received 2 doses of MMR vaccine (refer to 4.9.3 Epidemiology above). MMRV vaccines are not recommended for use in persons ≥14 years of age, due to a lack of data on safety and immunogenicity/efficacy in this age group. If a dose of MMRV vaccine is inadvertently given to an older person, this dose does not need to be repeated.

Healthcare workers and other occupations

All adolescents and adults (born during or since 1966) should have their vaccination records reviewed to ensure they have received 2 doses of MMR vaccine. This is important for all persons, but especially those working in certain occupations, such as healthcare workers, staff working in early childhood education and care, staff of long-term care facilities and staff of correctional facilities. Those who were born during or since 1966 and are non-immune, or who have only received 1 dose of MMR vaccine, should be vaccinated and have documented evidence of 2 doses of MMR vaccine or serological evidence of immunity to measles (refer to ‘Adults and adolescents’ above). (Refer also to 3.3 Groups with special vaccination requirements, Table 3.3.7 Recommended vaccinations for persons at increased risk of certain occupationally acquired vaccine-preventable diseases.)

Travellers

It is especially important that all persons born during or since 1966 have been given 2 doses of measles-containing vaccine (administered at least 4 weeks apart, with both doses administered at ≥12 months of age; refer to ‘Children’ above) before embarking on international travel if they do not have evidence of previous receipt of 2 doses of MMR vaccine or serological evidence of protection for measles, mumps and rubella (refer to ‘Adults and adolescents’ above).

Infants travelling to countries in which measles is endemic, or where measles outbreaks are occurring, may be given MMR vaccine from as young as 9 months of age, after an individual risk assessment. In these cases, 2 further doses of MMR vaccine are still required. The next dose of MMR vaccine should be given at 12 months of age or 4 weeks after the 1st dose, whichever is later. This should be followed by the routine administration of the next dose of measles-containing vaccine, as MMR vaccine, at 18 months of age.

Serological testing for immunity to measles

Serological testing for immunity to measles, mumps, rubella or varicella is not recommended before or after routine administration of the 2-dose childhood schedule of these vaccines. However, serological testing for immunity to measles can be performed in cases where a history of natural immunity or 2 doses of vaccine administration is uncertain (refer to ‘Adults and adolescents’ above). Serology is indicated in special situations, such as pre-pregnancy planning (refer also to 4.18 Rubella, 4.22 Varicella and 3.3.2 Vaccination of women who are planning pregnancy, pregnant or breastfeeding, and preterm infants). Serological tests to investigate immunity to measles are generally sensitive at detecting antibody produced by both prior natural infection and vaccination, although sensitivity varies by assay and the clinical setting (e.g. time since vaccination). Interpretation of the results of serological testing may be enhanced by discussion with the laboratory that performed the test, ensuring that relevant clinical information is provided. An alternative to serological testing is presumptive administration of MMR vaccine dose(s). There is no known increase in adverse events from vaccinating those with pre-existing immunity to one or more of the vaccine components (refer to 4.9.11 Adverse events below).

4.9.8 Pregnancy and breastfeeding

MMR-containing vaccines are contraindicated in pregnant women. Pregnancy should be avoided for 28 days after vaccination.

MMR vaccines can be given to breastfeeding women. (Refer also to 4.18 Rubella.)

MMR vaccines are not recommended for use in persons aged ≥14 years.

There is no risk to pregnant women from contact with recently vaccinated persons. The vaccine virus is not transmitted from vaccinated persons to susceptible contacts. (Refer also to 4.18 Rubella, 4.22 Varicella and 3.3 Groups with special vaccination requirements, Table 3.3.1 Recommendations for vaccination in pregnancy for more information.

4.9.9 Contraindications

Anaphylaxis to vaccine components

MMR and MMRV vaccines are contraindicated in persons who have had:

- anaphylaxis following a previous dose of any MMR-containing vaccine
Persons who are immunocompromised

Measles-, mumps- and rubella-containing vaccines contain live attenuated vaccine viruses and are contraindicated in persons who are immunocompromised. Thus, MMR-containing vaccines are contraindicated in the following groups:

- Persons immunocompromised due to HIV/AIDS. MMR vaccination of asymptomatic HIV-infected persons >12 months of age with an age-specific CD4\(^+\) count of ≥15% may be considered.\(^{42-45}\) (refer to ‘MMR vaccinated persons’ in 3.3.3 Vaccination of immunocompromised persons). Since studies have not been performed using combination MMRV vaccines in asymptomatic HIV-infected persons or persons with an age-specific CD4\(^+\) count of ≥15%, it is recommended that only MMR vaccine (and monovalent VV, refer to 4.22 Varicella) be considered for use in this setting.\(^{44,46-48}\)
- Persons with other medical conditions associated with significant immunocompromise (refer to 3.3.3 Vaccination of immunocompromised persons).
- Persons receiving high-dose systemic immunosuppressive therapy, such as chemotherapy, radiation therapy or oral corticosteroids. MMR-containing vaccines are contraindicated in persons taking high-dose oral corticosteroids for more than 1 week (in children equivalent to >2 mg/kg per day prednisolone, and in adults >60 mg per day) (refer to 3.3.3 Vaccination of immunocompromised persons). Those who have been receiving high-dose systemic steroids for more than 1 week may be vaccinated with live attenuated vaccines after corticosteroid therapy has been discontinued for at least 1 month.\(^{49}\) (refer to 4.9.10 Precautions below and 3.3.3 Vaccination of immunocompromised persons).

Refer also to 3.3 Groups with special vaccination requirements and 4.22 Varicella for more information.

Pregnant women

Refer to 4.9.8 Pregnancy and breastfeeding above.

4.9.10 Precautions

Vaccination with other live attenuated parenteral vaccines

If MMR or MMRV vaccine is not given simultaneously with other live attenuated parenteral vaccines (e.g. varicella, BCG, yellow fever), the vaccines should be given at least 4 weeks apart.

Vaccination after immunoglobulin or blood product administration

Administration of MMR or MMRV vaccine should be delayed after administration of immunoglobulin-containing products. After receipt of immunoglobulin-containing blood products, the expected immune response to measles, mumps, rubella and varicella vaccination may be impaired.\(^{20,38,50}\) MMR-containing vaccines should not be given for between 3 and 11 months following the administration of immunoglobulin-containing blood products. The interval between receipt of the blood product and vaccination depends on the amount of immunoglobulin in each product, and is indicated in 3.3 Groups with special vaccination requirements. Table 3.3.6 Recommended intervals between either immunoglobulins or blood products and MMR, MMRV or varicella vaccination.\(^{38}\) For further information, refer to 3.3.4 Vaccination of recent recipients of normal human immunoglobulin and other blood products.

Recent blood transfusion with washed red blood cells is not a contraindication to MMR or MMRV vaccines.

MMR vaccine may be administered concomitantly with, or at any time in relation to, anti-D immunoglobulin, but at a separate injection site. Anti-D immunoglobulin does not interfere with the antibody response to vaccine.

Immunoglobulin or blood product administration after vaccination

Immunoglobulin-containing products should not be administered for 3 weeks following vaccination with measles-containing vaccines, unless the benefits exceed those of vaccination. If immunoglobulin-containing products are administered within this interval, the vaccinated person should either be revaccinated later at the appropriate time following the product (as indicated in Table 3.3.6), or be tested for immunity 6 months later and then revaccinated if seronegative.

Rhesus (D) immunoglobulin (anti-D) may be given at the same time in different sites with separate syringes or at any time in relation to MMR vaccine, as it does not interfere with the antibody response to the vaccine.

HIV-infected persons

MMR vaccine can be given to asymptomatic HIV-infected persons >12 months of age with an age-specific CD4\(^+\) count of ≥15%.\(^{51}\) (refer to 3.3 Groups with special vaccination requirements, Table 3.3.4 Categories of immunocompromise in HIV-infected persons, based on age-specific CD4\(^+\) counts and percentage of total lymphocytes). This is because the risk posed by measles infection is considered to be greater than the likelihood of adverse events from vaccination.\(^{38}\) MMR vaccine is contraindicated in immunocompromised HIV-infected persons (refer to 4.9.9 Contraindications above).

As there are no data available on the safety, immunogenicity or efficacy of MMRV vaccines in HIV-infected children, MMRV vaccine should not be administered as a substitute for MMR vaccine when vaccinating these children.\(^{29,50}\)

Persons receiving immunosuppressive therapy

MMR-containing vaccines may be given to persons on low-dose systemic corticosteroid therapy (e.g. children on doses of ≤2 mg/kg per day for less than 1 week, and those on lower doses of 1 mg/kg per day or alternate-day regimens for longer periods). Persons receiving high-dose corticosteroids can receive MMR-containing vaccines after corticosteroid therapy has been discontinued for at least 1 month (refer to < a href="4-9-9">4.9.9 Contraindications above).\(^{48}\) Some experts suggest withholding lower doses of steroids 2 to 3 weeks prior to vaccination with live viral vaccines, if this is possible.\(^{49,55}\) (Refer also to 3.3.3 Vaccination of immunocompromised persons.)

Household contacts of persons who are immunocompromised

Household contacts of persons who are immunocompromised, should ensure that they are age-appropriately vaccinated against, or are immune to, measles, as well as mumps, rubella and varicella. MMR-containing vaccines can be safely administered to household contacts, as measles, mumps and rubella vaccine viruses are not transmissible from vaccinated persons to others.\(^{48}\) If using MMRV vaccine, refer to 4.22 Varicella for information regarding varicella vaccine virus transmission.

Persons receiving long-term aspirin or salicylate therapy

There is no need to avoid salicylates before or after MMR or MMRV vaccination. Persons receiving long-term salicylate therapy (aspirin) can be vaccinated with MMRV, if indicated, as the benefit is likely to outweigh any possible risk of Reyes syndrome occurring after vaccination with a varicella-containing vaccine (refer to 4.22 Varicella).

Persons with a history of thrombocytopenia

Thrombocytopenia is a rare adverse event following MMR vaccination (refer to also 4.9.11 Adverse events below).\(^{1,52,53}\) In children with a past history of an episode(s) of idiopathic thrombocytopenia purpura (ITP), the risk of vaccine-associated thrombocytopenia occurring following a dose of MMR vaccine has been uncertain.\(^{79,53}\) However, a recent systematic review concluded that MMR vaccination, either as a 1st or 2nd dose, did not lead to a recurrence of ITP.\(^{54}\)

Personal or close family history of seizures or convulsions
Tuberculin skin testing following MMR vaccination

Measles virus inhibits the response to tuberculin and tuberculin-positive persons may become tuberculin-negative for up to a month after measles infection.\(^{25,26}\) As such, tuberculin skin testing ( Mantoux test) may be unreliable for at least 4 weeks after the administration of measles-containing vaccines. There are no studies on the effect of MMR or MMRV vaccination on the results of interferon-gamma release assays (IGRAs).\(^{26}\)

### 4.9.11 Adverse events

If using MMRV vaccine, additional adverse events relating to the varicella vaccine component are outlined in 4.22 Varicella.

Adverse events following administration of MMR-containing vaccines are generally mild and well tolerated.\(^{2}\) Adverse events are much less common after the 2nd dose of MMR or MMRV vaccine than after the 1st dose.

Fever (with malaise and/or a rash, which is non-infectious) may occur after MMR vaccination, most commonly between 7 to 10 days (range 5 to 12 days) after vaccination and lasting about 2 to 3 days. This coincides with the period of peak measles vaccine virus replication. High fever (>39.4°C) occurs in approximately 5 to 15% of MMR vaccine recipients, and rash occurs in approximately 5%.\(^{2,28}\) There is also an increased risk for febrile seizures in the same time period of approximately 1 case per 3000 doses.\(^{24}\)

It is recommended that vaccine recipients or their parents/carers be advised about possible symptoms in the period 5 to 12 days after vaccination, and given advice on their management, including the use of paracetamol for fever (refer to 2.3.2 (Handbook10-home.handbook10part2-handbook10-2-3#2-3) Adverse events following immunisation).

Higher rates of fever were observed in clinical trials of both MMRV vaccines, particularly following dose 1, when compared with giving MMR vaccine and monovalent VV at the same time but at separate sites.\(^{31-34}\) Two post-marketing studies in the United States identified an approximately 2-fold increased risk of fever and febrile convulsions in 1st dose recipients of MMRV vaccine, who were predominantly 12–23 months of age, in the period 7 to 10 days\(^{57}\) (or 5 to 12 days)\(^{28}\) after vaccination, compared with recipients of separate MMR and VV vaccines. MMRV vaccination resulted in 1 additional febrile seizure for every 2300 doses compared to separate MMR and VV vaccination.\(^{57}\) An increase in fever or febrile convulsions has not been identified after the 2nd dose of MMRV vaccine in the United States, although most 2nd dose recipients were aged 4–6 years, an age at which the incidence of febrile convulsions is low.\(^{26}\) These post-marketing studies were in children who received ProQuad; however, it is anticipated that this side effect profile would be similar in Priorix-tetra recipients.

A varicellaiform rash may occur after MMR vaccination (refer to 4.22.11 Adverse events in 4.22 Varicella). The appearance of a rash after monovalent varicella vaccine occurs in less than 5% of vaccine recipients (usually within 5 to 26 days), and similar rates are observed with the use of MMRV vaccine.\(^{60}\)

Anaphylaxis following the administration of MMR vaccine is very rare (less than 1 in 1 million doses distributed).\(^{26}\) Although no cases of anaphylaxis were reported in MMRV vaccine clinical trials, the incidence is likely to be similar to that occurring with use of MMR vaccine. Anaphylaxis after vaccination is likely due to anaphylactic sensitivity to gelatin or neomycin, not egg allergy. Although measles and mumps (but not rubella or varicella) vaccine viruses are grown in chick embryo tissue cultures, it is now recognised that measles- and mumps-containing vaccines contain negligible amounts of egg ovalbumin (refer to 4.9.13 Variations from product information below and 3.3.1 Vaccination of persons who have had an adverse event following immunisation).

Persons with egg allergy can be safely given MMR or MMRV vaccine.\(^{1,61}\) Skin testing is not required prior to vaccine administration.\(^{1}\)

Thrombocytopenia (usually self-limiting) has been very rarely associated with the rubella or measles component of MMR vaccine, occurring in 3 to 5 per 100 000 doses of MMR vaccine administered.\(^{1,26,52,55}\) This is considerably less frequent than after natural measles, mumps and rubella infections.\(^{1,51}\) Any association with MMRV vaccine is expected to be similar.

It is uncertain whether encephalopathy occurs after measles vaccine. If it does, it may occur at least 1000 times less frequent than as a complication from natural infection.\(^{2,28}\)

Other rare adverse events attributed to MMR vaccine include transient lymphadenopathy and arthralgia (refer to 4.18.28). Parotitis has been reported rarely (refer to 4.11 Mumps).\(^{28}\)

Autism, autistic spectrum disorder and inflammatory bowel disease are not associated with the MMR vaccine. There has been no credible scientific evidence to support this claim and most proponents of the link have retracted this claim.\(^{32,63}\) There is now a substantial body of evidence to refute it\(^{64-67}\) (refer to Appendix 4 Commonly asked questions about vaccination).

### 4.9.12 Public health management of measles

Measles is a notifiable disease in all states and territories in Australia. The public health management of measles is described in 4.9.12 Public health management of measles.

Variations from product information

For more information please refer to 4.22 Varicella.

### 4.9.13 Variations from product information

Any association with MMRV vaccine is expected to be similar.

The appearance of a rash after monovalent varicella vaccine occurs in less than 5% of vaccine recipients (usually within 5 to 26 days), and similar rates are observed with the use of MMRV vaccine.\(^{60}\)

Anaphylaxis after vaccination is likely due to anaphylactic sensitivity to gelatin or neomycin, not egg allergy. Although measles and mumps (but not rubella or varicella) vaccine viruses are grown in chick embryo tissue cultures, it is now recognised that measles- and mumps-containing vaccines contain negligible amounts of egg ovalbumin (refer to 4.9.13 Variations from product information below and 3.3.1 Vaccination of persons who have had an adverse event following immunisation).

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#### Table 4.9.2: Post-exposure prophylaxis required within 72 hours of first exposure for persons exposed to measles

<table>
<thead>
<tr>
<th>Age or immune status</th>
<th>Measles-mumps-rubella (MMR) vaccination history</th>
</tr>
</thead>
<tbody>
<tr>
<td>0 doses MMR or unknown</td>
<td>1 dose MMR</td>
</tr>
<tr>
<td>Normal human immunoglobulin (NHIG)</td>
<td>0.5 mL/kg to maximum of 15 mL</td>
</tr>
<tr>
<td>Immunocompromised (any age)</td>
<td>0.5 mL/kg to maximum of 15 mL</td>
</tr>
<tr>
<td>Birth to 5 months</td>
<td>0.2 mL/kg</td>
</tr>
<tr>
<td>6 to 8 months</td>
<td>0.2 mL/kg</td>
</tr>
</tbody>
</table>
9 to 11 months

MMR now, then repeat dose at 12 months of age or 4 weeks later
(whichever is later)†

Not applicable

Not applicable

12 months to <18 months

MMR†

MMRV (or MMR if already immunised against varicella), at least 4 weeks after initial dose of MMR

Nil necessary

≥18 months and born during or since 1966

MMR if not pregnant†‡§

If pregnant: check IgG if time; offer NHIG (0.2 mL/kg to maximum of 15 mL)¶

MMR or MMRV (based on age) if not pregnant

If pregnant: check IgG if time; offer NHIG (0.2 mL/kg to maximum of 15 mL)¶

Nil necessary

* NHIG is required because maternal antibody will have partially waned and vaccination is not as reliably effective in this age group compared with older infants.
† The 2nd scheduled dose of MMR-containing vaccine (MMRV) should then be given at 18 months of age, with a minimum interval of 4 weeks after the previous dose of MMR vaccine (refer to 4.9.7 Recommendations above).
‡ A subsequent dose of MMR-containing vaccine (MMR or MMRV) should be provided at least 4 weeks after the 1st valid dose (a valid dose is one given at ≥12 months of age) to complete a 2-dose vaccine schedule (refer to 4.9.7 Recommendations above).
§ In children aged 2 to <14 years, MMRV vaccine could also be used as dose 1 if the child has not been previously immunised against varicella (refer to 4.9.7 Recommendations above).
¶ Consult public health authority (and/or obstetrician or GP) about interpretation of IgG results and use of NHIG.

4.9.13 Variations from product information

The product information for MMR and MMRV vaccines recommends that women of child-bearing age should be advised not to become pregnant for 3 months after vaccination. The ATAGI instead recommends avoiding pregnancy for 28 days after vaccination.†

The product information for Priorix, M-M-R II, Priorix-tetra and ProQuad states that persons with a history of anaphylactic or anaphylactoid reactions to egg should not be vaccinated. The ATAGI recommends instead that either Priorix, M-M-R II, Priorix-tetra or ProQuad can be given in this situation.²⁸

The product information for Priorix-tetra states that it should be given by SC injection. The ATAGI recommends that it may also be given by IM injection.

The product information for ProQuad states that this vaccine is indicated for vaccination in individuals 12 months through 12 years of age. The product information for Priorix-tetra states that this vaccine can be used in persons from 9 months of age. The ATAGI recommends instead that both MMRV vaccines can be given to persons up to 14 years of age. The ATAGI also recommends that MMRV vaccine should not be used routinely as the 1st dose of MMR-containing vaccine in children aged <4 years.

The product information for both MMRV vaccines states that salicylates should be avoided for 6 weeks after vaccination, as Reye syndrome has been reported following the use of salicylates during natural varicella infection. The ATAGI recommends instead that non-immune persons receiving long-term salicylate therapy can receive varicella-containing vaccine, as the benefit is likely to outweigh any possible risk of Reye syndrome occurring after vaccination.

References

4. World Health Organization (WHO). Western Pacific Region. Four Western Pacific countries and areas are the first in their Region to be measles-free. 2014 (http://www.wpro.who.int/mediacentre/releases/2014/20140320/en/). (accessed Mar 2015).


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4.10 Meningococcal disease

Please Note: This chapter is currently being reviewed and updated. For information regarding meningococcal disease, please refer to the National Centre for Immunisation Research and Surveillance Fact Sheets – Meningococcal vaccines for Australians and Meningococcal vaccines – frequently asked questions (http://www.ncirs.edu.au/provider-resources/ncirs-fact-sheets/).

This chapter has been amended on 22 June 2015.

4.10.1 Bacteriology

Meningococcal disease is caused by a Gram-negative bacterium, Neisseria meningitidis, commonly known as meningococcus. There are 13 known serogroups distinguished by differences in surface polysaccharides of the outer membrane capsule. Globally, serogroups A, B, C, W135 and Y most commonly cause disease. Meningococci can be further classified by differences in their outer membrane proteins.1

4.10.2 Clinical features

N. meningitidis can cause invasive meningococcal disease (IMD) which includes meningitis and septicaemia. Septicaemia, either on its own or with meningitis, can be particularly severe. N. meningitidis can also cause other localised infections, including pneumonia, arthritis and conjunctivitis, but these are less common.

The clinical manifestations of meningococcal septicaemia and meningitis may be non-specific and can include sudden onset of fever, rash (petechial, purpuric or maculopapular), headache, neck stiffness, photophobia, altered consciousness, muscle ache, cold hands, thirst, joint pain, nausea and vomiting.2-6 Not all symptoms or signs may be present at disease onset. The characteristic rash of meningococcal disease, which does not disappear with gentle pressure on the skin, is not always present. Meningococcal infections can progress rapidly to serious disease or death in previously healthy persons. The overall mortality risk for IMD is high (between 5 and 10%), despite appropriate antibiotic therapy. Approximately 10 to 30% of children and adolescents who survive develop permanent sequelae, including limb deformity, skin scarring, deafness and neuroplogic deficits.2,4,5 Humans are the only reservoir of N. meningitidis. Meningococcus is transmitted via droplets or direct contact and has an incubation period of between 2 and 10 days, but commonly 3 to 4 days.3 A proportion of the population carry N. meningitidis without developing disease. The prevalence and duration of asymptomatic nasopharyngeal carriage of meningococci vary over time and in different population and age groups. Prevalence of carriage is known to be higher when groups of people occupy small areas of living space.6,7

A number of medical conditions are known to increase the risk of an individual developing IMD. The magnitude of the risk varies with the primary underlying condition. Persons with a complement deficiency have an increased risk of meningococcal disease (estimated to range from 5- to 10 000-fold depending on the specific condition), and are also more likely to have a recurrence of infection.8,9 Persons with an absent or dysfunctional spleen are at a life-long increased risk of severe bacterial infection,10,11 including sepsis attributable to meningococcal disease. Other immunocompromising conditions which increase the risk of IMD include HIV infection12,13 and haematopoetic stem cell transplant.

Other individuals at greater risk of meningococcal infection include laboratory workers who handle meningococci, new military recruits14,15 and university students living in residential colleges (particularly in their first years).16-19 Studies have also reported that exposure to smokers (who are more likely to be carriers), intimate kissing with multiple partners, and recent or current viral infection of the upper respiratory tract may also contribute to an individual’s risk of contracting meningococcal disease.20-22 There is no definitive evidence that there is an increased risk of IMD among men who have sex with men (MSM); however, clusters or community outbreaks of serogroup C IMD among MSM have been reported.23-26

4.10.3 Epidemiology

Meningococcal disease may occur sporadically or in epidemics. In Australia, a large proportion of cases are reported during winter and early spring, demonstrating a seasonal trend which is also observed in other countries with temperate climates.27 The notification rates of IMD among Indigenous persons are several times higher than in non-Indigenous persons for most age groups, except in those aged 15–24 years.28,29 The dominant meningococcal serogroup(s) varies between geographical regions. Serogroup A disease occurs predominantly in low-income countries, particularly countries in sub-Saharan Africa. Meningococcal serogroup B (‘MenB’) is the major cause of sporadic meningococcal disease in many developed countries. In Australia, serogroup B has predominated, particularly since the meningococcal serogroup C (MenC) conjugate vaccine program began in 2003. Of the 194 cases of meningococcal disease notified in Australia in 2012, for which the serogroup could be determined, 83% were due to serogroup B. The remainder were due to serogroup C (6%), serogroup W135 (4%) and serogroup Y (8%).30

Trends in the incidence of meningococcal disease are hard to predict over time due to natural fluctuations in disease. In Australia, notification rates of meningococcal disease have been decreasing, from a peak of 3.5 cases per 100 000 in 2001 to 1.1 per 100 000 in 2011. This is due to a decline in serogroup C disease following the national meningococcal C vaccination program and also a substantial decline in serogroup B disease.27 In Australia in 2006–2011, the highest incidence of serogroup B disease was in children aged <5 years (5.7 cases per 100 000), particularly infants aged <1 year (14.0 cases per 100 000) and toddlers aged 12–23 months (6.3 cases per 100 000). There was also a lower, secondary peak in late adolescence and early adulthood (2.8 cases per 100 000 aged 15–19 years). The incidence of serogroup C disease has remained low at <0.3 cases per 100 000 since 2009 for all age groups, with no cases reported among those aged <20 years in 2011.27

4.10.4 Vaccines

Meningococcal vaccines available in Australia can be broadly categorised according to their formulation type (conjugate, polysaccharide or recombinant) and the serogroups which they are designed to protect against (A, B, C, W135 and/or Y). There is no single vaccine that offers protection against all meningococcal serogroups.

Conjugate meningococcal vaccines

Monovalent meningococcal C vaccines (MenCCV)

- **Meningitec** – Emerge Health (meningococcal serogroup C–CRM197 conjugate). Each 0.5 mL pre-filled syringe contains 10 µg Neisseria meningitidis serogroup C oligosaccharide conjugated to approximately 15 µg of non-toxic Corynebacterium diphtheriae CRM197 protein; aluminium phosphate.

- **Menjugate Syringe** – CSL Limited/Novartis Vaccines and Diagnostics Pty Ltd (meningococcal serogroup C–CRM197 conjugate). Lyophilised powder in a monodose vial with a pre-filled diluent syringe. Each 0.5 mL reconstituted dose contains 10 µg N. meningitidis serogroup C oligosaccharide conjugated to 12.5–25 µg of non-toxic C. diphtheriae CRM197 protein; 1.0 mg aluminium hydroxide.

Combination vaccine that contains meningococcal C (Hib-MenCCV)

- **Menitorix** – GlaxoSmithKline Australia Pty Ltd (Haemophilus influenzae type b (PRP-T)-meningococcal serogroup C–tetanus toxoid conjugate). Lyophilised powder in a monodose vial with a pre-filled diluent syringe. Each 0.5 mL reconstituted dose contains 5 µg Hib capsular polysaccharide (PRP) conjugated to 12.5 µg of tetanus toxoid, and 5 µg N. meningitidis serogroup C polysaccharide conjugated to 10–20 µg of tetanus toxoid; traces of trometamol and sucrose.

Quadrivalent meningococcal conjugate vaccines (4vMenCV)

- **Menactra** – Sanofi-Aventis Australia Pty Ltd (meningococcal serogroups A, C, W135, Y–diphtheria toxoid conjugate). Each 0.5 mL monodose vial contains 4 µg each of serogroup A, C, W135 and Y polysaccharides individually conjugated with up to approximately 48 µg of a diphtheria toxoid protein.

- **Menveo** – CSL Limited/Novartis Vaccines and Diagnostics Pty Ltd (meningococcal serogroups A, C, W135, Y–CRM197 conjugate). Lyophilised powder containing serogroup A (MenA) in a monodose vial with a pre-filled syringe or vial containing serogroups C, W135 and Y (MenCWY) in saline suspension. Each 0.5 mL reconstituted dose contains 10 µg of serogroup A and 5 µg each of serogroups C, W135 and Y oligosaccharides individually conjugated with to 33.3 µg of non-toxic C. diphtheriae CRM197 protein; sucrose.

- **Nimenrix** – GlaxoSmithKline Australia Pty Ltd (meningococcal serogroups A, C, W135, Y–tetanus toxoid conjugate). Lyophilised powder in a monodose vial with solvent supplied in a pre-filled syringe or ampoule. Each 0.5 mL reconstituted dose contains 5 µg each of serogroups A, C, W135 and Y polysaccharides conjugated with a total of 44 µg of tetanus toxoid; trometamol; sucrose.

Conjugate meningococcal vaccine formulations contain meningococcal serogroup antigens conjugated to a carrier protein. They include vaccines that only offer protection against serogroup C meningococcal disease – monovalent meningococcal C conjugate vaccines (MenCCV) and MenCCV in combination with Hib (Hib-MenCCV) – and vaccines which offer protection against disease caused by four serogroups, including meningococcal C (quadrivalent meningococcal conjugate vaccines, 4vMenCV).

Monovalent meningococcal C vaccines (MenCCV)

Following extensive assessment in clinical studies, MenCCVs are now routinely delivered to infants and young children in a number of countries, including Australia. The effectiveness of MenCCV following 1 dose has been estimated to range from 83 to 100%.

The population-wide use of this vaccine in national vaccination programs has resulted in marked reductions in serogroup C invasive disease in the eligible age groups, including in Australia.

There is also evidence that meningococcal C vaccination programs have offered indirect protection to older age groups who were not eligible to receive the vaccine.

Although waning of antibody levels has been observed following vaccination with MenCCVs, current serogroup C meningococcal disease epidemiology in Australia suggests ongoing protection in age groups who were previously vaccinated.

Combination vaccine that contains meningococcal C (Hib-MenCCV)

The combination vaccine containing meningococcal serogroup C and Haemophilus influenzae type b antigens (Hib-MenCCV) has been used under the National Immunisation Program (NIP) since July 2013. The MenCCV component has similar immunogenicity and safety to monovalent MenCCV.

Quadrivalent meningococcal conjugate vaccines (4vMenCV)

4vMenCVs are designed to provide protection against four serogroups of meningococci: A, C, W135 and Y. As it is not feasible to assess the efficacy of 4vMenCVs in clinical trials, immunogenicity outcomes have been used as a surrogate measure for vaccine efficacy. Each of the registered 4vMenCV formulations have been shown to be immunogenic in infants, children and adults, inducing serum bactericidal antibodies at levels that correlate with clinical protection approximately 1 month after a vaccine dose.

Although waning of antibody levels has been observed following vaccination with MenCCVs, there is some evidence that the immunogenicity of the different 4vMenCV formulations varies among adolescents and adults, but the clinical significance of the differences is uncertain and does not warrant a preference for one formulation over another in these age groups.

The vaccine effectiveness of a 4vMenCV adolescent vaccination program in the United States, consisting of a single dose, has been estimated at 80 to 85%.

Menevo is the only 4vMenCV which has been assessed in young infants (from 2 months of age). A clinical trial has shown that protective levels of antibody to serogroups C, W135 and Y are induced in >70% of infants after 2 vaccine doses, at 2 and 4 months of age, with a lower antibody response to serogroup A. However, protective levels of antibodies to all serogroups were achieved in >90% of infants after a 3rd dose at 6 months of age.

Protective antibody titres from 4vMenCV have been shown to persist for up to 3 years in clinical trials in children.

In adolescents and adults, a high proportion of vaccine recipients have been shown to maintain seroprotective antibody titres against most of the vaccine serogroups (except serogroup A) until up to 5 years after primary vaccination.

A few studies have demonstrated a poor immune response to a single dose of meningococcal conjugate vaccine (either MenCCV or 4vMenCV) in children and adults with asplenia and in HIV-infected persons.

The immune response to some serogroups improves following a 2nd vaccine dose.

Meningococcal B vaccine (MenBV)

- **Bexsero** – Novartis Vaccines and Diagnostics Pty Ltd (recombinant multicomponent meningococcal serogroup B vaccine). Each 0.5 mL pre-filled syringe contains 50 µg Neisseria meningitidis serogroup B Neisseria heparin binding antigen fusion protein, 50 µg Neisseria meningitidis serogroup B Neisseria adhesin A protein, 50 µg Neisseria meningitidis serogroup B factor H binding protein fusion protein, 25 µg outer membrane vesicles from Neisseria meningitidis serogroup B strain NZ98/254 (measured as amount of total protein containing the PorA P1.4), adsorbed onto aluminium hydroxide; sodium chloride; histidine; sucrose. May contain traces of kanamycin. Tip cap may contain traces of natural rubber latex.

MenBV is a recombinant multicomponent vaccine (also known as 4CMenB) designed to provide protection against multiple strains of meningococcal serogroup B. It contains four major protein antigens that are highly conserved across serogroup B strains. This vaccine differs from strain-specific meningococcal B vaccines that have been used in some countries, such as New Zealand, for the control of epidemics dominated by a single serogroup B strain.

As it is not feasible to assess the efficacy of MenBV in clinical trials, immunogenicity outcomes have been used as a surrogate measure for vaccine efficacy. Clinical studies have shown that MenBV induces bactericidal antibodies specific to the four vaccine antigens in infants, children, adolescents and younger adults at a level that correlates with protection against clinical disease.

There are currently no data on the use of MenBV in persons aged >50 years. MenBV is expected to protect against the majority of circulating meningococcal B strains.

Specialised laboratory testing (Meningococcal Antigen Typing System or MATS) has predicted that approximately 76% of all meningococcal B strains that caused disease in Australia from 2007 to 2011 would have been susceptible to effective killing by vaccine-induced antibodies.

The duration of clinical protection afforded by MenBV is currently unknown due to the limited data on persistence of vaccine-induced immunity.

Poly saccharide meningococcal vaccines

Quadrivalent meningococcal polysaccharide vaccines (4vMenPV)

- **Menevax ACWY** – GlaxoSmithKline Australia Pty Ltd (meningococcal serogroups A, C, W135 and Y polysaccharides). Lyophilised pellet in a monodose vial with separate saline diluent. Each 0.5 mL reconstituted dose contains 50 µg of each meningococcal serogroup polysaccharide; 12.6 mg sucrose; 0.1 mg trometamol.

- **Menomune** – Sanofi-Aventis Australia Pty Ltd (meningococcal serogroups A, C, W135 and Y polysaccharides). Lyophilised powder in a monodose vial with separate saline diluent. Each 0.5 mL reconstituted dose contains 50 µg of each meningococcal serogroup polysaccharide; 2.5–5 mg lactose.
4.10.5 Transport, storage and handling


**Conjugate vaccines**

Menjugate Syringe must be reconstituted by adding the entire contents of the diluent syringe to the vial and shaking gently until the powder is completely dissolved. Reconstituted vaccine should be used immediately.

Menitorix must be reconstituted by adding the entire contents of the diluent syringe to the vial and shaking well until the powder is completely dissolved. Reconstituted vaccine should be used promptly. If storage is necessary, hold at +2°C to +8°C for not more than 24 hours.

Menvax must be reconstituted by adding the entire contents of the liquid MenCWY vial to the lyophilised MenA vial and shaking vigorously until the powder is completely dissolved. Reconstituted vaccine should be used as soon as practicable. If storage is necessary, hold at +2°C to +8°C for not more than 24 hours.

Nimenrix must be reconstituted by adding the entire contents of the pre-filled syringe or ampoule of solvent to the vial and shaking well until the powder is completely dissolved. Reconstituted vaccine must be used promptly. Reconstituted vaccine is stable at temperatures up to 30°C for up to 8 hours.

**Polysaccharide vaccines**

Mencevax ACWY must be reconstituted by adding the entire contents of the diluent container to the vial and shaking until the powder is completely dissolved. Reconstituted vaccine should be used promptly. If storage is necessary, hold at +2°C to +8°C for not more than 8 hours.

Menomune must be reconstituted by adding the entire contents of the diluent container to the vial and swirling until the powder is completely dissolved. Reconstituted vaccine should be used immediately.

4.10.6 Dosage and administration

**Conjugate meningococcal vaccines**

The dose of all meningococcal conjugate vaccines (MenCCV, Hib-MenCCV, 4vMenCV) is 0.5 mL, to be given by IM injection.

Meningitec (MenCCV), Menjugate Syringe (MenCCV) and Menitorix (Hib-MenCCV) are registered for use from 6 weeks of age.

NeisVac-C (MenCCV) is registered for use from 8 weeks of age.

The recommended age for use of 4vMenCVs varies between vaccine brands. Menactra can be used from 2 years of age, Nimenrix from 12 months of age and Menvax from 2 months of age (refer to 4.10.13 Variations from product information below).

**Meningococcal B vaccine**

The dose of MenBV is 0.5 mL, to be given by IM injection. Refer to Table 4.10.1 for the recommended doses of MenBV for different age groups.

MenBV is registered for use from 2 months of age. However, the 1st dose can be given as early as 6 weeks of age to align with the schedule for other routine infant vaccines (refer to 4.10.13 Variations from product information below). If the 1st dose is given at 6 weeks of age, the next scheduled doses can be given at 4 and 6 months of age.

<table>
<thead>
<tr>
<th>Age at commencement of vaccine course</th>
<th>Number of doses required for primary immunisation</th>
<th>Recommended interval between primary doses</th>
<th>Recommended age for single booster dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>6 weeks – 5 months</td>
<td>3 doses</td>
<td>8 weeks</td>
<td>12 months</td>
</tr>
<tr>
<td>6–11 months</td>
<td>2 doses</td>
<td>8 weeks</td>
<td>12 months, or 8 weeks after previous dose, whichever is later</td>
</tr>
<tr>
<td>≥12 months†</td>
<td>2 doses</td>
<td>8 weeks</td>
<td>No booster required†</td>
</tr>
</tbody>
</table>

* MenBV is registered for use in persons ≥2 months of age; however, the 1st dose of MenBV can be given as early as 6 weeks of age (refer to 4.10.13 Variations from product information).
† There are currently no data on the use of MenBV in persons aged >50 years; however, it is recommended that MenBV can be used in older persons who are at increased risk of IMD (refer to 4.10.7 Recommendations below).
‡ The need for a booster dose for this age group is as yet uncertain.

**Polysaccharide meningococcal vaccines**

The dose of both 4vMenPVs is 0.5mL, to be given by SC injection.

4vMenPVs are registered for use in persons ≥2 years of age.

**Co-administration with other vaccines**

Meningococcal vaccines can be administered concurrently with other vaccines (refer to 4.10.13 Variations from product information below).

There is an increased risk of fever following the co-administration of MenBV with other vaccines routinely recommended for children <24 months of age, compared to when these vaccines are given separately (refer to 4.10.11 Adverse events below). Co-administration of MenBV with other routine infant vaccines in this age group is acceptable; however, prophylactic administration of paracetamol to reduce the risk of fever is recommended (refer to 4.10.10 Precautions below). Alternatively, MenBV can be administered separately from other routine infant vaccines, with a minimum interval of 3 days to minimise the risk of fever. In this circumstance, parents are advised that routinely recommended vaccines are not delayed.
Interchangeability of meningococcal vaccines

The different meningococcal vaccine formulations (conjugate, polysaccharide and recombinant) are not interchangeable.

4.10.7 Recommendations

Meningococcal vaccines are recommended for the following age and risk groups because of their greater risk of IMD.

Infants and children

Meningococcal C vaccines

A single dose of MenCCV-containing vaccine is recommended for all children at the age of 12 months. This can be provided as either MenCCV or the combination vaccine Hib-MenCCV (refer to 4.10.4 Vaccines above). Additional doses of MenCCV-containing vaccine are not recommended based on current disease epidemiology in Australia (refer to 4.10.3 Epidemiology above).

Children who missed receiving a dose of MenCCV-containing vaccine at 12 months of age should be given a single catch-up dose (refer to 2.1.5 Handbook10-home~handbook10part2~handbook10-2-1#2-1-5 Catch-up). Similarly, children (without medical risk factors for IMD) who have received a dose(s) of MenCCV-containing vaccine at age <12 months, such as migrants from overseas countries where different vaccine schedules are used, should be given a single dose at 12 months of age or 8 weeks after their last dose (refer to 2.1.5 Handbook10-home~handbook10part2~handbook10-2-1#2-1-5 Catch-up and 4.10.13 Variations from product information below).

Meningococcal B vaccine

MenBV is recommended for infants and young children, particularly those aged <2 years, due to their higher risk of serogroup B meningococcal disease (refer to 4.10.3 Epidemiology above). The number of doses required depends on the age at which the vaccine course is commenced (refer to Table 4.10.1 and 4.10.6 Dosage and administration above).

Prophylactic administration of paracetamol is recommended with every dose of MenBV in children <2 years of age due to the increased risk of fever following vaccine administration (refer to 4.10.10 Precautions below).

Adolescents and adults

Meningococcal B vaccine

MenBV is recommended in a 2-dose schedule for all adolescents aged 15–19 years due to their higher risk of serogroup B meningococcal disease compared with other ages (refer to Table 4.10.1 and 4.10.6 Dosage and administration above).

MenBV vaccine is particularly recommended for adolescents and young adults living in close quarters, such as new military recruits and students living in residential accommodation.

Vaccination should be given prior to entry to such risk settings or as soon as possible after entry (refer to 4.10.2 Clinical features).

Persons with condition(s) associated with an increased risk of meningococcal disease

A number of medical conditions or treatments increase a person’s risk of IMD (refer to List 4.10.1) and additional doses of 4vMenCV and MenBV are recommended for persons with these risk factors.

List 4.10.1: Conditions associated with an increased risk of invasive meningococcal disease (IMD) in children and adults

- defects in or deficiency of complement components, including factor H, factor D or properdin deficiency
- current or future treatment with eculizumab (a monoclonal antibody directed against complement component C5)
- functional or anatomical asplenia
- HIV infection, regardless of stage of disease or CD4+ count
- haematopoietic stem cell transplant

Meningococcal conjugate vaccines

4vMenCV is recommended for persons with conditions in List 4.10.1. The vaccine brand and doses required depend on the age at which the vaccine course is commenced (refer to Table 4.10.2).

Menveo is the only brand of 4vMenCV that should be used in infants <12 months of age. If Menveo is not available, specialist advice should be sought on the most appropriate vaccination schedule.

Persons who require 4vMenCV due to the presence of underlying at-risk conditions, who have previously received 4vMenPV, should receive 2 doses of 4vMenCV as outlined in Table 4.10.2. The first dose of 4vMenCV is recommended approximately 2 years after the most recent dose of 4vMenPV. However, if the first dose of 4vMenCV is required sooner, a minimum interval of 6 months after 4vMenPV is acceptable, based on limited immunogenicity studies.\(^28,48\)

Table 4.10.2: Recommended use of 4vMenCV by age group for persons with medical condition(s) associated with an increased risk of meningococcal disease

<table>
<thead>
<tr>
<th>Age at commencement of vaccine course</th>
<th>Recommended brand</th>
<th>Primary immunisation</th>
<th>Recommended interval between primary doses*</th>
<th>Timing of booster doses</th>
</tr>
</thead>
<tbody>
<tr>
<td>2–6 months</td>
<td>Menveo</td>
<td>3 doses</td>
<td>8 weeks</td>
<td>At age 12–18 months, then 3 years later, then every 5 years thereafter</td>
</tr>
<tr>
<td>7–11 months</td>
<td>Menveo</td>
<td>2 doses</td>
<td>12 weeks</td>
<td>3 years after the primary doses, then every 5 years thereafter</td>
</tr>
<tr>
<td>12–23 months</td>
<td>Menveo or Nimenrix</td>
<td>2 doses</td>
<td>12 weeks</td>
<td>3 years after the primary doses, then every 5 years thereafter</td>
</tr>
</tbody>
</table>

### Meningococcal B vaccine

MenBV is recommended for persons with conditions in List 4.10.1. For recommended doses of MenBV by age group refer to Table 4.10.1 in 4.10.6 Dosage and administration above.

### Travellers

A quadrivalent meningococcal vaccine is recommended for persons who are planning travel involving a greater risk of exposure to meningococcal serogroups A, C, W135 and Y. This includes:
- individuals who intend to travel to or reside in parts of the world where epidemics of group A, C, W135 or Y meningococcal disease occur, particularly the ‘meningitis belt’ of sub-Saharan Africa.
- individuals who intend to travel to mass gatherings, for example, pilgrims travelling to the Hajj. In some instances documentation of vaccination is required for country entry visas.

The vaccine brand and doses required depends on the age at which the vaccine course is commenced (refer to Table 4.10.3). Use of 4vMenCV is preferred, particularly in children aged <7 years and travellers of any age who anticipate ongoing or periodic travel-related exposure risk. 4vMenPV is suitable, however, when the need for repeat doses is not anticipated, as described in 4.10.4 Vaccines above.

In those with ongoing increased risk due to travel who have previously received 4vMenPV, 1 dose of 4vMenCV is recommended approximately 2 years after the most recent dose of 4vMenPV, with a recommended minimum interval of 6 months, with subsequent 4vMenCV vaccinations as outlined in Table 4.10.3.

### Use of vaccines for close contacts of meningococcal disease cases

Advice on the need for meningococcal vaccination of the close contacts of a meningococcal disease case (i.e. those with household or household-like contact) should be sought from the relevant state or territory public health authority (refer to 4.10.12 Public health management of meningococcal disease below).

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### Table 4.10.3: Recommended use of 4vMenCV by age group for persons travelling to areas where epidemics of group A, C, W135 or Y meningococcal disease occur or to mass gatherings

<table>
<thead>
<tr>
<th>Age at commencement of vaccine course</th>
<th>Recommended brand</th>
<th>Primary immunisation</th>
<th>Recommended interval between primary doses</th>
<th>Timing of booster doses of 4vMenCV if required</th>
</tr>
</thead>
<tbody>
<tr>
<td>2–6 years</td>
<td>Menveo</td>
<td>3 doses</td>
<td>8 weeks</td>
<td>At age 12–18 months, then 3 years later, then every 5 years thereafter</td>
</tr>
<tr>
<td>7–11 months</td>
<td>Menveo</td>
<td>2 doses</td>
<td>12 weeks</td>
<td>3 years after the primary doses, then every 5 years thereafter</td>
</tr>
<tr>
<td>12–23 months</td>
<td>Either</td>
<td>2 doses</td>
<td>12 weeks</td>
<td>3 years after the primary dose(s), then every 5 years thereafter</td>
</tr>
<tr>
<td></td>
<td>Menveo or</td>
<td></td>
<td></td>
<td>3 years after the primary dose(s), then every 5 years thereafter</td>
</tr>
<tr>
<td></td>
<td>Nimenrix†</td>
<td></td>
<td></td>
<td>3 years after the primary dose(s), then every 5 years thereafter</td>
</tr>
<tr>
<td>2–6 years</td>
<td>Menactra, Menveo</td>
<td>1 dose</td>
<td>Not applicable</td>
<td>3 years after the primary dose, then every 5 years thereafter</td>
</tr>
<tr>
<td></td>
<td>or Nimenrix†</td>
<td></td>
<td></td>
<td>3 years after the primary dose, then every 5 years thereafter</td>
</tr>
<tr>
<td>≥7 years</td>
<td>Menactra, Menveo</td>
<td>1 doses</td>
<td>Not applicable</td>
<td>Every 5 years after the previous dose†</td>
</tr>
<tr>
<td></td>
<td>or Nimenrix†</td>
<td></td>
<td></td>
<td>3 years after the primary dose, then every 5 years thereafter</td>
</tr>
</tbody>
</table>

* Refer to Table 2.1.7(Handbook10-home~handbook10part2~handbook10-2-1#2-1-7) Minimum acceptable dose intervals for children <10 years of age for advice on minimum intervals.

† 4vMenCV is preferred. However, 4vMenPV is a suitable alternative for travellers aged ≥7 years when the need for repeat doses is not anticipated (refer to ‘Travellers’ above).

#### Laboratory personnel who frequently handle Neisseria meningitidis

Laboratory personnel who are at occupational risk of exposure to Neisseria meningitidis are recommended to receive immunisation against all vaccine-preventable meningococcal serogroups as listed below.

#### Meningococcal conjugate vaccines

4vMenCV is recommended for laboratory personnel to offer protection against serogroups A, C, W135 and Y. Those with ongoing occupational exposure risks are recommended to receive a 4vMenCV booster dose every 5 years.

4vMenPV can be used if the risk of exposure is not expected to be ongoing and the need for repeat doses (which can result in immunological hyporesponsiveness, refer to 4.10.4 Vaccines) is not anticipated. However, for most laboratory personnel, there will be ongoing exposure risks and anticipated need for repeat doses of the vaccine and, in these instances, 4vMenCV is preferred.

In those with ongoing occupational exposure risks who have previously received 4vMenPV, a dose of 4vMenCV is recommended approximately 2 years after the most recent dose of 4vMenPV. The minimum interval between the 1st dose of 4vMenCV and the last dose of 4vMenPV is 6 months.82,84,85

#### Meningococcal B vaccine

MenBV in a 2-dose schedule is recommended for laboratory personnel to offer protection against meningococcal serogroup B. For recommended doses of MenBV by age group refer to Table 4.10.1 in 4.10.6 Dosage and administration above.
4.10.9 Contraindications

The only absolute contraindications to meningococcal vaccines are:

- anaphylaxis following a previous dose of any meningococcal vaccine
- anaphylaxis following any vaccine component.

Previous meningococcal disease, regardless of the serogroup, is not a contraindication to administration of any meningococcal vaccine.

Previous vaccination with the strain-specific meningococcal B vaccine used in New Zealand, MenNZB, is not a contraindication for receiving MenBV.

4.10.10 Precautions

Prophylactic administration of paracetamol with MenBV vaccination in children aged <2 years

Prophylactic administration of paracetamol with each dose of MenBV administered to children <2 years of age is recommended due to the increased risk of fever, including high fever, following MenBV.70 (refer to 4.10.11 Adverse events below). This is an exception to the general recommendation not to routinely give paracetamol at the time of vaccinations (refer to 2.3.2 (Handbook10-home-handbook10part2-handbook10-2-3#2-3-2) Adverse events following immunisation).

The 1st dose of paracetamol (15 mg/kg/dose) is recommended within the 30-minute period prior to, or as soon as practicable after, vaccination, regardless of the presence of fever. This can be followed by 2 more doses of paracetamol given 6 hours apart, regardless of the presence of fever. A clinical trial has shown that the prophylactic use of paracetamol in infants reduced the likelihood of high-grade fever by approximately half following any vaccine dose, with no overall impact on the immunogenicity of either MenBV or other vaccines given concurrently.91

Similarly, the use of prophylactic antipyretics in a population-based MenBV program in a region of Quebec, Canada, reduced the likelihood of fever in the first 48 hours following the 1st dose of MenBV by about 50% among over 1500 children <2 years of age92 (refer to 4.10.11 Adverse events below).

4.10.11 Adverse events

Conjugate meningococcal vaccines

Meningococcal conjugate vaccines are generally considered safe and well tolerated. Common adverse events are pain, redness and swelling at the injection site, fever, irritability, drowsiness, decreased appetite and headaches.32,38-41,44-46 There are some age-related differences in the type of adverse events following vaccination. For example, headache, anorexia, fever and chills are more likely to be reported in adolescents and adults than in children following administration of 4vMenCV.44-46 Among recipients of 4vMenCV, rash and nausea are common. However, serious general adverse events are rare.44-46

The range of adverse events occurring after Hib-MenCCV combination vaccine is similar to that after other childhood vaccines.38 Redness is the most frequently reported local symptom, with irritability the most frequently reported generalised reaction.38-40 Concomitant administration of Hib-MenCCV with MMR vaccine is not associated with an increased rate of adverse events for either vaccine.38

There is no evidence of an association between meningococcal conjugate vaccines and Guillain-Barré syndrome (GBS). An early report in the United States of a suspected temporal association between Menactra and GBS was followed by a large retrospective cohort study in the United States which found no evidence of an increased risk of GBS with the use of Menactra.38,39 Meningococcal conjugate vaccines can be administered to persons with a history of GBS for whom vaccination is indicated (refer to 4.10.13 Variations from product information below).

Meningococcal B vaccine

MenBV has an acceptable safety and tolerability profile based on clinical trial data. In clinical trials, fever was the most notable systemic reaction in infants and children, particularly those aged 2–12 months. Temperatures were highest 6 hours after vaccination, then decreased on day 2 and generally subsided by day 3.80 More than a quarter (26 to 41% depending on dose number) of infants who received MenBV alone developed fever ≥38°C and 4 to 8% had fever ≥39°C.70 In response to a community epidemic, approximately 44,000 individuals between 2 months and 20 years of age in a region of Quebec, Canada, received at least 1 dose of MenBV. About 15% (112,746) of infants who participated in the vaccine safety surveillance reported fever; among those who had their temperature measured in the first 48 hours (n=61), approximately 32% reported a peak temperature of 39–40.4°C, and <1% reported a peak temperature of ≥40.5°C.92

In a clinical trial, the frequency of fever was about 2 times higher when MenBV was administered with other infant vaccines, specifically DTPa-hepB-IPV-Hib and 7-valent pneumococcal conjugate vaccines, with 51 to 62% of infants reporting fever ≥38°C and 10 to 15% reporting fever ≥39°C within 7 days of any vaccine dose.70 Fever in infants given MenBV concurrently with other routine infant vaccines was reduced by prophylactic use of paracetamol.91 (Refer also to 4.10.10 Precautions above). In clinical studies, fever and other systemic reactions were less common after the booster dose of MenBV administered at 12 months of age.

Other common adverse events following MenBV included tenderness, swelling, induration and erythema at the injection site, as well as irritability, sleepiness, unusual crying and changes in appetite.69 These reactions were reported less often with increasing age. Pain at the injection site, malaise and headache were more commonly reported among adolescents and adults.71

Polysaccharide meningococcal vaccines

Local adverse events after 4vMenPV include erythema, induration, tenderness, pain and local axillary lymphadenopathy. However, these reactions are usually mild and infrequent. Fever and chills occur in approximately 2% of young children, and may persist for 48 hours or longer, but significant general adverse events are rare. Studies have indicated no consistently significant differences in adverse events following 4vMenPV and 4vMenCV.54

4.10.12 Public health management of meningococcal disease

Invasive meningococcal disease is notifiable in all states and territories in Australia. Prompt diagnosis and medical treatment of suspected cases of meningococcal disease is important.

The state/territory public health authority should be contacted as soon as possible for guidance on the public health management of suspected cases and their contacts (refer to Appendix 1 (Handbook10-home-handbook10-tools-handbook10-appendices-handbook10-appendix1) Contact details for Australian, state and territory government health authorities and communicable disease control).

Decisions about the need for meningococcal vaccination of the close contacts of a meningococcal disease case (i.e. those with household or household-like contact), or in an outbreak of meningococcal disease in an institutional or community setting, should be made by the local public health unit and/or the state or territory public health authority, according to the national guidelines.54

4.10.13 Variations from product information

The product information for meningococcal C conjugate vaccines states that, under the age of 12 months, either 2 (NeisVac-C) or 3 (Meningitec and Menjugate Syringe) doses of vaccine are required. The ATAGI recommends instead that meningococcal C vaccination is routinely not recommended before 12 months of age (unless specifically indicated).
The product information for NeisVac-C states that this vaccine should not be administered with PRP-OMP Haemophilus influenzae type b vaccine unless ‘medically important’. The ATAGI recommends instead that the vaccine may be administered simultaneously with other vaccines in the NIP.

The product information for Menveo states that this vaccine is indicated for use in persons ≥2 months of age. However, the ATAGI recommends instead that this vaccine can be given to infants concurrently with other infant vaccines from as early as 6 weeks of age, to align with the routine infant schedule.

The product information for NeisVac-C states that this vaccine is indicated for use in persons between 2 and 55 years of age. The ATAGI recommends instead that this vaccine can be given to persons ≥55 years of age.

The product information for Menactra states that this vaccine is indicated for use in persons between 2 and 55 years of age. The ATAGI recommends instead that this vaccine can be given to persons ≥2 months of age.

The product information for Menveo states that this vaccine is indicated for use in persons ≥2 months of age. However, the ATAGI recommends instead that this vaccine may be administered simultaneously with other vaccines in the NIP.

The product information for Menvec states that this vaccine should be administered as a single dose. The ATAGI recommends that these vaccines can be given in a 2- or 3-dose primary schedule to infants, children and adults who are at increased risk of IMD according to Tables 4.10.2 and 4.10.3.

References


McQuaid F, Snape MD, John TM, et al. Persistence of bactericidal antibodies to 5 years of age after immunization with serogroup B meningococcal vaccines at 6, 8, 12 and 40 months of age.

Snape MD, Philip J, John TM, et al. Bactericidal antibody persistence 2 years after immunization with 2 investigational serogroup B meningococcal vaccines at 6, 8 and 12 months.

Snape MD, Saroey P, John TM, et al. Persistence of bactericidal antibodies following early infant vaccination with a serogroup B meningococcal vaccine and immunogenicity of a preschool booster dose.

Novartis Vaccines and Diagnostics Pty Ltd. Product information: Bexsero.

O’Hallahan J, McNicholas A, Galloway Y, O’Leary E, Roseveare C. Delivering a safe and effective strain-specific vaccine to control an epidemic of group B meningococcal disease.

Licorice B, Costa LS, van der Heijden IM, Sato HK, Marques HR. Immunogenicity of a meningococcal serogroup C conjugate vaccine in HIV-infected children, adolescents, and young adults.


Bacterium pertussis (B. pertussis) is the cause of whooping cough. An adult dose of inactivated vaccine is given with the ACWY vaccine.


Bexsero is a meningococcal conjugate vaccine indicated for the prevention of meningococcal disease caused by serogroups A, C, W-135, and Y in individuals aged 2-35 years.

Inactivated meningococcal vaccines are used to prevent meningococcal disease caused by serogroups A, C, W-135, and Y. These vaccines are given as a series of 4 doses at 2, 3, 4, and 6 months of age.

The meningococcal meningitis type b vaccine is indicated for the prevention of meningococcal disease caused by Neisseria meningitidis serogroup B in children aged 2-10 years.

The meningococcal meningitis type b vaccine is indicated for the prevention of meningococcal disease caused by Neisseria meningitidis serogroup B in children aged 2-10 years.

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The meningococcal meningitis type b vaccine is indicated for the prevention of meningococcal disease caused by Neisseria meningitidis serogroup B in children aged 2-10 years.


4.11 Mumps

4.11.1 Virology

Mumps is a paramyxovirus, genus Rubulavirus, with a single-stranded RNA genome. It is rapidly inactivated by heat, formalin, ether, chloroform and light.1

4.11.2 Clinical features

Mumps is an acute viral illness with an incubation period of 12 to 25 days.2 Transmission is via respiratory secretions, including aerosol transmission, or by direct contact with saliva or possibly urine.3 Asymptomatic infection occurs in one-third of cases.3 Symptomatic disease ranges from mild upper respiratory symptoms to widespread systemic involvement.3 A high proportion of mumps infections involve non-specific symptoms including fever, headache, malaise, myalgia and anorexia.4 The characteristic bilateral, or occasionally unilateral, parotid swelling occurs in 60 to 70% of clinical cases.4,5 Maximum infectiousness occurs between 2 days before onset of illness and 4 days afterwards, but patients may be infectious from 7 days before parotid swelling to 9 days after.5 Meningeal symptoms and signs appear in approximately 10% of cases, but permanent neurologic sequelae are rare.5 Mumps encephalitis has been estimated to occur in 1–2 per 10 000 cases, with a case-fatality rate of around 1.0%.6 Deafness is relatively common in mumps meningoencephalitis, although permanent nerve deafness is rare (1 in 20 000 infections).7 Orbitis (usually unilateral) has been reported in up to 15 to 30% of clinical mumps cases in post-pubertal males, but subsequent stenitis is rare.8 Symptomatic involvement of other glands and organs has been observed less frequently (pancreatitis, oophoritis, hepatitis, myositis, thyroïditis, mastitis).9,10

Mumps infection during the first trimester of pregnancy may result in spontaneous abortion.11,12 Maternal infection is not associated with an increased risk of congenital malformation.13,14

4.11.3 Epidemiology

Mumps is worldwide. Prior to universal vaccination, mumps was primarily a disease of childhood with the peak incidence in the 5–9 years age group. However, since 2000, peak rates have been reported in older adolescents and young adults, especially the 20–34 years age group.7,9 Between 2002 and 2004, mumps notifications were the lowest recorded in Australia, averaging 0.4 per 100 000.15 In 2005, notifications increased to 1.2 per 100 000, peaking at 2.7 per 100 000 in 2007, but have since declined to less than 1 per 100 000 since 2010.3,15 There have also been recent outbreaks of mumps in the United States and Europe, where the peak rates of disease have been in the 18–24 years age group.12,15

Similar to measles, persons born in the late 1960s to mid-1980s (especially the 1978–1982 birth cohort) are recognised to be at a greater risk of mumps. Many missing being vaccinated or acquiring mumps infection as infants (when vaccine coverage was low and disease incidence was decreasing), and may also have missed catch-up vaccinations during their school years as part of either the Measles Control Campaign (which only targeted primary-school-aged children) or the Young Adult Measles Control Campaign (which did not result in high coverage).16,17 During outbreaks, mumps attack rates are lowest in persons who have received 2 doses of mumps-containing vaccines, as this provides optimal long-term protection.18,19 In Australia, over the 11-year period from 1996 to 2006, mumps was reported as the underlying cause of 5 deaths, all in adults aged over 80 years.7,9

4.11.4 Vaccines

Monovalent mumps vaccine is not available in Australia. Mumps vaccination is provided using either measles-mumps-rubella (MMR) or measles-mumps-rubella-varicella (MMRV) vaccines. Two combination vaccines containing live attenuated measles, mumps, rubella and varicella viruses (MMRV) are registered in Australia.

Clinical trials of MMR vaccine indicate 95% mumps seroconversion after a single dose and up to 100% after a 2nd dose.4 However, outbreak investigations and post-marketing studies have reported 1-dose vaccine effectiveness to be between 60 and 90%.13,14 A Cochrane review reported 1-dose vaccine effectiveness to be between 69% and 81% for the vaccine containing the Jeryl Lynn mumps strain and between 70% and 75% for the vaccine containing the Urabe strain.19 While protection is greater in 2-dose vaccine recipients, recent outbreaks have reported mumps in 2-dose vaccine recipients, particularly young adults who received their vaccines more than 10 years previously.14,15,19,20,21 Combination MMRV vaccines have been shown in clinical trials, to produce similar rates of seroconversion to all four vaccine components compared with MMR vaccine and monovalent varicella vaccines administered concomitantly at separate injection sites.22-25

Refer to further information on MMR and MMRV vaccines in 4.22 Varicella(Handbook10-home~handbook10part4~handbook10-4-9-4.9 <em>Measles</em></a> and <a href=).

Combination measles–mumps–rubella (MMR) vaccines

- **M-M-R II** – bscSIL Pty Ltd (live attenuated measles virus (Enders’ attenuated Edmonston strain), mumps virus (Jeryl Lynn B level strain) and rubella virus (Wistar RA 27/3 strain)). Lyophilised pellet in a monodose vial with separate diluent. Each 0.5 mL reconstituted dose contains ≥1000 tissue culture infectious dose 50% (TCID50) of measles virus, ≥1050 TCID50 of mumps virus, and ≥1000 TCD50 of rubella virus; 14.5 mg sorbitol; 1.9 mg sucrose; 14.5 mg hydrolysed porcine gelatin; ≤0.3 mg recombinant human albumin; <1 ppm fetal bovine serum; 25 μg neomycin.

- **Priorix** – Glaxo Smith Kline Australia Pty Ltd (live attenuated measles virus (Schwarz strain), mumps virus (RIT 4385 strain, derived from the Jeryl Lynn strain) and rubella virus (Wistar RA 27/3 strain)). Lyophilised pellet in a monodose vial with a pre-filled diluent syringe. Each 0.5 mL reconstituted dose contains ≥105 TCID50 of measles virus, ≥108 TCID50 of mumps virus, and ≥107 TCID50 of rubella virus; lactose; neomycin; sorbitol; mannitol.

Combination measles-mumps-rubella-varicella (MMRV) vaccines

- **Priorix-tetra** – GlaxoSmithKline Pty Ltd (live attenuated measles virus (Schwarz strain), mumps virus (RIT 4385 strain, derived from the Jeryl Lynn strain), rubella virus (Wistar RA 27/3 strain) and varicella-zoster virus (Oka strain)). Lyophilised pellet in a monodose vial with a pre-filled diluent syringe. Each 0.5 mL reconstituted dose contains ≥105 CCID50 of measles virus, ≥107 CCID50 of mumps virus, and ≥105 CCID50 of rubella virus; lactose; neomycin; sorbitol; mannitol.

- **ProQuad** – CSL Pty Ltd (live attenuated measles virus (Enders’ attenuated Edmonston strain), mumps virus (Jeryl Lynn B level strain), rubella virus (Wistar RA 27/3 strain) and varicella-zoster virus (Oka/Measles strain)). Lyophilised powder in a monodose vial with a pre-filled diluent syringe. Each 0.5 mL reconstituted dose contains ≥105 TCID50 of measles virus, ≥104 TCID50 of mumps virus, ≥106 TCID50 of rubella virus, and ≥105 PFU of varicella-zoster virus; 20 mg sucrose; 11 mg hydrolysed porcine gelatin; 2.5 mg urea; 16 mg sorbitol; 0.38 mg monosodium L-glutamate; 0.25 mg recombinant human albumin; 5 μg neomycin; residual components of MRC-5 cells; 0.5 μg bovine serum albumin.

4.11.5 Transport, storage and handling

Transport according to National vaccine storage guidelines: **Store** for 5.26 Store at +2°C to +8°C. Do not freeze. Protect from light.

Both MMR and MMRV vaccines must be reconstituted by adding the entire contents of the diluent container to the vial containing the pellet and shaking until the pellet is completely dissolved.

Reconstituted Priorix (MMR), M-M-R II (MMR) and Priorix-tetra (MMRV) vaccines should be used as soon as practicable. If storage is necessary, hold at +2°C to +8°C for not more than 8 hours.

Reconstituted ProQuad (MMR) vaccine should be used immediately. If storage is necessary, hold at +2°C to +8°C for not more than 2.5 hours or at +20°C to +25°C for not more than 1 hour.

4.11.6 Dosage and administration

The dose of Priorix (MMR) vaccine for both children and adults is 0.5 mL to be given by either SC or IM injection.

For children <14 years of age, the dose of MMRV vaccine is 0.5 mL to be given by SC injection. Priorix-tetra may also be given by IM injection.27

MMRV vaccines are not recommended for use in persons aged ≥14 years.

When 2 doses of MMR-containing vaccine are required, the minimum interval between doses is 4 weeks.

Co-administration with other vaccines

MMR or MMRV vaccines can be given at the same time as other live attenuated parenteral vaccines (e.g. varicella, BCG, yellow fever) or other inactivated vaccines (including DTpA, hepatitis B, Hib, IPV, MenCCV, hepatitis A and pneumococcal conjugate vaccine),28 using separate syringes and injection sites. If MMR or MMRV vaccine is not given simultaneously with other live attenuated parenteral vaccines, they should be given at least 4 weeks apart.

If MMR vaccine is given at the same time as monovalent varicella vaccine (VV), they should be given using separate syringes and injection sites. MMR vaccine and monovalent VV should not be mixed together prior to injection.

Separate administration of measles, mumps or rubella vaccine is not available as an alternative to MMR vaccine, although a monovalent varicella vaccine is available (refer to 4.22 Varicella (Handbook10-home-handbook10part4-handbook10-4-22)).

Interchangeability of MMR-containing vaccines

In general, the two brands of MMR vaccine can be considered interchangeable, that is, the 2nd MMR dose does not have to be of the same brand as the 1st. The same principle applies to the two available MMRV vaccines,29 although they are not routinely recommended in a 2-dose schedule.

4.11.7 Recommendations

Infants aged <12 months

MMR-containing vaccines are not routinely recommended for infants <12 months of age. However, MMR vaccine can be given to children from as early as 9 months of age in high-risk circumstances (refer to 4.9 Measles (Handbook10-home-handbook10part4-handbook10-4-9)).

If MMR vaccine is given at <12 months of age, there is still a need for 2 vaccine doses to be administered at ≥12 months of age (refer to 4.9 Measles (Handbook10-home-handbook10part4-handbook10-4-9)).

Children

Two doses of mumps-containing vaccine are recommended for all children. The 1st dose should be given at 12 months of age as MMR vaccine. MMRV vaccines are not recommended for use as the 1st dose of MMR-containing vaccine in children <4 years of age, due to a small but increased risk of fever and febrile seizures when given as the 1st MMR-containing vaccine dose in this age group (refer to Table 4.9.1 in 4.9 Measles (Handbook10-home-handbook10part4-handbook10-4-9)).

If MMR vaccine is given at <12 months of age, there is still a need for 2 vaccine doses to be administered at ≥12 months of age (refer to 4.9 Measles (Handbook10-home-handbook10part4-handbook10-4-9)).

If MMR vaccine is inadvertently administered as dose 1 of MMR-containing vaccine, the dose does not need to be repeated (providing it was given at ≥12 months of age); however, parents/carers should be advised regarding the small but increased risk of fever and febrile seizures (compare with that expected following MMR vaccine).

Adults and adolescents

Two doses of mumps-containing vaccine are recommended for all non-immune adolescents and adults (refer to 4.9 Measles (Handbook10-home-handbook10part4-handbook10-4-9)). All persons born during or since 1966 who are ≥18 months of age (or, until catch-up following the move of the 2nd NIP dose of vaccines-containing vaccine to 18 months of age is completed, are ≥4 years of age) should have documented evidence of 2 doses of MMR-containing vaccine (administered at least 4 weeks apart with both doses administered at ≥12 months of age) or have serological evidence of protection for measles, mumps and rubella.

It is recommended that all adolescents and young adults have their vaccination records reviewed to ensure they have received 2 doses of MMR vaccine (refer to 4.11.3 Epidemiology above).

MMRV vaccines are not recommended for use in persons ≥14 years of age, due to a lack of data on safety and immunogenicity/efficacy in this age group. If a dose of MMRV vaccine is inadvertently given to an older person, this dose does not need to be repeated.

For further information on the recommendations for MMR and MMRV vaccines, refer to 4.9 Measles (Handbook10-home-handbook10part4-handbook10-4-9) and 4.22 Varicella (Handbook10-home-handbook10part4-handbook10-4-22).

Serological testing for immunity to mumps

Serological testing for immunity to mumps (and measles, rubella and varicella) is not recommended before or after routine administration of the 2-dose childhood schedule of these vaccines. However, serological testing for mumps (and measles and rubella) can be performed in cases where a history of natural immunity or 2 doses of vaccine administration is uncertain (refer to Adults and adolescents above). Serology is indicated in special situations, such as pre-pregnancy planning (refer also to 4.9 Measles (Handbook10-home-handbook10part4-handbook10-4-9), 4.18 Rubella (Handbook10-home-handbook10part4-handbook10-4-18) and 4.22 Varicella (Handbook10-home-handbook10part4-handbook10-4-22)). Serological tests to investigate immunity to mumps are generally sensitive at detecting antibody produced by both prior natural infection and vaccination, although sensitivity varies by assay and the clinical setting (e.g. time since vaccination). Interpretation of the results of serological testing may be enhanced by discussion with the laboratory that performed the test, ensuring that relevant clinical information is provided. An alternative to serological testing is presumptive administration of MMR vaccine (Handbook10-home-handbook10part3-handbook10-3-3). There is no known increase in adverse events from vaccinating those with pre-existing immunity to one or more of the vaccine components (refer to 4.11.11 Adverse events below).

4.11.8 Pregnancy and breastfeeding

MMR-containing vaccines are contraindicated in pregnant women. Pregnancy should be avoided for 28 days after vaccination.29

MMR vaccines can be given to breastfeeding women. (Refer also to 4.18 Rubella (Handbook10-home-handbook10part4-handbook10-4-18).)

MMRV vaccines are not recommended for use in persons aged ≥14 years.

For children <14 years of age, the dose of MMRV vaccine is 0.5 mL to be given by SC injection. Priorix-tetra may also be given by IM injection.27

MMRV vaccines are not recommended for use in persons aged ≥14 years.

Interchangeability of MMR-containing vaccines

In general, the two brands of MMR vaccine can be considered interchangeable, that is, the 2nd MMR dose does not have to be of the same brand as the 1st. The same principle applies to the two available MMRV vaccines,29 although they are not routinely recommended in a 2-dose schedule.

4.11.7 Recommendations

Infants aged <12 months

MMR-containing vaccines are not routinely recommended for infants <12 months of age. However, MMR vaccine can be given to children from as early as 9 months of age in high-risk circumstances (refer to 4.9 Measles (Handbook10-home-handbook10part4-handbook10-4-9)).

If MMR vaccine is given at <12 months of age, there is still a need for 2 vaccine doses to be administered at ≥12 months of age (refer to 4.9 Measles (Handbook10-home-handbook10part4-handbook10-4-9)).

If MMR vaccine is inadvertently administered as dose 1 of MMR-containing vaccine, the dose does not need to be repeated (providing it was given at ≥12 months of age); however, parents/carers should be advised regarding the small but increased risk of fever and febrile seizures (compare with that expected following MMR vaccine).

Adults and adolescents

Two doses of mumps-containing vaccine are recommended for all non-immune adolescents and adults (refer to 4.9 Measles (Handbook10-home-handbook10part4-handbook10-4-9)). All persons born during or since 1966 who are ≥18 months of age (or, until catch-up following the move of the 2nd NIP dose of vaccines-containing vaccine to 18 months of age is completed, are ≥4 years of age) should have documented evidence of 2 doses of MMR-containing vaccine (administered at least 4 weeks apart with both doses administered at ≥12 months of age) or have serological evidence of protection for measles, mumps and rubella.

It is recommended that all adolescents and young adults have their vaccination records reviewed to ensure they have received 2 doses of MMR vaccine (refer to 4.11.3 Epidemiology above).

MMRV vaccines are not recommended for use in persons ≥14 years of age, due to a lack of data on safety and immunogenicity/efficacy in this age group. If a dose of MMRV vaccine is inadvertently given to an older person, this dose does not need to be repeated.

For further information on the recommendations for MMR and MMRV vaccines, refer to 4.9 Measles (Handbook10-home-handbook10part4-handbook10-4-9) and 4.22 Varicella (Handbook10-home-handbook10part4-handbook10-4-22).

Serological testing for immunity to mumps

Serological testing for immunity to mumps (and measles, rubella and varicella) is not recommended before or after routine administration of the 2-dose childhood schedule of these vaccines. However, serological testing for mumps (and measles and rubella) can be performed in cases where a history of natural immunity or 2 doses of vaccine administration is uncertain (refer to Adults and adolescents above). Serology is indicated in special situations, such as pre-pregnancy planning (refer also to 4.9 Measles (Handbook10-home-handbook10part4-handbook10-4-9), 4.18 Rubella (Handbook10-home-handbook10part4-handbook10-4-18) and 4.22 Varicella (Handbook10-home-handbook10part4-handbook10-4-22)). Serological tests to investigate immunity to mumps are generally sensitive at detecting antibody produced by both prior natural infection and vaccination, although sensitivity varies by assay and the clinical setting (e.g. time since vaccination). Interpretation of the results of serological testing may be enhanced by discussion with the laboratory that performed the test, ensuring that relevant clinical information is provided. An alternative to serological testing is presumptive administration of MMR vaccine (Handbook10-home-handbook10part3-handbook10-3-3). There is no known increase in adverse events from vaccinating those with pre-existing immunity to one or more of the vaccine components (refer to 4.11.11 Adverse events below).
4.11.10 Precautions

For additional precautions related to MMR and MMRV vaccines, refer to 4.9 Measles (Handbook10-home~handbook10part4~handbook10-4-9) and 4.22 Varicella (Handbook10-home~handbook10part4~handbook10-4-22).

Vaccination with other live attenuated parenteral vaccines

If MMR or MMRV vaccine is not given simultaneously with other live attenuated parenteral vaccines (e.g. varicella, BCG, yellow fever), the vaccines should be given at least 4 weeks apart.

4.11.11 Adverse events

Adverse events following administration of MMR-containing vaccines are generally mild and well tolerated. Adverse events are much less common after the 2nd dose of MMR or MMRV vaccine than after the 1st dose.

The most common adverse events following mumps vaccination are fever and parotitis. Parotitis occurs most commonly from 10 to 14 days after vaccination. The incidence varies by vaccine strain; in studies of the Jeryl Lynn vaccine strain, parotid and/or submandibular swelling occurred in 0.5 to 1.6% of recipients.

An increased risk of aseptic meningitis has been observed after vaccination with the Urabe strain of mumps vaccine in some countries. However, the Urabe strain is not used in Australia. MMR and MMRV vaccines available in Australia contain a Jeryl Lynn-derived strain of mumps, which is not associated with an increased risk of aseptic meningitis.

Persons with egg allergy can be safely given MMR or MMRV vaccine (refer to MMR and MMRV vaccines available in Australia contain a Jeryl Lynn-derived strain of mumps, which is not associated with an increased risk of aseptic meningitis. Persons with egg allergy can be safely given MMR or MMRV vaccine (refer to MMR and MMRV vaccines available in Australia contain a Jeryl Lynn-derived strain of mumps, which is not associated with an increased risk of aseptic meningitis.

For further information on the adverse events associated with MMR and MMRV vaccines, refer to 4.9 Measles (Handbook10-home~handbook10part4~handbook10-4-9) and 4.22 Varicella (Handbook10-home~handbook10part4~handbook10-4-22).

4.11.12 Public health management of mumps

Mumps is a notifiable disease in all states and territories in Australia.


4.12 Pertussis

4.12.1 Bacteriology

Pertussis (whooping cough) is caused by Bordetella pertussis, a fastidious, Gram-negative, pleomorphic bacillus. There are other organisms (such as Bordetella parapertussis, Mycoplasma pneumoniae and Chlamydia pneumoniae) that can cause a pertussis-like syndrome.1

4.12.2 Clinical features

Pertussis is a respiratory infection with an incubation period of 7 to 20 days. In unvaccinated persons, B. pertussis is highly infectious, spreading by aerosols to 90% of susceptible household contacts.2 Natural infection does not provide long-term protection and repeat infection can occur.2 The characteristic paroxysmal cough with inspiratory whoop seen in unvaccinated children is less common in individuals who have varying degrees of immunity acquired from vaccination or infection.3 It has been estimated that B. pertussis accounts for up to 7% of cough illnesses per year in adults and, each year, more than 25% of adults experience a coughing illness of at least 5 days duration.4 Even in adults, pertussis can be associated with significant morbidity, with cough persisting for up to 3 months, and other significant symptoms, such as sleep disturbance or, rarely, rib fracture.5 Identification of pertussis is limited by patient and physician awareness and, in some cases, the limited sensitivity of diagnostic tests; it is generally believed to be significantly under-diagnosed (refer to 4.12.11 Public health management of pertussis below).

Death due to pertussis is rare in people aged 10–70 years. However, the case-fatality rate in unvaccinated infants <6 months of age is estimated to be 0.8%.6,7 The most common cause of death in persons with pertussis infection is pertussis pneumonia, sometimes complicated by seizures and hypoxic encephalopathy.3

4.12.3 Epidemiology

Despite a long-standing immunisation program, pertussis remains highly prevalent in Australia and the least well controlled of all vaccine-preventable diseases. Epidemics occur every 3 to 4 years. In unvaccinated populations, these outbreaks can be very large. In vaccinated populations, outbreaks are smaller, with greatly reduced mortality and morbidity, and may continue to occur every 3 to 4 years or be more widely spaced.8 The maximal risk of infection and severe morbidity is before infants are old enough to have received at least 2 vaccine doses.9 In recent years, among highly immunised communities, many cases of pertussis have occurred in adults and adolescents due to waning immunity.9,10 These persons are a significant reservoir of infection. Evidence from studies of infant pertussis cases indicates that household contacts and carers are frequently the source of infection, with parents identified as the source for more than 50% of cases.11 However, Australian studies have shown that in settings where notification rates in children are high, siblings are a significant source of infant infections.12,13 There have also been case reports documenting nosocomial infection in young infants acquired from healthcare workers.14-17 Pertussis hospitalisation rates for persons aged ≥60 years are higher than for other adults.18 Between 1995 and 2012, multiple epidemics of pertussis occurred in Australia; however, the timing and frequency of these varied by geographical location. The highest annual incidence of notifications (173 cases per 100,000 population) was reported in 2011, with 38,732 notified cases.19 There have been a number of changes introduced to the NIP schedule over time in an attempt to improve control of pertussis. Introduction of a 5th dose of diphtheria, tetanus and whole-cell pertussis vaccine (DTPw) for 4–5-year-old children in August 1994 was followed by a decrease in notifications consistent with a vaccine effect; first among children aged 5 and 6 years, then by those in the 7–9 years age group.20 Subsequently, the average age of pertussis notifications continued to increase. By 2005, the proportion of notifications in adults >20 years of age had reached 83%,21 compared with 40% in the early 1990s.

Acellular pertussis vaccine (DTPa) replaced DTPw for booster doses in 1997, and for all doses from 1999. In 2003, the DTPa booster dose at 18 months of age was removed from the NIP, moving the 1st booster dose to 4 years of age. The removal of the 18-month booster dose from the schedule was based on evidence from an Italian longitudinal study of DTPa trial participants. The study found that a primary DTPa course at 2, 4 and 6 months of age provided 76 to 80% protection from prolonged cough disease and this was maintained until 8 years of age.22 In contrast to preceding epidemics, in the 2008–2011 epidemic period the highest notification rates in Australia were in children <15 years of age and the proportion of notifications in older adolescents and adults decreased. Notable increases in pertussis notifications occurred for children between 3 and 9 years of age.19 Although more accessible and sensitive diagnostic testing with polymerase chain reaction (PCR) contributed to the rise in notified cases,23-25 waning of DTPa vaccine-induced immunity has also been demonstrated to be a factor (refer to 4.12.4 Vaccines below).26-28 Although increased notification rates were observed in the most recent epidemic, hospitalisation and death rates from pertussis did not increase substantially.27 A high proportion of hospitalisations, and almost all deaths, attributed to pertussis occur in infants too young to have received more than 1 dose of pertussis-containing vaccine.18,19 The prevention of severe pertussis morbidity and deaths, particularly in infants <3 months of age, is a major goal in Australia and similar countries. Two vaccination strategies have been considered to achieve this – indirect protection from immunisation of household contacts and carers of newborn infants, known as the ‘cocoon’ strategy,29 and direct protection from immunisation of the mother during the last trimester of pregnancy30 (refer to 4.12.4 Vaccines and 4.12.7 Recommendations below).

4.12.4 Vaccines

Pertussis vaccine is only available in Australia in combination with diphtheria and tetanus, with or without other antigens such as inactivated poliomyelitis, hepatitis B and Haemophilus influenzae type b. The acronym DTPa, using capital letters, signifies child formulations of diphtheria, tetanus and acellular pertussis-containing vaccines. The acronym dTpa is used for formulations that contain substantially lesser amounts of diphtheria toxoid and pertussis antigens than child (DTPa-containing) formulations; dTpa vaccines are usually used in adolescents and adults.

Acellular pertussis-containing vaccines have been used for both primary and booster vaccination of children in Australia since 1999. Whole-cell pertussis-containing vaccines were used exclusively before 1997. Between 1997 and 1999 acellular vaccines were used for booster doses. There are a number of acellular pertussis-containing vaccines that contain two or more purified components of B. pertussis. In the 2-component vaccine these are pertussis toxin (PT) and filamentous haemagglutinin (FHA); in the 3-component vaccines, pertactin (PRN) is also included; and in the 5-component vaccines, two fimbrial (FIM) antigens are also included. In the last decade, 3-component vaccines have been predominantly used in the childhood immunisation schedule in Australia.

Pertussis vaccines provide good protection against severe and typical pertussis, but substantially less against milder coughing illness.31,32 Vaccine efficacy of DTPa vaccines with three or more antigens has been reported as 71 to 78% for preventing mild symptoms of pertussis and 84% for preventing typical disease.32 Epidemiological data suggest that receipt of the 1st dose of the primary DTPa course significantly reduces the incidence of severe pertussis disease in young infants, as measured by hospitalisation rates.33-35 However, there is a growing body of evidence from both observational and experimental studies that vaccination of household contacts and carers of newborn infants (the ‘cocoon’ strategy) improves the control of pertussis in the community.36-38 Pertussis vaccines are recommended for all infants aged 2 months or older, in the following schedule:

- 2 months
- 3 months
- 4 months
- 5 months
- 6 months

- 11–12 months
- 15–16 months

These persons are a significant reservoir of infection, and direct protection from immunisation of household contacts and carers of newborn infants, known as the ‘cocoon’ strategy, is considered to achieve this – indirect protection from immunisation of household contacts and carers of newborn infants, known as the ‘cocoon’ strategy,39 and direct protection from immunisation of the mother during the last trimester of pregnancy40 (refer to 4.12.4 Vaccines and 4.12.7 Recommendations below).
Antigen content formulation, dTpa vaccines are immunogenic. A randomised trial in adults reported a point estimate of 92% efficacy against culture/nucleic acid test-positive disease within 2.5 years of vaccination with a 3-component monovalent pertussis vaccine. Data on the duration of immunity to pertussis following a single booster dose of dTpa are limited. Long-term follow-up of adults vaccinated with dTpa has shown a rapid decline in levels of pertussis antibodies within the first 2 years after vaccination, with a continued steady decline out to 10 years after vaccination, although antibody levels remained above baseline. A similar long-term follow-up of adolescents demonstrated a more rapid decline, with pertussis antibody levels decreasing to or approaching pre-vaccination levels after 10 years. The rate of decline in clinical protection is unknown, but some protection against clinical disease may persist for up to 10 years. Recent studies have indicated that dTpa vaccine is immunogenic in the elderly.

Vaccination of pregnant women with dTpa has been shown to be effective in preventing pertussis disease in newborn infants via the transfer of maternal antibodies in utero. Vaccination of mothers at least 7 days before delivery reduced pertussis disease by 91% in infants <3 months of age. However, the level of pertussis antibody required in the pregnant woman to achieve this level of protection and the impact of waning pertussis immunity in the mother are not known. On the one hand, pertussis-specific IgG levels in maternal and umbilical cord serum of mother-and-newborn pairs show significant antibody decay over a 2-year interval between pregnancies. On the other hand, pertussis antibody levels in the cord blood of infants whose mothers were vaccinated approximately 13 months previously (following birth of an older sibling) were significantly higher than those in cord blood of the older sibling prior to maternal vaccination.

Studies have shown lower levels of anti-pertussis antibodies at 7 months of age in children born to women vaccinated with dTpa during pregnancy, compared to children of mothers who were not vaccinated. However, when children were given a booster dose of DTpa-containing vaccine at 12–18 months of age, levels of anti-pertussis antibodies 1 month later were similar irrespective of whether the child’s mother was vaccinated during pregnancy or not. Vaccination of pregnant women with dTpa has been shown to be effective in preventing pertussis disease in newborn infants via the transfer of maternal antibodies in utero. Vaccination of mother-and-newborn pairs show significant antibody decay over a 2-year interval between pregnancies. On the other hand, pertussis antibody levels in the cord blood of infants whose mothers were vaccinated approximately 13 months previously (following birth of an older sibling) were significantly higher than those in cord blood of the older sibling prior to maternal vaccination.

Cocoon vaccination is an alternative vaccination strategy expected to reduce infection risk to infants, especially the youngest of infants, through the vaccination of household contacts and carers who are known to be an important source of pertussis infection (refer to Cocoon vaccination is an alternative vaccination strategy expected to reduce infection risk to infants, especially the youngest of infants, through the vaccination of household contacts and carers who are known to be an important source of pertussis infection (refer to Cocoon vaccination is an alternative vaccination strategy expected to reduce infection risk to infants, especially the youngest of infants, through the vaccination of household contacts and carers who are known to be an important source of pertussis infection (refer to Cocoon vaccination is an alternative vaccination strategy expected to reduce infection risk to infants, especially the youngest of infants, through the vaccination of household contacts and carers who are known to be an important source of pertussis infection (refer to 4.12.3 Epidemiology above). However, the emerging data on the effectiveness of indirect protection to infants from the cocoon approach suggest only a modest benefit.

Formulations for children aged <10 years

- **Hemaxim** – Sanofi-Aventis Australia Pty Ltd (DTpa-hepB-IPV/Hib; diphtheria-tetanus-acellular pertussis-hepatitis B-inactivated poliovirus-Haemophilus influenzae type b). Each 0.5 mL pre-filled syringe contains ≥20 IU diphtheria toxoid, ≥40 IU tetanus toxoid, 25 µg pertussis toxoid (PT), 25 µg filamentous haemagglutinin (FHA), 10 µg recombinant HBSAg, 40 D-antigen units inactivated poliovirus type 1 (Mahoney), 8 D-antigen units type 2 (MEF-1), 32 D-antigen units type 3 (Saukett) and 12 µg purified Hib capsular polysaccharide (PRP) conjugated to 22–36 µg tetanus toxoid, adsorbed onto 0.6 mg aluminium as aluminium hydroxide. May contain traces of glatirameracetate, formaldehyde, neomycin, streptomycin and polymyxin B.

- **Infanrix** – GlaxoSmithKline Australia Pty Ltd (DTPa-hepB-HB/HB). Each 0.5 mL pre-filled syringe contains ≥30 IU diphtheria toxoid, ≥40 IU tetanus toxoid, 25 µg PT, 25 µg FHA, µg pertactin (PRN), adsorbed onto 0.5 mg aluminium as aluminium hydroxide.

- **Infanrix** – GlaxoSmithKline Australia Pty Ltd (DTPa-hepB-IPV/Hib; diphtheria-tetanus-acellular pertussis-hepatitis B-inactivated poliovirus-Haemophilus influenzae type b). Each 0.5 mL pre-filled syringe contains ≥30 IU diphtheria toxoid, ≥40 IU tetanus toxoid, 25 µg PT, 25 µg FHA, µg pertactin (PRN), adsorbed onto 0.5 mg aluminium as aluminium hydroxide.

- **Infanrix hexa** – GlaxoSmithKline Australia Pty Ltd (DTPa-hepB-IPV/Hib; diphtheria-tetanus-acellular pertussis-hepatitis B-inactivated poliovirus-Haemophilus influenzae type b). The vaccine consists of both a 0.5 mL pre-filled syringe containing ≥30 IU diphtheria toxoid, ≥40 IU tetanus toxoid, 25 µg PT, 25 µg FHA, 8 µg PRN, 10 µg recombinant HBSAg, 40 D-antigen units inactivated poliovirus type 1 (Mahoney), 8 D-antigen units type 2 (MEF-1) and 32 D-antigen units type 3 (Saukett), adsorbed onto aluminium hydroxide phosphate; traces of formaldehyde, polysorbate 80, poloxamers 20, poloxamers and neomycin; and a vial containing a lyophilised pellet of 10 µg purified Hib capsular polysaccharide (PRP) conjugated to 20–40 µg tetanus toxoid. May contain yeast proteins.

- **Quadrotal** – Sanofi-Aventis Australia Pty Ltd (DTPa-hepB-IPV; diphtheria-tetanus-acellular pertussis-hepatitis B-inactivated poliovirus-Haemophilus influenzae type b). Each 0.5 mL pre-filled syringe contains ≥30 IU diphtheria toxoid, ≥40 IU tetanus toxoid, 20 µg PT, 20 µg FHA, 3 µg PRN, 5 µg FIM 2+3, 40 D-antigen units inactivated poliovirus type 1 (Mahoney), 8 D-antigen units type 2 (MEF-1) and 32 D-antigen units type 3 (Saukett), adsorbed onto aluminium hydroxide phosphate; traces of formaldehyde, polysorbate 80, polyvinyl and neomycin.

- **Tridecal** – Sanofi-Aventis Australia Pty Ltd (DTPa-hepB-IPV/Hib; diphtheria-tetanus-acellular pertussis-hepatitis B-inactivated poliovirus-Haemophilus influenzae type b). Each 0.5 mL pre-filled syringe contains ≥30 IU diphtheria toxoid, ≥40 IU tetanus toxoid, 10 µg PT, 5 µg FHA, 3 µg PRN, 5 µg FIM 2+3, 1.5 mg aluminium phosphate; 3.4 mg phenoxethanol.

Reduced antigen formulations for adults, adolescents and children aged ≥10 years

- **Adacel** – Sanofi-Aventis Australia Pty Ltd (dTpa; diphtheria-tetanus-acellular pertussis). Each 0.5 mL monodose vial contains ≥2 IU diphtheria toxoid, ≥20 IU tetanus toxoid, 2.5 µg PT, 5 µg FHA, 3 µg PRN, 5 µg FIM 2+3, 0.33 mg aluminium as aluminium phosphate; phenoxethanol; traces of formaldehyde and glutaraldehyde.

- **Adacel Polio** – Sanofi Pasteur Pty Ltd (DTPa-IPV; diphtheria-tetanus-acellular pertussis-inactivated poliovirus). Each 0.5 mL monodose vial or pre-filled syringe contains ≥2 IU diphtheria toxoid, ≥20 IU tetanus toxoid, 2.5 µg PT, 5 µg FHA, 3 µg PRN, 5 µg FIM 2+3, 40 D-antigen units inactivated poliovirus type 1 (Mahoney), 8 D-antigen units type 2 (MEF-1) and 32 D-antigen units type 3 (Saukett); 0.33 mg aluminium as aluminium phosphate; phenoxethanol; traces of formaldehyde, glutaraldehyde, polysorbate 80, polyvinyl and neomycin and streptomycin.

- **Boostrix** – GlaxoSmithKline Australia Pty Ltd (dTpa; diphtheria-tetanus-acellular pertussis). Each 0.5 mL monodose vial or pre-filled syringe contains ≥2 IU diphtheria toxoid, ≥20 IU tetanus toxoid, 8 µg PT, 8 µg FHA, 2.5 µg PRN, adsorbed onto 0.5 mg aluminium as aluminium hydroxide phosphate; traces of formaldehyde, polysorbate 80 and glycine.

- **Boostrix-IPV** – GlaxoSmithKline Australia Pty Ltd (dTpa; diphtheria-tetanus-acellular pertussis-inactivated poliovirus). Each 0.5 mL pre-filled syringe contains ≥2 IU diphtheria toxoid, ≥20 IU tetanus toxoid, 8 µg PT, 8 µg FHA, 2.5 µg PRN, 40 D-antigen units inactivated poliovirus type 1 (Mahoney), 8 D-antigen units type 2 (MEF-1) and 32 D-antigen units type 3 (Saukett), adsorbed onto 0.5 mg aluminium as aluminium hydroxide phosphate; traces of formaldehyde, polysorbate 80, polyvinyl and neomycin.
Booster doses

Two booster doses of pertussis-containing vaccine are recommended during childhood to provide ongoing protection against pertussis throughout early adolescence (refer to ‘Older children and adolescents’ below).

The first booster dose of pertussis-containing vaccine (dose 4 in the childhood series), usually provided as DTPa, is recommended at 18 months of age. This booster dose is required due to waning of pertussis immunity following receipt of the primary schedule (refer to 4.12.4 Vaccines above).26

The second booster dose of pertussis-containing vaccine (dose 5 in the childhood series), usually provided as DTPa-IPV, is recommended at 4 years of age. This second booster dose is essential to maximise pertussis immunity during childhood as waning occurs progressively with age.21,24

For details on the management of children who require catch-up vaccination for pertussis, including minimum acceptable intervals between vaccine doses, refer to 2.1.5 (Handbook10-home-handbook10part2-handbook10-2-1#table-2-1-5) Catch-up.

In addition, household contacts and carers of infants should be age-appropriately immunised to minimise the risk of severe disease occurring in young infants prior to completion of the primary course (refer to ‘Older children and adolescents’ and ‘Adults’ below).

Older children and adolescents

An additional booster dose of pertussis-containing vaccine (i.e. in addition to those recommended for young children, refer above) is recommended for adolescents between 10 and 17 years of age, using the reduced antigen content dTpa. The optimal age for administering this dose is 11–13 years, due to waning of the antibody response following the booster dose recommended at 4 years of age.23,26 This adolescent booster dose of pertussis-containing vaccine is essential for maintaining immunity to pertussis (and diphtheria and tetanus) into adulthood.50

For details on the management of children and adolescents who require catch-up vaccination for pertussis, refer to 2.1.5 (Handbook10-home-handbook10part2-handbook10-2-1#table-2-1-5) Catch-up.

Adults

Vaccination with dTpa is recommended for any adult who wishes to reduce their likelihood of becoming ill with pertussis. Vaccination is particularly important if the adult meets the criteria of a special risk group (refer to ‘Persons in contact with infants and others at increased risk from pertussis’ below).

dTpa vaccine should be used in place of dT at the age routinely recommended for a tetanus and diphtheria booster (50 years). There is currently insufficient evidence to recommend routine 10-yearly booster doses of dTpa vaccine for all adults (who do not meet the criteria of a special risk group below). However, due to the increased morbidity associated with pertussis in the elderly,18 adults aged ≥65 years should be offered a single dTpa booster if they have not received one in the previous 10 years.18,51 Adults of all ages who require a booster dose of dT vaccine should be encouraged to do so with dTpa vaccine, particularly if they have not received a dTpa dose previously (refer to 4.19 (Handbook10-home-handbook10part4-handbook10-4-19) Tetanus and 4.2 (Handbook10-home-handbook10part4-handbook10-4-2) Diphtheria).52

Travellers should receive a booster dose of dT (or dTpa if not given previously) if more than 10 years have elapsed since the last dose of dT-containing vaccine. For persons undertaking high-risk travel, consider giving a booster dose of either dTpa or dT (as appropriate) if more than 5 years have elapsed since the last dose of a dT-containing vaccine (refer to 4.19 (Handbook10-home-handbook10part4-handbook10-4-19) Tetanus and 4.2 (Handbook10-home-handbook10part4-handbook10-4-2) Diphtheria).52

For those adults requiring additional protection from polio (refer to 4.14 Poliomyelitis), dTpa-IPV can be used.

For additional information on adults with no history of a primary course of dT or pertussis-containing vaccine requiring catch-up, refer to 4.19 (Handbook10-home-handbook10part4-handbook10-4-19) Tetanus and 2.1.5 (Handbook10-home-handbook10part2-handbook10-2-1) Catch-up.

Persons in contact with infants and others at increased risk from pertussis

There is significant morbidity associated with pertussis infection in infants <6 months of age, particularly those <3 months of age who are not yet old enough to be immunised or have received only their 1st vaccine dose.18 The source of infection in infants is often a household contact, most frequently the infant’s mother.11 (Also refer to 4.12.3 Epidemiology above.) To reduce the risk of pertussis occurring in infants, pertussis vaccination is recommended for their close contacts as outlined below. Pertussis vaccination is also recommended for healthcare workers to reduce the risk of pertussis being transmitted to vulnerable patients.

Women who are pregnant or post-partum

dTpa vaccine is recommended as a single dose during the third trimester of each pregnancy (refer to 3.3 (Handbook10-home-handbook10part3-handbook10-3-3) Groups with special vaccination requirements). Vaccination during pregnancy has been shown to be more effective in reducing the risk of pertussis in young infants than vaccination of the mother post partum.42

This added benefit is due to direct passive protection of the newborn by transplacental transfer of high levels of pertussis antibodies from the vaccinated woman to the fetus. As pertussis antibody levels do not peak until approximately 2 weeks after vaccination53 and active transport of maternal antibody to the fetus occurs predominantly from 30 weeks gestation onwards,94 the optimal time for vaccination is early in the third trimester (between 28 and 32 weeks). However, if the vaccine is not given during this period it should still be given at any time during the third trimester up to delivery, noting greatest levels of infant pertussis antibodies have been observed in the infant when the interval between maternal vaccination and delivery is at least 4 weeks.95 If the dose of dTpa vaccine is given earlier than the third trimester, a repeat dose during that same pregnancy is not required. Early evidence has demonstrated transfer of pertussis antibodies to the infant in women who received dTpa vaccine as early as 13 weeks gestation.96

Vaccination is recommended with each pregnancy to provide maximal protection to every infant; this includes pregnancies which are closely spaced (e.g. <2 years) (refer to ‘Interval between dTpa and other tetanus/diphtheria-containing vaccines’ below). Vaccine-induced pertussis antibodies wane over time and the protective antibody level required in mothers to pass on immunity to pertussis (and diphtheria and tetanus) into adulthood.

If the dose of dTpa vaccine is given earlier than the third trimester, a repeat dose during that same pregnancy is not required. Early evidence has demonstrated transfer of pertussis antibodies to the infant in women who received dTpa vaccine as early as 13 weeks gestation.96

Vaccination is recommended with each pregnancy to provide maximal protection to every infant; this includes pregnancies which are closely spaced (e.g. <2 years) (refer to ‘Interval between dTpa and other tetanus/diphtheria-containing vaccines’ below). Vaccine-induced pertussis antibodies wane over time and the protective antibody level required in mothers to pass on immunity to newborn infants is unknown (refer to 4.12.4 Vaccines above). It is therefore possible that if a mother is not revaccinated during a subsequent pregnancy (even if closely spaced), her newborn will not be adequately protected against severe pertussis illness.

For any pregnancy where antenatal vaccination does not occur, maternal vaccination during the post-partum period will reduce the likelihood of pertussis occurring in the mother and thus provide some indirect protection to the infant. However, infant protection will be substantially less than that achieved from a dose administered to the mother in the third trimester of pregnancy. (Refer to 4.12.4 below). If a mother requires a post-partum dose of dTpa vaccine, it should be administered as soon as possible after delivery of the infant (preferably before hospital discharge). This timing is optimal as the risk of severe pertussis disease in the infant is greatest in the first weeks and months of life, and vaccine protection in the mother takes approximately 2 weeks to fully establish. There may still be some benefit from receipt of a post-partum dose until the infant has completed their primary vaccination course at 6 months of age. For any future pregnancies, the woman should receive the recommended dose of dTpa vaccine in the third trimester of the pregnancy, even if pregnancies are closely spaced (e.g. <2 years) (refer to ‘Interval between dTpa and other tetanus/diphtheria-containing vaccines’ below).

Other adult household contacts and carers of infants <6 months of age

Adult household contacts and carers (e.g. fathers, grandparents) of infants <6 months of age should ideally receive a dTpa vaccine at least 2 weeks before beginning close contact with the infant. A booster dose of dTpa is recommended if 10 years have elapsed since a previous dose.40,41

Healthcare workers

All healthcare workers should receive dTpa vaccine because of the significant risk of nosocomial transmission of pertussis to vulnerable patients.14-17 (Refer also to 3.3 (Handbook10-home-handbook10part3-handbook10-3-3) Groups with special vaccination requirements, Table 3.3.7 (Handbook10-home-handbook10part1-handbook10-3-3#table-3-3-7) Recommended vaccinations for persons at increased risk of certain occupationally acquired vaccine-preventable diseases.) A booster dose of dTpa is recommended if 10 years have elapsed since the previous dose.40,41

Interval between dTpa and other tetanus/diphtheria-containing vaccines

In circumstances where protection against pertussis is required as soon as possible, a single dose of dTpa vaccine can be administered at any time after a dose of tetanus- and diphtheria-containing vaccine. If providing dTpa vaccine as part of a dT catch-up schedule in adults or children aged ≥10 years, the recommended minimum intervals between doses should be met (refer to 2.2 Administration of vaccines). Studies indicate that the adverse reactions to a single dose of DTPa are similar whether administered shortly after (18 months), or at a longer interval after, a previous dose of a vaccine containing tetanus/diphtheria toxoids. Where a tetanus- and diphtheria-containing vaccine has been given less than 18 months previously, the benefits of protection against pertussis gained from using dTpa vaccine, where recommended (e.g. in the third trimester of pregnancy), are likely to outweigh the risk of an adverse event (refer to 'dTpa vaccines in pregnant women' in 4.12.10 Adverse events below).

Persons with a history of pertussis infection

Administration of pertussis vaccine in children, adolescents or adults who have had laboratory-confirmed pertussis infection is safe and is necessary, as natural immunity does not confer lifelong protection. In particular, incompletely vaccinated infants <6 months of age who develop pertussis may not mount an adequate immune response following infection and should receive all routinely scheduled pertussis-containing vaccines.

4.12.8 Pregnancy and breastfeeding

dTpa vaccine is recommended for pregnant women (in the third trimester of each pregnancy) (refer to ‘Women who are pregnant or post-partum’ in 4.12.7 Recommendations above).

dTpa vaccine can be given to breastfeeding women.

Refer to 3.3 (Handbook10-home-handbook10part3-handbook10-3-3) Groups with special vaccination requirements, Table 3.3.1 (Handbook10-home-handbook10part3-handbook10-3-3#Table) Recommendations for vaccination in pregnancy for more information.

4.12.9 Contraindications

The only absolute contraindications to acellular pertussis-containing vaccines are:

- anaphylaxis following a previous dose of any acellular pertussis-containing vaccine
- anaphylaxis following any vaccine component.

4.12.10 Adverse events

DTPa-containing vaccines in children

Acellular pertussis vaccines are associated with a much lower incidence of fever (approximately 20%) and local adverse events (approximately 10%) than whole-cell pertussis vaccines (approximately 45% and 40%, respectively), which are no longer used in Australia.61.62

Extensive limb swelling, defined as swelling and/or redness involving at least half the circumference of the limb and the joints both above and below the injection site, is a recognised adverse event that occurs rarely following booster doses of DTPa. Such reactions commence within 48 hours of vaccination, last for 1 to 7 days and resolve completely without sequelae.63 The pathogenesis of extensive limb swelling is poorly understood. In an analysis of 4th and 5th dose follow-up studies that examined 12 different DTPa vaccines, entire thigh swelling was reported in 2% of 1015 children who received consecutive doses of the same DTPa vaccine reported. All of these episodes resolved completely without intervention.61 A history of extensive limb swelling after a booster dose of DTPa vaccine is not a contraindication to further DTPa doses recommended during childhood or the reduced antigen formulations of dTpa vaccine at 11–13 years of age (or older) (refer to 4.12.7 Recommendations above).63 Parents of children about to receive a booster dose of a DTPa-containing vaccine should be informed of the small but well-defined risk of this adverse event which, even when extensive, is usually not associated with significant pain or limitation of movement and requires no specific treatment.

Febrile convulsions are very infrequently reported following DTPa-containing vaccines, within 48 hours of vaccination. The risk is even lower in infants who complete their primary course at 6 months of age, as febrile convulsions are uncommon in children <6 months of age. Children who experience a febrile convulsion after a dose of DTPa-containing vaccine have a slightly greater risk of a further febrile convulsion following a subsequent dose of a DTPa-containing vaccine. This risk can be minimised by appropriate measures to prevent fever, so vaccination is still recommended.

Hypotonic-hyporesponsive episodes (HHE), defined as an episode of pallor, limpness and unresponsiveness, occur rarely following DTPa vaccine. 1 to 48 hours after vaccination. Shallow respiration and cyanosis may also occur in an HHE. An HHE may last from a few minutes to 36 hours. In Australia during 2009, 3.2 cases of HHE were reported per 100 000 doses of DTPa-containing vaccine given to children <1 year of age.64 Follow-up of children with HHE shows no long-term neurological or other sequelae and they can receive further doses of DTPa-containing vaccines.65 Children who have an HHE following DTPa-containing vaccines should receive further doses as recommended. Supervision may be required under some circumstances; advice can be obtained from clinicians specialising in the management of adverse events following immunisation (refer to Appendix 1 (Handbook10-home-handbook10-tools-handbook10-appendices-handbook10-appendix1) Contact details for Australian, state and territory government health authorities and communicable disease control).

Pertussis-containing vaccines do not cause infantile spasms or epilepsy. Infants and children known to have active or progressive neurological disease can be safely vaccinated with DTPa-containing vaccines. A large Canadian study found no evidence of encephalopathy following acellular pertussis vaccines.66 Pertussis-containing vaccines have a slight risk of causing infantile spasms or epilepsy in certain circumstances. A history of infantile spasms or epilepsy in a family increases the risk of encephalopathy following vaccination with pertussis-containing vaccines.67 For infants and children with stable neurological disease (including cerebral palsy), or a family history of idiopathic epilepsy or other familial neurological disorder, the risk of adverse events following DTPa-containing vaccines is the same as for other infants of the same age.

Sudden infant death syndrome (SIDS) is not associated with either DTPa or any pertussis-containing vaccine.68 Some studies suggest a decreased risk of SIDS in children who have been vaccinated.69-70

dTpa-containing vaccines in adolescents and adults

Reduced antigen content dTpa vaccines are safe and well-tolerated in adults when given as a 3-dose primary series or as a booster dose.71-73 The incidence of fever is low, and comparable in vaccine and placebo recipients in clinical trials.73,74 Studies investigating revaccination within 10 years (and some within 2 years) after a tetanus toxoid-, dT- or dTpa-containing vaccine in non-pregnant adolescents and adults have found no increase in moderate or severe adverse events or subjective fever. However, an increase in mild transient injection site pain is often reported following dTpa-containing booster doses.40,58,75,76 Limb swelling reactions after dTpa-containing booster doses are rare.40,41,74 In adults who report a history of adverse event(s) following whole-cell pertussis-containing vaccine given in childhood, dTpa can almost always be given (refer to 3.3.1 (Handbook10-home-handbook10part3-handbook10-3-1) Vaccination of persons who have had an adverse event following immunisation).

Brachial neuritis (inflammation of a nerve in the arm, causing weakness or numbness) has been described following the administration of tetanus toxoid-containing vaccines, with an estimated excess risk of approximately 0.5-1 in 100 000 doses in adults.75,76
Although dTpa vaccine is generally safe and well-tolerated in adults, there is a small risk that significant injection site reactions following subsequent doses might occur in some women who receive dTpa vaccines during successive closely spaced pregnancies (refer to ‘dTpa-containing vaccines in adolescents and adults’ above). However, a retrospective study of more than 29,000 women who received dTpa vaccine during pregnancy reported no increased risk of acute adverse events (fever, allergy or local reactions) among women who had received a tetanus-containing vaccine less than 2 years or 2 to 5 years previously, compared with women who had received a dose more than 5 years previously.42

4.12.11 Public health management of pertussis

Pertussis (both suspected and confirmed) is a notifiable disease in all states and territories in Australia. Detailed information regarding case definitions and the management of pertussis cases and contacts can be found in the national guidelines for control of pertussis(http://www.health.gov.au/internet/nucleus.nsf/Content/PHN-Infant-health-handbook10#immunise).

Further instructions about the public health management of pertussis can also be obtained from state/territory public health authorities (refer to Appendix 1 (Handbook10-home-handbook10-tools-handbook10-appendices-handbook10-appendix1) Contact details for Australian, state and territory government health authorities and communicable disease control).

Suspected cases of pertussis should be investigated, regardless of vaccination status, as immunisation is not 100% effective and immunity wanes over time. The diagnosis of pertussis can be confirmed by either culture or nucleic acid testing of a per-nasal swab or nasopharyngeal aspirate specimen, or by serology. The appropriate diagnostic test depends on the age, vaccination history and duration of symptoms. PCR is usually the diagnostic method of choice, particularly if pertussis is suspected in someone who has received a pertussis-containing vaccine within the previous 5 years.84

To reduce the risk of transmission of B. pertussis, persons with pertussis infection should commence appropriate antibiotic therapy on clinical suspicion, if within 21 days of the onset of coryza. Antibiotic treatment does not shorten the course of the illness, but reduces infectivity if provided early in the illness. Detailed information regarding appropriate macrolide antibiotics and dosing can be found in the national guidelines for control of pertussis.83,85

Management of contacts of cases

Vaccination

Since a primary vaccination course requires three or more injections to protect against pertussis, infant vaccination cannot be effectively used to protect unimmunised infants. Vaccination has not been shown to have a role in controlling outbreaks at any age, even in closed settings. However, unvaccinated or partially vaccinated contacts, up to their 10th birthday, should be offered DTPa-containing vaccines, and older contacts should be offered dTpa (refer to 2.1.5(Handbook10-home-handbook10part2-handbook10-2-1) Catch-up).

Passive immunisation with normal human immunoglobulin is not effective in the prevention of pertussis.

Chemoprophylaxis

The benefit of chemoprophylaxis in preventing the secondary transmission of pertussis is limited due to multiple factors, including delayed clinical presentation, delayed diagnosis and imperfect compliance.86 The use of chemoprophylaxis for prevention of secondary cases should be limited to high-risk close contacts of cases. Further recommendations regarding chemoprophylaxis of close contacts can be found in the national guidelines for control of pertussis.83

4.12.12 Variations from product information

The product information for Infantrix states that this vaccine is indicated for primary immunisation of infants from the age of 2 months to 12 months and as a booster dose for children from 15 months to 6 years of age who have previously been vaccinated against diphtheria, tetanus and pertussis. The ATAGI recommends that this vaccine may also be used for catch-up of the primary schedule or as a booster in children <10 years of age. The ATAGI also recommends that the primary schedule may be commenced at 6 weeks of age, if required.

The product information for Infantrix hexa states that this vaccine is indicated for primary immunisation of infants from the age of 6 weeks and as a booster dose for children 18 months of age if boosting is required for all antigens. The ATAGI recommends that this vaccine may also be used for catch-up of the primary schedule or as a booster in children <10 years of age.

The product information for Infantrix IPV states that this vaccine is indicated for use in a 3-dose primary schedule for immunisation of infants from the age of 6 weeks and as a single booster dose for children ≥6 years of age who have previously been vaccinated against diphtheria, tetanus, pertussis and poliomyelitis. In addition, the ATAGI recommends that this product may also be used for catch-up of the primary schedule or as a booster in children <10 years of age.

The product information for Quadracel states that this vaccine is indicated for use in a 3-dose primary schedule from the age of 2 months to 12 months and may also be used as a booster dose for children from 15 months to 6 years of age who have previously been vaccinated against diphtheria, tetanus, pertussis and poliomyelitis. The ATAGI recommends that, when appropriate, this product may also be used for either catch-up of the primary schedule or as a booster dose in children aged <10 years. The ATAGI also recommends that the primary schedule may be commenced at 6 weeks of age, if required.

The product information for Tripacel states that this vaccine is indicated for use in a 3-dose primary schedule from the age of 2 months to 12 months and may also be used as a booster dose for children from 15 months to 6 years of age who have previously been vaccinated against diphtheria, tetanus and pertussis. The ATAGI recommends that, when appropriate, this product may also be used for either catch-up of the primary schedule or as a booster dose in children aged <10 years. The ATAGI also recommends that the primary schedule may be commenced at 6 weeks of age, if required.

The product information for Adacel and Boostrix (reduced antigen content dTpa) states that these vaccines are indicated for booster doses only. The ATAGI recommends instead that, when a 3-dose primary course of diphtheria/tetanus toxoids is given to an adolescent/adult, dTpa should replace the 1st dose of dT, with 2 subsequent doses of dT. If dT is not available, dTpa can be used for all 3 primary doses.

The product information for Adacel states that vaccination in pregnancy is not recommended unless there is a definite risk of acquiring pertussis. The product information for Boostrix states that the vaccine should be used during pregnancy only when clearly needed, and the possible advantages outweigh the possible risks for the fetus. The ATAGI recommends that pregnant women receive a dose with every pregnancy.

The product information for Adacel and Boostrix state that there is no recommendation regarding the timing and frequency of booster doses against pertussis in adults. However, the ATAGI recommends that pregnant women receive a booster dose with every pregnancy and that other adults in contact with infants and/or at increased risk from pertussis can receive a booster dose every 10 years.

The product information for Boostrix, Boostrix-IPV and Adacel states that dTpa-containing vaccine should not be given within 5 years of a tetanus toxoid-containing vaccine. The product information for Adacel Polio states that dTpa-containing vaccine should not be given within 3 years of a tetanus toxoid-containing vaccine. The ATAGI recommends instead that, if protection against pertussis is required, dTpa-containing vaccines can be administered at any time following receipt of a dT-containing vaccine.

The product information for Adacel, Adacel Polio, Boostrix, Boostrix-IPV, Infantrix, Infantrix hexa, Infantrix IPV, Quadracel and Tripacel states that these vaccines are contraindicated in children with encephalopathy of unknown aetiolog or with neurologic complications occurring within 7 days following a vaccine dose. The ATAGI recommends instead that the only contraindication is a history of anaphylaxis to a previous dose or to any of the vaccine components.

References


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Booy R, Van Der Meeren O, Ng SP, et al. A decennial booster dose of reduced antigen content diphtheria, tetanus, acellular pertussis vaccine (Boostrix™) is immunogenic and well tolerated in adults. Vaccine 2010;28:45-50.


Healy CM, Rench MA, Baker CJ. Importance of timing of maternal combined tetanus, diphtheria, and acellular pertussis (Tdap) immunization and protection of young infants. Clinical Infectious Diseases 2013;56:53-49.


In Australia, vaccination with 7-valent pneumococcal conjugate vaccine (7vPCV) was first included in (46%) and not included in (57%) 23vPPV.

In non-Indigenous adults, the prevalence of risk factors among those with IPD was 29% lower in 2006–2007 than in 2002–2004. This was mostly due to a 53% decrease in the incidence of serotypes included in 7vPCV, despite increases in IPD caused by serotypes also a marked reduction in pneumonia hospitalisations, presumed to be attributable to 7vPCV vaccination, in children <2 and 2–4 years of age (of 38% and 28%, respectively).

In Indigenous adults, there is a high prevalence of risk factors in IPD cases of all ages.


4.13.11 Adverse events

Household crowding, exposure to cigarette smoke, childcare attendance, excessive alcohol consumption and certain non-immunocompromising chronic medical conditions are also associated with greater risk and/or severity of IPD.1,2,10,11 Indigenous populations in developed countries, including Aboriginal and Torres Strait Islander people in Australia, have a disproportionately high burden of IPD.1,12,13

4.13.12 Clinical features

Person-to-person transmission of S. pneumoniae occurs via contact with respiratory droplets of colonised persons. Almost all pneumococcal disease probably begins with the establishment of nasopharyngeal colonisation. From the nasopharynx, pneumococci may spread locally into adjacent sites to cause sinusitis, otitis media or pneumonia. Pneumococci may enter the bloodstream, and also localise in the meninges, causing meningitis, or at other sites including bones, joints and soft tissues.1,3,4 For disease surveillance purposes, detection of S. pneumoniae in a normally sterile site, such as blood, cerebrospinal fluid or pleural fluid, by culture or nucleic acid testing, is classified as IPD. The major clinical categories of IPD are meningitis, bacteraemic pneumonia, and bacteraemia without focus. In adults, pneumonia with bacteraemia is the most common manifestation of IPD. Although more difficult to measure for non-bacteraemic cases, it is estimated that pneumococci account for over one-third of all community-acquired pneumonia and up to half of hospitalised pneumonia in adults.2,4 In children, the most common manifestation is bacteraemia without focus, accounting for approximately 70% of IPD, followed by pneumonia with bacteraemia. Meningitis, although least common, is the most severe category of IPD and has an estimated case-fatality rate of about 30%.1,2 Acute otitis media (AOM) is the most common non-invasive manifestation of pneumococcal disease in children. S. pneumoniae is detected in 28 to 55% of middle ear aspirates from children with AOM.2,3,9

Immunocompromised persons who are unable to mount an adequate immune response to pneumococcal capsular antigens, including those with asplenia, have the highest risk of IPD.1,2,4 Household crowding, exposure to cigarette smoke, childcare attendance, excessive alcohol consumption and certain non-immunocompromising chronic medical conditions are also associated with greater risk and/or severity of IPD.1,2,10,11 Indigenous populations in developed countries, including Aboriginal and Torres Strait Islander people in Australia, have a disproportionately high burden of IPD.1,12,13

The highest incidence of IPD is seen at the extremes of age, in young children and the elderly.5,6 In Australia, vaccination with 7-valent pneumococcal conjugate vaccine (7vPCV) was first funded under the NIP from mid-2001, to 5 years of age for Indigenous children living in Central Australia and children with specified predisposing medical conditions, and to 2 years of age for non-Indigenous children living in Central Australia and Indigenous children in the rest of the country. One dose of the 23-valent pneumococcal polysaccharide vaccine (23vPPV) at 18–24 months of age, as a booster following a primary 7vPCV schedule, was also funded for Indigenous children with predisposing medical conditions living in jurisdictions with the highest incidence of IPD (the Northern Territory, Queensland, South Australia and Western Australia). From January 2005, NIP-funded 7vPCV was extended to all infants nationally, together with catch-up vaccination for all children aged <2 years. High vaccination uptake of over 90% has been maintained since the inception of universal infant pneumococcal vaccination.

The introduction of 7vPCV led to a dramatic reduction in the overall incidence of IPD in Australia, which was greatest in the primary target group of children <2 years of age and for IPD caused by the seven vaccine serotypes. Among non-Indigenous children <2 years of age, the overall notification rate of IPD declined by 75%, from 78 per 100 000 in the pre-vaccination period (2002–2004) to 19.5 per 100 000 in the post-vaccination period (2007); IPD due to 7vPCV serotypes decreased by 97%, from 60.9 to 2.1 per 100 000, respectively.14,15 There was also a marked reduction in pneumonia hospitalisations, presumed to be attributable to 7vPCV vaccination, in children <2 and 2–4 years of age (of 38% and 28%, respectively).15 Reductions in IPD were also observed in age groups not targeted for vaccination (‘herd immunity’ effect); the incidence of IPD due to 7vPCV serotypes declined by between 50 and 60% in various age groups >5 years of age.14

Although 7vPCV use resulted in a marked reduction in rates of IPD due to vaccine serotypes, IPD among Indigenous children remains disproportionately higher than in non-Indigenous children, due to significantly higher rates of IPD caused by non-7vPCV serotypes.7,15,16 (Refer also to 3.1 Vaccination for Aboriginal and Torres Strait Islander people (Handbook 10-home-handbook10part3-handbook10part3-1-1.).)

Serotype distribution of pneumococcal disease is more diverse in adults than in children, and more diverse in Aboriginal and Torres Strait Islanders than in other Australians. Prior to universal infant vaccination, 85% of IPD in children aged <2 years was caused by the seven vaccine serotypes;18 however, the proportion differed substantially between Indigenous children (46%) and non-Indigenous children (85%).19,20 Since the implementation of the universal 7vPCV program, increases in rates of IPD caused by certain serotypes not contained in 7vPCV (replacement diseases) have been observed in Australia and several other countries. This is particularly so among non-Indigenous children aged <2 years, in whom 44% of IPD in 2007 was due to serotype 1A.19 In 2009 and 2010, two extended-valency pneumococcal conjugate vaccines (the 10-valent [10vPCV] and the 13-valent [13vPCV], respectively) became available in Australia. In the Northern Territory, 10vPCV replaced 7vPCV from October 2009. In other jurisdictions, 13vPCV (which includes serotype 19A) replaced 7vPCV under the NIP for infants in July 2011, and in the Northern Territory replaced 10vPCV from September 2011.

Vaccination using 23vPPV was introduced in 1999 for all Indigenous adults aged ≥50 years and younger Indigenous adults with risk factors. Since January 2005, 23vPPV has also been funded under the NIP for non-Indigenous adults aged 65 years. Persons aged <65 years with a condition(s) associated with an increased risk of IPD can access 23vPPV through the Pharmaceutical Benefits Scheme. Most IPD isolates in adults belong to serotypes contained in 23vPPV.7,21 In non-Indigenous adults, the prevalence of risk factors among those with IPD increases with age. In contrast, among Indigenous adults, there is a high prevalence of risk factors in IPD cases of all ages.21 Overall, among adults aged ≥65 years, the incidence of IPD was 29% lower in 2006–2007 than in 2002–2004. This was mostly due to a 53% decrease in the incidence of serotypes included in 7vPCV, despite increases in IPD caused by serotypes both included in (46%) and not included in (57%) 23vPPV.14

4.13.4 Vaccines

There are two different types of pneumococcal vaccines – pneumococcal conjugate vaccine (PCV) and pneumococcal polysaccharide vaccine (PPV). Among the pneumococcal conjugate vaccines, formulations vary in the number of pneumococcal serotypes included and the conjugating proteins used. Pneumococcal conjugate vaccines are immunogenic in young infants and can induce an immune memory response. In contrast, 23vPPV is poorly immunogenic for most serotypes in children aged <2 years and does not induce immune memory; however, 23vPPV contains more serotypes.

Pneumococcal conjugate vaccines

- **Synflorix** – GlaxoSmithKline Australia Pty Ltd (10-valent pneumococcal conjugate vaccine; 10vPCV). Each 0.5 mL monodose vial or pre-filled syringe contains 1 µg of pneumococcal capsular polysaccharide of serotypes 1, 2, 3, 4, 5, 6A, 7F, 7V, 9N, 14, 18C, 19F, 23F, and 3 µg of serotype 4, conjugated to 5–10 µg of tetanus toxoid carrier protein, and 3 µg of serotype 19F conjugated to 3–6 µg of diphtheria toxoid carrier protein, adsorbed onto 0.5 mg aluminium as aluminium phosphate.
- **Prevenar 13** – Pfizer Australia Pty Ltd (13-valent pneumococcal conjugate vaccine; 13vPCV). Each 0.5 mL monodose pre-filled syringe contains 2.2 µg each of pneumococcal capsular polysaccharide of serotypes 1, 3, 4, 5, 6A, 7F, 9V, 14, 18C, 19A, 19F, 23F and 4.4 µg of serotype 6B, conjugated to non-toxic Corynebacterium diphtheriae CRM197 protein, adsorbed onto 0.566 mg aluminium phosphate; succinic acid; polysorbate 80.

7-valent pneumococcal conjugate vaccine (7vPCV)

A 7vPCV with the mutant non-toxic diphtheria CRM197 protein as the conjugating protein (Prevenar) became available in Australia in 2001. Efficacy data on the 7vPCV from a pivotal trial in the United States found greater than 95% protective efficacy against IPD caused by the serotypes contained in the vaccine.22 A Cochrane review of clinical trials estimated an efficacy of 80% against vaccine-type IPD for PCVs (most, but not all, of which used CRM197 as the conjugating protein) in children <2 years of age.23 Based on the included studies, the effectiveness against IPD of any serotype among these children was 58%,23 noting that the proportion of IPD due to vaccine serotypes varies among different populations. Effectiveness against X-ray confirmed pneumonia (using World Health Organization [WHO] criteria) was lower, at 27%.

A 3-dose primary vaccination schedule for 7vPCV consisting of doses at 2, 4 and 6 months of age without a booster in the 2nd year of life was recommended in Australia from 2001 (except for persons at increased risk of IPD). This recommendation was initially based on data suggesting similar efficacy against type-specific IPD with either 3 or 4 doses.22 Subsequent Australian data have shown similar degrees of direct and indirect reduction in IPD and pneumonia hospitalisations as those seen in countries with alternate schedules.24-27

7vPCV is no longer available, having been replaced in 2011 by 13vPCV made by the same manufacturer.

10-valent pneumococcal conjugate vaccine (10vPCV)

10vPCV has been registered for use in Australia since 2009 and is included under the NIP. The protein D of non-typeable H. influenzae (NTHi) is one of the main conjugating proteins in this vaccine. This vaccine was used for all children aged <2 years in the Northern Territory from October 2009 to September 2011, after which 13vPCV was used. (Refer also to 3.1 Vaccination for Aboriginal and Torres Strait Islander people (Handbook10-home-handbook10part3-handbook10-3-1)).

Clinical trials on 10vPCV with efficacy outcomes are not yet published; registration of 10vPCV in Australia was based on immunogenicity data.28-32 A clinical study of a prototype 11-valent pneumococcal vaccine (containing the 10 serotypes in 10vPCV plus serotype 3), also conjugated to NTHi protein D, showed significant protective efficacy of approximately 58% against acute otitis media caused by vaccine serotypes (as well as protective efficacy of approximately 38% against AOM caused by H. influenzae).33 10vPCV has been shown to produce robust antibody responses to all 10 serotypes contained in the vaccine after a 4th (booster) dose in the 2nd year of life, but lesser antibody responses after 3 primary doses given in infancy.33-35

Although 10vPCV does not contain specific antigens for serotypes 6A or 19A, there were also measurable levels of antibody against these cross-reacting serotypes in functional antibody assays.31,32

13-valent pneumococcal conjugate vaccine (13vPCV)

13vPCV has been registered in Australia since 2010, and used in the NIP since July 2011. A single supplementary dose of 13vPCV for children aged 12–35 months who completed primary vaccination with 7vPCV was available under the NIP for 12 months from October 2011.

Registration of 13vPCV was based on immunogenicity studies showing non-inferiority for the 7vPCV serotypes and comparable antibody response to the additional serotypes.34-38 This includes serotype 19A, for which high levels of functional antibody have been demonstrated. Early data from 13vPCV use in England and Wales in 2011 have shown an impact against IPD caused by the additional serotypes contained in the vaccine.40

Based on the substantial impact of the 7vPCV program on serotype-specific IPD, the similar composition of 13vPCV and 7vPCV, and immunogenicity data, a 2, 4, 6 month schedule without a booster is also recommended for 13vPCV (except for those with a medical condition(s) associated with an increased risk of IPD or Indigenous children living in high-incidence regions). The comparative effectiveness of this schedule will continue to be monitored.

13vPCV has also been registered since October 2011 for use in adults aged ≥50 years, based on immunogenicity data showing equivalent or better antibody responses than those provided by 23vPPV for the shared vaccine serotypes. Since May 2014, the registered age of use for 13vPCV has been extended to include any person from 6 weeks of age. There are currently no data on clinical outcomes for 13vPCV, but a study examining its efficacy against pneumonia in adults is underway.41 In the absence of evidence of superior effectiveness against IPD or non-influenza pneumonia, the relative benefit of 13vPCV over 23vPPV for adults is uncertain, since the serotype coverage of 13vPCV is more limited. It is also uncertain whether the level of reduction in pneumonia (using World Health Organization [WHO] criteria) was lower, at 27%.

Pneumococcal polysaccharide vaccine

- **Pneumovax 23** – bioCSL Pty Ltd/Merck Sharp & Dohme (Australia) Pty Ltd (23-valent pneumococcal polysaccharide vaccine; 23vPPV). Each 0.5 mL monodose vial contains 25 µg each of pneumococcal capsular polysaccharide of serotypes 1, 2, 3, 4, 5, 6B, 7F, 8, 9N, 9V, 10A, 11A, 12F, 14, 15B, 17F, 18C, 19F, 19A, 20, 22F, 23F and 33F; 0.25% phenol.

23vPPV contains polysaccharides derived from the 23 most frequent or most virulent capsular types of S. pneumoniae isolated from sterile fluids in the United States in the 1970s/early 1980s, with worldwide serotype distribution and potential cross-reactive serotypes also taken into consideration.42 These serotypes are responsible for most IPD cases in adults in Australia. 23vPPV induces significant immune responses in immunocompetent adults, including the elderly, with no substantial differences in immune response between older and younger subjects, but poor responses in the immunocompromised.43 In children <2 years of age, the antibody response is limited to a small number of serotypes without previous 7vPCV vaccination.44

A Cochrane review published in 2008 found an estimated overall protective efficacy of 74% for pneumococcal polysaccharide vaccines against IPD, based on randomised controlled trials (RCTs). The review also found a vaccine effectiveness of 52% against IPD in older adults or adults with conditions associated with an increased risk of IPD, based on observational studies, but lower efficacy against all-cause pneumonia, based on RCTs (29%).45 Evidence from more recent controlled trials and observational studies using 23vPPV in the elderly population is similar.46-52 Data from England and Wales reported 23vPPV vaccine effectiveness of 48% against IPD within 2 years of vaccination for adults aged ≥65 years, but effectiveness waned and became insignificant beyond 5 years. In the subset of adults aged 65–74 years with no risk factors, 23vPPV effectiveness was higher (65% within 2 years) and was maintained for longer.53 In Victoria, 23vPPV vaccine effectiveness was estimated to be 71% for adults aged >65 years.54

4.13.5 Transport, storage and handling

Transport according to National vaccine storage guidelines: Strive for 5°C to +8°C. Do not freeze.

10vPCV should be protected from light.

4.13.6 Dosage and administration

The dose of pneumococcal conjugate vaccines (10vPCV, 13vPCV) is 0.5 mL, to be given by IM injection, in the opposite limb to other injectable vaccines, if possible.

The dose of pneumococcal polysaccharide vaccine (23vPPV) is 0.5 mL, to be given by either IM or SC injection, in the opposite limb to other injectable vaccines, if possible. The IM route is preferred, as a 3-fold greater rate of injection site reactions is found following administration of 23vPPV by the SC route.82 However, a vaccine dose administered subcutaneously does not need to be repeated.

10vPCV (Synflorix) is registered for use in infants and children aged 6 weeks up to 5 years.

13vPCV (Prevenar 13) is registered for use in children aged ≥6 weeks and in adults.

23vPPV (Pneumovax 23) is registered for use in children aged ≥2 years and in adults.

Co-administration with other vaccines

10vPCV may be concurrently administered with other vaccines routinely used in the infant schedule.

13vPCV may be concurrently administered with other vaccines in the infant schedule, including inactivated trivalent influenza vaccine. However, parents/carers of infants or children who are recommended to receive both influenza vaccine and 13vPCV should be advised of a possible small increased risk of fever following concomitant administration of these vaccines (refer to 4.13.10 Precautions below).

Pneumococcal polysaccharide vaccine can be concurrently administered with Zostavax using separate syringes and injection sites.63-65 (Refer also to 4.24 Zoster (Handbook10-home-handbook10part4-handbook10-4-24#4-24).)

Interchangeability of 10vPCV and 13vPCV

There are no available specific data on the interchangeability of 10vPCV and 13vPCV. Although completion of a primary course of pneumococcal conjugate vaccine with the same formulation is generally preferred, if vaccination with 10vPCV is commenced (e.g. in children born overseas), completion of the course with 13vPCV is acceptable.

4.13.7 Recommendations


Children aged <2 years

All children are recommended to receive a complete course of pneumococcal conjugate vaccination. The total number of doses recommended depends on the vaccine type used, on whether the child has a medical condition(s) associated with an increased risk of IPD (refer to List 4.13.1), on the child’s Indigenous status and on whether the child is living in a jurisdiction with a high incidence of IPD (the Northern Territory, Queensland, South Australia or Western Australia).

If 10vPCV is used for primary vaccination in infants, a total of 4 doses are recommended, regardless of the child’s Indigenous status or place of residence, or whether the child has any underlying medical condition(s) associated with an increased risk of IPD. The recommended schedule is 3 primary doses, at 2, 4 and 6 months of age, followed by 1 booster dose at between 12 and 18 months of age (at least 6 months after the 3rd primary dose) (a ‘3+1’ schedule).

If 13vPCV is used for primary vaccination in infants, the total recommended schedule for most children is 3 primary doses, at 2, 4 and 6 months of age (a ‘3+0’ schedule); however, additional doses are required for some children, as summarised in Table 4.13.1. A booster dose of 13vPCV is recommended for young Indigenous children living in the four jurisdictions specified above. In these children, the risk of IPD is comparable to the risk of IPD in children with certain medical conditions (refer to List 4.13.1).

The 1st dose of pneumococcal conjugate vaccine can be given as early as 6 weeks of age. If the 1st dose is given at 6 weeks of age, the next scheduled doses should still be given at 4 months and 6 months of age.

Table 4.13.1: Recommendations for pneumococcal vaccination for children aged <5 years

<table>
<thead>
<tr>
<th>Recommended age for pneumococcal vaccine doses</th>
<th>2 months*</th>
<th>4 months</th>
<th>6 months</th>
<th>12 months</th>
<th>12–18 months</th>
<th>4–5 years</th>
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<tr>
<td><strong>Children without any medical conditions associated with an increased risk of invasive pneumococcal disease (IPD)</strong></td>
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<tr>
<td><strong>If 10vPCV is used for the primary course:</strong></td>
<td></td>
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<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>All children</td>
<td>10vPCV</td>
<td>10vPCV</td>
<td>10vPCV</td>
<td>–</td>
<td>10vPCV</td>
<td>–</td>
</tr>
<tr>
<td><strong>If 13vPCV is used for the primary course:</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Non-Indigenous children and Indigenous children in ACT, NSW, Tas or Vic</td>
<td>13vPCV</td>
<td>13vPCV</td>
<td>13vPCV</td>
<td>–</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>Indigenous children in NT, Qld, SA or WA</td>
<td>13vPCV</td>
<td>13vPCV</td>
<td>13vPCV</td>
<td>–</td>
<td>13vPCV ‡</td>
<td>–</td>
</tr>
<tr>
<td><strong>Children with a medical condition(s) associated with an increased risk of IPD ‡</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>All children</td>
<td>13vPCV</td>
<td>13vPCV</td>
<td>13vPCV</td>
<td>13vPCV ‡</td>
<td>–</td>
<td>23vPPV</td>
</tr>
</tbody>
</table>

* The 1st dose can be given as early as 6 weeks of age; the next scheduled doses should still be given at 4 months and 6 months of age.

Table 4.13.2 indicates which vaccines are recommended, depending on prior vaccination history. The need for additional doses of pneumococcal vaccine is based on the continuing higher risk of invasive pneumococcal disease (IPD) in the first 5 years of life and in immunocompromised persons, including more specific revaccination recommendations for haematopoietic stem cell transplant recipients.

For children aged 7–23 months who have not completed a full course of pneumococcal conjugate vaccines, the timing and number of further doses for ‘catch-up’ vaccination depends on age and previous doses administered. For recommendations, refer to the following three tables in 2.1.5 Catch-up (Handbook10-home-handbook10part2-handbook10-2-1#table-2-1-11):

- Table 2.1.9 Catch-up schedule for 13vPCV (Prevenar 13) for non-Indigenous children, and Indigenous children residing in the Australian Capital Territory, New South Wales, Tasmania and Victoria, who do not have any medical condition(s) associated with an increased risk of invasive pneumococcal disease (IPD), aged <5 years.
- Table 2.1.10 Catch-up schedule for 13vPCV (Prevenar 13) for Indigenous children residing in the Northern Territory, Queensland, South Australia or Western Australia ONLY, who do not have any medical condition(s) associated with an increased risk of invasive pneumococcal disease (IPD), aged <5 years.
- Table 2.1.11 Catch-up schedule for 13vPCV (Prevenar 13) and 23vPPV (Pneumovax 23) in children with a medical condition(s) associated with an increased risk of IPD, presenting at age <2 years (for children aged 7–23 months with a medical condition(s) associated with an increased risk of IPD who have not completed a full course of pneumococcal conjugate vaccines).

If catch-up is required in a child who has commenced vaccination with 10vPCV, subsequent doses should be with 13vPCV. If 13vPCV is not available, 10vPCV may be used, and catch-up vaccination should be provided according to the rules in Table 2.1.10.

List 4.13.1: Conditions associated with an increased risk of invasive pneumococcal disease (IPD) in children and adults, by severity of risk

**Category A: Conditions associated with the highest increased risk of IPD**

- functional or anatomical asplenia, including:
  - sickle cell disease or other haemoglobinopathies
  - congenital or acquired asplenia (e.g. splenectomy), splenic dysfunction
- immunocompromising conditions, including:
  - congenital or acquired immune deficiency, including symptomatic IgG subclass or isolated IgA deficiency (Note: children who require monthly immunoglobulin infusion are unlikely to benefit from vaccination)
- immunosuppressive therapy (including corticosteroid therapy ≥2 mg/kg per day of prednisolone or equivalent for more than 1 week) or radiation therapy, where there is sufficient reconstitution for vaccine response to be expected
- haematological and other malignancies
- solid organ transplant
- haematopoietic stem cell transplant (HSCT)
- HIV infection (including AIDS)
- chronic renal failure, or relapsing or persistent nephrotic syndrome
- proven or presumptive cerebrospinal fluid (CSF) leak
- cochlear implants
- intracranial shunts

**Category B: Conditions associated with an increased risk of IPD**

- chronic cardiac disease
- particularly cyanotic heart disease or cardiac failure in children
- excluding hypertension only (in adults)
- chronic lung disease, including:
  - chronic lung disease in preterm infants
  - cystic fibrosis
  - severe asthma in adults (requiring frequent hospital visits and use of multiple medications)
- diabetes mellitus
- Down syndrome
- alcoholism
- chronic liver disease
- preterm birth at <28 weeks gestation
- tobacco smoking

* Refer also to 3.3.3 Vaccination of immunocompromised persons (Handbook10-home-handbook10part3-handbook10-3-3#3-3-3) for more recommendations for immunocompromised persons, including more specific revaccination recommendations for haematopoietic stem cell transplant recipients.
† Recommendations for pneumococcal vaccination differ for those aged >5 years (but not for those aged <5 years) between categories in this table, i.e. depending on whether the person is in Category A: Conditions associated with the highest increased risk of IPD or Category B: Conditions associated with an increased risk of IPD. Refer also to relevant sections below.
‡ HSCT recipients require 3 doses of 13vPCV post-transplantation, followed by 23vPPV, irrespective of previous vaccine doses received (refer to Table 3.3.3 Recommendations for revaccination following HSCT in children and adults, irrespective of previous immunisation history).
§ All infants born at <28 weeks gestation should receive vaccines recommended for those up to age 5 years with a medical condition(s) associated with an increased risk of IPD, according to Table 4.13.1. Thereafter, they only require further pneumococcal vaccine doses if they have chronic lung disease, and/or other chronic medical conditions as specified above.
¶ Tobacco smoking is not a medical condition, but is associated with an increased risk of IPD.

Children aged 2–5 years

Children aged 2–5 years who do not have a medical condition associated with an increased risk of IPD are not routinely recommended to receive further pneumococcal vaccine doses. If they have not previously received any PCV doses, or had only 1 dose of a pneumococcal conjugate vaccine before 12 months of age, a single dose of 13vPCV is recommended (refer to 2.1.5 Catch-up (Handbook10-home-handbook10part2-handbook10-2-1#table-2-1-5)).

Table 2.1.9 Catch-up schedule for 13vPCV (Prevenar 13) for non-Indigenous children, and Indigenous children residing in the Australian Capital Territory, New South Wales, Tasmania and Victoria, who do not have any medical condition(s) associated with an increased risk of invasive pneumococcal disease (IPD), aged <5 years.

Table 2.1.10 Catch-up schedule for 13vPCV (Prevenar 13) for Indigenous children residing in the Northern Territory, Queensland, South Australia or Western Australia ONLY, who do not have any medical condition(s) associated with an increased risk of IPD, aged <5 years.

Table 2.1.11 Catch-up schedule for 13vPCV (Prevenar 13) and 23vPPV (Pneumovax 23) in children with a medical condition(s) associated with an increased risk of IPD, presenting at age <2 years (for children aged 7–23 months with a medical condition(s) associated with an increased risk of IPD who have not completed a full course of pneumococcal conjugate vaccines).

Children who have a medical condition(s) associated with an increased risk of IPD, as described in List 4.13.1 (Categories A and B), should receive a dose of 23vPPV at 4–5 years of age. Table 4.13.2 indicates which vaccines are recommended, depending on prior vaccination history. The need for additional doses of pneumococcal vaccine is based on the continuing higher susceptibility of these children to IPD at older ages, and extrapolation from data showing that boosting of immune responses to certain 7vPCV serotypes occurs when a dose of 23vPPV is administered.
Although 13vPCV is registered for use in adults, there is currently insufficient evidence to routinely recommend its use in preference to 23vPPV at the individual or population level for limiting the total lifetime number of 23vPPV doses to 3.

Prevalence of conditions associated with an increased risk of IPD and incidence of IPD in this population; this dose should be considered as a dose received in adulthood for the purpose of recommendations given in Table 4.13.3. In the Northern Territory, a dose of 23vPPV is provided to all Indigenous adolescents at approximately 15 years of age, based on the very high prevalence of conditions associated with an increased risk of IPD and incidence of IPD in this sub-population (refer to ‘Adults aged ≥18 years’ below and 3.1 Vaccination for Aboriginal and Torres Strait Islander people (Handbook10-home-handbook10-part3-handbook10-3-1)).

For children with a medical condition(s) associated with an increased risk of IPD, further pneumococcal vaccine doses are recommended, as discussed below, depending on the child’s level of risk.

Those with the highest increased risk of IPD (List 4.13.1, Category A)

Children aged >5 to <18 years with a pre-existing chronic medical condition(s) associated with the highest increased risk of IPD (List 4.13.1, Category A), who were previously vaccinated according to the recommendations in Table 4.13.2, should receive another 23vPPV dose 5 years after their 1st 23vPPV dose, at approximately 10 years of age. Their next 23vPPV dose should be approximately 10 years later, at age 18–20 years. (Refer also to ‘Adults with a condition(s) associated with an increased risk of IPD’ below.) If a child in this category has never received a dose of 13vPCV previously, 1 dose of 13vPCV should be administered, with the exception of HSCT recipients who should receive 3 doses of 13vPCV (refer to Table 3.3.3 Recommendations for revaccination following HSCT in children and adults, irrespective of previous immunisation history (Handbook10-home-handbook10-part3-handbook10-3-3table-3-3-3)). This should then be followed by 23vPPV approximately 2 months later (if no prior 23vPPV dose has been received), or a minimum of 5 years after a prior 23vPPV dose (refer above). The minimum interval between a previous 23vPPV dose and the single 13vPCV dose, if required, is 12 months.

Children in this age group with a newly identified medical condition(s) associated with the highest increased risk of IPD (List 4.13.1, Category A) are recommended to receive a dose of 23vPPV at diagnosis, if they have not previously received a dose of 13vPCV, they should receive one 13vPCV dose at diagnosis, followed by their 1st 23vPPV dose a minimum of 2 months later. A further dose of 23vPPV is recommended 5 years after the 1st 23vPPV dose (minimum 2 months after 13vPCV). Their next 23vPPV dose should be approximately 10 years later, or at age 18–20 years, whichever is later (refer to ‘Adults with a condition(s) associated with an increased risk of IPD’ below).

Those with an increased risk of IPD (List 4.13.1, Category B)

Children aged >5 to <18 years with a pre-existing medical condition(s) associated with an increased risk of IPD (List 4.13.1, Category B) who received a dose of 23vPPV at 4–5 years of age should receive a 2nd dose of 23vPPV approximately 10 years later, at 15–18 years of age. That dose should be counted as their 1st adult 23vPPV dose.

For children in this age group with a newly identified medical condition(s) associated with an increased risk of IPD (List 4.13.1, Category B), a single dose of 23vPPV is recommended at the time of diagnosis. In the rare situation where a previous dose of 23vPPV has been given (e.g. in Indigenous children in some jurisdictions), this dose should be given at least 5 years after the previous 23vPPV dose. The next 23vPPV dose should be given approximately 5–10 years after the 1st 23vPPV dose and counted as their 1st adult 23vPPV dose (refer to ‘Adults with a condition(s) associated with an increased risk of IPD’ below).

Adults aged ≥18 years

The recommendations for use of 23vPPV in adults who do not have a condition(s) associated with an increased risk of IPD are summarised in Table 4.13.3. Recommendations for pneumococcal vaccination using 23vPPV in adults who do not have a condition(s) associated with an increased risk of invasive pneumococcal disease (IPD). Recommendations for the use of 13vPCV and/or 23vPPV in adults with a condition(s) associated with an increased risk of IPD (List 4.13.1, Category A or B) are described in the text below.

The number of doses recommended depends on age, Indigenous status and the presence of a condition(s) associated with an increased risk of IPD. Up to 3 doses (i.e. 2 revaccinations) of 23vPPV in adulthood are recommended, depending on these factors. This is based on limited data on adverse events and effectiveness, as well as uncertainty regarding the clinical significance of blunting of antibody response (immune hyporesponsiveness) following revaccination with 23vPPV, especially with multiple revaccinations.

For adults, prior childhood doses of 23vPPV that may have been given at either 18–24 months and/or 4–5 years of age should not be counted; that is, they are not relevant to the recommendations given in Table 4.13.3. In the Northern Territory, a dose of 23vPPV is provided to all Indigenous adolescents at approximately 15 years of age, based on the very high prevalence of conditions associated with an increased risk of IPD and incidence of IPD in this population; this dose should be considered as a dose received in adulthood for the purpose of limiting the total lifetime number of 23vPPV doses to 3.

Although 13vPCV is registered for use in adults, there is currently insufficient evidence to routinely recommend its use in preference to 23vPPV at the individual or population level for persons aged ≥18 years who do not have a condition(s) associated with an increased risk of IPD (refer to 4.13.4 Vaccines above). Updated recommendations on the use of 13vPCV in adults will be made when more data are available (refer to Immunise Australia website/(home)).

Non-Indigenous adults


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Use of 13vPCV

Adults with a medical condition(s) associated with the highest increased risk of IPD in List 4.13.1, Category A (immunocompromising conditions, functional or anatomical asplenia, CSF leak, cochlear implant), are recommended to receive a single dose of 13vPCV,\(^\dagger\) with the exception of HSCT recipients who should receive 3 doses of 13vPCV (refer to Table 3.3.3 Recommendations for revaccination following HSCT in children and adults, irrespective of previous immunisation history). For those with a newly diagnosed (or newly recognised for the purposes of requiring vaccination) condition, the dose of 13vPCV should be given at the time of diagnosis and followed by 23vPPV doses. The 1st 23vPPV dose should be given a minimum of 2 months after 13vPCV (refer to ‘Use of 23vPPV’ below). For adults with a pre-existing condition listed in Category A, who have received 1 or more prior doses of 23vPPV, the dose of 13vPCV should be given at least 12 months after the most recent dose of 23vPPV. (Refer also to ‘Persons with functional or anatomical asplenia’ in 3.3.3 Vaccination of immunocompromised persons). Although data on clinical benefit from 13vPCV in persons at increased risk of IPD are not yet available, providing a dose of 13vPCV to adults at the highest increased risk of IPD (Category A) is likely to be beneficial based on extrapolations from data on 7vPCV.\(^\dagger\) Adults who have a condition listed in Category B in List 4.13.1 are not recommended to receive 13vPCV.

Use of 23vPPV

All adults with a condition(s) associated with an increased risk of IPD (List 4.13.1, Categories A and B) are recommended to receive additional doses of 23vPPV (compared with those who do not have an increased risk).

In adults with a pre-existing condition (List 4.13.1, Categories A and B) the 1st adult dose of 23vPPV is recommended at approximately 18 years of age (refer to ‘Children aged >5 years to <18 years’ above), or a minimum of 5 years after the most recent dose of 23vPPV, and is to be followed by up to 2 additional doses. For those newly diagnosed, or who have never received pneumococcal vaccination, a 1st dose of 23vPPV is recommended at identification of the risk condition if they are in Category B. If the adult has a condition(s) associated with the highest increased risk of IPD (listed in Category A), they should receive a single dose of 13vPCV at time of diagnosis (refer above), followed by a 1st dose of 23vPPV a minimum of 2 months later. A 2nd dose of 23vPPV is recommended for all at-risk adults in Categories A and B at approximately 5–10 years (minimum of 5 years) after the 1st dose of 23vPPV. A 3rd dose of 23vPPV is recommended at the age of 50 years for Indigenous adults and 65 years for non-Indigenous adults, or a minimum of 5 years after the 2nd dose, whichever is later. For older adults with a newly diagnosed condition who have already received an age-based 1st dose of 23vPPV at age 65 years (non-Indigenous) or 50 years (Indigenous), a single catch-up dose of 23vPPV should be offered as soon as possible. Routine revaccination with 23vPPV for non-Indigenous adults without a condition(s) associated with an increased risk of IPD is not recommended (refer to Table 4.13.3).

Aboriginal and Torres Strait Islander (Indigenous) adults

A 1st dose of 23vPPV is recommended for all Indigenous adults reaching the age of 50 years (Table 4.13.3). This is based on the increased risk of IPD in Indigenous adults compared with non-Indigenous adults, and the high prevalence of conditions associated with an increased risk of IPD (including tobacco smoking) in Indigenous adults after 50 years of age, compared with younger ages. A 2nd dose of 23vPPV is recommended 5 years after the 1st dose. For those aged ≥50 years who have never received a dose of 23vPPV, a 1st dose should be offered as soon as possible, with a 2nd dose recommended 5 years after the 1st dose.

Indigenous adults aged <50 years with a condition(s) associated with an increased risk of IPD (List 4.13.1), should be vaccinated according to the recommendation for ‘Adults with a condition(s) associated with an increased risk of IPD’ below.

### Table 4.13.3: Recommendations for pneumococcal vaccination using 23vPPV for adults who do not have a condition(s) associated with an increased risk of invasive pneumococcal disease (IPD)*

<table>
<thead>
<tr>
<th>Age Group</th>
<th>1st dose of 23vPPV</th>
<th>2nd dose of 23vPPV</th>
<th>3rd dose of 23vPPV</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;65 years</td>
<td>Not recommended †</td>
<td>Not recommended</td>
<td>Not recommended</td>
</tr>
<tr>
<td>≥65 years</td>
<td>Give now †</td>
<td>Not recommended</td>
<td>Not recommended</td>
</tr>
</tbody>
</table>

### Table 4.13.3: Recommendations for pneumococcal vaccination using 23vPPV for adults who do not have a condition(s) associated with an increased risk of invasive pneumococcal disease (IPD)*

<table>
<thead>
<tr>
<th>Age Group</th>
<th>1st dose of 23vPPV</th>
<th>2nd dose of 23vPPV</th>
<th>3rd dose of 23vPPV</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;50 years</td>
<td>Not recommended †</td>
<td>Not recommended</td>
<td>Not recommended</td>
</tr>
<tr>
<td>≥50 years</td>
<td>Give now †</td>
<td>5 years after 1st dose †</td>
<td>Not recommended</td>
</tr>
</tbody>
</table>

* Refer to List 4.13.1 for conditions associated with an increased risk of IPD. Recommendations for those who have a condition(s) that places them at an increased risk of IPD are listed in the text below.

† In the Northern Territory, a dose of 23vPPV is provided to all Indigenous adolescents at approximately 15 years of age, based on the very high prevalence of conditions associated with an increased risk of IPD and incidence of IPD in this sub-population. This dose should be considered a dose received in adulthood for the purpose of limiting the total lifetime number of 23vPPV doses to 3.

‡ The minimum interval between any 2 doses of 23vPPV should be 5 years, and no more than 3 lifetime adult doses of 23vPPV are recommended.

Pneumococcal vaccines are not routinely recommended for pregnant women.
13-valent pneumococcal conjugate vaccine and inactivated influenza vaccines

One study has demonstrated a slightly higher risk of fever and febrile convulsions in children aged 6 months to <5 years (especially those aged 12–24 months) with the concurrent administration of 13vPCV and inactivated trivalent influenza vaccine (compared with giving the vaccines separately).\(^7\) The risk was estimated to be about 18 excess cases per 100 000 doses in children aged 6–59 months, with a peak of 45 per 100 000 doses in those aged 16 months. Given that the reported increase in risk was relatively small, and a more recent study did not demonstrate the same association between febrile seizures and the concurrent administration of these two vaccines,\(^7\) administration of 13vPCV and inactivated influenza vaccine at the same visit is acceptable when both vaccines are indicated. (Refer also to 4.7 Influenza)(Handbook10-home-handbook10part3-handbook10-4-7) However, immunisation service providers should advise parents of the possible risk and provide the option of administering these two vaccines on separate days (with an interval of not less than 3 days).

4.13.10 Precautions

13-valent pneumococcal conjugate vaccine

The safety profile of 10vPCV is similar to that of 7vPCV,\(^7\) with no clinically relevant difference when co-administered with routine childhood vaccines.\(^8\) In clinical trials, erythema, pain, or swelling of any degree at the injection site each occurred in approximately 30 to 50% of 10vPCV recipients. Erythema of >30 mm occurred in up to about 5% of 10vPCV recipients in the primary course. The frequency of local adverse events was higher after the booster dose. Irritability and drowsiness were reported in about 50% of 10vPCV recipients when co-administered with a DTpa-combination vaccine, but severe reactions occurred in fewer than 5%. When co-administered with DTpa-based combination vaccines, fever with temperature ≥38°C was reported in about 33% of 10vPCV recipients after primary or booster doses. Approximately 2 to 6% of 10vPCV recipients reported rectal temperature >39°C after primary vaccination and 1.5 to 3% after booster vaccination.\(^7\)

The product information for Prevenar 13 recommends 4 doses of 13vPCV for vaccination commencing at 6 weeks of age, with further doses at 4, 6 and 12–15 months of age; 3 doses for vaccination commencing between 7 and 11 months of age; and 2 doses for vaccination commencing between 12 and 23 months of age. The ATAGI recommends instead that 1 dose less be given for vaccination commencing between 7 and 11 months of age; and 2 doses for vaccination commencing between 12 and 23 months of age.

4.13.12 Variations from product information

The product information for Pneumovax 23 states that Pneumovax 23 and Zostavax should not be given concurrently. The ATAGI instead recommends that Pneumovax 23 can be concurrently administered with Zostavax.


4.14 Poliomyelitis

4.14.1 Virology

Polioviruses are classified as enteroviruses in the family Picornaviridae. They have an RNA genome, and can inhabit the gastrointestinal tract transiently. There are three poliovirus serotypes, referred to as either type 1, type 2 or type 3. The virus enters through the mouth, multiplies in the pharynx and gut and is excreted in the stools for several weeks. The virus invades local lymphoid tissue, enters the bloodstream and may then infect and replicate in cells of the central nervous system.

4.14.2 Clinical features

Poliomyelitis is an acute illness following gastrointestinal infection by one of the three types of poliovirus. Transmission is through faecal-oral and, occasionally, oral-oral spread. The infection may be clinically inapparent. If symptoms occur, they may include headache, gastrointestinal disturbance, malaise and stiffness of the neck and back, with or without paralysis. Paralysis is classically asymmetrical. Paralytic polio is a complication of poliovirus aseptic meningitis, and may be spinal (79%), bulbar (2%) or bulbospinal (19%). The case-fatality rate in paralytic polio is 2 to 5% in children and 15 to 30% in adults. The case-fatality rate in bulbar polio is up to 75%. The infection rate in households with susceptible young children can reach 100%. The ratio of asymptomatic to paralytic infection may be as high as 1000:1 in children and 75:1 in adults, depending on the poliovirus type and social and environmental conditions.

The incubation period ranges from 3 to 21 days. Infected persons are most infectious from 7 to 10 days before to 7 to 10 days after the onset of symptoms. The oral vaccine virus may be shed in the faeces for 6 weeks or more, and for up to several years in people who are immunocompromised. Oral vaccine strains shed for many years may mutate into potentially neurovirulent strains.

4.14.3 Epidemiology

The incidence of poliomyelitis has been dramatically reduced worldwide through an intensified Global Polio Eradication Initiative by the World Health Organization (WHO). In 1994, the continents of North and South America were certified to be free of polio. The last case of wild poliomyelitis in Australia occurred in 2007 in an overseas-born student who acquired the disease during a visit to Pakistan. In Australia, the peak incidence of poliomyelitis was 39.1/100,000 in 1938. There has been a dramatic fall in incidence since 1952, but epidemics occurred in 1956 and 1961–62. The last laboratory-confirmed case of wild poliomyelitis in Australia occurred in 2007 in an overseas-born student who acquired the disease during a visit to Pakistan. The last case of wild poliomyelitis prior to this was in 1977, due to an importation from Turkey, but two vaccine-associated cases were notified in 1986 and 1995.

The advantage of using IPV is that it cannot cause vaccine-associated paralytic poliomyelitis (VAPP). Emergence of highly evolved vaccine-derived polioviruses (VDPV) in persons with primary immunodeficiency (IIVDPV) with long-term excretion, and polio outbreaks due to circulating VDPV (cVDPV), particularly in areas with low vaccine coverage, are associated with oral poliomyelitis vaccine (OPV) administration.

4.14.4 Vaccines

Inactivated poliomyelitis vaccine

- **IPOL** – Sanofi-Aventis Australia Pty Ltd (IPV; inactivated poliovirus). Each 0.5 mL pre-filled syringe contains 40 D-antigen units inactivated poliovirus type 1 (Mahoney), 8 D-antigen units type 2 (MEF-1) and 32 D-antigen units type 3 (Saukett); 2–3 µL phenoxyethanol; 20–40 µg formaldehyde; polysorbate 80; traces of neomycin, streptomycin, polymyxin B and bovine serum albumin.

Combination vaccines that contain IPV

Formulations for children aged <10 years

- **Hexaxim** – Sanofi-Aventis Australia Pty Ltd (DTPa-hepB-IPV-Hib; diphtheria-tetanus-acellular pertussis-hepatitis B-inactivated poliovirus-Haemophilus influenzae type b). Each 0.5 mL pre-filled syringe contains ≥20 IU diphtheria toxoid, ≥40 IU tetanus toxoid, 25 µg pertussis toxoid (PT), ≥25 µg filamentous haemagglutinin (FHA), 10 µg recombinant HBsAg, 40 D-antigen units inactivated poliovirus type 1 (Mahoney), 8 D-antigen units type 2 (MEF-1), 32 D-antigen units type 3 (Saukett) and 12 µg purified Hib capsular polysaccharide (PRP) conjugated to 22–36 µg tetanus toxoid, adsorbed onto 0.6 mg aluminium as aluminium hydroxide. May contain traces of aluminium hydroxide, formaldehyde, neomycin, streptomycin and polymyxin B.

- **Infanrix hexa** – GlaxoSmithKline Australia Pty Ltd (DTPa-hepB-IPV-Hib; diphtheria-tetanus-acellular pertussis-hepatitis B-inactivated poliovirus-Haemophilus influenzae type b). Each 0.5 mL pre-filled syringe contains ≥30 IU diphtheria toxoid, ≥40 IU tetanus toxoid, ≥25 µg PT, ≥25 µg FHA, ≥8 µg pertactin (PRN), 10 µg recombinant HBsAg, 40 D-antigen units inactivated poliovirus type 1 (Mahoney), 8 D-antigen units type 2 (MEF-1) and 32 D-antigen units type 3 (Saukett), adsorbed onto aluminium hydroxide/phosphate; traces of formaldehyde, polysorbate 80, polysorbate 20, polymyxin and neomycin; and a vial containing a lyophilised pellet of 10 µg purified Hib capsular polysaccharide (PRP) conjugated to 20–40 µg tetanus toxoid. May contain yeast proteins.

- **Infanrix IPV** – GlaxoSmithKline Australia Pty Ltd (DTPa-hepB-IPV-Hib; diphtheria-tetanus-acellular pertussis-inactivated poliovirus). Each 0.5 mL pre-filled syringe contains ≥30 IU diphtheria toxoid, ≥40 IU tetanus toxoid, ≥25 µg PT, ≥25 µg FHA, ≥8 µg PRN, 40 D-antigen units inactivated poliovirus type 1 (Mahoney), 8 D-antigen units type 2 (MEF-1) and 32 D-antigen units type 3 (Saukett), adsorbed onto aluminium hydroxide; traces of formaldehyde, polysorbate 80, polymyxin and neomycin.

- **Quadracel** – Sanofi-Aventis Australia Pty Ltd (DTPa-IPV-Hib; diphtheria-tetanus-acellular pertussis-inactivated poliovirus). Each 0.5 mL monodose vial contains ≥30 IU diphtheria toxoid, ≥40 IU tetanus toxoid, ≥25 µg PT, ≥25 µg FHA, 5 µg FIM 2+3, 40 D-antigen units inactivated poliovirus type 1 (Mahoney), 8 D-antigen units type 2 (MEF-1) and 32 D-antigen units type 3 (Saukett); 1.5 mg aluminium phosphate; ≤50 ng bovine serum albumin; phenoxyethanol as preservative; traces of formaldehyde, glutaraldehyde, polysorbate 80, polymyxin and neomycin.

Reduced antigen formulations for adults, adolescents and children aged ≥10 years


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Adverse events

4.14.10.1

The only absolute contraindications to IPV (IPOL) or IPV-containing vaccines are:

Contraindications

4.14.9

IPV (IPOL) or IPV-containing vaccines are not routinely recommended for pregnant or breastfeeding women, but can be given where vaccination is considered necessary (refer to recommendations in response to new evidence of the spread of wild poliovirus (refer to International travel requirements)).

Documented evidence of polio vaccination is not routinely required for travellers under International Health Regulations but may be temporarily recommended in accordance with WHO recommendations on vaccinations for travellers (http://www.who.int/ith/en/).

4.14.14.10.2

Advisory note: Live-attenuated poliovirus vaccines (oral polio vaccine, OPV) are not advised for people with kidney disease, who are immunocompromised, or who are not at increased risk of acquiring poliomyelitis.

If storage is necessary, hold at room temperature for not more than 8 hours. Infanrix hexa must be reconstituted by adding the entire contents of the syringe to the vial and shaking until the pellet is completely dissolved. Reconstituted vaccine should be used as soon as practicable. If storage is necessary, hold at room temperature for not more than 8 hours.

4.14.14.10.3

OPV is no longer in use in Australia. OPV and IPV are interchangeable. Children commenced on OPV should complete their polio vaccination schedule using IPV (IPOL) or IPV-containing vaccines.

4.14.14.10.4

Recommended doses and schedule

- IPV (IPOL) or IPV-containing vaccines are recommended for infants at 2, 4 and 6 months of age. The 1st dose of an IPV-containing vaccine can be given as early as 6 weeks of age. If the 1st dose is given at 6 weeks of age, the next scheduled doses should still be given at 4 months and 6 months of age. An open, randomised, multi-centre trial comparing the hexavalent and pentavalent IPV-containing vaccines found that infants receiving either vaccine at 2, 4 and 6 months of age had seroprotective levels of antibody to poliovirus types 1, 2 and 3. Extra doses of IPV (IPOL) or IPV-containing vaccines are not needed for babies born prematurely.

- Other antigens including poliomyelitis are required, INFANRIX IPV or INFANRIX hexa can be used for catch-up vaccination in children aged <10 years (refer to Catch-up (Handbook10-home-handbook10part2-handbook10-2-14-1-5)).

Booster doses for children

A booster dose of IPV (IPOL) or IPV-containing vaccine is recommended at 4 years of age. This is commonly provided as DTPa-IPV, which can be given as early as 3.5 years (refer also to Pertussis (Handbook10-home-handbook10part4-handbook10-4-12) and Tetanus (Handbook10-home-handbook10part4-handbook10-10-4-19)).

A completed poliomyelitis vaccination schedule for children is 3 primary doses and 1 booster dose of IPV (IPOL) or IPV-containing vaccine.

- Where a child received their 3rd primary dose of IPV or an IPV-containing vaccine after the age of 3.5 years, a booster dose is not required.

Primary vaccination of adults

A course of 3 doses of IPV (IPOL) or IPV-containing vaccines is recommended for the primary vaccination of adults. No adult should remain unvaccinated against poliomyelitis. For more information refer to 2.1.5 Catch-up (Handbook10-home-handbook10part2-handbook10-2-14-1-5).

Booster doses for adults

Booster doses for adults are not recommended unless there is an individual risk, such as:

- travellers to areas or countries where poliomyelitis is epidemic or endemic; refer also to WHO recommendations on vaccinations for travellers (http://www.who.int/ith/en/) and 3.2 Vaccination for international travel (http://www.cmpd01.central.health/internet/immunise/publishing.nsf/Content/Handbook10-home-handbook10part3-handbook10-3-3).

- healthcare workers, including laboratory workers, in possible contact with poliomyelitis cases or poliomyelitis virus.

For those exposed to a continuing risk of infection, booster doses are desirable every 10 years. dTpa-IPV combination vaccines can be used where otherwise indicated.

International travel requirements

Documented evidence of polio vaccination is not routinely required for travellers under International Health Regulations but may be temporarily recommended in accordance with WHO recommendations on response to new evidence of the spread of wild poliovirus (refer to 3.2 Vaccination for international travel).

Pregnancy and breastfeeding

IPV (IPOL) or IPV-containing vaccines are not routinely recommended for pregnant or breastfeeding women, but can be given where vaccination is considered necessary (refer to 4.14.7 Recommendations above).

Refer to 3.3 Groups with special vaccination requirements (Handbook10-home-handbook10part3-handbook10-3-3), Table 3.3.1 Recommendations for vaccination in pregnancy (Handbook10-home-handbook10part3-handbook10-3-3-table-3-3-1) for more information.

Contraindications

The only absolute contraindications to IPV (IPOL) or IPV-containing vaccines are:

- anaphylaxis following a previous dose of any IPV-containing vaccine
- anaphylaxis following any vaccine component.

Adverse events

4.14.10

Adverse events

The only absolute contraindications to IPV (IPOL) or IPV-containing vaccines are:

Contraindications

4.14.9

IPV (IPOL) or IPV-containing vaccines are not routinely recommended for pregnant or breastfeeding women, but can be given where vaccination is considered necessary (refer to recommendations in response to new evidence of the spread of wild poliovirus (refer to International travel requirements)).

Documented evidence of polio vaccination is not routinely required for travellers under International Health Regulations but may be temporarily recommended in accordance with WHO recommendations on response to new evidence of the spread of wild poliovirus (refer to 3.2 Vaccination for international travel).

4.14.8

Pregnancy and breastfeeding

IPV (IPOL) or IPV-containing vaccines are not routinely recommended for pregnant or breastfeeding women, but can be given where vaccination is considered necessary (refer to 4.14.7 Recommendations above).

Refer to 3.3 Groups with special vaccination requirements (Handbook10-home-handbook10part3-handbook10-3-3), Table 3.3.1 Recommendations for vaccination in pregnancy (Handbook10-home-handbook10part3-handbook10-3-3-table-3-3-1) for more information.

4.14.9

Contraindications

The only absolute contraindications to IPV (IPOL) or IPV-containing vaccines are:

- anaphylaxis following a previous dose of any IPV-containing vaccine
- anaphylaxis following any vaccine component.
Repeate doses of IPV or IPV-containing vaccines have not been associated with increased adverse events and, where extra doses are required, are safe.

4.14.11 Public health management of poliomyelitis

Poliomyelitis is a notifiable disease in all states and territories in Australia.

Further instructions about the public health management of poliomyelitis, including management of cases of poliomyelitis and their contacts, should be obtained from state/territory public health authorities (refer to Appendix 1 Contact details for Australian, state and territory government health authorities and communicable disease control (Handbook 10-home-handbook10-tools-handbook10-appendices-handbook10-appendix1)).

4.14.12 Variations from product information

The product information for Infanrix hexa states that this vaccine is indicated for primary immunisation of infants from the age of 6 weeks and as a booster dose for children 18 months of age if boosting is required for all antigens. The ATAGI recommends that this vaccine may also be used for catch-up of the primary schedule in children <10 years of age.

The product information for Infanrix IPV states that this vaccine is indicated for use in a 3-dose primary schedule for immunisation of infants from the age of 6 weeks and as a single booster dose for children ≥6 years of age who have previously been vaccinated against diphtheria, tetanus, pertussis and poliomyelitis. In addition, the ATAGI recommends that this product may also be used for catch-up of the primary schedule or as a booster in children <10 years of age.

The product information for Quadracel states that this vaccine is indicated for use in a 3-dose primary schedule from the age of 2 months to 12 months and may also be used as a booster dose for children from 15 months to 6 years of age who have previously been vaccinated against diphtheria, tetanus, pertussis and poliomyelitis. The ATAGI recommends that, when appropriate, this product may also be used for either catch-up of the primary schedule or as a booster dose in children aged <10 years. The ATAGI also recommends that the primary schedule may be commenced at 6 weeks of age, if required.

The product information for Boostrix-IPV states that dTpa-containing vaccines should not be given within 5 years of a tetanus toxoid-containing vaccine. The product information for Adacel Polio states that dTpa-containing vaccine should not be given within 3 years of a tetanus toxoid-containing vaccine. The ATAGI recommends instead that, if protection against pertussis is required, dTpa-containing vaccines can be administered at any time following receipt of a dT-containing vaccine.

The product information for Adacel Polio, Boostrix-IPV, Infanrix hexa, Infanrix IPV and Quadracel states that these vaccines are contraindicated in children with encephalopathy of unknown aetiology or with neurologic complications occurring within 7 days following a vaccine dose. The ATAGI recommends instead that the only contraindication is a history of anaphylaxis to a previous dose or to any of the vaccine components.

References

A full reference list is available on the electronic Handbook or Immunise Australia website (http://www.immunise.health.gov.au/).

8. Kimman TG, Koopmans MP, van der Avoort HG. Ending polio immunisation: when and how are we sure that the needle is out of the haystack? Vaccine 1999;17:624-7.
4.15 Q fever

4.15.1 Bacteriology

Q fever is caused by Coxiella burnetii, an obligate intracellular bacterium. The organism is inactivated at pasteurisation temperatures. It survives well in air, soil, water and dust, and may also be disseminated on fomites such as wool, hides, clothing, straw and packing materials. C. burnetii has been weaponised and is considered a Category B biothreat agent.

4.15.2 Clinical features

Q fever can be acute or chronic, and there is increasing recognition of long-term sequelae. Infection is asymptomatic in at least half of cases. Acute Q fever usually has an incubation period of 2 to 3 1/2 weeks, depending on the inoculum size and other variables (range from 4 days up to 6 weeks). Clinical symptoms vary by country, but, in Australia, the most common presentation is rapid onset of high fever, rigors, profuse sweat, extreme fatigue, muscle and joint pain, severe headache and photophobia. As the attack progresses, there is usually evidence of hepatitis, occasionally with frank jaundice; a proportion of patients may have pneumonia, which is usually mild but can require mechanical ventilation. If untreated, the acute illness lasts 1 to 3 weeks and may be accompanied by substantial weight loss in more severe cases. Infection often results in time off work, lasting a few days to several weeks.

C. burnetii may cause chronic manifestations, the most commonly reported being subacute endocarditis. Less common presentations include granulomatous lesions in bone, joints, liver, lung, testis and soft tissues. Infection in early pregnancy, or even before conception, may recrudesce at term and cause fetal damage.

Studies have also identified a late sequela to infection, post Q fever fatigue syndrome (QFS), which occurs in about 10 to 15% of patients who have previously had acute Q fever. Research suggests that non-infective antigenic complexes of C. burnetii persist for many years after acute Q fever, and the maintenance of immune responses to these antigens might be the biological basis by which QFS occurs.

4.15.3 Epidemiology

C. burnetii infects both wild and domestic animals and their ticks, with cattle, sheep and goats being the main sources of human infection. Companion animals such as cats and dogs may also be infected, as well as native Australian animals such as kangaroos, and introduced animals such as feral cats and camels. The animals shed C. burnetii into the environment through their placental tissue or birth fluids, which contain exceptionally high numbers of Coxiella organisms, and also via their milk, urine and faeces. C. burnetii is highly infectious and can survive in the environment. The organism is transmitted to humans via the inhalation of infected aerosols or dust. Those most at risk include workers from the meat and livestock industries and shearers, with non-immune new employees or visitors being at highest risk of infection. Nevertheless, Q fever is not confined to occupationally exposed groups; there are numerous reports of sporadic cases or outbreaks in the general population in proximity to infected animals in stockyards, feedlots, processing plants or farms. Although most notifications occur among men from rural areas or with occupational exposure, a recent serosurvey from Queensland indicated a high rate of exposure among urban residents, including women and children.

Use of Q fever vaccine in Australia can be considered in 4 periods: from 1991 to 1993, when vaccine was used in a limited number of abattoirs; from 1994 to 2000, when vaccination steadily increased to cover large abattoirs in most states; from 2001 to 2006, during the period of the Australian Government sponsored National Q fever Management Program (NQFMP); and the period since 2007 after the NQFMP finished, where the vaccination remains available on the private market. The NQFMP funded screening and vaccination of abattoir workers and shearers, with non-immune new employees or visitors being at highest risk of infection. Nevertheless, Q fever is not confined to occupationally exposed groups; there are numerous reports of sporadic cases or outbreaks in the general population in proximity to infected animals in stockyards, feedlots, processing plants or farms. Although most notifications occur among men from rural areas or with occupational exposure, a recent serosurvey from Queensland indicated a high rate of exposure among urban residents, including women and children.

4.15.4 Vaccine

- Q-Vax – CSL Limited (Q fever vaccine). Each 0.5 mL pre-filled syringe contains 25 μg purified killed suspension of Coxiella burnetii; thiomersal 0.01% w/v. Traces of formalin. May contain egg proteins.
- Q-Vax Skin Test – CSL Limited (Q fever skin test). Each 0.5 mL liquid vial when diluted to 15 mL with sodium chloride contains 16.7 ng of purified killed suspension of C. burnetii in each vial; contained in a unit dose vial for dilution. Traces of formalin. May contain egg proteins.
The Q fever vaccine and skin test consist of a purified killed suspension of vaccine antigen grown in the yolks of embryonated hen eggs. The organisms are extracted, inactivated with formalin, and freed from excess egg proteins by fractionation and ultracentrifugation. Thioumerosal 0.01% w/v is added as a preservative.

Phase I whole-cell vaccines have been shown to be highly antigenic and protective against challenge, both in laboratory animals and in volunteer trials. Serological response to the vaccine is chiefly IgM antibody to C. burnetii Phase I and II antigens. Lack of seroconversion is not a reliable marker of lack of vaccination. Although the seroconversion rate may be low, long-term cell-mediated immunity develops and estimates of vaccine efficacy have ranged from 83 to 100%, based on the results of open and placebo-controlled trials, and post-marketing studies. It is important that vaccination status is reported for all notified cases and apparent vaccine failures are investigated.

It should be noted that vaccination during the incubation period of a natural attack of Q fever does not prevent the development of the disease.

The Q fever vaccine and skin test are available for purchase in Australia through the private market. The Australian Government may fund the vaccine and skin test in emergency situations where there is a Q fever outbreak.

### 4.15.5 Transport, storage and handling

Transport the vaccine according to National vaccine storage guidelines: Store at +2°C to +8°C. Do not freeze or store in direct contact with ice packs. If vaccine has been exposed to temperatures less than 0°C, do not use it. Protect from light.

Diluted Q-Vax Skin Test should be freshly prepared, stored at +2°C to +8°C and used within 6 hours.

### 4.15.6 Dosage and administration

The dose of Q fever vaccine is 0.5 mL, to be given by SC injection, after ascertaining that serological and skin testing have been performed and that both tests are negative (see 'Pre-vaccination testing' below).

Q fever vaccination and skin testing training is undertaken via an educational video available online. Please contact the manufacturer for access details.

### 4.15.7 Recommendations

#### Children aged <15 years

Q fever vaccine is not recommended in children aged <15 years. There are no data on the safety or efficacy of Q fever vaccine in this age group.

#### Adolescents aged ≥15 years and adults

Q fever vaccine is recommended for those at risk of infection with C. burnetii. This includes abattoir workers, farmers, stockyard workers, shearsers, animal transporters, and others exposed to cattle, camels, sheep, goats and kangaroos (or their products (including products of conception). It also includes veterinarians, veterinary nurses, veterinary students, professional dog and cat breeders, agricultural college staff and students, wildlife and zoo workers (working with high-risk animals) and laboratory personnel handling veterinary specimens or working with the organism (see also 3.3.7 Vaccination of persons at occupational risk|Handbook10-home|handbook10part3|handbook10-3-3#table-3-3-7). Table 3.3.7 Recommended vaccinations for persons at increased risk of certain occupationally acquired vaccine-preventable diseases|Handbook10-home|handbook10part3|handbook10-3-3#table-3-3-7).

Workers at pig abattoirs do not require Q fever vaccination.

#### Pre-vaccination testing

- Before vaccination, persons with a negative history of previous infection with Q fever must have serum antibody estimations and skin tests to exclude those likely to have hypersensitivity reactions to the vaccine resulting from previous (possibly unrecognized) exposure to the organism.
- If the person has a positive history of previous infection with Q fever, or has already been vaccinated for Q fever, vaccination is contraindicated and therefore skin testing and serology are not required. (See also below.)
- It is essential to take a detailed history and to obtain documentation of previous Q fever vaccination or laboratory results confirming Q fever disease in all potential vaccinees. Some persons who have had verified Q fever disease in the past may show no response to serological or skin testing; however, they may still experience serious reactions to Q fever vaccine. Persons who have worked in the livestock or meat industries for some time should be questioned particularly carefully. The Australian Q Fever Register(http://www.qfever.org), established by Meat and Livestock Australia (MLA), has records of receipt of Q fever vaccination for some individuals, which can be accessed by registered users. If there is any doubt about serological or skin test results, testing should be repeated 2 to 3 weeks later (see below for interpretation).
- Serological and skin test results should be taken into account, according to Table 4.15.1, before vaccination. Antibody studies were originally done by complement fixation (CF) tests at serum dilutions of 1 in 2, 5, 5 and 10 against the Phase II antigen of C. burnetii. Although this is generally satisfactory, many testing laboratories now use enzyme immunoassay (EIA) or immunofluorescent antibody (IFA) to detect IgG antibody to C. burnetii as an indicator of past exposure. Subjects who are CF antibody positive at 1 in 2.5, IFA positive at 1 in 10 or more, or with a definite positive absorbance value in the EIA, should not be vaccinated.
- Skin testing and interpretation should only be carried out by experienced personnel. Details of immunisation service providers trained in the administration of Q fever skin testing can be obtained online from the Australian Q Fever Register(http://www.qfever.org). Skin testing is performed by diluting 0.5 mL of the Q-Vax Skin Test in 14.5 mL of sodium chloride (injection grade). Diluted Q-Vax Skin Test should be freshly prepared, stored at +2°C to +8°C and used within 6 hours. A 0.1 mL dose of the diluted Q-Vax Skin Test is injected intradermally into the volar surface of the forearm. Commercial isopropyl alcohol skin wipes should not be used. If the skin is not visibly clean, then methylated spirits may be used. Skin reactions are common 3 to 4 days after skin testing; however, these reactions generally resolve by day 7 when the skin test is read. A positive reaction is indicated by any indentation at the site of injection after 7 days. Individuals giving such a reaction must not be vaccinated, because they may develop severe local reactions.
- The result of testing is considered 'indeterminate' when skin test induration is just palpable and the antibody test is either equivocal or negative, or when there is no skin induration and therefore skin testing and serology are not performed (see Table 4.15.1).

An indeterminate result, which occurs in only a small proportion of subjects, may be the consequence of past infection with Q fever. It may also merely indicate the presence in the subject of antibodies to antigens shared between C. burnetii and other bacteria. Australian Q fever vaccine providers have dealt with this finding in one of two ways:

- Repeat the skin test and interpret as per the guidelines for initial testing. Collect serum 2 to 3 weeks later to look for a rise in titre of C. burnetii antibodies in the IFA test, using Phase I and Phase II antigens and immunoglobulin class analysis. A significant increase (defined as a 4-fold rise in titre of paired sera) indicates previous Q fever infection and vaccination is then contraindicated.
- Vaccinate the subject using SC injection of a 5 µg (0.1 mL) dose instead of a 25 µg (0.5 mL) dose of the vaccine. If there are no adverse events (e.g. severe local induration or severe systemic effects, perhaps accompanied by fever) 48 hours after the injection, a further 0.4 mL (20 µg) dose of the vaccine is given within the next 2 to 3 weeks, that is, before the development of cell-mediated immunity to the 1st dose.

<table>
<thead>
<tr>
<th>Serology</th>
<th>Skin test</th>
<th>Interpretation/Action</th>
</tr>
</thead>
<tbody>
<tr>
<td>Positive antibody test*</td>
<td>Any skin test result</td>
<td>Sensitised: do not vaccinate</td>
</tr>
</tbody>
</table>

Table 4.15.1: Interpretation and action for serological and skin test results (with modifications from A guide to Q fever and Q fever vaccination (CSL Biotherapies, 2009))

4.15.13 Variations from product information

Further instructions about the public health management of Q fever, including management of cases of Q fever, should be obtained from state/territory public health authorities (see Appendix 1 Contact details for Australian, state and territory government health authorities and communicable disease control (Handbook10-home~handbook10-tools~handbook10-appendices~handbook10-appendix1)).
recommends instead that experienced Q fever vaccinators may elect to give reduced vaccine doses in subjects who have indeterminate results on either serological or skin testing.
4.16 Rabies and other lyssaviruses (including Australian bat lyssavirus)

Lyssaviruses are single-stranded RNA viruses in the family Rhabdoviridae, genus Lyssavirus. There are 12 known species within the genus Lyssavirus, including the classical rabies virus and other closely related lyssaviruses such as the Australian bat lyssavirus (ABL) and European bat lyssaviruses.  

4.16.1 Virology

Lyssaviruses are single-stranded RNA viruses in the family Rhabdoviridae, genus Lyssavirus. There are 12 known species within the genus Lyssavirus, including the classical rabies virus and other closely related lyssaviruses such as the Australian bat lyssavirus (ABL) and European bat lyssaviruses.  

4.16.2 Clinical features

Rabies is a zoonotic disease caused by human exposure to saliva or nerve tissue of an animal infected with rabies virus or other lyssaviruses. As the clinical disease caused by classical rabies virus and other lyssaviruses is indistinguishable, the term 'rabies' refers to disease caused by any of the known lyssavirus species.  

4.16.3 Epidemiology

The epidemiology of rabies varies depending on the lyssavirus species and the animal host. Lyssaviruses have been found in all continents, except Antarctica. Rabies that is due to the classical rabies virus and occurs in land dwelling (terrestrial) mammals is present throughout much of Africa, Asia, the Americas and Europe, where the virus is maintained in certain species of mammals, particularly dogs. In countries where rabies vaccination of domestic animals is widespread (North America and Europe), wild animals such as raccoons and foxes are important reservoirs. The continual maintenance of rabies in animal populations in these countries is referred to as enzootic rabies. Australia, New Zealand, Japan, Papua New Guinea and Pacific island nations are currently free of rabies in terrestrial mammals. However, a country's status can change at any time. For example, in 2008 on the island of Bali, Indonesia, rabies was reported in dogs, with cases later reported in humans. Prior to this, Bali had been considered free of rabies, although rabies was known to occur in other areas of Indonesia.

In some parts of the world, bats are important reservoirs of classical rabies as well as other lyssaviruses, with bat lyssaviruses found in areas that are considered free from terrestrial rabies. ABLV was first reported in bats in 1996; since then, three cases of fatal encephalitis caused by ABLV have been reported in Australians, in 1996, 1998 and 2013. It should therefore be assumed that all Australian bats have the potential to be infected with ABLV. Different regions in Australia have reported higher risk of potential ABLV exposures. ABLV has not been isolated from bats outside Australia. However, closely related lyssaviruses are found in bats in other countries. For example, European bat lyssavirus 1 and European bat lyssavirus 2 have been isolated in bats in some parts of Europe. Four human deaths from European bat lyssavirus variants have been reported in Europe, all with no record of prorhabdovirus rabies immunisation. As such, bats anywhere in the world should be considered a potential source of lyssaviruses and a potential risk for acquiring rabies, depending on the exposure. There are rare reports of bat lyssavirus infections in other animals. The first confirmed cases of ABLV in terrestrial mammals in Australia occurred in two horses in Queensland in 2013.

Information on the global occurrence of rabies can be obtained from reputable international authorities.  

4.16.4 Rabies vaccines

- Mérieux Inactivated Rabies Vaccine – Sanofi Pasteur Pty Ltd (human diploid cell vaccine [HDCV]). Lyophilised powder in a monodose vial with 1.0 mL distilled water as diluent. Each 1.0 mL reconstituted dose contains ≥2.5 IU inactivated rabies virus; 100–150 µg neomycin; ≤70 µg human serum albumin; trace of phenol red (indicator). May contain trace amounts of bovine gelatin and β-propiolactone.

- Rabipur Inactivated Rabies Virus Vaccine – CSL Limited/Novartis Vaccines and Diagnostics Pty Ltd (purified chick embryo cell vaccine [PCECV]). Lyophilised powder in a monodose vial with 1.0 mL distilled water as diluent. Each 1.0 mL reconstituted dose contains ≥2.5 IU inactivated rabies virus; trace amounts of neomycin, chlortetracycline, tyrometamol, β-propiolactone, monopotasium glutamate and ammonium B. May contain trace amounts of bovine gelatin and egg protein.

There are two inactivated rabies cell culture-derived vaccines available in Australia. The Mérieux vaccine is a lyophilised, stabilised suspension of inactivated Wistar rabies virus that has been cultured on human diploid cells and then inactivated by β-propiolactone. This human diploid cell vaccine (HDCV) is coloured off-white, but after reconstitution with the diluent it turns a pinkish colour due to the presence of phenol red. The vaccine does not contain a preservative.

Rabipur is a lyophilised, stabilised suspension of inactivated Flury LEP rabies virus that has been cultured on purified chick embryo cells and then inactivated by β-propiolactone. This purified chick embryo cell vaccine (PCECV) does not contain a preservative.
4.16.5 Rabies immunoglobulin

- Imgam Rabies Pasteurized – Sanofi Pasteur Pty Ltd (human rabies immunoglobulin [HRIG]). Each 1.0 mL contains IgG class human rabies antibodies with a minimum titre of 150 IU; 22.5 mg glycerine; 1 mg sodium chloride. Supplied in 2 mL vials.

Human rabies immunoglobulin (HRIG) is prepared by cold ethanol fractionation from the plasma of hyperimmunised human donors. In exceptional circumstances, such as product shortages, other HRIG products may be made available for use in Australia. For example, KamRAB Rabies Immune Globulin (Kamada, Israel), although not registered by the TGA, has been made available under the Special Access Scheme due to a critical shortage of alternative products. Advice on the use of HRIG products will be provided by state and territory health authorities (refer also to 4.16.12 Public health management of lyssavirus infections above).

4.16.6 Transport, storage and handling

Rabies vaccine

Transport according to National vaccine storage guidelines: Strive for 5. Store at +2°C to +8°C. Do not freeze.

Both rabies vaccines must be reconstituted by adding the entire contents of the diluent container to the vial and shaking until the powder is completely dissolved. Reconstituted vaccine should be used immediately.

Human rabies immunoglobulin

Transport according to National vaccine storage guidelines: Strive for 5. Store at +2°C to +8°C. Do not freeze. Protect from light.

HRIG should be used immediately once the vial is opened.

4.16.7 Dosage and administration

Rabies vaccine

The dose of rabies vaccine for use in PreP and PEP is 1.0 mL, to be given by IM injection and is the same for infants, children and adults.

HDCV can also be given by SC injection; however, if PCECV is inadvertently given via the SC route, the dose should be repeated.

Note: Rabies vaccination administered via the intradermal (ID) route is not routinely used in Australia and is not recommended. The use of the ID route for rabies vaccination is the practitioner’s own responsibility, as rabies vaccines are not registered for use via this route in Australia. ID administration should be particularly discouraged for post-exposure prophylaxis. For detailed information on the restrictions that apply to the use of ID vaccination, if undertaken for PreP, refer to ‘Pre-exposure prophylaxis administered via the intradermal route’ below.

Rabies vaccine should be given in the deltoid area, as rabies virus neutralising antibody (VNAb) titres may be reduced after administration in other sites. In particular, vaccine should never be given in the buttock, as failure of pre-exposure prophylaxis has been reported when given by this route.38 In infants <12 months of age, administration into the anterolateral aspect of the thigh is recommended.

Pre-exposure prophylaxis (PreP)

The recommended schedule for pre-exposure prophylaxis (PreP) for rabies or other lyssavirus infection consists of a total of 3 doses of vaccine: the 1st dose of vaccine is given on day 0, and subsequent doses on days 7 and 21–28. Although the 3rd dose can be given as early as 21 days, there are no data to support the use of an even more accelerated schedule for those with limited time before travel to a rabies-enzootic area.

Post-exposure prophylaxis (PEP)

In persons previously unvaccinated, the recommended schedule for post-exposure prophylaxis (PEP) for immunocompetent persons consists of 4 doses of vaccine. The 1st dose of vaccine is given as soon as practicable (day 0), and subsequent doses are given on days 3, 7 and 14; deviations of a few days from this schedule are probably unimportant.27

The recommended schedule for PEP for previously unvaccinated immunocompromised persons consists of 5 doses of vaccine. The 1st dose of vaccine is given as soon as practicable (day 0), and subsequent doses are given on days 3, 7, 14 and 28; deviations of a few days from this schedule are probably unimportant.

The recommended schedule for PEP for people who have been previously vaccinated against rabies consists of 2 doses of rabies vaccine on days 0 and 3 (noting caveats in Figures 4.16.1 and 4.16.2).

For more detailed information refer to 4.16.8 Recommendations below.

Human rabies immunoglobulin

When HRIG is indicated, the dose is 20 IU per kilogram of body mass and is the same for infants, children and adults. HRIG should be administered at the same time as the 1st dose (day 0) of rabies vaccine. Do not administer HRIG if more than 7 days have elapsed since the 1st dose of vaccine, as the HRIG may interfere with the immune response to the vaccine. For more detailed information refer to 4.16.8 Recommendations below.

HRIG must be infiltrated in and around all wounds using as much of the calculated dose as possible. The remainder of HRIG that cannot safely be infiltrated in and around the wound, or in situations where there is no wound (such as for mucous membrane exposures), HRIG should be administered intramuscularly at a site away from the rabies vaccine injection site (e.g. the alternative deltoid, lateral thigh or gluteal muscle, depending on volume). If the wounds are severe and the calculated volume of HRIG is inadequate for complete infiltration of all wounds (e.g. extensive dog bites in a young child), the HRIG should be diluted in saline to make up an adequate volume for the careful infiltration of all wounds.

Wounds to fingers and hands may be small, particularly following exposures to bats, and infiltration of HRIG into these wounds is likely to be both technically difficult and painful for the recipient. However, due to the extensive nerve supply to these sites, it is important that as much of the calculated dose of HRIG as possible should be infiltrated into finger and hand wounds using either a 25 or 26 gauge needle. To avoid the development of a compartment syndrome, the HRIG should be infiltrated very gently, and should not cause the adjacent finger tissue to go frankly pale or white. It may be necessary to give a ring-block using a local anaesthetic.

Interchangeability of rabies vaccines

The World Health Organization (WHO) does not recommend interchanging rabies cell culture-derived vaccines (CCV), but states that, in situations where it is unavoidable, a PreP or PEP course can be completed with an alternative rabies CCV, providing the vaccine is WHO-endorsed (also termed ‘pre-qualified’).27 Various international vaccine advisory groups state that rabies CCVs are interchangeable. This is supported by the similarities in tissue culture vaccine production methods as well as antibody responses and adverse reactions following vaccination. In one study that specifically assessed the interchangeability of HDCV and PCECV, 165 subjects were randomised to receive rabies PreP (days 0, 7, 21–28) using either HDCV or PCECV.38 One year following PreP, each group received 1 or 2 booster doses of PCECV. The booster dose resulted in an anamnestic response (geometric mean titre several orders of magnitude >0.5 IU/mL) in all subjects by day 7, independent of the vaccine that was used to deliver the primary course. It is expected that this response would be similar with other rabies CCVs.

 Measures to avoid potential rabies virus and other lyssavirus (including ABLV) exposures

Travellers to rabies-enzootic regions should be advised to avoid close contact with either wild or domestic animals; this is particularly important for children. They should be advised about pre-travel (i.e. pre-exposure) rabies vaccination (or, if appropriate, booster doses), and on what to do should they be either bitten or scratched by an animal while abroad. It is recommended that prior to travel, travellers be educated regarding first aid treatment for rabies exposures, irrespective of prior vaccination.

Recommendaions to decrease the risk of exposure to rabies include:

- Do not allow young children to feed, pat or play with animals. The height of young children makes bites to the face and head more likely.
- Avoid contact with stray dogs or cats. Remain vigilant when walking, running or cycling.
- Do not carry food, and do not feed or pat monkeys, even in popular areas around temples or markets where travellers may be encouraged to interact with the monkeys. In particular, avoid focusing attention on monkeys carrying their young, as they may feel threatened and bite suddenly.

In addition, contact with bats should be avoided anywhere in the world, including Australia. Only appropriately vaccinated and trained persons should handle bats. If bats must be handled, safety precautions, such as wearing protective gloves and clothing, should be observed.

Pre-exposure prophylaxis for rabies virus and other lyssaviruses (including ABLV)

PreP with rabies vaccine is recommended for:

- Persons liable to receive bites or scratches from bats (this includes bat handlers, veterinarians, wildlife officers and others who come into direct contact with bats) in any country, including Australia
- Travellers and expatriates who will be spending time in rabies-enzootic areas; PreP should occur following a risk assessment that takes into consideration the likelihood of interaction with animals and access to emergency medical attention
- Persons working with terrestrial animals in rabies-enzootic areas
- Research laboratory personnel working with any live lyssaviruses.

Parents travelling with children to rabies-enzootic areas should consider PreP for younger children, as many children, if bitten by dogs, are often bitten on the face and hands because they are at an optimal height for such contact.

Serological testing to confirm seroconversion is only necessary in certain circumstances (refer to ‘Serological testing following rabies vaccination’ below).

PreP simplifies the management of a subsequent exposure because fewer doses of vaccine are needed and because rabies immunoglobulin (RIG) is not required (refer to ‘Post-exposure prophylaxis for rabies virus and other lyssavirus (including ABLV) exposures’ below). This is particularly important as RIG (human or equine) is often difficult to obtain in many developing countries and its safety may not be guaranteed.

Pre-exposure prophylaxis administered via the intradermal route

Intraderal PreP is not recommended because, although initial antibody titles may be higher, titles at 14 days are lower and wane more rapidly after ID administration of rabies vaccine than after either IM or SC administration. There may also be a slow initial immune response following exposure to rabies virus in those given ID rabies vaccine. For these reasons, it is strongly recommended that the IM route (IM or SC if HDCV is used) be used for pre-exposure prophylaxis. (Refer also to 4.16.7 Dosage and administration above.)

However, if ID rabies PreP is considered (using a dose of 0.1 mL on days 0, 7 and 28) it is essential that:

- It is given by vaccine providers with not only expertise in, but also regular practice of, the ID technique
- It is not administered to anyone who is immunocompromised
- It is not administered to persons taking either chloroquine or other antimalarials structurally related to chloroquine (e.g. mefloquine), at either the time of, or within a month following, vaccination
- Any remaining vaccine is discarded at the end of the session during which the vial is opened (8 hours)
- The rabies VNAb level is checked 14 to 21 days following completion of the pre-exposure course of ID vaccine (refer to ‘Serological testing following rabies vaccination’ below)
- It is only used for PreP for classical rabies exposures (there are no data on the protection provided by ID rabies vaccination for the prevention of infection with other lyssaviruses, including ABLV).

Post-exposure prophylaxis for rabies virus and other lyssavirus (including ABLV) exposures

PEP for rabies virus and other lyssavirus exposures consists of prompt wound management, vaccination and HRIG administration. The appropriate combination of these components depends on a detailed risk assessment, including determining the extent of the exposure, the animal source of the exposure, the person’s immune status and their previous vaccination history. The different PEP pathways are described in more detail below and PEP management algorithms are outlined in Figures 4.16.1 and 4.16.2.

Types of potential rabies virus and other lyssavirus (including ABLV) exposures

Three different categories of lyssavirus exposure are outlined in Table 4.16.1, based on those already described by the World Health Organization (WHO). The appropriate PEP pathway following each of the different exposure categories depends on whether the source of exposure was a terrestrial animal or a bat. Different PEP pathways are required following potential bat exposures compared with terrestrial animal exposures because the risk from wounds from bats is often hard to determine due to the limited injury inflicted, and there is evidence that superficial bat exposures are more likely to result in human infection compared to superficial bites from terrestrial animals.

Risk assessment should be conducted for exposures to both live and dead animals. An in-vivo study of mice inoculated with a laboratory strain of rabies virus remained viable for up to 3 days post-mortem in brain tissue extracted from whole carcasses decomposing at 25°C to 35°C and for up to 18 days at lower temperatures. Every effort should be made following a potential exposure to have the animal tested so that unnecessary treatment is avoided (refer to ‘Wound management in post-exposure prophylaxis’ below).

An algorithm detailing the appropriate PEP pathway following potential lyssavirus exposure from a terrestrial animal is provided in Figure 4.16.1; an algorithm for use following potential lyssavirus exposure from a bat is provided in Figure 4.16.2.

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Table 4.16.1: Lyssavirus exposure categories, to be used in conjunction with Figure 4.16.1 or 4.16.2 to determine appropriate post-exposure prophylaxis

<table>
<thead>
<tr>
<th>Type of exposure</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Category I</td>
<td>Touching or feeding animals, licks on intact skin, as well as exposure to blood, urine or faeces</td>
</tr>
<tr>
<td>Category II</td>
<td>Nibbling of uncovered skin, minor scratches or abrasions without bleeding</td>
</tr>
<tr>
<td>Category III</td>
<td>Single or multiple transdermal bites or scratches, contamination of mucous membrane with saliva from licks, licks on broken skin</td>
</tr>
</tbody>
</table>

Source: Modified from WHO 2017

The relevant state/territory health authority should be contacted about any of the following potential exposures, in order to conduct a detailed risk assessment and advise on management. (Refer also to 4.16.12 Public health management of lyssavirus infections below.)
Post-exposure prophylaxis of persons who are previously unvaccinated

Vaccine

After performing wound management, rabies vaccine should be administered with or without HRIG (refer to ‘Human rabies immunoglobulin’ below), depending on the category and source of exposure, as outlined in Figure 4.16.1 or 4.16.2 and described below.

Persons who have not previously received a complete rabies vaccine course, and are immunocompetent, should receive a total of 4 doses of rabies vaccine (refer to 4.16.7 Dosage and administration above). Although no clinical trial has assessed the efficacy of rabies vaccine, the rationale supporting the use of a 4-dose schedule in immunocompetent persons is based on 11 studies where the immunogenicity of either cell culture-derived vaccine was consistently >0.5 IU/mL by day 30 (after 4 doses) and, in a majority of participants, was >0.5 IU/mL by day 14 (after 3 doses). Antibody responses observed after the 4th and 5th doses were both several orders of magnitude larger than the WHO cut-off of 0.5 IU/mL and were similar in value. As the additional immune boosting following a 5th dose is minimal, a 5th dose is not required in immunocompetent persons.52,62

Persons who have not previously received a complete rabies vaccine course and who have either an immunocompromising illness, or are taking immunosuppressant medications, should receive a 5-dose vaccine schedule (refer to 4.16.7 Dosage and administration above).53-56 The rabies VNA titre should be measured 14 to 21 days after the 5th dose and a further dose given if the titre is reported as inadequate (i.e. <0.5 IU/mL). Serological testing should be repeated following the 6th dose, and, if titres remain <0.5 IU/mL, infectious disease specialist advice should be sought (refer to ‘Serological testing following rabies vaccination’ below).

Corticosteroids and immunosuppressive therapy can interfere with the development of active immunity and, therefore, if possible, should not be administered during the period of post-exposure prophylaxis.66

Human rabies immunoglobulin

The administration of a single dose of HRIG (refer to 4.16.7 Dosage and administration above), in addition to vaccination, in previously unvaccinated persons is only indicated in certain circumstances as outlined in Figure 4.16.1 or Figure 4.16.2, and as described below. HRIG is given to provide localised anti-rabies antibody protection while the person responds to the rabies vaccine. This should follow adequate wound care (refer to ‘Wound management in post-exposure prophylaxis’ above).

HRIG is not recommended in persons who:
- received the 1st dose (day 0) of vaccine more than 7 days prior to presenting for HRIG (i.e. more than 7 days have elapsed since the 1st dose of vaccine was given)
- have a documented history of previous completed recommended PreP or PEP (refer to 4.16.7 Dosage and administration above)
- have documented evidence of adequate VNA titres (refer to ‘Serological testing following rabies vaccination’ below).

Such persons should receive rabies vaccine only (refer to ‘Post-exposure prophylaxis of persons who have been previously vaccinated’ below).

Although data are limited on the effectiveness of rabies vaccine and HRIG as PEP against infection with lyssaviruses other than classical rabies virus, the available animal data and clinical experience support their use.20,29,34

Post-exposure prophylaxis of persons who have been previously vaccinated

Wound management must still be carried out irrespective of prior rabies vaccination.

Persons who have evidence of a previous completed recommended PreP or PEP regimen, or who have a previously documented adequate VNA titre, require a total of 2 doses of rabies vaccine (refer to Figure 4.16.1 or 4.16.2). This includes immunocompromised individuals; however, VNA levels should be checked after the 2nd dose to ensure they are adequate (refer to ‘Serological testing following rabies vaccination’ below).

Note: PreP or PEP vaccine administered via the ID route is not considered appropriate previous vaccination unless documentation of an adequate VNA titre is available (refer to ‘Serological testing following rabies vaccination’ below).

HRIG is not required and should not be administered, as its use may suppress the level of anamnestic response and circulating VNA.

In cases where a person's vaccination status is unclear but the documentation of a full course of rabies vaccine is not available, the full PEP regimen should be administered.

Post-exposure prophylaxis commenced overseas

Australians travelling abroad who are exposed to a potentially rabid animal (including bats from any country) may be given PEP using vaccines and schedules not used in Australia. In very rare circumstances, if an older nerve tissue-derived rabies vaccine has been administered, any doses given should be disregarded (refer to Table 4.16.2). However, it is most likely that a person vaccinated overseas will have received a cell culture-derived vaccine (refer to ‘Interchangeability of rabies vaccines’ in 4.16.7 Dosage and administration above).27,39 If a person has received a cell culture-derived vaccine abroad, it is recommended that the standard post-exposure prophylaxis regimen be continued in Australia with either HDCV or PCECV.

WHO-approved post-exposure rabies vaccination regimens include:
- Zagreb (2 doses on day 0, doses on days 7 and 21; annotated as 2-0-1-1)
- Essen (doses given on days 0, 3, 7, 14 and 28 (or 30); annotated as 1-1-1-1-1)
- Modified Essen (doses given on days 0, 3, 7 and 14; annotated as 1-1-1-1).

If the PEP was started overseas but HRIG or equine RIG was not given, and the person presents in Australia within 7 days of commencing PEP, HRIG should be given as soon as is practicable (and within 7 days of the 1st rabies vaccine dose). If the person presents in Australia more than 7 days after commencing PEP, then HRIG should not be administered and the appropriate number of remaining doses of rabies vaccine administered.
For these and other scenarios that may arise, Table 4.16.2 outlines the most common PEP regimens that may be commenced overseas and the recommended schedule to complete PEP in Australia.

In the case of PEP commenced overseas, every traveller should be advised to request a PEP certificate from the vaccination centre and to obtain or record the following information (preferably in English):

- the contact details for the clinic attended (telephone and email address)
- the batch and source of RIG used (Note: equine RIG rather than human RIG may be used in some countries)
- the volume of RIG administered
- the type of cell culture vaccine used
- the vaccine batch number
- the number of vials used
- the route of vaccine administration
- the date of RIG and/or vaccine administration.

These details help inform decisions about PEP on return home.

Table 4.16.2: Post-exposure prophylaxis commenced overseas and recommended completion in Australia

<table>
<thead>
<tr>
<th>Vaccine type/route administered overseas/rabies immunoglobulin (RIG)</th>
<th>Rabies vaccine schedule in Australia</th>
<th>HRIG Category III terrestrial animal exposures and Category II and III bat exposures only*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nerve tissue vaccine</td>
<td>Recomence schedule starting from day 0</td>
<td>Administer HRIG if no RIG already given Do not give HRIG if more than 7 days since 1st dose of vaccine (day 0)</td>
</tr>
<tr>
<td>Unsure/unknown/poor documentation</td>
<td>Recomence schedule starting from day 0</td>
<td>Administer HRIG if no RIG already given Do not give HRIG if more than 7 days since 1st dose of vaccine (day 0)</td>
</tr>
<tr>
<td>Well documented, RIG (equine or human) given, plus vaccine given either IM or ID</td>
<td>Align with nearest due dose and resume schedule administering vaccine IM (IM or SC if HDCV used)</td>
<td>No HRIG needed</td>
</tr>
<tr>
<td>2 vaccine doses given IM on day 0</td>
<td>Give a further 2 doses; the 1st dose on day 7 and the 2nd dose on day 14</td>
<td>Administer HRIG if no RIG already given Do not give HRIG if more than 7 days since 1st doses of vaccine (day 0)</td>
</tr>
<tr>
<td>Immunocompromised with vaccines administered</td>
<td>Irrespective of number of previous doses, administer a 5-dose schedule IM (IM or SC if HDCV used) and check serology (refer to ‘Serological testing following rabies vaccination’ below)</td>
<td>Administer HRIG if no RIG already given Do not give HRIG if more than 7 days since 1st dose of vaccine (day 0)</td>
</tr>
</tbody>
</table>

* Refer to Table 4.16.1 (Handbook10-home~handbook10part4~handbook10-4-16#table-4-16-1) Lyssavirus exposure categories and Figures 4.16.1 and 4.16.2 for further information of PEP pathways, including HRIG administration following either a terrestrial animal or bat exposure.

Figure 4.16.1: Post-exposure prophylaxis algorithm for potential exposure to lyssavirus from a terrestrial animal in a rabies-endemic area

Figure 4.16.1: Post-exposure prophylaxis algorithm for potential exposure to lyssaviruses from bats in Australia or overseas

Note: This algorithm is also suitable for potential exposure to a terrestrial animal with a laboratory-confirmed lyssavirus infection in an area where rabies is not enzootic, such as Australia.

* If in doubt, treat as non-immune.
† Previously immunised – documentation of a completed recommended PreP or PEP rabies vaccine regimen. This is irrespective of the time period since the last dose was administered. This may either be a completed primary pre-exposure course or post-exposure course and includes those where subsequent boosting has occurred, or documented rabies antibody (VNAb) titres of ≥0.5 IU/mL.
‡ Non-immune – person who has never received pre- or post-exposure immunisation with rabies vaccine, has had incomplete/inadequate primary vaccination course.
§ Immunocompromised persons, not previously vaccinated, should receive 5 doses of vaccine on days 0, 3, 7, 14 and 28. Serology should be checked 14 to 21 days post dose 5 and a further dose offered if the result is <0.5 IU/mL. In immunocompromised persons, HRIG should be administered if a Category II or III exposure.
¶ Immunocompromised persons, previously immunised, should have serological testing 14 to 21 days after the 2nd dose to confirm acceptable VNAb levels. If the result is <0.5 IU/mL, expert advice should be sought regarding the total number of doses required for PEP.
* If in doubt, treat as non-immune.
† Includes situations where the exposure may be difficult to categorise because a person is unaware or unable to communicate that an exposure has occurred when in close proximity to a bat. ‡ Previously immunised – documentation of a completed recommended PreP or PEP rabies vaccine regimen. This is irrespective of the time period since the last dose was administered. This may either be a completed primary pre-exposure course or post-exposure course and includes those where subsequent boosting has occurred, or documented rabies antibody (VNAb) titres of ≥0.5 IU/mL.
§ Non-immune – person who has never received pre- or post-exposure immunisation with rabies vaccine or has had incomplete/inadequate primary vaccination course.
¶ Immunocompromised persons, previously immunised, should have serological testing 14 to 21 days after the 2nd dose to confirm acceptable VNAb levels. If the result is <0.5 IU/mL, expert advice should be sought regarding the total number of doses required for PEP.
# Immunocompromised persons, not previously vaccinated, should receive 5 doses of vaccine on days 0, 3, 7, 14 and 28. Serology should be checked 14 to 21 days post dose 5 and a further dose offered if the result is <0.5 IU/mL. In immunocompromised persons, HRIG should be administered if a Category II or III exposure.

**Booster doses**

A recent WHO position paper applied a quality assessment of a moderate level of scientific evidence to support that cell culture-derived rabies vaccines induce long-term immunity of at least 10 years. The WHO states that booster doses are not required for persons who are travelling to, or living in, an area of high rabies risk and who have completed a primary course, either pre- or post-exposure, using either of the currently available cell culture-derived vaccines.

Booster doses of rabies vaccine are recommended for immunised persons who have ongoing occupational exposure to lyssaviruses in Australia or overseas (refer to Figure 4.16.3). These include:

- Persons who work with live lyssaviruses in research laboratories who should have rabies neutralising antibody titres measured every 6 months. If the titre is reported as inadequate (<0.5 IU/mL), they should have a booster dose.
- Others with exposures to bats in Australia or overseas, and those who are likely to be exposed to potentially rabid terrestrial mammals overseas, who should have rabies antibody titres measured every 2 years. If the titre is reported as inadequate (<0.5 IU/mL), they should have a booster dose. Alternatively, a booster dose may be offered every 2 years without determining the antibody titre.

Points that should be considered as to whether a person should receive a booster dose of rabies vaccine because their antibody level falls below 0.5 IU/mL are:

- anticipated risk of exposure (i.e. routinely handling sick animals or rabies reservoir species in enzootic areas)
- length of time until the next antibody measurement
- individual health status (consider immunocompromising conditions or a history of poor vaccine response)
- timely access to vaccine and administration should a potential exposure occur.

**Figure 4.16.3: Booster algorithm for persons at ongoing risk of exposure to either rabies or other lyssaviruses, including Australian bat lyssavirus (ABLV)**

Serological testing following rabies vaccination

The WHO defines adequate immunity to rabies virus as the presence of a VNAb titre ≥0.5 IU/mL. Routine serological testing for rabies following PreP or PEP vaccination is not usually necessary. However, persons who are immunocompromised should have their VNAb titres determined 14 to 21 days after the 3rd dose of vaccine in a PreP schedule or after the 5th dose of vaccine in a PEP schedule; a further dose should be given if the titre is reported as inadequate (i.e. <0.5 IU/mL). Serological testing should then be repeated and, if titres remain <0.5 IU/mL, infectious disease specialist advice should be sought.

If PreP was administered via the ID route, the rabies antibody level should be checked 14 to 21 days following completion of the pre-exposure course to ensure VNAb levels are adequate. If inadequate, expert advice should be sought.

Persons who are at risk of repeated exposure to rabies or other lyssaviruses, including ABLV, should have their VNAb titre determined every 6 months to 2 years, depending on the risk of exposure, to assess the need for booster vaccination (refer to ‘Booster doses’ above).

4.16.9 Pregnancy and breastfeeding

Rabies vaccine and HRIG are recommended in pregnant or breastfeeding women following a potential exposure to rabies virus, ABLV or another bat lyssavirus (refer to 4.16.8 Recommendations above and 3.3/Handbook10-home-handbook10part3-handbook10-3-3#3-3) Groups with special vaccination requirements, Table 3.3.1 (Handbook10-home-handbook10part3-handbook10-3-3#table-3-3-1) Recommendations for vaccination in pregnancy).

4.16.10 Contraindications

There are no absolute contraindications to use of either rabies vaccine or HRIG as post-exposure prophylaxis in persons with a potential exposure to rabies or other lyssaviruses, including ABLV. This is because rabies disease is almost always lethal.

Persons with an anaphylactic sensitivity to eggs, or to egg proteins, should not receive PCECV. HDCV should be used instead.

Refer also to 4.16.11 Adverse events below.

4.16.11 Adverse events

Cell culture-derived vaccines are generally well tolerated. In a large study, the following adverse events were reported after administration of HDCV to adults: sore arm (in 15 to 25% of vaccine recipients), headache (in 5 to 8%), malaise, nausea or both (in 2 to 5%), and allergic oedema (in 0.1%). Similar adverse event profiles have been reported for the PCECV; these reactions occur at the same rates in children. Although anaphylactic reactions are rare (approximately 1 per 10 000 vaccinations) following administration of HDCV, approximately 6% of persons receiving booster doses may experience allergic reactions. The reactions typically occur 2 to 21 days after a booster dose, and are characterised by generalised urticaria, sometimes with arthralgia, arthritis, oedema, nausea, vomiting, fever and malaise. These reactions are not life-threatening; they have been attributed to the presence of β-propiolactone-altered human albumin in the implicated vaccines. HRIG has an excellent safety profile and, in general, no chance of immediate hypersensitivity reactions as is more often the case with some equine sources of rabies immunoglobulin.

Management of adverse events

Once initiated, rabies post-exposure prophylaxis should not be interrupted or discontinued because of local reactions or mild systemic reactions. Such reactions can usually be managed with simple analgesics.

Because rabies disease is almost always lethal, the recommended vaccination regimen, in particular the PEP regimen, should be continued even if a significant allergic reaction occurs following a dose of rabies vaccine. Antihistamines can be administered in an attempt to ameliorate any subsequent reactions.

A patient’s risk of developing either lyssavirus infection or rabies must be carefully considered before deciding to discontinue vaccination.

4.16.12 Public health management of lyssavirus infections

Classical rabies virus and ABLV virus infections in humans are notifiable diseases in all states and territories in Australia.

Other lyssavirus cases that do not meet the case definition for ABLV or rabies virus infection are also notifiable in all states and territories in Australia.

Detailed information regarding the management of disease from rabies and other lyssaviruses, including ABLV, can be found in the national guidelines for public health units (http://www.health.gov.au/cdnasongs) and (www.health.gov.au/cdnasongs).

Both HRIG and rabies vaccine are available for PEP from the relevant state/territory health authorities (refer to Appendix 1 Contact details for Australian, state and territory government health authorities and communicable disease control).
Neither of the product information sheets for the two vaccines available in Australia mentions that they can be used for both PreP or PEP as per 4.16.8 Recommendations above. The product information for HDCV recommends a routine 6th dose at 90 days in a PEP regimen. The ATAGI instead recommends that, where indicated, either of the available rabies vaccines can be used as PreP or PEP as per 4.16.8 Recommendations above.

The product information for PCECV recommends a routine 5th dose at 28 days in a PEP regimen and the product information for HDCV recommends a routine 5th and 6th dose at days 30 and 90 respectively, in a PEP regimen. The ATAGI recommends instead that a 4-dose schedule with either cell culture-derived vaccine be used for PEP in immunocompetent persons. A 5th dose at day 28 should be offered to persons who are immunocompromised. Further doses should be offered to persons who are immunocompromised and have an inadequate antibody level following the 5th dose of PEP.

References

...
4.17 Rotavirus

4.17.1 Virology
Rotaviruses are non-enveloped RNA viruses that are classified according to the two surface proteins they contain: VP7, the ‘G’ glycoprotein, and VP4, the protease-cleaved ‘P’ protein. The G and P proteins are targets for the neutralising antibodies that contribute to protection against reinfection and disease.1,2 The two gene segments that encode these proteins can segregate independently, and a binary typing system, consisting of both P and G types, has been developed. Rotavirus strains are most commonly referred to by their G serotype, with G1, G2, G3, G4 and G9 accounting for around 90% of serotypes, both globally and in Australia.3,4 The most common P types found in combination with these G types are P1A[8] (found with all common G types except G2) and P1B[4], usually found in combination with G2.5

4.17.2 Clinical features
Rotavirus is the predominant agent of severe dehydrating gastroenteritis in infants and young children in both developed and developing countries.1,2 The spectrum of rotavirus infection ranges from asymptomatic infection, to mild, watery diarrhoea of limited duration, to severe dehydrating diarrhoea with vomiting, fever, electrolyte imbalance, shock and death. Rotavirus infections are often more severe than other common causes of diarrhoea, and are more likely to result in dehydration and hospitalisation.1,6 The incubation period is 1 to 3 days, after which illness can begin abruptly, with vomiting often preceding the onset of diarrhoea.6 Up to one-third of patients have a temperature of >39°C in the first few days of illness. Symptoms generally resolve in 3 to 7 days.

4.17.3 Epidemiology
Rotaviruses are shed in high concentrations in the stools of infected children and are transmitted by the faecal-oral route, both through close person-to-person contact and via fomites.7 In some instances, rotaviruses might also be transmitted by other modes, such as faecally contaminated food, water and respiratory droplets.4,8

Infection in early childhood is thought to be universal. Although individuals can be infected several times during their lives, the first infection, typically between 3 and 36 months of age, is most likely to cause severe diarrhoea and dehydration.9,10 The degree of protection following natural infection varies. After a single natural infection, 40% of children are protected against any subsequent infection with rotavirus, 75% are protected against diarrhoea from a subsequent rotavirus infection, and 88% are protected against severe diarrhoea.10 Repeat infections provide even greater protection. Prior to the introduction of rotavirus vaccines in Australia, the best available estimates were that approximately 10 000 hospitalisations due to rotavirus occurred each year in children <5 years of age,11 equating to around half the hospitalisations for acute gastroenteritis in this age group.12,13 and affecting 3.8% of all children (1 in 27) by the age of 5 years. In addition to hospitalisations, an estimated 115 000 children <5 years of age visited a GP, and 22 000 children required an emergency department visit due to rotavirus.12,13

Figure 4.17.1: Rotavirus-coded hospitalisations per month, Australia, 2001 to 201017

4.17.4 Vaccines
Two oral rotavirus vaccines are available in Australia, and their efficacy and safety in the prevention of rotavirus gastroenteritis have been extensively evaluated.23-29 Both are live attenuated vaccines administered orally to infants, but the component vaccine viruses differ. The human rotavirus vaccine, Rotarix (GlaxoSmithKline), is a live attenuated vaccine containing one strain of attenuated human rotavirus (G1P[1A][8] strain). Rotarix protects against non-G1 serotypes on the basis of other shared epitopes. A pentavalent vaccine, RotaTeq (CSL Limited/Merck & Co Inc), contains five human–bovine rotavirus reassortants with the human serotypes G1, G2, G3, G4 and P1A[8] and the bovine serotypes G6 and P7.


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There are no data from clinical trials on the use of rotavirus vaccines given in older age groups (refer to available rotavirus vaccines).

Completion of a course of rotavirus vaccine should be with vaccine from the same manufacturer whenever possible. There are very few studies that address the interchangeability of the two available rotavirus vaccines. However, rotavirus circoviruses have been never shown to cause illness in humans and are considered non-pathogenic.

Rotarix – GlaxoSmithKline (live attenuated RIX4414 human rotavirus strain, type G1P1A[8]). Each 1.5 mL monodose pre-filled oral applicator or squeezable tube contains ≥10^9 cell culture infectious dose 50% (CCID50) of the RIX4414 strain; di-sodium adipate; Dulbecco’s Modified Eagle Medium; sterile water. Manufacture involves exposure to bovine-derived material.

RotaTeq – CSL Limited/Merck & Co Inc (live attenuated human-bovine reassortant rotavirus strains, types G1, G2, G3, G4 and P1A[8]). Each 2.0 mL monodose pre-filled dosing tube contains a minimum dose level of at least 2.0 x 10^6 infectious units of each of the rotavirus reassortants G1, G2, G3, G4 and P1A[8]; sodium citrate; sodium phosphate monobasic monohydrate; sodium hydroxide; polysorbate 80; cell culture medium. Manufacture involves exposure to bovine-derived material.

There are no restrictions on the timing of administration of any other live vaccines in relation to rotavirus vaccines, including BCG or oral poliomyelitis vaccine (OPV), for example, in infants who have received OPV overseas. Delay of rotavirus vaccination for 4 weeks following vaccination with BCG or vice versa is not necessary.

Interchangeability of rotavirus vaccines

Completion of a course of rotavirus vaccine should be with vaccine from the same manufacturer whenever possible. There are very few studies that address the interchangeability of the two available rotavirus vaccines. However, if either dose 1 or 2 of vaccine is given as RotaTeq, a 3rd dose of either rotavirus vaccine may be given, provided that the upper age limit and inter-vaccine interval, as defined in Table 4.17.1, are met.

Co-administration with other vaccines

There are no restrictions on the timing of administration of any other live vaccines in relation to rotavirus vaccines, including BCG or oral poliomyelitis vaccine (OPV), for example, in infants who have received OPV overseas. Delay of rotavirus vaccination for 4 weeks following vaccination with BCG or vice versa is not necessary.

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4.17.7 Recommendations

Infants

Administration of a course of oral rotavirus vaccination is recommended for all infants in the first half of the 1st year of life. Vaccination of older infants and children is not recommended as there are theoretical concerns regarding use in older age groups (refer to 4.17.4 Vaccines above). Vaccination should occur at either 2 and 4 months of age (Rotarix), or 2, 4 and 6 months of age (RotaTeq), according to the following schedules and upper age limits (refer to Table 4.17.1). The 1st dose of either rotavirus vaccine can be given as early as 6 weeks of age, where necessary (refer to Table 4.17.1). If the 1st dose is given at 6 weeks of age, the next scheduled rotavirus vaccine dose(s) should still be given according to the age limits specified for dosing in Table 4.17.1 below.

Rotarix (human monovalent rotavirus vaccine)
Infants with underlying conditions predisposing to severe rotavirus gastroenteritis

Infants with underlying conditions predisposing to severe rotavirus gastroenteritis should not be vaccinated until after recovery from their acute illness. Infants with mild gastroenteritis (including mild diarrhoea) can be vaccinated. The use of rotavirus vaccines has not been studies in infants with acute gastroenteritis.

Refer also to 4.17.10 Precautions below for other special risk groups and hospitalised infants.

4.17.8 Pregnancy and breastfeeding

There are no restrictions on the infant’s consumption of food or liquid, including breast milk, either before or after vaccination with either rotavirus vaccine.8,62

Infants living in households of pregnant women can receive rotavirus vaccines. Most pregnant women will have pre-existing immunity to rotavirus, but protection from transmission of wild-type infection through the vaccination of infant contacts may benefit adults, including pregnant women, and outweighs any theoretical concern regarding exposure to vaccine viruses.

4.17.9 Contraindications

The contraindications to rotavirus vaccines are:

- anaphylaxis following a previous dose of either rotavirus vaccine
- anaphylaxis following any vaccine component
- previous history of intussusception or a congenital abnormality that may predispose to IS

The risk of recurrence of IS unrelated to rotavirus vaccination is in the order of 10%.61 In addition, certain congenital malformations affecting the gut (e.g. Meckel’s diverticulum) increase the risk of IS. Because of the possible association of rotavirus vaccination with an increased risk of IS (refer to 4.17.11 Adverse events below), it is considered prudent to withhold administration of rotavirus vaccines to an infant with a previous history of IS or with a known uncorrected congenital malformation associated with increased risk of IS.

- severe combined immunodeficiency (SCID) in infants

Case reports from the United States68-70 indicate prolonged vaccine virus-associated gastrointestinal disease following receipt of rotavirus vaccines among infants with SCID. Because these infants are unlikely to generate a protective immune response to vaccination and because of potential harm, rotavirus vaccines are contraindicated for infants with SCID. For infants with less severe forms of immunocompromise, the risk of vaccine-associated disease is likely to be less than the risk of natural infection (refer to 4.17.10 Precautions below).

4.17.10 Precautions

Infants with acute gastroenteritis

Infants with moderate to severe acute gastroenteritis should not be vaccinated until after recovery from their acute illness. Infants with mild gastroenteritis (including mild diarrhoea) can be vaccinated. The use of rotavirus vaccines has not been studied in infants with acute gastroenteritis.

Infants with moderate to severe illness

As with other vaccines, infants with a moderate to severe illness should be vaccinated after recovery. In addition to the factors mentioned above, this avoids superimposing potential adverse events related to vaccination with the concurrent illness.

Table 4.17.1: Upper age limits for dosing of oral rotavirus vaccines

<table>
<thead>
<tr>
<th>Doses</th>
<th>Age of routine oral administration</th>
<th>Recommended age limits for dosing - 1st dose</th>
<th>Recommended age limits for dosing - 2nd dose</th>
<th>Recommended age limits for dosing - 3rd dose</th>
<th>Minimum interval between doses</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rotarix (GSK)</td>
<td>2 oral doses (1.5mL/dose)</td>
<td>2 and 4 months</td>
<td>6–14* weeks</td>
<td>10–24* weeks</td>
<td>N/A</td>
</tr>
<tr>
<td>RotaTeq (CSL, Limited/Merck &amp; Co Inc)</td>
<td>3 oral doses (2 mL/dose)</td>
<td>2, 4 and 6 months</td>
<td>6–12† weeks</td>
<td>10–32† weeks</td>
<td>14–32† weeks</td>
</tr>
</tbody>
</table>

* The upper age limit for receipt of the 1st dose of Rotarix is immediately prior to turning 15 weeks old, and the upper age limit for receipt of the 2nd dose is immediately prior to turning 25 weeks old.
† The upper age limit for receipt of the 1st dose of RotaTeq is immediately prior to turning 13 weeks old. The 2nd dose of vaccine should preferably be given by 28 weeks of age to allow for a minimum interval of 4 weeks before receipt of the 3rd dose. The upper age limit for the 3rd dose is immediately prior to turning 33 weeks old. For infants presenting for their 2nd dose after reaching 28 weeks of age, a 2nd and final dose can be given, provided the upper age limit of 32 weeks (immediately prior to turning 33 weeks old) has not been reached.

For infants in whom the 1st dose of rotavirus vaccine is inadvertently administered at an age greater than the suggested cut-off (i.e. after the 14th week of age for Rotarix or the 12th week of age for RotaTeq), the remaining vaccine doses should be administered as per the schedule, providing the minimum interval between doses can be maintained within the recommended age limits for subsequent doses. The timing of the 1st dose should not affect the safety and efficacy of the 2nd and 3rd doses. Infants who develop rotavirus gastroenteritis before receiving the full course of rotavirus vaccination should still complete the full 2- or 3-dose schedule (dependent on the brand of vaccine), because one rotavirus infection only provides partial immunity.

Older infants

Vaccination of older infants, children or adults is not recommended. Infants should commence the course of rotavirus vaccination within the recommended age limits for the 1st dose and doses should not be given beyond the upper age limit for the final dose of the vaccine course (refer to ‘Infants’ above). The incidence of severe rotavirus infections decreases with increasing age and the benefit and safety profile of rotavirus vaccination in older infants and children has not been established.

Preterm infants

Vaccination of preterm infants using either rotavirus vaccine is indicated at a chronologic age (without correction for prematurity) of at least 6 weeks, if the infant is clinically stable. Preterm infants (born at <32 weeks gestation) appear to be at increased risk of hospitalisation from viral gastroenteritis.64 In clinical trials, RotaTeq or placebo was administered to 2070 preterm infants (25–36 weeks gestational age; median 34 weeks) who experienced rates of adverse events after vaccination similar to matched placebo recipients.65 Efficacy against rotavirus gastroenteritis of any severity appeared comparable to efficacy in full-term infants (73%; 95% CI: 62 to 85%).66 These conclusions would also be expected to apply to Rotarix vaccine, which appears safe and immunogenic in preterm infants.67 If standard infection control precautions are maintained, administration of rotavirus vaccine to hospitalised infants, including hospitalised preterm infants, would be expected to carry a low risk for transmission of vaccine viruses.

Refer also to 4.17.10 Precautions below for other special risk groups and hospitalised infants.


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Infants who are immunocompromised

There are theoretical concerns that vaccine-associated gastrointestinal disease could occur in immunocompromised infants who receive rotavirus vaccines, and infants with the most severe forms of immunocompromise (SCID) should not receive rotavirus vaccine (refer to 4.17.9 Contraindications above). However, the risk for those infants with less severe immunocompromise may be less than the risk from natural disease. The risks and benefits of vaccination should be considered in the context of the infant’s specific immunocompromise with appropriate specialist advice (refer to 3.3.3 (Handbook 10-home-handbook 10-part3-handbook10-3-383-3-3) Vaccination of immunocompromised persons).

Rotavirus vaccines have been administered to HIV-infected infants in clinical trial settings. 23-38 Specific data on the safety and efficacy of rotavirus vaccines in these infants are limited, but suggest that the vaccines are safe and immunogenic in HIV-infected, but clinically stable, children. 24-27 (Refer also to 3.3.3 (Handbook 10-home-handbook 10-part3-handbook10-3-383-3-3) Vaccination of immunocompromised persons and Table 3.3.4 Categories of immunocompromise in HIV-infected persons, based on age-specific CD4+ counts and percentage of total lymphocytes.) There are no data on the use of rotavirus vaccines in infants born to women who have received immunosuppressive therapy in pregnancy (refer to ‘Use of immunosuppressive therapy during pregnancy’ in 3.3.2 (Handbook 10-home-handbook 10-part3-handbook10-3-383-3-3) Vaccination of women who are planning pregnancy, pregnant or breastfeeding, and preterm infants).

Infants living in households with people who are immunocompromised

Infants living in households with immunocompromised persons should be vaccinated. In general, immunocompromised household members are afforded protection by vaccination of young children in the household and this is considered to outweigh the risk of transmitting vaccine virus shed in stools to the immunocompromised household member. However, there have been no studies to specifically address this question. 28 Hand washing and the careful disposal of soiled nappies are likely to minimise any risk of vaccine transmission to other household members. (Refer also to 3.3.3 (Handbook 10-home-handbook 10-part3-handbook10-3-383-3-3) Vaccination of immunocompromised persons.)

Recent administration of antibody-containing blood products

Infants who have recently received antibody-containing blood products and are at an eligible age should be vaccinated. The interval between vaccination and receipt of the blood product should be as long as possible, but without delaying administration of vaccine beyond the suggested age limits for dosing (as per Table 4.17.1 above). This recommendation for maximising the interval between receipt of antibody-containing blood products and rotavirus vaccination is based on theoretical concern that passively acquired antibody to rotavirus may interfere with vaccine immunogenicity. 6

Hospitalised infants

Administration of rotavirus vaccine to hospitalised infants, including premature infants, is likely to carry a low risk for transmission of vaccine viruses if standard infection control precautions are maintained. Provided that the infant is medically stable, vaccination should not be delayed, particularly if the delay would result in an infant being beyond the upper age limit for vaccination (refer to 4.17.7 Recommendations above). If a recently vaccinated child is hospitalised for any reason, no precautions other than routine standard precautions need to be taken to prevent the spread of vaccine virus in the hospital setting.

4.17.11 Adverse events

Intussusception

Although clinical trials of the two available vaccines did not find an association between vaccination and intussusception (IS) 39 (refer to 4.17.4 Vaccines above), one post-marketing study in Australia found evidence of a 4- to 5-fold increase in the risk of IS in the 7 days following the 1st dose of either Rotarix or RotaTeq. 40 However, no overall increase in the risk of IS was detectable over the first 9 months of life. 41 A similar apparent increase in risk for IS following the 1st dose of Rotarix has been observed in Mexico, and a smaller increase after the 2nd dose of Rotarix in Brazil. 42 A study in the United States found no increased risk of IS following RotaTeq; however, the study was limited by small numbers, which reduced power to determine a lower range risk increase. 43 A subsequent Australian study estimated the increased risk of IS to be approximately 9-fold in the 1st 7 days after dose 1, and 2-fold in the first 7 days after dose 2 of either vaccine. 44 The baseline risk of intussusception for Australian infants is around 80 cases per 100,000 infants. 45 The increased risk of IS following rotavirus vaccination, from the most recent Australian study, is estimated as approximately 6 additional cases of intussusception among every 100,000 infants vaccinated, or 14 additional cases per year in Australia. 46 This estimate assumes that infants in which an episode of IS occurs shortly after vaccination (refer to 4.17.9 Contraindications above). However, the risks and benefits of vaccination should be considered in the context of the infant’s specific immunocompromise and how to be alert for the signs and symptoms of the condition.

Rotavirus vaccine should not be given to an infant who has had a confirmed intussusception because there may be an increased risk of the condition recurring (refer to 4.17.9 Contraindications above).

Other adverse events

No significant increase in post-vaccination vomiting, diarrhoea or fever has been reported during follow-up of several thousand recipients of Rotarix compared to those who were unvaccinated. 36-37 Detailed follow-up of 11,700 recipients of RotaTeq or placebo reported no increase in fever or irritability in the week after vaccination among vaccinated infants, but a small increase in the incidence of vomiting (7% versus 5%) and diarrhoea (10% versus 9%). 38 Vomiting and diarrhoea have not emerged as important adverse events following immunisation in post-marketing surveillance of rotavirus vaccines.

Infants who report an episode of diarrhoea or vomiting following vaccination should still receive subsequent rotavirus vaccine doses, as required and age eligible. The potential causes of diarrhoea/vomiting following vaccination include: gastroenteritis unrelated to rotavirus vaccination or infection (e.g. another viral agent); natural rotavirus infection (as vaccination is neither indicated, nor contraindicated in that condition); other naturally occurring or vaccine virus (as vaccine virus shedding occurs commonly after vaccination (refer to 4.17.4 Vaccines above). Specific testing is required to differentiate between vaccine virus and natural infection; however, this is rarely clinically indicated.

4.17.12 Variations from product information

The product information for Rotarix states that the vaccine should not be administered to subjects with any chronic gastrointestinal disease. The ATAGI recommends instead that pre-existing chronic gastrointestinal disease is not a contraindication to rotavirus vaccination, with the exception of those conditions that may predispose to IS (refer to 4.17.9 Contraindications and 4.17.10 Precautions above).

The product information for RotaTeq states that in the event that a dose of vaccine is spat out or vomited post vaccination, a replacement dose should not be given. The ATAGI recommends instead that if most of a dose is spat out or vomited then a single replacement dose may be given (refer to 4.17.6 Dosage and administration above.)

References


Infectious Diseases


Rubella is an envelo povirus, genus Rubivirus. The virus has an RNA genome and is closely related to group A arboviruses, but does not require a vector for transmission. It is relatively unstable, and is inactivated by lipid solvents, trypsin, formalin, extremes of heat and pH, and light.1

4.18.2 Clinical features
Rubella is generally a mild and self-limiting infectious disease, spread from person to person by respiratory secretions, possibly including aerosol transmission.1,2 It causes a transient, generalised, erythematous, maculopapular rash; lymphadenopathy involving the post-auricular and sub-occipital glands; and, occasionally, arthritis and arthralgia. Other complications, such as neurological disorders and thrombocytopenia, may occur but are rare. Clinical diagnosis is unreliable since the symptoms are often fleeting and can be caused by other viruses; in particular, the rash is not unique to rubella and may be absent.1,2 Up to 50% of rubella virus infections are subclinical or asymptomatic.1 A history of rubella should, therefore, not be accepted without serological evidence of previous infection.1 The incubation period is 14 to 21 days, and the period of infectivity is from 1 week before until 4 days after the onset of the rash.2

Rubella infection in pregnancy can result in fetal infection, causing congenital rubella syndrome (CRS) in a high proportion of cases. Up to 90% of infants born to women who had rubella infection in the first trimester of pregnancy have abnormalities (often multiple) characteristic of CRS.3-5 The risk of damage declines to 10 to 20% by 16 weeks gestation. After this stage of pregnancy, fetal damage is rare but has been reported up to 20 weeks gestation.2 The characteristics of CRS include intellectual disabilities, cataracts, deafness, cardiac abnormalities, intrauterine growth retardation, and inflammatory lesions of the brain, liver, lungs and bone marrow.2 Any combination of these defects may occur, but defects that commonly occur alone following infection after the first 8 weeks of pregnancy are deafness and pigmentary retinopathy. Some infected infants may appear normal at birth, but defects, especially sensorineural deafness, may be detected later.6

Rubella vaccination has been reported in some persons who already have either natural or vaccine-induced antibody.5 Occasional cases of CRS after reinfection in pregnancy have been documented. However, fetal damage is very rare in cases of infection in women in whom antibody has previously been detected.4,5-8

4.18.3 Epidemiology
Evidence suggests that endemic rubella is well controlled in Australia.10 The incidence of rubella has fallen rapidly since vaccine registration, and notifications of rubella have been low since high vaccine coverage was achieved with the National Measles Control Campaign in late 1998 and then maintained.15 Since 2003, rubella notifications in Australia have been less than 0.3 per 100 000. There has been a shift in the age distribution of cases, with comparatively more cases seen in older age groups, particularly the 25–29 years age group.15

Rubella vaccines have been registered in Australia since 1970, and mass vaccination of schoolgirls commenced in 1971.1,13 Non-pregnant, seronegative adult women were also vaccinated. These programs were successful and there was a significant reduction in the incidence of CRS from 1977.12-14 Successful vaccination campaigns and high vaccination coverage resulted in no cases of congenital rubella syndrome occurring in infants of Australian-born mothers between 1982 and 2002. However, 5 cases resulting from infection acquired outside of Australia were reported during this time.13 In 2003, 2 cases of CRS occurred in Australian-born mothers from infection that occurred in Australia,15 which reinforces the need for high vaccination coverage of women of child-bearing age. Between 2004 and 2008, 2 confirmed cases of CRS were reported in Australia, in children whose mothers were born outside Australia.16,17,19

There has also been a significant increase in the percentage of pregnant women immune to rubella (e.g. in New South Wales from 62% in 1971 to 96% in 1983).20 Based on a study conducted in Melbourne in 2000, it was estimated that only 2.5% of women of child-bearing age in Australia were seronegative.21 However, susceptibility was higher among certain groups of women, particularly overseas-born women (refer to ‘Women of child-bearing age, including post-partum women’ in 4.18.7 Recommendations below).21

Young adults may not be immune to rubella, because they did not receive a measles-mumps-rubella (MMR) vaccine.22 The MMR vaccination program for all adolescents replaced the rubella program for girls in 1993/94.17 A serosurvey conducted in 1999 showed that only 84% of males aged 14–18 years (compared to 95% of females) and 89% of males aged 19–49 years (compared to 98% of females) were immune to rubella.23 For this reason, young adult males, as well as females, who do not have a documented history of receipt of 2 doses of MMR vaccine should be vaccinated (refer to 4.18.7 Recommendations below).21 This is both for their own protection and to prevent transmission of the infection in the community.

Goals for the elimination of rubella and CRS have been set by a number of World Health Organization (WHO) regions, and elimination has been declared for the Pan American Organization.22 The WHO Western Pacific Region has set goals for increased rubella and CRS control efforts, with a number of member states yet to incorporate rubella vaccination into their routine schedule.23 As with elimination of measles, rubella and CRS elimination requires continued strengthening of immunisation and surveillance efforts, particularly identification of rubella virus genotypes to confirm the absence of an endemic strain.24

4.18.4 Vaccines
Monovalent rubella vaccine is not available in Australia. Rubella vaccination is provided using either MMR or measles-mumps-rubella-varicella (MMRV) vaccines. Two combination vaccines containing live attenuated measles, mumps, rubella and varicella viruses (MMRV) are registered in Australia.

A single dose of rubella vaccine produces an antibody response in over 95% of vaccine recipients, but antibody levels are lower than after natural infection.2,7,8 A 2nd dose aims to confer immunity in those who fail to seroconvert to the 1st dose. Vaccine-induced antibodies have been shown to persist for at least 16 years in the absence of endemic disease.4,5,8,24,27 Protection against clinical rubella appears to be long-term in those who seroconvert.9

Combination MMRV vaccines have been shown, in clinical trials, to produce similar rates of seroconversion to all four vaccine components compared with MMR and monovalent varicella vaccines administered concomitantly at separate injection sites.26-31

Combination measles-mumps-rubella (MMR) vaccines

- **M-M-R II** – bioCSL Pty Ltd (live attenuated measles virus (Enders’ attenuated Edmonston strain), mumps virus (Jeryl Lynn B level strain) and rubella virus (Wistar RA 27/3 strain)). Lyophilised pellet in a monodose vial with separate diluent. Each 0.5 mL reconstituted dose contains ≥1000 tissue culture infectious dose 50% (TCID50) of measles virus, ≥12 500 TCID50 of mumps virus, and ≥1000 TCID50 of rubella virus; 14.5 mg sorbitol; 1.9 mg sucrose; 14.5 mg hydrolysed porcine gelatin; ≤0.3 mg recombinant human albumin; ≤1 ppm fetal bovine serum; 25 µg neomycin.
Combination measles-mumps-rubella-varicella (MMRV) vaccines

- **Priorix-tetra** – GlaxoSmithKline Australia Pty Ltd (live attenuated measles virus (Schwarz strain), mumps virus (RIT 4385 strain, derived from the Jeryl Lynn strain), rubella virus [Wistar RA 27/3 strain] and varicella-zoster virus (Oka strain)). Lyophilised pellet in a monodose vial with a pre-filled diluent syringe. Each 0.5 mL reconstituted dose contains ≥10^10 TCID\text{50} of measles virus, ≥10^7 TCID\text{50} of mumps virus, and ≥10^3.00 TCID\text{50} of rubella virus; lactose; neomycin; sorbitol; mannitol.

- **ProQuad** – bioCSL Pty Ltd (live attenuated measles virus [Enders’ attenuated Edmonston strain], mumps virus [Jeryl Lynn B level strain], rubella virus [Wistar RA 27/3 strain] and varicella-zoster virus [Oka/Merck strain]). Lyophilised powder in a monodose vial with a pre-filled diluent syringe. Each 0.5 mL reconstituted dose contains ≥10^5.00 TCID\text{50} of measles virus, ≥10^4.00 TCID\text{50} of mumps virus, ≥10^3.20 TCID\text{50} of rubella virus, and ≥10^3.99 PFU of varicella-zoster virus; 20 mg sucrose; 11 mg hydrosolysed porcine gelatin; 2.5 mg urea; 16 mg sorbitol; 0.38 mg monosodium L-glutamate; 0.25 mg recombinant human albumin; 5 µg neomycin; residual components of MRC-5 cells; 0.5 µg bovine serum albumin.

4.18.5 Transport, storage and handling

Transport according to National vaccine storage guidelines: Strive for 5. Store at +2°C to +8°C. Do not freeze. Protect from light.

Both MMR and MMRV vaccines must be reconstituted by adding the entire contents of the diluent container to the vial containing the pellet and shaking until the pellet is completely dissolved.

Reconstituted Priorix (MMR) and Priorix-tetra (MMRV) vaccines should be used as soon as practicable. If storage is necessary, hold at +2°C to +8°C for not more than 8 hours.

Reconstituted ProQuad (MMRV) vaccine should be reconstituted immediately. If storage is necessary, hold at +2°C to +8°C for not more than 2.5 hours or at +20°C to +25°C for not more than 1 hour.

4.18.6 Dosage and administration

The dose of Priorix (MMR) vaccine for both children and adults is 0.5 mL, to be given by either SC or IM injection.

The dose of M-M-R II (MMR) vaccine for both children and adults is 0.5 mL, to be given by SC injection.

For children <14 years of age, the dose of MMRV vaccine is 0.5 mL, to be given by SC injection. Priorix-tetra may also be given by IM injection.

MMRV vaccines are not recommended for use in persons aged ≥14 years.

When 2 doses of MMR-containing vaccine are required, the minimum interval between doses is 4 weeks.

Co-administration with other vaccines

MMR or MMRV vaccines can be given at the same time as other live attenuated parenteral vaccines (e.g. varicella, BCG, yellow fever) or other inactivated vaccines (including DTPa, hepatitis B, Hib, IPV, MenCCV, hepatitis A and pneumococcal conjugate vaccine), using separate syringes and injection sites. If MMR or MMRV vaccine is not given simultaneously with other live attenuated parenteral vaccines, they should be given at least 4 weeks apart.

If MMR vaccine is given at the same time as monovalent varicella vaccine (VV), they should be given using separate syringes and injection sites. MMR vaccine and monovalent VV should not be mixed together prior to injection.

Separate administration of measles, mumps or rubella vaccine is not available as an alternative to MMR vaccine, although a monovalent varicella vaccine is available (refer to 4.22).

Interchangeability of MMR-containing vaccines

In general, the two brands of MMR vaccine can be considered interchangeable, that is, the 2nd MMR dose does not have to be of the same brand as the 1st. The same principle applies to the two available MMRV vaccines, although they are not routinely recommended in a 2-dose schedule.

4.18.7 Recommendations

For further information on the recommendations for MMR and MMRV vaccines, refer to 4.9. Measles and 4.22. Vircella.

The principal aim of rubella vaccination is to prevent congenital rubella syndrome by stopping the circulation of rubella virus in the community. Susceptible pregnant women will continue to be at risk of rubella infection in pregnancy until the transmission of rubella virus is interrupted by continued high-level coverage of rubella-containing vaccine.

A history of rubella is not a contraindication to vaccination. Persons who are already immune to rubella have no increased risk of side effects from vaccination.

Infants aged <12 months

MMR-containing vaccines are not routinely recommended for infants <12 months of age. However, MMR vaccine can be given to children from as early as 9 months of age in high-risk circumstances (refer to 4.9).

If MMR vaccine is given <12 months of age, there is still a need for 2 vaccine doses to be administered at ≥12 months of age (refer to 4.9).

Children

Two doses of rubella-containing vaccine are recommended for all children. The 1st dose should be given at 12 months of age as MMR vaccine. MMRV vaccines are not recommended for use as the 1st dose of MMR-containing vaccine in children <4 years of age, due to a small but increased risk of fever and febrile seizures when given as the 1st MMR-containing vaccine dose in this age group (refer to Table 4.9.1).

If MMR vaccine is given <12 months of age, there is still a need for 2 vaccine doses to be administered at ≥12 months of age (refer to 4.9).

The 2nd dose of rubella-containing vaccine is recommended to be given routinely at 18 months of age as MMR vaccine. This is to commence from July 2013, once MMR vaccine(s) are available under the NIP (refer to Table 4.9.1).

The recommended age for administration of the 2nd dose of rubella-containing vaccine will be moved down from 4 years of age, to provide earlier 2-dose protection against measles, mumps and rubella, and to improve vaccine uptake (refer to 4.18.3 Epidemiology above).

Persons who are immunocompromised
Anaphylaxis to vaccine components
Refer also to 3.3
There is no risk to pregnant women from contact with recently vaccinated persons. The vaccine virus is not transmitted from vaccinated persons to susceptible contacts.

MMRV vaccines are not recommended for use in persons aged ≥14 years.
because of breastfeeding.

Rubella-containing vaccines are contraindicated for use in persons aged ≥14 years. However, parents/carers should be advised regarding the small but increased risk of fever and febrile seizures (compared with that expected following MMR vaccine).

Adults and adolescents
Two doses of rubella-containing vaccine are recommended for all non-immune adolescents and adults (refer to 4.9/Handbook10-home-handbook10part4-handbook10-4-9#4-9) Measles.

All persons born between or after 1966 who are ≥18 months of age (or, until catch-up following the move of the 2nd NIP dose of measles-containing vaccine to 18 months of age is completed, are ≥4 years of age) should have documented evidence of 2 doses of MMR-containing vaccine (administered at least 4 weeks apart with both doses administered at ≥12 months of age) or have serological evidence of protection for measles, mumps and rubella.

It is particularly important to ensure that women of child-bearing age are immune to rubella (refer to ‘Women of child-bearing age, including post-partum women’ below). It is recommended that all males born during or after 1966 (particularly those born from 1966 up to the 1990s) have their vaccination records reviewed to ensure they have received 2 doses of MMR vaccine, as they are more likely, than females, to have not received 2 doses of rubella-containing vaccine (refer to 4.18.3 Epidemiology above).

If a dose of MMR vaccine is inadvertently given to an older person, this dose does not need to be repeated.

Healthcare workers and those who work with children
All healthcare workers and persons working with children, born during or since 1966, either without vaccination records or seronegative upon screening, should receive 2 doses of MMR vaccine, both for their own protection and to avoid the risk of transmitting rubella to pregnant women25 (refer to 3.3/Handbook10-home-handbook10part3-handbook10-3-3) Groups with special vaccination requirements, Table 3.3.7(Handbook10-home-handbook10part3-handbook10-3-3#table-3-3-7) Recommended vaccinations for persons at increased risk of certain occupationally acquired vaccine-preventable diseases).

Women of child-bearing age, including post-partum women
Every effort should be made to identify and immunise non-pregnant seronegative women of child-bearing age (refer to ‘Serological testing for immunity to rubella’ below). The following women are more likely to be seronegative to rubella: women born overseas (especially in Asia, Pacific islands, sub-Saharan Africa and South America) who entered Australia after the age of routine vaccination; Indigenous women living in rural and remote regions; non-English speaking women; women over the age of 35 years; and Australian-born Muslim women.12,13,21,36-38

Seronegative women should be given MMR vaccine and advised to avoid pregnancy for 28 days after vaccination. Vaccinated women should be tested for seroconversion 6 to 8 weeks after vaccination (refer to ‘Serological testing for immunity to rubella’ below). Women who have negative or very low antibody levels after vaccination should be revaccinated. However, if antibody levels remain low after a 2nd documented vaccination, it is unlikely that further vaccinations will improve this.2 Further testing and vaccination is not usually warranted; however, consultation with the laboratory that performed the serological testing may also be helpful (refer also to ‘Serological testing for immunity to rubella’ below). Negative serology after 2 documented doses of rubella-containing vaccine may represent a false negative (i.e. an antibody titre too low to be detected using routine commercial assays).

Although 2 doses of MMR vaccine are routinely recommended, if rubella immunity is demonstrated after receipt of 1 dose of a rubella-containing vaccine, no further dose is required, unless indicated by subsequent serological testing (refer to ‘Serological testing for immunity to rubella’ below) or if indicated for protection against measles and mumps (refer to 4.9 (Handbook10-home-handbook10part4-handbook10-4-9) Measles and 4.11(Handbook10-home-handbook10part4-handbook10-4-11) Mumps).

Women found to be seronegative on antenatal testing for rubella immunity should be vaccinated after delivery and before discharge from the maternity unit, as discussed above. These women should be tested for rubella immunity 6 to 8 weeks following vaccination.1,7 (Refer also to ‘Serological testing for immunity to rubella’ below.)

Serological testing for immunity to rubella
Serological testing for immunity to rubella after routine vaccination of children is not recommended. However, serological testing for rubella immunity can be performed in cases where a history of natural immunity or 2 doses of vaccine administration is uncertain. It is particularly important to ensure that women of child-bearing age are immune to rubella (refer to ‘Women of child-bearing age, including post-partum women’ above).

A number of commercial assays for testing immunity to rubella are available. These vary according to the method used to determine the positive cut-off value (the WHO cut-off is 10 IU/mL, but, at present, there is no recommended Australian minimal level). Available data support the presumption that an antibody level found by use of a licensed assay to be above the standard positive cut-off for that assay can be considered evidence of past exposure to rubella virus.7 Rubella virus induces immune responses that are similar in quality, but lesser in quantity, than those after natural disease.7 Measurement of antibody by commercial assays is not a perfect correlate of protection in vaccinated persons.8 While on the one hand, those with low levels of vaccine-induced antibodies are often protected, conversely, reinfection may take place in some individuals with measurable antibodies. If a person is found to be rubella IgG seronegative, vaccination should be provided according to the recommendations above. Interpretation of the results of serological testing may be enhanced by discussion with the laboratory that performed the test, ensuring that relevant clinical information is provided. In addition, expert consultation and referral of sera to a reference laboratory are recommended if there is difficulty interpreting results, particularly for women of child-bearing age (refer to ‘Women of child-bearing age, including post-partum women’ above).

All women of child-bearing age should be advised by a medical practitioner of the result of their antibody test, as it is a clinically significant test.9 Women should be screened for rubella antibodies shortly before every pregnancy, or early in the pregnancy, or if pregnancy is contemplated, irrespective of a previous positive rubella antibody result.3,4 Very occasionally, errors may result in patients who are seronegative being reported as seropositive. Specimens from pregnant women are required to be stored until the completion of the pregnancy for parallel serological testing if required.40

4.18.8 Pregnancy and breastfeeding
Rubella-containing vaccines are contraindicated in pregnant women (refer to 4.18.9 Contraindications below). Pregnancy should be avoided for 28 days after vaccination.61

MMR vaccines can be given to breastfeeding women. The rubella vaccine virus may be secreted in human breast milk, and rare cases of transmission of vaccine virus through breast milk have been reported. However, symptoms in the newborn have been absent or mild.42-44 Post-partum vaccination of women without evidence of rubella immunity need not be delayed because of breastfeeding.

MMRV vaccines are not recommended for use in persons aged ≥14 years.

There is no risk to pregnant women from contact with recently vaccinated persons. The vaccine virus is not transmitted from vaccinated persons to susceptible contacts.1 Refer also to 3.3 Groups with special vaccination requirements, Table 3.3.1 Recommendations for vaccination in pregnancy for more information.

4.18.9 Contraindications
Anaphylaxis to vaccine components
MMR and MMRV vaccines are contraindicated in persons who have had:

• anaphylaxis following a previous dose of any MMR-containing vaccine
• anaphylaxis following any vaccine component.

Persons who are immunocompromised
Measles-, mumps-, and rubella-containing vaccines contain live attenuated vaccine viruses and are contraindicated in persons who are immunocompromised. Thus, MMR-containing vaccines are contraindicated in the following groups: http://www.immunise.health.gov.au/internet/immunise/publishing.nsf/Content/Handbook10-home 213/278
susceptible women were inadvertently vaccinated while pregnant or became pregnant within 3 months after vaccination. There were no CRS-related abnormalities among the infants born to these women.\(^{54}\) Based on this evidence, the vaccine cannot be considered to be teratogenic, and termination of pregnancy following inadvertent vaccination is not indicated.\(^{1,8}\) (Refer also to 3.3.2(Handbook10-home\~handbook10part3\~handbook10-3-3) Vaccination of women who are planning pregnancy, pregnant or breastfeeding, and preterm infants.)

4.18.10 Precautions

For additional precautions related to MMR and MMRV vaccines, refer to 4.9(Handbook10-home\~handbook10part4\~handbook10-4-9) Measles and 4.22(Handbook10-home\~handbook10part4\~handbook10-4-22) Varicella.

Vaccination with other live attenuated parenteral vaccines

If MMR or MMRV vaccine is not given simultaneously with other live attenuated parenteral vaccines (e.g. varicella, BCG, yellow fever), the vaccines should be given at least 4 weeks apart.

Vaccination after immunoglobulin or blood product administration

Administration of a MMR or MMRV vaccine should be delayed after administration of immunoglobulin-containing products. After receipt of immunoglobulin-containing blood products, the expected immune response to measles, mumps, rubella and varicella vaccination may be impaired.\(^{7,55-58}\) MMR-containing vaccines should not be given for between 3 and 11 months following the administration of immunoglobulin-containing blood products. The interval between receipt of the blood product and vaccination depends on the amount of immunoglobulin in each product, and is indicated in 3.3 Groups with special vaccination requirements, Table 3.3.6 Recommended intervals between either immunoglobulins or blood products and MMR, MMRV or varicella vaccination.\(^{59}\) For further information, refer to 3.3.3(Handbook10-home\~handbook10part3\~handbook10-3-3) Vaccination of recent recipients of normal human immunoglobulin and other blood products.

Recent blood transfusion with washed red blood cells is not a contraindication to MMR or MMRV vaccines.

MMR vaccine may be administered concomitantly with, or at any time in relation to, anti-D immunoglobulin, but at a separate injection site. Anti-D immunoglobulin does not interfere with the antibody response to vaccine.\(^{1,3,8}\)

Immunoglobulin or blood product administration after vaccination

Immunoglobulin-containing products should not be administered for 3 weeks following vaccination with rubella-containing vaccines, unless the benefits exceed those of vaccination. If immunoglobulin-containing products are administered within this interval, the vaccinated person should either be revaccinated later at the appropriate time following the product (as indicated in Table 3.3.6), or be tested for immunity 6 months later and then revaccinated if seronegative.

Rh (D) immunoglobulin (anti-D) may be given at the same time in different sites with separate syringes or at any time in relation to MMR vaccine, as it does not interfere with the antibody response to the vaccine.

4.18.11 Adverse events

Adverse events following administration of MMR-containing vaccines are generally mild and well tolerated.\(^{7}\) Adverse events are much less common after the 2nd dose of MMR or MMRV vaccine than after the 1st dose.

Mild adverse events such as fever, sore throat, lymphadenopathy, rash, arthralgia and arthritis may occur following MMR vaccination.\(^{1,7}\) Symptoms most often begin 1 to 3 weeks after vaccination and are usually transient.

Thrombocytopenia (usually self-limiting) has been very rarely associated with the rubella or measles component of MMR vaccine, occurring in 3 to 5 per 100000 doses of MMR vaccine administered.\(^{7,57-58}\) This is considerably less frequent than after natural measles, mumps and rubella infections.\(^{59}\) Persons with egg allergy can be safely given MMR or MMRV vaccine (refer to 4.9.11 Adverse events in 4.9 Measles).

For further information on adverse events related to MMR and MMRV vaccines, refer to 4.9(Handbook10-home\~handbook10part4\~handbook10-4-9) Measles and 4.22(Handbook10-home\~handbook10part4\~handbook10-4-22) Varicella.

4.18.12 Public health management of rubella

Rubella is a notifiable disease in all states and territories in Australia.

Further instructions about the public health management of rubella, including management of cases of rubella and their contacts, should be obtained from state/territory government health authorities (refer to Appendix 1(Handbook10-home\~handbook10-part10\~handbook10-appendices\~handbook10-appendix1) Contact details for Australian, state and territory government health authorities and communicable disease control).

Rubella-containing vaccine does not provide protection if given after exposure to rubella.\(^{7}\) However, if the exposure did not result in infection, the vaccine would induce protection against subsequent infection. Normal human immunoglobulin (NHIG) has been shown not to be of value in post-exposure prophylaxis for rubella.\(^{7}\) However, NHIG may be recommended in certain circumstances (refer to ‘Use of normal human immunoglobulin in pregnant women exposed to rubella’ below).

Suspected rubella contacts

All contacts of persons with suspected rubella infection should be identified, especially those who are pregnant (refer to ‘Pregnant women with suspected rubella or exposure to rubella’ below).
The product information for MMR and MMRV vaccines recommends that women of child-bearing age should be advised not to become pregnant for 3 months after vaccination. According to variations from product information indicated for such women with low antibody titres in high-risk occupations, pregnant women should be counselled to restrict contact with persons with confirmed, probable or suspected rubella for 6 weeks (2 incubation periods). Exposed healthcare workers without adequate proof of immunity should be excluded from work for 21 days from exposure or for at least 4 days after the onset of rash.

Testing for rubella infection

All cases of suspected rubella infection should be laboratory tested and false positive results excluded (refer to ‘Serological testing for immunity to rubella’ in 4.18.7 Recommendations above).

Acute rubella infection is indicated by the presence of rubella IgM or a 4-fold or greater increase in rubella IgG. Rubella IgM may not appear until a week after clinical symptoms. Sera for testing should be taken to be examined between days 7 to 10 days after onset of illness and repeated to 3 weeks later. The most recent date of potential exposure should be obtained, if possible, to calculate the potential incubation period. Some patients may have more than one exposure to a person with a rubella-like illness, and because exposure may occur over a prolonged period, it is important to ascertain the dates of the first and last exposures. Testing for infection can also be done, particularly early in the course of a clinical illness, using virus-detection methods, such as nucleic acid amplification testing (PCR).

Infected persons should be excluded from school/work/institution and should avoid contact with women of child-bearing age for at least 4 days after the onset of rash.

Pregnant women with suspected rubella or exposure to rubella

All pregnant women with suspected rubella or exposure to rubella should be serologically tested (for IgM and IgG), irrespective of a history of prior vaccination, clinical rubella or a previous positive rubella antibody result (for more details, refer to ‘Testing for rubella infection’ above). Testing is essential because of the serious consequences of the infection, the rash of rubella is not diagnostic, asymptomatic infection can occur, and the diagnosis requires confirmation by laboratory tests. In addition, infection has been reported in women who have previous evidence of antibody.

Serologic specimens should include information regarding the date of the last menstrual period and the date of presumed exposure (or date of onset of symptoms) if the woman has an antibody titre below the protective level, or a low level of antibodies and remains asymptomatic, a second specimen should be collected 28 days after the exposure (or onset of symptoms) and tested in parallel with the first. Alternatively, if the woman develops symptoms/signs of rubella infection, a second serum specimen should be tested as soon as possible. A third blood specimen may be required in some circumstances. Testing for infection can also be done, particularly early in the course of a clinical illness, using virus-detection methods, such as nucleic acid amplification testing (PCR).

Pregnant women should be counselled to restrict contact with persons with confirmed, probable or suspected rubella for 6 weeks (2 incubation periods). Counselling of pregnant women with confirmed rubella infection should include preventing the risk to the fetus should be given in conjunction with the woman’s obstetric service.

Use of normal human immunoglobulin in pregnant women exposed to rubella

Post-exposure prophylaxis with normal human immunoglobulin (NHIG) does not prevent infection in non-immune contacts and is, therefore, of little value for protection of susceptible contacts exposed to rubella. However, it may prolong the incubation period. If given to non-immune pregnant contacts, this may marginally reduce the risk to the fetus. It may also reduce the likelihood of clinical symptoms in the mother. In such cases, IM administration of 20 mL of NHIG within 72 hours of rubella exposure might reduce, but will not eliminate, the risk for rubella. Serological follow-up of recipients is essential, and should continue for up to 2 months.

There is some evidence to suggest that, in outbreak situations, pre-exposure NHIG may be effective in preventing infection in women who are likely to be pregnant, and its use may be indicated for such women with low antibody titres in high-risk occupations.

4.18.13 Variations from product information

The product information for MMR and MMRV vaccines recommends that women of child-bearing age should be advised not to become pregnant for 3 months after vaccination. The ATAGI instead recommends avoiding pregnancy for 28 days after vaccination.

For further information on MMR and MMRV vaccines, refer to 4.9-handbook10-home (handbook10part4-handbook10-4-9) Measles and 4.22 (Handbook10-home-handbook10part4-handbook10-4-22) Varicella.

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4.19 Tetanus

4.19.1 Bacteriology

Tetanus is caused by Clostridium tetani, a motile, non-capsulated, Gram-positive rod that forms endospores. Spores of the bacillus are found in manured soil and can enter wounds. Once in a wound site, the bacillus can grow anaerobically. C. tetani produces a potent protein toxin, which has two components, tetanospasmin (a neurotoxin) and tetanolysin (a haemolysin).

4.19.2 Clinical features

Tetanus is an acute, often fatal, disease caused by the toxin produced by C. tetani. The neurotoxin acts on the central nervous system to cause muscle rigidity with painful spasms. The disease usually occurs after an incubation period of 3 to 21 days (range 1 day to several months), with a median time of onset after injury of 10 days. Generally, a shorter incubation period is associated with a more heavily contaminated wound, more severe disease and a worse prognosis. Generalised tetanus, the most common form of the disease, is characterised by increased muscle tone and generalised spasms. Early symptoms and signs include increased tone in the masseter muscles (trismus, or lockjaw), dysphagia, and stiffness or pain in the neck, shoulder and back muscles. Some patients develop paroxysmal, violent, painful, generalised muscle spasms. A constant threat during generalised spasms is reduced ventilation, apnoea or laryngospasm. The patient may be febrile, although many have no fever; mental state is unimpaired. Sudden cardiac arrest sometimes occurs, but its basis is unknown. Other complications include pneumonia, fractures, muscle rupture, deep vein thrombophlebitis, pulmonary emboli, decubitus ulcers and rhabdomyolysis. Death results from respiratory failure, hypertension, hypothermia or cardiac arrhythmia.

Tetanus is uncommon in people who have received 4 or more doses of a tetanus-containing vaccine and in those who received their last dose within 10 years. However, cases have been reported and clinicians should consider tetanus when there are appropriate symptoms and signs, irrespective of the person’s vaccination status. A high level of diagnostic awareness of tetanus is particularly important in the elderly in industrialised countries, including Australia, as most deaths occur in people over 70 years of age, especially women, and may be associated with apparently minor injury.

Neonatal tetanus is usually associated with generalised symptoms, and fatal if left untreated. It usually occurs following contamination of the umbilical cord stump. Neonatal tetanus was effectively eliminated in Australia and other developed countries over a century ago. Introduction of maternal immunisation during pregnancy with tetanus toxoid has seen neonatal tetanus almost eliminated in developing countries.

4.19.3 Epidemiology

In Australia, tetanus is rare, occurring primarily in older adults who have never been vaccinated or who were vaccinated in the remote past. There were 24 notified cases of tetanus during 2001–2007, but 156 hospitalisations (July 2000–June 2007) where tetanus was coded as the principal diagnosis. This discrepancy suggests under-notification. During 2001–2006, there were 3 deaths recorded from tetanus. The case-fatality rate in Australia is about 2%. Effective protection against tetanus can be provided only by active immunisation. This is because the amount of tetanus toxin required to produce clinical symptoms is too small to induce a protective antibody response; second cases of tetanus in unimmunised persons have been recorded. Tetanus vaccine was introduced progressively into the childhood vaccination schedule after World War II. The effectiveness of the vaccine was demonstrated in that war; all Australian servicemen were vaccinated against tetanus and none contracted the disease. As tetanus can follow apparently trivial, even unnoticed wounds, active immunisation is the only certain protection. A completed course of vaccination provides protection for many years.

4.19.4 Vaccines

Tetanus toxoid is available in Australia only in combination with diphtheria, with or without other antigens such as pertussis, inactivated poliomyelitis, hepatitis B and Haemophilus influenzae type b.

The acronym DTaP, using capital letters, signifies child formulations of diphtheria, tetanus and acellular pertussis-containing vaccines. The acronym dTPa is used for formulations that contain substantially less amounts of diphtheria toxoid and pertussis antigens than child (dTPa-containing) formulations; dTaP vaccines are usually used in adolescents and adults.

Tetanus vaccine stimulates the production of antitoxin. Hence, vaccination does not prevent growth of C. tetani in contaminated wounds, but protects against the toxin produced by the organism. The immunogen is prepared by treating a cell-free preparation of toxin with formaldehyde, thereby converting it into the innocuous tetanus toxoid. Tetanus toxoid is usually adsorbed onto an adjuvant, either aluminium phosphate or aluminium hydroxide, to increase its immunogenicity. Antigens from Bordetella pertussis, in combination vaccines, also act as an effective adjuvant.

Complete immunisation (4 doses) during childhood and into adulthood is strongly recommended. By middle age, about 50% of vaccinees will have low or undetectable levels.

A single dose of tetanus toxoid produces a rapid anamnestic response in such persons.

Formulations for children aged <10 years

- **Hexaxim** – Sanofi-Aventis Australia Pty Ltd (DTPa-hepB-IPV-Hib; diphtheria-tetanus-acellular pertussis-hepatitis B-inactivated poliovirus-Haemophilus influenzae type b). Each 0.5 mL pre-filled syringe contains ≥20 IU diphtheria toxoid, ≥40 IU tetanus toxoid, 25 µg pertussis toxoid (PT), 25 µg filamentous haemagglutinin (FHA), 10 µg recombinant HBsAg, 40 D-antigen units inactivated poliovirus type 1 (Mahoney), 8 D-antigen units type 2 (MEF-1), 32 D-antigen units type 3 (Saukett) and 12 µg purified Hib capsular polysaccharide (PRP) conjugated to 22–36 µg tetanus toxoid, adsorbed onto 0.6 mg aluminium as aluminium hydroxide. May contain traces of glutaraldehyde, formaldehyde, neomycin, streptomycin and polymyxin B.

- **Infanrix** – GlaxoSmithKline Australia Pty Ltd (DTPa; diphtheria-tetanus-acellular pertussis). Each 0.5 mL monodose vial or pre-filled syringe contains ≥30 IU diphtheria toxoid, ≥40 IU tetanus toxoid, 25 µg PT, 25 µg FHA, 8 µg pertactin (PRN), adsorbed onto 0.5 mg aluminium as aluminium hydroxide.

- **Infanrix heza** – GlaxoSmithKline Australia Pty Ltd (DTPa-hepB-IPV-Hib; diphtheria-tetanus-acellular pertussis-hepatitis B-inactivated poliovirus-Haemophilus influenzae type b). The vaccine consists of both 0.5 mL pre-filled syringe containing ≥40 IU diphtheria toxoid, ≥40 IU tetanus toxoid, 25 µg PT, 25 µg FHA, 8 µg PRN, 10 µg recombinant HBsAg, 40 D-antigen units inactivated poliovirus type 1 (Mahoney), 8 D-antigen units type 2 (MEF-1) and 32 D-antigen units type 3 (Saukett), adsorbed onto aluminium hydroxide/phosphate; traces of formaldehyyde, polysorbate 80, polysorbate 20, polymyxin and neomycin; and a vial containing a lyophilised pellet of 10 µg purified Hib capsular polysaccharide (PRP) conjugated to 20–40 µg tetanus toxoid. May contain yeast proteins.


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4.19.5 Transport, storage, and handling

Transport according to National vaccine storage guidelines: Strive for 5°C to +8°C. Do not freeze. Protect from light.

Infanrix hexa must be reconstituted by adding the entire contents of the syringe to the vial and shaking until the pellet is completely dissolved. Reconstituted vaccine should be used as soon as practicable. If storage is necessary, hold at room temperature for not more than 8 hours.

4.19.6 Dosage and administration

The dose of all tetanus-containing vaccines is 0.5 mL, to be given by IM injection.

Do not mix DTPa- or dTpa-containing vaccines or dT vaccine with any other vaccine in the same syringe, unless specifically registered for use in this way.

4.19.7 Recommendations

Infants and children

Primary doses

Tetanus toxoid is given in combination with diphtheria toxoid and acellular pertussis as DTPa-containing vaccines. The recommended 3-dose primary schedule is at 2, 4 and 6 months of age. The 1st dose can be given as early as 6 weeks of age, due to the high morbidity and occasional mortality associated with pertussis in very young infants. If the 1st dose is given at 6 weeks of age, the next scheduled doses should still be given at 4 months and 6 months of age (refer to 4.12(Handbook10-home–handbook10part4–handbook10-4-12#4-12) Pertussis).

Booster doses

Two booster doses of DTPa-containing vaccine are recommended during childhood (at 18 months and 4 years of age) to provide ongoing protection against pertussis through to early adolescence (refer to 4.12(Handbook10-home–handbook10part4–handbook10-4-12#4-12) Pertussis).

For details on the management of children who require catch-up vaccination for tetanus, including minimum acceptable intervals between vaccine doses, refer to 2.1.5 (Handbook10-home–handbook10part2–handbook10-2-1#2-1-5) Catch-up.

Older children and adolescents

An additional dose (i.e. in addition to those recommended for young children, refer above) is recommended for adolescents between 10 and 17 years of age, using the reduced antigen content dTpa. The optimal age for administering this dose is 11–13 years, particularly due to waning of the pertussis antibody response following the booster dose recommended at 4 years of age. (Refer to 4.12(Handbook10-home–handbook10part4–handbook10-4-12#4-12) Pertussis.) This adolescent booster dose of tetanus-containing vaccine is also essential for maintaining immunity to tetanus (and diphtheria and pertussis) into adulthood.

It is recommended to use the reduced antigen content of DTPa for booster doses. However, when necessary, dT can also be used for the booster dose or, if necessary, for the primary dT course, in persons aged ≥10 years (refer to 4.19.14 Variations from product information below).

For details on the management of children and adolescents who require catch-up vaccination for tetanus, refer to 2.1.5(Handbook10-home–handbook10part2–handbook10-2-1#2-1-5) Catch-up.

Adults

Booster doses

All adults who reach the age of 50 years without having received a booster dose of dT in the previous 10 years should receive a further tetanus booster dose. This should be given as dTpa, to also provide protection against pertussis (refer to 4.12(Handbook10-home–handbook10part4–handbook10-4-12#4-12) Pertussis). This stimulates further production of circulating tetanus antibodies at an age when waning of diphtheria and tetanus immunity is commencing in the Australian population.8

A single booster dose of dTpa is also recommended for adults aged ≥65 years (if not received in the previous 10 years), for protection against pertussis (refer to 4.12(Handbook10-home–handbook10part4–handbook10-4-12#4-12) Pertussis). This booster dose of tetanus-containing vaccine is also essential for maintaining immunity to tetanus (and diphtheria and pertussis) in older age groups.

Travellers to countries where health services are difficult to access should be adequately protected against tetanus before departure. They should receive a booster dose of dT (or dTpa if not previously given) if more than 10 years have elapsed since the last dose of dT-containing vaccine.

For persons undertaking travel with a high risk of sustaining a tetanus-prone wound, consider giving a booster dose of either dTpa or dT (as appropriate) if more than 5 years have elapsed since the last dose of a dT-containing vaccine.

4.12 Pertussis

For details on the management of children who require catch-up vaccination for pertussis, refer to 4.12(Handbook10-home–handbook10part4–handbook10-4-12#4-12) Pertussis.

Triacel

Sanofi-aventis Australia Pty Ltd (dTpa; diphtheria-tetanus-acellular pertussis). Each 0.5 mL monodose vial contains ≥30 IU diphtheria toxoid, ≥40 IU tetanus toxoid, 20 µg PT, 20 µg FHA, 3 µg PRN, 5 µg FIM 2+3, 40 D-antigen units inactivated poliovirus type 1 (Mahoney), 8 D-antigen units type 2 (IMF-1) and 32 D-antigen units type 3 (Saukett). 1.5 mg aluminium phosphate; ≤50 µg bovine serum albumin; phenoxylethanol as preservative; traces of formaldehyde, glutaraldehyde, polysorbate 80, polymyxin and neomycin.

Tripacel

Sanofi-Aventis Australia Pty Ltd (dTpa; diphtheria-tetanus-acellular pertussis). Each 0.5 mL monodose vial contains ≥30 IU diphtheria toxoid, ≥40 IU tetanus toxoid, 10 µg PT, 5 µg FHA, 3 µg PRN, 5 µg FIM 2+3, 1.5 mg aluminium phosphate; 3.4 µg phenoxylethanol.

Reduced antigen formulations for adults, adolescents and children aged ≥10 years

• **ADT Booster** – CSL Limited/Statens Serum Institut (dT; diphtheria-tetanus). Each 0.5 mL monodose vial or pre-filled syringe contains ≥2 IU diphtheria toxoid and ≥20 IU tetanus toxoid, adsorbed onto 0.5 mg aluminium as aluminium hydroxide.

• **Adacel** – Sanofi-aventis Australia Pty Ltd (dTpa; diphtheria-tetanus-acellular pertussis). Each 0.5 mL monodose vial contains ≥2 IU diphtheria toxoid, ≥20 IU tetanus toxoid, 2.5 µg PT, 5 µg FHA, 3 µg PRN, 5 µg FIM 2+3, 0.33 mg aluminium as aluminium phosphate; phenoxylethanol; traces of formaldehyde and glutaraldehyde.

• **Adacel Polio** – Sanofi-aventis Australia Pty Ltd (dT-pa; diphtheria-tetanus-acellular pertussis-inactivated poliovirus). Each 0.5 mL monodose vial or pre-filled syringe contains ≥2 IU diphtheria toxoid, ≥20 IU tetanus toxoid, 2.5 µg PT, 5 µg FHA, 3 µg PRN, 5 µg FIM 2+3, 40 D-antigen units inactivated poliovirus type 1 (Mahoney), 8 D-antigen units type 2 (MEF-1) and 32 D-antigen units type 3 (Saukett). 0.33 mg aluminium as aluminium phosphate; phenoxylethanol; traces of formaldehyde and glutaraldehyde, polysorbate 80, polymyxin, neomycin and streptomycin.

• **Boostrix** – GlaxoSmithKline Australia Pty Ltd (dTpa; diphtheria-tetanus-acellular pertussis). Each 0.5 mL monodose vial or pre-filled syringe contains ≥2 IU diphtheria toxoid, ≥20 IU tetanus toxoid, 8 µg PT, 8 µg FHA, 2.5 µg PRN, adsorbed onto 0.5 mg aluminium as aluminium hydroxide/phosphate; traces of formaldehyde, polysorbate 80 and glycine.

• **Boostrix-IPV** – GlaxoSmithKline Australia Pty Ltd (dT-pa-IPV; diphtheria-tetanus-acellular pertussis-inactivated poliovirus). Each 0.5 mL pre-filled syringe contains ≥2 IU diphtheria toxoid, ≥20 IU tetanus toxoid, 8 µg PT, 8 µg FHA, 2.5 µg PRN, 40 D-antigen units inactivated poliovirus type 1 (Mahoney), 8 D-antigen units type 2 (MEF-1) and 32 D-antigen units type 3 (Saukett). adsorbed onto 0.5 mg aluminium as aluminium hydroxide/phosphate; traces of formaldehyde, polysorbate 80, polymyxin and neomycin.

4.19.14 Variations from product information

Below is a list of information that is not provided in the product information and is being included for clinical use. This information must only be used by healthcare professionals.

**Notes:**

• **Adacel** contains 0.9 mg polysorbate 80, 0.0009 mg streptomycin and 0.0018 mg neomycin.
For those who have not received any tetanus vaccines are also likely to receive TdT or dTpa (where appropriate, see Table 4.19.1) at least 4 weeks after skin 'popping' is practised.

Appropriate tetanus prophylaxis measures in wound management, including use of tetanus immunoglobulin (TIG), are outlined in Table 4.19.1.

Adults who have sustained injuries deemed to be tetanus-prone (all wounds other than clean minor cuts) should receive a booster dose of dT if more than 5 years have elapsed since the last dose of tetanus-containing vaccine (refer to Table 4.19.1). As an alternative to dT vaccine after a tetanus-prone wound, adults can receive dTpa vaccine (refer to 4.12 (Handbook10-home-handbook10part4-handbook10-4-12#4-12) Pertussis)). If providing dT or dTpa vaccine as part of a dT catch-up schedule in adults or children aged ≥10 years, the recommended minimum intervals between doses should be met (refer to 2.3.2 (Handbook10-home-handbook10part2-handbook10-2-2) Administration of vaccines).

4.19.9 Tetanus-prone wounds

The definition of a tetanus-prone injury is not straightforward, as tetanus may occur after apparently trivial injury, such as from a rose thorn, or with no history of injury. It is for this reason that all wounds other than clean, minor cuts are considered ‘tetanus-prone’. However, there are certain types of wounds that are more likely to cause tetanus. These include compound fractures, bite wounds, deep penetrating wounds, wounds containing foreign bodies (especially wood splinters), wounds complicated by pyogenic infections, wounds with extensive tissue damage (e.g. contusions or burns) and any superficial wound obviously contaminated with soil, dust or horse manure (especially if topical disinfection is delayed more than 4 hours). Reimplantation of an avulsed tooth is also a tetanus-prone event, as minimal washing and cleaning of the tooth is conducted to increase the likelihood of successful reimplantation.

Persons who inject drugs are also at risk of tetanus, particularly if skin ‘popping’ is practised. Appropriate tetanus prophylaxis measures in wound management, including use of tetanus immunoglobulin (TIG), are outlined in Table 4.19.1.

Adults who have sustained injuries deemed to be tetanus-prone (all wounds other than clean minor cuts) should receive a booster dose of dT if more than 5 years have elapsed since the last dose of tetanus-containing vaccine (refer to Table 4.19.1). As an alternative to dT vaccine after a tetanus-prone wound, adults can receive dTpa vaccine (refer to 4.12 (Handbook10-home-handbook10part4-handbook10-4-12#4-12) Pertussis)) to provide additional protection against pertussis. In children <10 years of age, this dose of vaccine should be given as DTPa or a DTPa-combination vaccine, consistent with the child’s vaccination history and the recommended schedule. For details on the management of children who have missed doses in the recommended schedule, refer to 2.1.5 (Handbook10-home-handbook10part2-handbook10-2-1#2-1-5) Catch-up. If there is any doubt about the adequacy of previous tetanus immunisation in a person who has a tetanus-prone wound, TIG must be given as soon as possible, as well as tetanus toxoid-containing vaccine, to provide both immediate passive and active protection (refer to Table 4.19.1). The recommended dose for TIG is 250 IU, given by IM injection, as soon as practicable after the injury. If more than 24 hours have elapsed, 500 IU should be given. Persons with a significant humoral immune deficiency may not have developed or maintained adequate immunity to tetanus, despite vaccination, and require TIG for tetanus-prone wounds.

Clean minor cuts are not categorised as tetanus-prone wounds and, for these wounds, TIG is unnecessary, independent of previous tetanus vaccination history.

Information regarding accessing tetanus immunoglobulin (for intramuscular use for management of tetanus-prone wounds, or intravenous tetanus immunoglobulin for the treatment of clinical tetanus) should be obtained from the Australian Red Cross Blood Service (refer to Part 5 (Handbook10-home-handbook10part5) Passive immunisation). For further information on TIG refer to 4.19.13 Public health management of tetanus below.

General measures for treatment of tetanus-prone wounds

Whatever the immune status of a person with a tetanus-prone wound, local disinfection and, where appropriate, surgical treatment of tetanus-prone wounds, must never be omitted. Antibiotic prophylaxis is not indicated for the prevention of tetanus; however, the use of antibiotics (such as penicillin, amoxycillin + clavulanate, or metronidazole) for preventing other bacterial infection of the wound is a matter for clinical judgment.

<table>
<thead>
<tr>
<th>History of tetanus vaccination</th>
<th>Time since last dose</th>
<th>Type of wound</th>
<th>DTPa, DTPa-combinations, dT, dTpa, as appropriate</th>
<th>Tetanus immunoglobulin* (TIG)</th>
</tr>
</thead>
<tbody>
<tr>
<td>≥3 doses</td>
<td>&lt;5 years</td>
<td>Clean minor wounds</td>
<td>NO</td>
<td>NO</td>
</tr>
<tr>
<td>≥3 doses</td>
<td>&lt;5 years</td>
<td>All other wounds†</td>
<td>NO</td>
<td>NO²</td>
</tr>
<tr>
<td>≥3 doses</td>
<td>5–10 years</td>
<td>Clean minor wounds</td>
<td>NO</td>
<td>NO</td>
</tr>
<tr>
<td>≥3 doses</td>
<td>5–10 years</td>
<td>All other wounds†</td>
<td>YES</td>
<td>NO</td>
</tr>
<tr>
<td>≥3 doses</td>
<td>&gt;10 years</td>
<td>Clean minor wounds</td>
<td>YES</td>
<td>NO</td>
</tr>
<tr>
<td>≥3 doses</td>
<td>&gt;10 years</td>
<td>All other wounds†</td>
<td>YES</td>
<td>NO²</td>
</tr>
<tr>
<td>&lt;3 doses or uncertain§</td>
<td>&gt;10 years</td>
<td>Clean minor wounds</td>
<td>YES</td>
<td>NO</td>
</tr>
<tr>
<td>&lt;3 doses or uncertain§</td>
<td>&gt;10 years</td>
<td>All other wounds†</td>
<td>YES</td>
<td>YES</td>
</tr>
</tbody>
</table>

* The recommended dose for TIG is 250 IU, given by IM injection, as soon as practicable after the injury. If more than 24 hours have elapsed, 500 IU should be given. Because of its viscosity, TIG should be given to adults using a 21 gauge needle. For children, it can be given slowly using a 23 gauge needle.

† Individuals with a humoral immune deficiency (including HIV-infected persons who have immunodeficiency) should be given TIG if they have received a tetanus-prone injury, regardless of the time since their last dose of tetanus-containing vaccine.

‡ All wounds, other than clean minor wounds, should be considered ‘tetanus-prone’. For more detail, refer to 4.19.9 Tetanus-prone wounds above.

4.19.10 Contraindications

The only absolute contraindications to tetanus-containing vaccines are:

- anaphylaxis following a previous dose of any tetanus-containing vaccine
- anaphylaxis following any vaccine component.

If a person has a tetanus-prone wound and has previously had a severe adverse event following tetanus vaccination, alternative measures, including the use of tetanus immunoglobulin, can be considered.

4.19.11 Adverse events

Mild discomfort or pain at the injection site persisting for up to a few days is common.

Administration of more than 1 dose of a dT-containing vaccine in a 5-year period in previously immunised adults had previously been thought to be associated with an increased risk of injection site reactions. However, recent studies indicate that, in adults and adolescents, the adverse reactions to a single dose of dTpa are similar whether administered shortly (18 months) or at a longer interval after a previous dose of a vaccine containing tetanus/diphtheria toxoids.27–30 (Refer also to 4.12) Pertussis.

Uncommon general adverse events following dT vaccine include headache, lethargy, malaise, myalgia and fever. Anaphylaxis, urticaria and peripheral neuropathy occur very rarely. Brachial neuritis (inflammation of a nerve in the arm, causing weakness or numbness) has been described following the administration of tetanus toxoid-containing vaccines, with an estimated excess risk of approximately 0.5–1 in 100 000 doses in adults.31–32 For specific adverse events following combination vaccines containing both tetanus and pertussis antigens, refer to 4.12 Pertussis.

4.19.12 Public health management of tetanus

Tetanus is a notifiable disease in all states and territories in Australia.

Further instructions about the public health management of tetanus, including management of cases of tetanus, should be obtained from state/territory public health authorities (refer to Appendix 1).

For information on the definition and management of tetanus-prone wounds, refer to 4.19.9 Tetanus-prone wounds and Table 4.19.1 above. To access tetanus immunoglobulin (for intramuscular use for management of tetanus-prone wounds, or intravenous tetanus immunoglobulin for the treatment of clinical tetanus), contact the Australian Red Cross Blood Service (refer to Part 5).

4.19.13 Variations from product information

The product information for Infanrix states that this vaccine is indicated for primary immunisation of infants from the age of 2 months to 12 months and as a booster dose for children from 15 months to 6 years of age who have previously been vaccinated against diphtheria, tetanus and pertussis. The ATAGI recommends that this vaccine may also be used for catch-up of the primary schedule or as a booster in children <10 years of age. The ATAGI also recommends that the primary schedule may be commenced at 6 weeks of age, if required.

The product information for Infanrix hexa states that this vaccine is indicated for primary immunisation of infants from the age of 6 weeks and as a booster dose for children 18 months of age if boosting is required for all antigens. The ATAGI recommends that this vaccine may also be used for catch-up of the primary schedule or as a booster in children <10 years of age.

The product information for Quadracel states that this vaccine is indicated for use in a 3-dose primary schedule from the age of 2 months to 12 months and may also be used as a booster dose for children from 15 months to 6 years of age who have previously been vaccinated against diphtheria, tetanus, pertussis and poliomyelitis. In addition, the ATAGI recommends that this product may also be used for catch-up of the primary schedule or as a booster in children <10 years of age.

The product information for Triacel states that this vaccine is indicated for use in a 3-dose primary schedule from the age of 2 months to 12 months and may also be used as a booster dose for children from 15 months to 6 years of age who have previously been vaccinated against diphtheria, tetanus, pertussis and poliomyelitis. The ATAGI recommends that, when appropriate, this product may also be used for either catch-up of the primary schedule or as a booster dose in children aged <10 years. The ATAGI also recommends that the primary schedule may be commenced at 6 weeks of age, if required.

The product information for ADT Booster states that this vaccine is indicated for use as a booster dose only in children aged ≥5 years and adults who have previously received at least 3 doses of diphtheria and tetanus vaccines. The ATAGI recommends instead that, where a dT vaccine is required, ADT Booster can be used, including for primary immunisation against diphtheria and tetanus (for any person ≥10 years of age).

The product information for Adacel and Boostrix states that these vaccines are indicated for booster doses only. The ATAGI recommends instead that, when a 3-dose primary course of diphtheria/tetanus toxoids is given to an adolescent/adult, dTpa should replace the 1st dose of dT, with 2 subsequent doses of dT. If dT is not available, dTpa can be used for all 3 primary doses.

The product information for Adacel and Boostrix states that vaccination in pregnancy is not recommended unless there is a definite risk of acquiring pertussis. The product information for Boostrix states that the vaccine should be used during pregnancy only when clearly needed, and the possible advantages outweigh the possible risks for the fetus. The ATAGI recommends instead that pregnant women receive a dose with every pregnancy.

The product information for Adacel and Boostrix states that there is no recommendation regarding the timing and frequency of booster doses against pertussis in adults. However, the ATAGI recommends that pregnant women receive a booster dose with every pregnancy and that other adults in contact with infants and/or at increased risk from pertussis can receive a booster dose every 10 years.
Immunise - The Australian Immunisation Handbook 10th Edition

References

A full reference list is available on the electronic Handbook or Immunise Australia website (http://www.immunise.health.gov.au).

**Tuberculosis**

The BCG vaccine is a suspension of a live attenuated strain of *M. bovis*. Worldwide, there are many BCG vaccines available, but they are all derived from the strain propagated by the Institute Pasteur, which was first tested in humans in 1921. BCG vaccination probably has little effect on preventing infection per se, or reactivation among those already infected with TB, so the role of BCG vaccination in preventing overall transmission is probably limited. However, there is strong evidence that BCG vaccination in infancy provides greater protection against severe disseminated forms of TB disease in young children, including miliary TB and TB meningitis. It can be difficult to diagnose in young children and progression to disseminated TB can be rapid; they are therefore the primary target for the use of BCG vaccine. The efficacy of BCG vaccine against pulmonary disease in adults is less consistent and has ranged from no protection to 80% in controlled trials. The greatest protection has been observed among skin test-negative adults in North America and Europe, and the lowest among skin test-positive persons in tropical settings. The reason for the wide variation in measured effectiveness is not clear, but has been attributed to variability in study quality, differences in BCG strains, host factors such as age at vaccination and nutritional status, and differences in the prevalence of infection with environmental mycobacteria. The duration of protection following BCG vaccination has been difficult to measure because the interval between infection and disease may extend to decades. Benefit from infant vaccination has been found in studies with follow-up of up to 12 years, but protection is commonly thought to decline over 10 to 20 years. There is evidence that memory responses persist for up to 10 to 50 years.

BCG vaccination has been shown to offer some protection against *Mycobacterium leprae*, the causative agent of leprosy.

BCG vaccine is not used in the treatment of tuberculosis disease. BCG may be used as a therapeutic modality for transitional cell carcinoma of the bladder.

### 4.20.4 Vaccine

**BCG vaccine** – Sanofi-Aventis Australia Pty Ltd (live vaccine prepared from an attenuated strain of *Mycobacterium bovis*). 1.5 mg lyophilised powder in a multi-dose vial with separate diluent. Reconstituted vaccine contains 8–32 x 10⁹ colony forming units per mL and monosodium glutamate 1.5% w/v. May contain traces of polysorbate 80. Reconstituted volume provides about 10 adult or 20 infant doses.

### 4.20.5 Transport, storage and handling

Transport according to **National vaccine storage guidelines**: Strive for 5°C to +8°C. Do not freeze. Protect from light.

BCG vaccine must be reconstituted by adding the entire contents of the diluent container to the vial and shaking until the powder is completely dissolved. Reconstituted vaccine is very unstable and must be stored at +2°C to +6°C and used within one working session of 4 to 6 hours.

### 4.20.6 Dosage and administration

The dose of BCG vaccine in newborns and infants <12 months of age is 0.05 mL, given by intradermal injection.
BCG vaccine is given as a single dose. Due to the lack of evidence, BCG revaccination is not recommended in any person. BCG vaccine is available from state/territory tuberculosis services.

**Before vaccination**

**Tuberculin skin test (Mantoux)**

All individuals, except infants <6 months of age, should undergo a tuberculin skin test (TST, Mantoux) before BCG vaccination. A hypersensitivity reaction to tuberculin purified protein derivative (PPD; Tuberculin) used in the TST assists in the identification of those infected with M.TB. A hypersensitivity reaction may also occur in those infected with other mycobacteria and those previously vaccinated with BCG. Only immunocompetent persons who have induration <5 mm following correctly administered and interpreted TST should receive BCG vaccination. Guidelines to assist in the undertaking and interpretation of TST are available by contacting local state/territory tuberculosis services.

It should be noted that live viral vaccines inhibit the response to tuberculin and tuberculin-positive persons may become tuberculin-negative for up to a month after measles infection. As such, tuberculin skin testing may be unreliable for at least 4 weeks after the administration of live viral vaccines.

**Interferon-gamma (γ) release assays**

Newly available blood tests (Interferon-gamma release assays; IGRA)s are available for the detection of tuberculosis infection. TST, however, remains the preferred method of screening for tuberculosis infection, pending further evaluation of IGRA.s Guidelines for the use of IGRA in Australia have been developed by the National Tuberculosis Advisory Committee.

**BCG vaccination procedures**

BCG vaccination should only be given by medical or nursing staff who are trained in BCG vaccination procedures.

- Use a short (10 mm) 26–27 gauge needle with a short bevel. The risk of spillage can be minimised by using an insulin syringe to which the needle is already attached.
- Wear protective eye-wear. The person to be vaccinated (and the parent/carer holding a small child being vaccinated) should also wear protective eye-wear. Eye splashes may ulcerate; if an eye splash occurs, wash the eye with saline or water immediately.

**Response to BCG vaccination**

In response to BCG vaccination, a small red papule forms and eventually ulcerates, usually within 2 to 3 weeks of vaccination. The ulcer heals with minimal scarring over several weeks. There may be swelling and tenderness in local lymph nodes. While a local reaction represents a normal response to BCG vaccination, more extensive local reactions are less common (refer to 4.20.11 Adverse events below). Subjects who have been given BCG vaccine despite latent or previous TB infection are likely to experience an accelerated response characterised by induration within 24 to 48 hours, pustule formation in 5 to 7 days, and healing within 10 to 15 days.

Clinical trials have not shown a consistent relationship between the size of tuberculin reactions after BCG vaccination and the level of protection provided. TST is not recommended to demonstrate immunity after BCG vaccination.

**Co-administration with other vaccines**

BCG can be administered at the same time as, or at any time following receipt of, other inactivated vaccines (e.g. tetanus-containing vaccines). If required.

If administration of both BCG and another live parenteral vaccine (e.g. MMR or yellow fever) is indicated, the vaccines should be given either on the same day or at least 4 weeks apart.

There are no restrictions on the timing of BCG vaccine in relation to oral live vaccines, including rotavirus and oral poliomyelitis vaccine (OPV) (e.g. in infants who have received OPV overseas).

**4.20.7 Recommendations**

BCG is not recommended for routine use in the general population, given the low incidence of TB in Australia and the variable efficacy reported in adults. However, some groups are at increased risk of tuberculosis and BCG vaccination may be warranted for these persons, based on a risk assessment. BCG should be specifically considered for the following groups.

**Aboriginal and Torres Strait Islander neonates**

In some parts of Australia, the incidence of TB is appreciably higher among Aboriginal and Torres Strait Islander people than Australian-born non-Indigenous Australians, and BCG is recommended for neonates living in those regions. State and territory guidelines should be consulted for local recommendations and the geographic areas where BCG vaccination of Aboriginal and Torres Strait Islander neonates is conducted (refer to Appendix 1(Handbook10-home~handbook10-tools~handbook10-appendices~handbook10-appendix1) Contact details for Australian, state and territory government health authorities and communicable disease control). (Refer also to 3.1(Handbook10-home~handbook10part3~handbook10-3-1) Vaccination for Aboriginal and Torres Strait Islander people.)

**Infants born in Australia to migrant parents**

TB is rare in infants and young children born in Australia, but infants born to parents who have migrated from countries with a high TB incidence (i.e. >40 cases per 100 000 population per year – refer to 4.20.3 Epidemiology above) may be at higher risk of TB exposure in their early life. BCG vaccination of these infants is not routinely recommended because of the uncertainty of the risks and benefits.

**Children who will be travelling to high TB incidence settings**

The risk of TB disease in children travelling to countries with a high TB incidence (i.e. >40 cases per 100 000 population per year – refer to 4.20.3 Epidemiology above) depends on the age of the child, the duration of stay, and the TB incidence at the destination. Country-specific incidence data are available from the World Health Organization.

The need for BCG vaccination should be assessed for young children, particularly those aged <5 years, who will be travelling to a country with high TB incidence for an extended period. This is best discussed with local state/territory TB services or with a paediatric infectious diseases specialist. BCG vaccination should ideally occur at least 3 months before departure and therefore consideration should be given to future travel plans at birth.

**Neonates born to parents with leprosy or a family history of leprosy**

There is strong evidence that BCG provides some protection against Mycobacterium leprae.

**Occupational groups**
4.20.8 Pregnancy and breastfeeding

BCG vaccine is contraindicated in pregnant women.

BCG vaccine can be given to breastfeeding women.

Refer to 3.3.(Handbook10-home~handbook10part3~handbook10-3-3) Groups with special vaccination requirements, Table 3.3.1 (Handbook10-home~handbook10part3~handbook10-3-3#Table-3-3-1) Recommendations for vaccination in pregnancy for more information.

4.20.9 Contraindications

BCG is a live vaccine and its use is contraindicated in the following groups:

- Persons with known or suspected HIV infection, even if asymptomatic or with normal immune function, because of the risk of disseminated BCG infection.
- Persons treated with corticosteroids or other immunosuppressive therapy, including monoclonal antibodies against tumour necrosis factor-alpha (TNF-alpha) (e.g. infiximab, etanercept, adalimumab) (refer to 3.3.(Handbook10-home~handbook10part3~handbook10-3-3) Groups with special vaccination requirements).
- Infants born to mothers treated with DMARDS (e.g. TNF-alpha blocking monoclonal antibodies) in the third trimester of pregnancy frequently have detectable antibodies for several months and they should not be vaccinated with BCG. (Refer also to ‘Use of immunosuppressive therapy during pregnancy’ in 3.3.2 (Handbook10-home~handbook10part3~handbook10-3-3#Vaccination of women who are planning pregnancy, pregnant or breastfeeding, and preterm infants.)
- Persons with congenital cellular immunodeficiencies, including specific deficiencies of the interferon-gamma pathway.
- Persons with malignancies involving bone marrow or lymphoid systems (refer also to 3.3.(Handbook10-home~handbook10part3~handbook10-3-3) Groups with special vaccination requirements).
- Persons with any serious underlying illness, including severe malnutrition.
- Pregnant women (BCG vaccine has not been shown to cause fetal damage, but use of live vaccines in pregnancy is not recommended).
- Persons who have previously had TB or a large (≥5 mm) reaction to a tuberculin skin test.

4.20.10 Precautions

For those who would otherwise be candidates for BCG, vaccination should be deferred in the following groups:

- Neonates who are medically unstable, until the neonate is in good medical condition and ready for discharge from hospital.
- Infants born to mothers who are suspected or known to be HIV-positive, until HIV infection of the infant can be confidently excluded.
- Persons with active skin disease such as eczema, dermatitis or psoriasis at or near the site of vaccination.
- Persons being treated for latent TB infection, as the therapy is likely to inactivate the BCG vaccine.
- Persons with significant febrile illness, until 1 month after recovery.

Vaccination before or after immunoglobulin or blood product administration

BCG vaccine can be given at any time before or after administration of immunoglobulin or any antibody-containing blood product as there is minimal interaction between these preparations and BCG vaccine. (Refer also to 3.3.4.(Handbook10-home~handbook10part3~handbook10-3-4) Vaccination of recent recipients of normal human immunoglobulin and other blood products.)

4.20.11 Adverse events

The normal reaction to BCG vaccination has been described above (refer to 4.20.6 Dosage and administration). About 5% of vaccinated persons experience adverse events. Injection site abscesses occur in 2.5% of vaccinated persons and lymphadenitis in 1%, while up to 1% require medical attention. Gross supplicative or generalised complications of BCG vaccination have been treated with anti-tuberculosis drugs; however, there is no consensus on the management of these complications and specialist advice should be sought from local state/territory tuberculosis services. Anaphylactic reactions have also been reported. Keloid formation can occur, but the risk is minimised if the injection is not given higher than the level of insertion of the deltoid muscle into the humerus. The overall risk of fatal disseminated infection is extremely low (approximately 1 case per million vaccinated persons).

4.20.12 Public health management of tuberculosis

Tuberculosis is a notifiable disease in all states and territories in Australia.

Further instructions about the public health management of tuberculosis, including management of cases of tuberculosis and their contacts, should be obtained from state/territory public health authorities (refer to Appendix 1 (Handbook10-home~handbook10-tools~handbook10-appendices~handbook10-appendix1) Contact details for Australian, state and territory government health authorities and communicable disease control).

In special circumstances, such as during shortages of the currently registered vaccine, state and territory public health authorities can also provide advice on the use of alternative vaccine products.

4.20.13 Variations from product information

Although the product information for BCG vaccine specifies that vaccine must be used within 8 hours of reconstitution, the National Tuberculosis Advisory Committee (NTAC) guidelines recommend that any unused vaccine is discarded after a working period of 4 to 6 hours.

The product information for BCG vaccine states that the vaccine is contraindicated in individuals with generalised skin disease such as eczema, furunculosis, atopic dermatitis or other exudative or inflammatory dermatologic conditions. The ATAGI recommends instead that BCG vaccination should be considered for TST-negative healthcare workers who are at high risk of exposure to drug-resistant TB, due to the difficulty in treating drug-resistant infection.

References


4.21 Typhoid

4.21.1 Bacteriology

Typhoid fever is a clinical syndrome caused by a systemic infection with Salmonella enterica subspecies enterica serovar Typhi (S. Typhi). Paratyphoid fever, caused by infection with S. enterica serovar Paratyphi A or B, is similar to, and often indistinguishable from, typhoid fever.\(^1\) The two infections are collectively known as enteric fever, have largely overlapping geographic distributions, and, although there is no vaccine specifically targeted against paratyphoid fever, there is evidence to suggest some cross-protection from the oral live attenuated typhoid vaccine against Paratyphi B.\(^2,4\)

4.21.2 Clinical features

Typhoid fever has a usual incubation period of 7 to 14 days (range 3 to 60 days).\(^5\) Although clinical presentations of typhoid fever can be quite variable, a typical case presents with a low-grade fever, dull frontal headache, malaise, myalgia, anorexia and a dry cough.\(^6\) The fever tends to increase as the disease progresses; constipation (more typically diarrhoea in young children), abdominal tenderness, relative bradycardia and splenomegaly are common. Complications occur in 10 to 15% of patients and tend to occur in patients who have been ill for more than 2 weeks. The more important complications include gastrointestinal bleeding, intestinal perforation and typhoid encephalopathy.\(^5\)

Relapse occurs in up to 10% of patients, usually 2 to 3 weeks after the initial fever resolves. Chronic asymptomatic biliary carriage of S. Typhi occurs in up to 5% of patients with typhoid fever, even after treatment. Chronic carriage is defined by the continued shedding of the organism for longer than 1 year. Carriers serve as an important reservoir in endemic areas and are of public health significance (e.g. if a carrier works in the food industry).\(^5\)

4.21.3 Epidemiology

Humans are the sole reservoir of S. Typhi. It is shed in the faeces of those who are acutely ill and those who are chronic asymptomatic carriers of the organism; transmission usually occurs via the ingestion of faecally contaminated food or water.

The vast majority of typhoid fever cases occur in less developed countries, where poor sanitation, poor food hygiene and untreated drinking water all contribute to endemic disease, with moderate to high incidence and considerable mortality.\(^6\) Geographic regions with high incidence (>100 cases per 100,000 population per year) include the Indian subcontinent, most Southeast Asian countries and several South Pacific nations, including Papua New Guinea. Estimates of incidence from African countries are more limited. In many regions, particularly the Indian subcontinent, strains partially or completely resistant to many antibiotics (including ciprofloxacin) are detected with increasing frequency.\(^7\)

In developed countries, typhoid fever is predominantly a travel-related disease, with a considerably greater risk following travel to the Indian subcontinent than to other regions.\(^8,9\) Those who travel to endemic regions to visit friends and relatives (e.g. immigrants who travel to their former homelands) appear to be at considerably greater risk of acquiring typhoid fever than other travellers.\(^10,11\) There are typically fewer than 150 cases of typhoid fever reported in Australia each year, with most following travel to regions with endemic disease.\(^11\)

4.21.4 Vaccines

Monovalent typhoid vaccines

- **Vivotif Oral** – Seqirus Pty Ltd (oral live attenuated typhoid vaccine). Each enteric-coated capsule contains ≥2 x 10\(^8\) viable organisms of attenuated S. Typhi strain Ty21a; gelatin (bovine derived); ethylene glycol; sucrose. 3 capsules in a blister pack.
- **Typherix** – GlaxoSmithKline Australia Pty Ltd (purified Vi capsular polysaccharide vaccine). Each 0.5 mL pre-filled syringe contains 25 µg Vi polysaccharide of S. Typhi strain Ty2; phenol; phosphate buffer.
- **Typhim Vi** – Sanofi Aventis Australia Pty Ltd (purified Vi capsular polysaccharide vaccine). Each 0.5 mL pre-filled syringe contains 25 µg Vi polysaccharide of S. Typhi strain Ty2; <1.25 mg phenol; phosphate buffer.

Combination vaccine that contains S. Typhi

- **Vivaxim** – Sanofi Aventis Australia Pty Ltd (formaldehyde-inactivated hepatitis A virus (GBM strain) and typhoid Vi capsular polysaccharide). Supplied in a dual-chamber syringe which enables the two vaccines to be mixed just before administration. Each 1.0 mL dose of mixed vaccine contains 160 antigen units of inactivated hepatitis A virus antigen, 25 µg purified typhoid Vi capsular polysaccharide strain Ty2; 0.3 mg aluminium as aluminium hydroxide; 2.5 µL phenoxyethanol; 12.5 µg formaldehyde; ≤5 µg neomycin; <10 ng bovine serum albumin; traces of polysorbate 80.

The attenuated non-pathogenic S. Typhi strain Ty21a was derived by chemical attenuation of a wild-type strain. Attenuated features of Ty21a include the absence of the enzyme UDP-galactose-4-epimerase and the Vi capsular polysaccharide antigen (an important virulence determinant of S. Typhi). These features partially contribute to the non-pathogenicity and, therefore, the safety of the oral live vaccine.\(^12\)

The oral vaccine Ty21a strain cannot be detected in faeces more than 3 days after administration of the vaccine. It stimulates serum IgG, vigorous secretory intestinal IgA and cell-mediated immune responses.\(^10\) Clinical trials, with different formulations of the vaccine and with a variety of schedules, have been undertaken in several countries with endemic typhoid fever (Egypt, Chile, Indonesia). These have documented varying degrees of protection against the disease.\(^11,12\)

Parenteral Vi polysaccharide vaccines are produced by fermentation of the Ty2 strain, followed by inactivation with formaldehyde, and then extraction of the polysaccharide from the supernatant using a detergent.\(^12\) The vaccines elicit prompt serum IgG anti-Vi responses in 85 to 95% of adults and children ≥2 years of age. The vaccines have also been used in clinical trials in endemic regions (Nepal, South Africa, China), indicating moderate protection against typhoid fever.\(^5,12\) As with oral typhoid vaccine, herd protection of unvaccinated persons living in areas with moderate coverage of parenteral vaccine has been demonstrated.\(^13,14\)

Neither the oral nor the parenteral vaccines have been studied in prospective clinical trials in endemic travellers. Because many travellers do not have any naturally acquired immunity, the protection conferred through typhoid vaccination may be less than that documented in the clinical trials mentioned above. However, there is circumstantial evidence that the vaccines do provide protection in travellers to endemic regions\(^9,9\) and that 3-weekly dosing can be used to simplify the course of providing the protection.\(^15\)
4.21.6 Dosage and administration

Oral live attenuated vaccine

The vaccine is registered for use in persons ≥6 years of age; it is presented in a pack of 3 capsules. Each dose (a whole capsule) is the same for both adults and children.

The vaccination schedule consists of 1 capsule of vaccine on days 1, 3 and 5, taken 1 hour before food. The capsule must be swallowed whole with water and must not be chewed, since the organisms can be killed by gastric acid. Do not give the vaccine concurrently with antibiotics, or other drugs that are active against Salmonellae. If possible, antibiotics and other relevant drugs should be delayed for 3 days after the last dose of the vaccine (refer to 4.21.10 Precautions below).

A 4th capsule taken on day 7 has been shown in one large clinical trial to result in a lower incidence of typhoid fever compared with 3 doses. However, giving a 4th dose requires partial use of a second pack.

Co-administration with other vaccines

Oral typhoid vaccine can be administered at the same time as any of the live parenteral vaccines (including yellow fever vaccine or BCG). Where continued exposure to Salmonellae exists (such as occurs with either prolonged travel or residence in an endemic region), the oral live attenuated vaccine is contraindicated in pregnant women (refer to 4.21.9 Contraindications below).

4.21.7 Recommendations

It is recommended that travellers be advised about personal hygiene, food safety and drinking boiled or bottled water only. They should be advised that raw (or undercooked) shellfish, salads, cold meats, untreated water and ice (in drinks) are all potentially ‘high-risk’, as are short (day) trips away from higher quality accommodation venues.

Oral live attenuated vaccine

Children aged <6 years

Oral typhoid vaccine is not recommended for use in children aged <6 years.

Children aged ≥6 years and adults

Oral typhoid vaccine in either a 3- or 4-dose schedule is recommended for children aged ≥6 years and adults who are:

- travelling to endemic regions, where food hygiene may be suboptimal and drinking water may not be adequately treated
- travelling to endemic regions to visit friends and relatives
- military personnel
- laboratory personnel routinely working with S. Typhi.

The addition of a 4th oral dose, on day 7, is an option as there is evidence that 4 doses provides greater protection. However, giving a 4th dose requires partial use of a second pack.

Revaccination of children aged ≥6 years and adults

The optimal timing of revaccination against typhoid fever is uncertain and, therefore, international recommendations vary considerably. Where continued exposure to S. Typhi exists (such as occurs with either prolonged travel or residence in an endemic region) and the oral live attenuated vaccine was used initially, a repeat 3-dose or 4-dose course can be given 3 years after a 3-dose course, or 5 years after a 4-dose course.

Parenteral Vi polysaccharide vaccines

Both monovalent typhoid vaccines (Typherix and Typhim Vi) are registered for use in persons ≥2 years of age. The dose of both vaccines is 0.5 mL (for both adults and children), to be given by IM injection.

The dose of the combination typhoid Vi polysaccharide/hepatitis A vaccine (Vivaxim) is 1 mL to be given by IM injection. Vivaxim is registered for use in persons aged ≥16 years. (Refer also to 4.4/Handbook10-home~handbook10part4~handbook10-4-4) Hepatitis A.)

Co-administration with other vaccines

Parenteral Vi polysaccharide typhoid vaccines can be given with, or at any time before or after, other travel vaccines, such as oral cholera or yellow fever vaccines.

4.21.8 Pregnancy and breastfeeding

The oral live attenuated typhoid vaccine is contraindicated in pregnant women (refer to 4.21.9 Contraindications below).
4.21.9 Contraindications
The only absolute contraindications to typhoid vaccines are:

- anaphylaxis following a previous dose of any typhoid vaccine
- anaphylaxis following any vaccine component.

Oral live attenuated vaccine
The oral live attenuated vaccine should not be administered to:

- children <6 years of age; parenteral Vi polysaccharide vaccine should be used instead in children 2–5 years of age
- pregnant women; parenteral Vi polysaccharide vaccine should be used instead
- persons who are immunocompromised, including those with known HIV infection; parenteral Vi polysaccharide vaccine should be used instead
- persons taking antibiotics; parenteral Vi polysaccharide vaccine should be used instead.

Parenteral Vi polysaccharide vaccines
The parenteral Vi polysaccharide vaccines should not be administered to children <2 years of age.

4.21.10 Precautions
The oral live attenuated vaccine may be destroyed by gastric acid, so capsules must be swallowed whole, rather than chewed or opened.

There should be an interval of at least 8 hours between the administration of the oral live attenuated typhoid vaccine and the inactivated oral cholera vaccine, as the buffer in the cholera vaccine may affect the transit of the capsules of oral typhoid vaccine through the gastrointestinal tract.

The oral live attenuated typhoid vaccine may be susceptible to inactivation by some antibiotics and antimalarial agents, although concurrent administration of either mefloquine or atovaquone/proguanil combination (Malarone) has not been shown to interfere with immune responses or efficacy. If the oral vaccine is used, it is recommended that vaccination should be timed so that the last dose of vaccine is administered at least 3 days before starting antibiotics or antimalarial prophyaxis.

4.21.11 Adverse events
Typhoid vaccines, both oral and parenteral, are associated with very few adverse events and, when adverse events do occur, they tend to be mild and transient. 18

Oral live attenuated vaccine
Abdominal discomfort, diarrhoea, nausea, vomiting and rashes have occasionally been reported.

Parenteral Vi polysaccharide vaccines
Local adverse events such as erythema, swelling and pain at the injection site occur very commonly in 10 to 20% of vaccine recipients. Systemic adverse events are common and include fever (3% of recipients), malaise and nausea.

4.21.12 Public health management of typhoid fever
Typhoid fever is a notifiable disease in all states and territories in Australia.

Further instructions about the public health management of typhoid fever, including management of cases of typhoid fever and their contacts, should be obtained from state/territory public health authorities (refer to Appendix 1 (Handbook10-home-handbook10-tools-handbook10-appendices-handbook10-appendix1) Contact details for Australian, state and territory government health authorities and communicable disease control).

4.21.13 Variations from product information
The Australian product information for Vivifol Oral live attenuated vaccine does not mention the use of a 4-dose course of the vaccine for either initial or repeat vaccination, although this vaccine is registered for use in some other countries (e.g. Canada and the United States) in a 4-dose schedule. The ATAGI recommends that a 4-dose course can be given to provide increased protection against typhoid fever.

The product information for Vivofol Oral live attenuated vaccine does not include pregnancy among the listed contraindications. The ATAGI recommends that pregnancy is a contraindication to the oral live attenuated typhoid vaccine.

The product information for Typhim Vi recommends a booster dose every 2 to 3 years, and the product information for Vivofol Oral live attenuated vaccine recommends a booster every 3 years. The ATAGI also recommends, for those at continuing risk, revaccination with a dose of parenteral Vi polysaccharide vaccine every 3 years after a previous dose, or revaccination with a 3- or 4-dose course of the oral live attenuated vaccine 3 years after a 3-dose course or 5 years after a 4-dose course.

References
4.22 Varicella

4.22.1 Virology

Varicella-zoster virus (VZV) is a DNA virus within the herpes virus family.1 Primary infection with VZV causes varicella (chickenpox). Following primary infection, VZV establishes latency in the dorsal root ganglia. Reactivation of the latent virus manifests as herpes zoster (shingles)2 (refer to 4.24 Zoster (Handbook10-home~handbook10part4~handbook10-4-24)).

4.22.2 Clinical features

Varicella is usually a mild disease of childhood. However, complications occur in approximately 1% of cases.3 It is more severe in adults and in persons of any age who are immunocompromised, in whom complications, disseminated disease and fatal illness can occur.4 The average incubation period is 14 to 16 days (range 10 to 21 days), but may be longer in persons who are immunocompromised, especially after receipt of zoster immunoglobulin (ZIG).5 The period of infectivity is from 48 hours before the onset of rash until crusting of all lesions has occurred.6 A short prodromal period of 1 to 2 days may precede the onset of the rash, especially in adults.7 In otherwise healthy children, skin lesions usually number between 200 and 500.8 Acute varicella may be complicated by secondary bacterial skin infection, pneumonia, acute cerebellar ataxia (1 in 4000 cases), aseptic meningitis, transverse myelitis, encephalitis (1 in 100 000 cases) and thrombocytopenia. In rare cases, it involves the viscera and joints.9

Congenital varicella syndrome has been reported after varicella infection in pregnancy and may result in skin scarring, limb defects, ocular anomalies and neurologic malformations.10,11 There is a higher risk to the fetus if maternal infection occurs in the second trimester compared with infection in the first trimester (1.4% versus 0.5%).5 Infants with intrauterine exposure also risk developing herpes zoster in infancy (0.8–1.7%), with the greatest risk following exposure in the third trimester.12 Severe neonatal varicella infection can result from perinatal maternal varicella.7 The onset of varicella in pregnant women from 5 days before delivery to 2 days after delivery is estimated to result in severe varicella in 17 to 30% of their newborn infants.1,13 Reactivation of latent VZV as a result of waning cellular immunity results in herpes zoster (HZ), a localised vesicular rash. HZ can occur at any age, but is more common in older adults and persons who are immunocompromised. Complications may include post-herpetic neuralgia and disseminated zoster with visceral, central nervous system and pulmonary involvement1 (refer to 4.24 Zoster (Handbook10-home~handbook10part4~handbook10-4-24)).

There is no specific therapy for uncomplicated varicella infection. Antiviral therapy is used in the treatment of complicated or severe varicella, herpes zoster disease, and disease in persons who are immunocompromised.

4.22.3 Epidemiology

In an unimmunised population in temperate climates, the annual number of cases of varicella approximates the birth cohort.8 Tropical regions have a higher proportion of cases in adults. Approximately 5% of cases are subclinical. A serosurvey conducted in 1997–1998 found that 83% of the Australian population were seropositive by 10–14 years of age.9 Prior to the introduction of a varicella vaccination program in Australia, there were about 240 000 cases, 1500 hospitalisations and an average of 7 to 8 deaths each year from varicella in Australia.10-12 The highest rates of hospitalisation occur in children <5 years of age.13

In Australia, there was a 69% decline in varicella hospitalisations in children aged 1–4 years in the first 2.5 years following the inclusion of varicella vaccine on the NIP in late 2005;14 Declines have also been observed in hospitalisation rates in other age groups and in general practice consultations.15-17 In the United States, where universal varicella vaccination has been in place since 1995, there has been an even greater decline in varicella disease (85%) and hospitalisations (70–88%).17-19 The greatest decline in hospitalisation rates has been in 0–4-year olds. However, reductions in hospitalisation rates have also occurred in infants,20 older children and adults, due to herd immunity.17

There has been no evidence of a change in the rates of herpes zoster incidence, healthcare utilisation or hospitalisations in the United States21 or hospitalisations in Australia14,15 attributable to the introduction of the varicella vaccine, although herpes zoster rates in children have declined in the United States20,24

4.22.4 Vaccines

Live attenuated varicella vaccine (VV) is currently available as a monovalent vaccine. Two combination vaccines containing live attenuated measles, mumps, rubella and varicella viruses (MMRV) are also registered in Australia.

All available varicella-containing vaccines are derived from the Oka VZV strain, but have some genetic differences.25 Monovalent VVs have been available in Australia since 2000, and, since November 2005, a single dose of VV has been funded under the NIP for all children at 18 months of age, with a catch-up dose funded for children 10 to 14 years of age who have not received varicella vaccine and who have not had the disease.26 At the time of implementation of a universal varicella vaccination program in Australia, a single dose was considered adequate for protection of infants and children <14 years of age. However, recent data from the United States suggest that a 2nd dose of varicella-containing vaccine in children is optimal to provide an immune response more like that acquired after natural infection, reducing the risk of vaccine failure and increasing population immunity.27 Vaccine failure, also known as breakthrough varicella, is defined as a case of wild-type varicella occurring more than 42 days after vaccination. The majority of cases of breakthrough varicella are mild with fewer lesions than natural infection. However, breakthrough varicella infections can be contagious, particularly if many lesions are present.28

Post-marketing studies in the United States have estimated the effectiveness of 1 dose of VV in children to be 80 to 85% against any disease and 95 to 98% against severe varicella.29-32 Although earlier data suggested persistence of immunity in most healthy vaccine recipients,1 some, but not all, long-term follow-up studies have shown that rates of vaccine failure increased over time in 1-dose vaccine recipients. For example, in one study, vaccine failure was increased 2.6 times in children who received 1 dose of vaccine more than 5 years previously, compared with those who had received 1 dose of vaccine within 5 years.33 Follow-up from a randomised controlled trial in children 12 months to 12 years of age, comparing 1 dose with 2 doses of VV over a 10-year period, showed significantly higher protection with 2 doses (98.3% versus 94.4%).34 Based on current evidence, 2 doses of a varicella-containing vaccine in children from 12 months of age will minimise the risk of breakthrough varicella (refer to 4.22.7 Recommendations below).

Healthy adolescents (≥14 years of age) and adults require 2 doses of varicella vaccine, at least 4 weeks apart, as the response to a single dose of VV decreases progressively as age increases and is insufficient to provide adequate protection.35
Monovalent varicella vaccines (VV)

- **Varilrix** – GlaxoSmithKline Australia Pty Ltd (live attenuated Oka strain of varicella-zoster virus). Lyophilised powder in a monodose vial with separate diluent. Each 0.5 mL reconstituted dose contains ≥10<sup>3.7</sup> plaque-forming units (PFU) of varicella-zoster virus; human albumin; lactose; mannitol; sorbitol; neomycin.

- **Varivax Refrigerated** – bioCSL Pty Ltd (live attenuated Oka/Merck strain of varicella-zoster virus). Lyophilised powder in a monodose vial with a pre-filled diluent syringe. Each 0.5 mL reconstituted dose contains ≥1500 PFU of attenuated varicella-zoster virus; 18 mg sucrose; 8.9 mg hydrolysed porcine gelatin; 3.6 mg urea; 0.36 mg monosodium glutamate; residual components of MRC-5 cells; traces of neomycin and bovine serum.

Combination measles-mumps-rubella-varicella (MMRV) vaccines

- **Priorix-tetra** – GlaxoSmithKline Australia Pty Ltd (live attenuated measles virus (Schwarz strain), mumps virus (RIT 4385 strain, derived from the Jeryl Lynn strain), rubella virus (Wistar RA 273 strain) and varicella-zoster virus (Oka strain)). Lyophilised pellet in a monodose vial with a pre-filled diluent syringe. Each 0.5 mL reconstituted dose contains ≥10<sup>3.0</sup> cell culture infectious dose 50% (CCID<sub>50</sub>) of measles virus, ≥10<sup>6.4</sup> CCID<sub>50</sub> of mumps virus, ≥10<sup>3.5</sup> CCID<sub>50</sub> of rubella virus, and ≥10<sup>3.3</sup> PFU of varicella-zoster virus; lactose; neomycin; sorbitol; mannitol.

- **ProQuad** – bioCSL Pty Ltd (live attenuated measles virus (Enders’ attenuated Edmonston strain), mumps virus (Jeryl Lynn B level strain), rubella virus (Wistar RA 273/3 strain) and varicella-zoster virus (Oka/Merck strain)). Lyophilised powder in a monodose vial with a pre-filled diluent syringe. Each 0.5 mL reconstituted dose contains ≥10<sup>5.00</sup> infectious dose 50% (ID<sub>50</sub>) of measles virus, ≥10<sup>3.00</sup> TCID<sub>50</sub> of mumps virus, ≥10<sup>3.00</sup> TCID<sub>50</sub> of rubella virus, and ≥10<sup>3.00</sup> PFU of varicella-zoster virus; 20 mg sucrose; 11 mg hydrolysed porcine gelatin; 2.5 mg urea; 16 mg sorbitol; 0.38 mg monosodium L-glutamate; 0.25 mg recombinant human albumin; 5 µg neomycin; residual components of MRC-5 cells; 0.5 µg bovine serum albumin.

4.22.5 Transport, storage and handling

Transport according to National vaccine storage guidelines: Store at +2°C to +8°C. Do not freeze. Protect from light. Varicella-containing vaccines are less stable than other commonly used live viral vaccines, and adherence to storage and reconstitution requirements is very important. All vaccines must be reconstituted by adding the entire contents of the diluent to the vial containing the pellet, and shaking until the pellet is completely dissolved. Available monovalent VVs and MMRV vaccines have different requirements following reconstitution.

Reconstituted Varilrix vaccine should be used as soon as practicable. If storage is necessary, hold at 25°C for not more than 90 minutes, or at +2°C to +8°C for not more than 8 hours. Reconstituted Varivax Refrigerated vaccine must be used within 2½ hours.

Reconstituted Priorix-tetra (MMRV) vaccine should be used as soon as practicable. If storage is necessary, hold at +2°C to +8°C for not more than 8 hours.

Reconstituted ProQuad (MMRV) vaccine should be used immediately. If storage is necessary, hold at +20°C to +25°C for not more than 1 hour or at +2°C to +8°C for not more than 2.5 hours.

4.22.6 Dosage and administration

The dose of VV and MMRV vaccines is 0.5 mL, to be given by SC injection. Priorix-tetra may also be given by IM injection. MMRV vaccines are not recommended for use in persons aged ≥14 years. The minimum interval between doses of varicella-containing vaccine is 4 weeks.

Co-administration with other vaccines

VV and MMRV vaccines can be given at the same time as other live attenuated parenteral vaccines (e.g. BCG, yellow fever) or other inactivated vaccines (including DTPa, hepatitis B, Hib, IPV, MenCCV, hepatitis A and pneumococcal conjugate vaccine),<sup>40</sup> using separate syringes and injection sites. If VV or MMRV vaccine is not given simultaneously with other live attenuated parenteral vaccines, they should be given at least 4 weeks apart.

If VV is given at the same time as MMR vaccine, they should be given using separate syringes and injection sites. MMR vaccine and monovalent VV should not be mixed together prior to injection.

Interchangeability of varicella-containing vaccines

In general, the two brands of varicella vaccine can be considered interchangeable; that is, the 2nd varicella dose does not have to be of the same brand as the 1st. The same principle applies to the two available MMRV vaccines,<sup>40</sup> although they are not routinely recommended in a 2-dose schedule.

4.22.7 Recommendations

Children (aged <14 years)

It is recommended that at least 1 dose of a varicella-containing vaccine be given to all children <14 years of age. One dose of varicella-containing vaccine is recommended to be given routinely at 18 months of age or as MMR vaccine; refer to Table 4.22.1. (Refer also to 4.9 Measles[Handbook10-home-handbook10part4-handbook10-4-9].) Prior varicella infection is not a contraindication and such children can still receive either VV or MMRV, as appropriate. (Refer also to ‘Serological testing for varicella immunity from infection and/or vaccination’ below). There is no known increase in adverse events from vaccinating those with pre-existing immunity to one or more of the vaccine components (refer to 4.22.11 Adverse events below).

Administration of varicella vaccine from as early as 12 months of age will provide earlier protection from varicella and can be considered on a case-by-case basis when appropriate, for example, in the context of travel or a varicella outbreak. However, note that MMRV vaccine is not recommended for use as the 1st dose of MMR-containing vaccine in children aged <4 years, due to a small but increased risk of fever and febrile seizures when given as the 1st MMR-containing vaccine dose in this age group (refer to 4.9 Measles[Handbook10-home-handbook10part4-handbook10-4-9] and 4.22.11 Adverse events below). If MMRV is inadvertently administered as dose 1 of MMRV-containing vaccine, the dose does not need to be repeated (providing it was given at ≥12 months of age); however, parents/carers should be advised regarding the small but increased risk of fever and febrile seizures (compared with that expected following MMR vaccine).

Receipt of 2 doses of varicella-containing vaccine provides increased protection and minimises the chance of breakthrough varicella in children <14 years of age.<sup>34</sup> However, routine administration of a 2nd dose of varicella-containing vaccine for children is not included on the NIP schedule. If parents/carers wish to minimise the risk of breakthrough varicella, administration of 2 doses of varicella-containing vaccine is recommended (refer to 4.22.4 Vaccines above). MMRV vaccine is also suitable for use as the 2nd dose of varicella-containing vaccine in children <14 years of age. (For further information, refer to also 4.9 Measles[Handbook10-home-handbook10part4-handbook10-4-9].) The minimum interval between doses of varicella-containing vaccine in children (and adults) is 4 weeks.


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Adolescents (aged ≥14 years) and adults

Vaccination is recommended for all non-immune adolescents (≥14 years of age) and adults. Every effort should be made to identify and immunise non-pregnant seronegative women of child-bearing age (refer to 4.22.2 Clinical features above). Adolescents (≥14 years of age) and adults must receive 2 doses of varicella vaccine to achieve adequate protection from varicella.[44,45] The 2 doses should be administered at least 4 weeks apart. However, a longer interval between vaccine doses is acceptable. Lack of immunity to varicella should be based on a negative history of previous varicella infection and can be supplemented by serological testing for evidence of past infection (refer to ‘Serological testing for varicella immunity from infection and/or vaccination’ below).

MMRV vaccines are not recommended for use in persons ≥14 years of age, due to a lack of data on safety and immunogenicity/efficacy in this age group. If a dose of MMRV vaccine is inadvertently given to an older person, this dose need not be repeated. Vaccination of household contacts of persons who are immunocompromised is strongly recommended. This is based on evidence that transmission of varicella vaccine virus strain is as likely as transmission of varicella-zoster virus in persons who are immunocompromised. [46,47] If vaccinated persons develop a rash, they should cover the rash and avoid contact with persons who are immunocompromised for the duration of the rash. Zoster immunoglobulin (ZIG) need not be given to an immunocompromised contact of a vaccinated person with a rash, because the disease associated with this type of transmission (should it occur) is expected to be mild (refer to 4.22.12 Public health management of varicella below).

Serological testing for varicella immunity from infection and/or vaccination

Children who have an uncertain clinical history or no documentation of age-appropriate varicella vaccination should be considered susceptible and offered vaccination. Although a reliable history of varicella infection correlates highly with serological evidence of immunity in young children,[44,45] due to the decreasing incidence of varicella in Australia and reduced familiarity with the disease, vaccination should be offered, unless confident clinical diagnosis of prior natural infection is made. Testing of children to assess serologic status prior to vaccination is generally not recommended. Provided there are no contraindications, children can safely receive either varicella or MMRV vaccine, even if prior infection with varicella has occurred (refer to ‘Children (aged <14 years)’ above).

In older adolescents and adults with a negative history of varicella infection and no documented history of age-appropriate vaccination, serological testing before vaccination is more likely to be helpful, as a majority of those with a negative history are immune, and thus may not require vaccination.[46,47] Screening for varicella immunity (from natural infection) or a past history of vaccination should be undertaken as part of pre-pregnancy planning and varicella vaccine given to non-immune women prior to conception. Testing to check for seroconversion after varicella vaccination is not recommended. Commerially available laboratory tests are not usually sufficiently sensitive to detect antibody levels following vaccination, which may be up to 10-fold lower than levels induced by natural infection.[46,47] Protection (commensurate with the number of vaccine doses received, refer to 4.22.4 Vaccines above) should be assumed if a child or adult has documented evidence of receipt of age-appropriate dose(s) of a varicella-containing vaccine. If serological tests to investigate existing immunity to varicella are performed, interpretation of the results may be enhanced by discussion with the laboratory that performed the test, ensuring the relevant clinical information described above is provided.

Post-exposure vaccination

If varicella-containing vaccines are not contraindicated, vaccination can be offered to non-immune age-eligible children and adults who have a significant exposure to varicella or HZ, and wish to be protected against primary infection with VZV. (Refer also to 4.22.12 Post-exposure vaccination requirements). Post-exposure vaccination is generally successful when given within 3 days, and up to 5 days after exposure, with earlier administration being preferable.[51-55] MMRV vaccine can be given to children in this setting, particularly if MMR vaccination is also indicated (refer to 4.22.7 Recommendations above).

Household contacts of persons who are immunocompromised

Vaccination of household contacts of persons who are immunocompromised is strongly recommended. This is based on evidence that transmission of varicella vaccine virus strain is extremely rare and it is likely to cause only mild disease (refer to 4.22.11 Adverse events below). This compares with the relatively high risk of severe varicella disease from exposure to wild-type varicella-zoster virus in persons who are immunocompromised.[46,47] If vaccinated persons develop a rash, they should cover the rash and avoid contact with persons who are immunocompromised for the duration of the rash. Zoster immunoglobulin (ZIG) need not be given to an immunocompromised contact of a vaccinated person with a rash, because the disease associated with this type of transmission (should it occur) is expected to be mild (refer to 4.22.12 Public health management of varicella below).

Healthcare workers, staff working in early childhood education and care, and in long-term care facilities

Refer to 3.3 Groups with special vaccination requirements, Table 3.3.7 Recommended vaccinations for persons at increased risk of certain occupationally acquired vaccine-preventable diseases (Handbook10-home=handbook10part13=handbook10-3-3table-3-3-7) for more information.

Vaccination against varicella is recommended for all non-immune adults, but especially for all healthcare workers (HCW), staff working in early childhood education and care, and staff working in long-term care facilities. Persons in such occupations who have a negative or uncertain history of varicella infection, and who do not have documentation of 2 doses of varicella vaccine, should be vaccinated with 2 doses of varicella vaccine or have serological evidence of immunity to varicella[52] (refer to ‘Adolescents (aged ≥14 years) and adults’ above). Testing to check for seroconversion after VV is not recommended (refer to ‘Serological testing for varicella immunity from infection and/or vaccination’ above). However, since varicella vaccination is not 100% effective, HCWs and other carers should still be advised of the signs and symptoms of infection and how to manage them appropriately according to local protocols if they develop varicella.

4.22.8 Pregnancy and breastfeeding

Varicella-containing vaccines are contraindicated in pregnant women (refer to 4.22.9 Contraindications below). Pregnancy should be avoided for 28 days after vaccination. Varicella-containing vaccines can be given to breastfeeding women. Most live vaccines have not been demonstrated to be secreted in breast milk. Women who received varicella vaccine while breastfeeding showed no evidence of VZV DNA in breast milk samples, and no effects on breastfed infants have been reported.[56] Post-partum vaccination of women without evidence of varicella immunity need not be delayed because of breastfeeding.

MMRV vaccines are not recommended for use in persons aged ≥14 years.

Refer to 3.3 Groups with special vaccination requirements, Table 3.3.1 Recommendations for vaccination in pregnancy (Handbook10-home=handbook10part13=handbook10-3-3table-3-3-1) for more information.

4.22.9 Contraindications

Anaphylaxis to vaccine components

Serious and life-threatening allergic reactions (anaphylaxis) have been reported following varicella vaccination. Varicella vaccines should not be given to individuals who have a history of anaphylaxis or other severe allergic reactions to vaccines or vaccine components. Reactions to other vaccines, especially to the varicella-zoster virus (VZV) vaccine, also need to be considered. The varicella vaccine contains endotoxin from Neisseria meningitidis. It is therefore contraindicated in persons with known or suspected endotoxin reactions. Anaphylactic reactions have also been associated with the tetanus toxoid component of the MMR vaccine. Labelling of the MMR vaccine refers to ‘anaphylaxis to vaccine components’ as a contraindication. This is considered a precautionary measure, as no reactions to the varicella component of the MMR vaccine have been reported.

Varicella-containing vaccines are contraindicated in persons with a history of anaphylaxis to vaccine components, or any other serious allergic reaction to components of the vaccine.

Lack of immunity to meningococcal meningitis. Meningococcal meningitis is a serious complication of varicella infection and should be treated with antibiotics. If meningococcal meningitis is diagnosed, further varicella vaccination should be delayed until the infection is fully treated.

Varicella vaccine is only recommended for use in persons aged ≥12 months.

The 2nd dose of MMR-containing vaccine is recommended to be provided at 18 months of age to improve 2-dose coverage and protection against measles in young children. However, until June 2013 the 2nd dose of MMR vaccine is included under the NIP schedule for administration at 4 years of age. From July 2013, the 2nd dose of MMR vaccine will move to the 18-month NIP schedule point and be provided as MMRV vaccine.


c## Vaccines | Schedule point (age) 12 months | Schedule point (age) 18 months | Schedule point (age) 4 years
--- | --- | --- | ---
(a) Only monovalent varicella vaccine available | MMR | VV | MMR*
(b) When MMRV vaccine available (from July 2013) | MMR | MMRV | —
Persons who are immunocompromised

Measles-, mumps-, rubella- and varicella-containing vaccines contain live attenuated vaccine viruses and are contraindicated in persons who are immunocompromised. Thus, both VV and MMRV vaccines are contraindicated in the following groups:

- Persons immunocompromised due to HIV/AIDS. Vaccination with live attenuated vaccines can result in a more extensive vaccine-associated rash or disseminated infection in persons with AIDS.69-72 However, varicella vaccination (with a 2-dose schedule of VV) of asymptomatic HIV-infected persons >12 months of age with an age-specific CD4+ count of ≥15% may be considered.69-72 (refer to ‘HIV-infected persons’ in 3.3.3 Vaccination of immunocompromised persons). Since studies have not been performed using combination MMRV vaccines in asymptomatic HIV-infected persons or persons with an age-specific CD4+ count of ≥15%, it is recommended that only MMR vaccine and monovalent VV be considered for use in this setting.69-72

- Persons with other medical conditions associated with significant immune compromise (refer to 3.3.3 Vaccination of immunocompromised persons (Handbook10-home-handbook10part3-handbook10-3-3#3-3-3)).

- Persons receiving high-dose systemic immunosuppressive therapy, such as chemotherapy, radiation therapy or oral corticosteroids. Varicella-containing vaccines are contraindicated in persons taking high-dose oral corticosteroids for more than 1 week (in children equivalent to >2 mg/kg per day prednisolone, and in adults >60 mg per day) (refer to 3.3.3 Vaccination of immunocompromised persons). Those who have been receiving high-dose systemic steroids for more than 1 week may be vaccinated with live attenuated vaccines after corticosteroid therapy has been discontinued for at least 1 month68 (refer to 3.3.3 Vaccination of immunocompromised persons (Handbook10-home-handbook10part3-handbook10-3-3#3-3-3)).

Refer also to 3.3. Groups with special vaccination requirements (Handbook10-home-handbook10part3-handbook10-3-3#3-3-4) and 4.9 Measles (Handbook10-home-handbook10part4-handbook10-4-9) for more information.

Pregnant women

Refer also to 4.22.8 Pregnancy and breastfeeding above.

Varicella-containing vaccines are contraindicated in pregnant women.

This is due to the theoretical risk of transmission of the varicella component of the vaccine to a susceptible fetus. However, no evidence of vaccine-induced congenital varicella syndrome has been reported. A registry in place from 1995 to 2013 in the United States recorded the maternal-fetal outcomes of pregnant women who were inadvertently administered ZV-containing vaccine within 3 months before or at any time during pregnancy. Data from the registry showed that, among the 860 prospectively enrolled women (including 96 live births to women known to be ZVV-seronegative who were exposed during the first or second trimester when the risk for congenital varicella syndrome is greatest), there was no evidence of congenital varicella syndrome.67 The overall occurrence of major congenital anomalies among live born infants was 2.2%, similar to reported rates in the general United States population.

A non-immune pregnant household contact is not a contraindication to vaccination with varicella-containing vaccines of a healthy child or adult in the same household. The benefit of reducing the exposure to varicella by vaccinating healthy contacts of non-immune pregnant women outweighs any theoretical risks of transmission of vaccine virus to these women.

4.22.10 Precautions

For additional precautions related to MMRV vaccines, refer to 4.9 Measles (Handbook10-home-handbook10part4-handbook10-4-9).

Vaccination with other live attenuated parenteral vaccines

If a varicella-containing vaccine is not given simultaneously with other live attenuated parenteral vaccines (e.g. MMR, BCG, yellow fever), the vaccines should be given at least 4 weeks apart.

Vaccination after immunoglobulin or blood product administration

Administration of MMR or MMRV vaccine should be delayed after administration of immunoglobulin-containing products. After receipt of immunoglobulin-containing blood products, the expected immune response to measles, mumps, rubella and varicella vaccination may be impaired.68-72 VV or MMRV vaccine should not be given for between 3 and 11 months following the administration of immunoglobulin-containing products. The interval between receipt of the blood product and vaccination depends on the amount of immunoglobulin in each product, and is indicated in 3.3 Groups with special vaccination requirements. Table 3.3.6 Recommended intervals between either immunoglobulins or blood products and MMR, MMRV or varicella vaccination (Handbook10-home-handbook10part3-handbook10-3-3#Table-3-3-4).68 For further information, refer to 3.3.4 Vaccination of recent recipients of normal human immunoglobulin and other blood products (Handbook10-home-handbook10part3-handbook10-3-3#3-3-4) and 4.22.13 Variations from product information below.

Recent blood transfusion with washed red blood cells is not a contraindication to VV or MMRV vaccines.

Varicella vaccine may be administered concomitantly with, or at any time in relation to, anti-D immunoglobulin, but at a separate injection site. Anti-D immunoglobulin does not interfere with the antibody response to vaccine.

Immunoglobulin or blood product administration after vaccination

Immunoglobulin-containing products should not be administered for 3 weeks following vaccination with varicella-containing vaccines, unless the benefits exceed those of vaccination. If immunoglobulin-containing products are administered within this interval, the vaccinated person should be revaccinated later at the appropriate time following the product (as indicated in Table 3.3.6 Recommended intervals between either immunoglobulins or blood products and MMR, MMRV or varicella vaccination (Handbook10-home-handbook10part3-handbook10-3-3#Table-3-3-4)).

Rh (D) immunoglobulin (anti-D) may be given at the same time, in different sites with separate syringes, or at any time in relation to varicella vaccine, as it does not interfere with the antibody response to the vaccine.

Persons receiving long-term aspirin or salicylate therapy

Persons receiving long-term salicylate therapy (aspirin) should be vaccinated if indicated, as the benefit is likely to outweigh any possible risk of Reye syndrome occurring after vaccination. Natural varicella infection and salicylate use has been associated with an increased risk of developing Reye syndrome. However, there have been no reports of an association between Reye syndrome and varicella vaccination (refer to 4.22.13 Variations from product information below).

4.22.11 Adverse events

If using MMRV vaccine, additional adverse events relating to the measles, mumps and rubella vaccine components are discussed in 4.9 Measles (Handbook10-home-handbook10part4-handbook10-4-9). 4.11 Mumps (Handbook10-home-handbook10part4-handbook10-4-11) and 4.18 Rubella. (Handbook10-home-handbook10part4-handbook10-4-11)

Adverse events following administration of varicella-containing vaccines are generally mild and well tolerated.71

Injection site reactions (pain, redness or swelling) are the most common adverse events reported after varicella vaccination, occurring in 7 to 30% of vaccine recipients, but are generally well tolerated.71

A maculopapular or papulovesicular rash may develop after varicella vaccination (usually within 5 to 26 days). A VV-associated rash is likely to occur in less than 5% of vaccine recipients, and to last for less than 1 week.72-77 Rashes typically consist of 2 to 5 lesions and may be generalised (3-5%), or also commonly occur at the injection site (3-5%).68 VV-associated rash may be atypical and may not be vesicular. Most varicellaiform rashes that occur within the first 2 weeks after vaccination are due to wild-type ZVV, with median onset 8 days after vaccination (range 1 to 24 days), while vaccine-strain VZV rashes occur at a median of 21 days after vaccination (range 5 to 42 days).74-75
Fever >39°C has been observed in 15% of healthy children after varicella vaccination, but this is comparable to that seen in children receiving placebo.66 In adults and adolescents, fever has been reported in 10% of VV recipients. It is recommended that parents/caregivers/vaccine recipients be advised about possible symptoms in the period 5 to 12 days after vaccination, and given advice on their management, including the use of paracetamol for fever (refer to 2.3.2 Adverse events following immunisation (Handbook10-home-handbook10part2-handbook10-2-3#2.3.2)). Higher rates of fever were observed in clinical trials of both MMRV vaccines, particularly following dose 1, when compared with giving MMR vaccine and monovalent VV at the same time but at separate sites.36–39 Two post-marketing-studies in the United States identified an approximately 2-fold increased risk of fever and febrile convulsions in 1st dose recipients of MMRV vaccine, who were predominantly 12–23 months of age, in the period 7 to 10 days39 (or 5 to 12 days)26 after vaccination, compared with recipients of separate MMR and VV vaccines. MMRV vaccination resulted in 1 additional febrile seizure for every 2300 doses compared to separate MMR and VV vaccination.26 An increase in fever or febrile convulsions has not been identified after the 2nd dose of MMRV vaccine in the United States, although most 2nd dose recipients were aged 4–6 years, an age at which the incidence of febrile convulsions is low.61 These post-marketing studies were in children who received ProQuad; however, it is anticipated that this side effect profile would be similar in Priorix-tetra recipients.

A post-marketing study in the United States reported serious adverse events temporally, but not necessarily causally, linked to varicella vaccination, such as encephalitis, ataxia, thrombocytopenia and anaphylaxis, were very rare and occurred in <0.01% of doses distributed.48,70 There were no neurological adverse events following VV in which the Oka vaccine virus strain was detected in cerebrospinal fluid (CSF).

Herpes zoster (HZ) has been reported rarely in vaccine recipients and has been attributed to both the vaccine strain and to wild-type varicella virus reactivation.14 Reactivation of the vaccine virus resulting in HZ is rare and most cases of HZ in vaccine recipients can be attributed to reactivation of wild-type virus following unrecognised prior infection. The risk of developing HZ is currently thought to be lower after vaccination than after natural varicella virus infection, and reported cases have been mild.2 Rates of herpes zoster in children 0–8 years of age after natural VZV infection were estimated to be between 30 and 74 per 100 000 per year,29 while a rate of 22 per 100 000 person-years was reported in a 9-year follow-up of 7000 varicella vaccinated children.27 (Refer also to 4.24 Zoster (Handbook10-home-handbook10part4-handbook10-4-24.).)

Persons with egg allergy can be safely given MMRV vaccine (refer to 4.9.11 Adverse events in 4.9 Measles).

### 4.22.12 Public health management of varicella

Varicella is a notifiable disease in most states and territories in Australia. Further instructions about the public health management of varicella, including management of cases of varicella and their contacts, should be obtained from state/territory public health authorities (refer to Appendix 1 Contact details for Australian, state and territory government health authorities and communicable disease control (Handbook10-home-handbook10-tools-handbook10-appendices-handbook10-appendix1)).

- **Zoster Immunoglobulin-VF (human)** – CSL Limited. 160 mg/mL immunoglobulin (mainly IgG) prepared from human plasma containing high levels of antibody to the varicella-zoster virus. Single vials contain 200 IU of varicella-zoster antibody, with the actual volume stated on the label on the vial. Also contains glycine.

High-titre zoster immunoglobulin (ZIG) is available from the Australian Red Cross Blood Service on a restricted basis for the prevention of varicella in high-risk subjects who report a significant exposure to varicella or HZ. ZIG has no proven use in the treatment of established varicella or zoster infection. ZIG is highly efficacious, but is often in short supply. Normal human immunoglobulin (NHIG) can be used for the prevention of varicella if ZIG is unavailable. Post-exposure prophylaxis using varicella vaccine may also be indicated, if vaccination is not contraindicated (refer to below).

Zoster immunoglobulin should only be given by IM injection.

‘Significant exposure’ to VZV is defined as living in the same household as a person with active varicella or HZ, or direct face-to-face contact with a person with varicella or HZ for at least 5 minutes, or being in the same room for at least 1 hour. In the case of varicella infection, the period of infectivity is from 48 hours before the onset of rash until crusting of all lesions has occurred. Transmission from a person with localised zoster is less likely than from a person with varicella.4

Immunocompetent varicella contacts should be tested for varicella-zoster antibodies. ZIG must be given early in the incubation period (within 96 hours of exposure), but may have some efficacy if administered out to as late as 10 days post exposure. ZIG is able to prevent or ameliorate varicella in infants <1 month of age, in children who are being treated with immunosuppressive therapy, and in pregnant women. Persons with primary or acquired diseases associated with cellular immune deficiency and those receiving immunosuppressive therapy should be tested for varicella-zoster antibodies before contacting with a person with confirmed varicella. However, testing should not delay ZIG administration after initial exposure to a case.4

ZIG administration (preferably within 96 hours and up to 10 days after exposure) is required for the following groups and should not be delayed by testing (if indicated below):

- Pregnant women who are presumed to be susceptible to varicella infection. If practicable, they should be tested for varicella-zoster antibodies before ZIG is given.3
- Neonates whose mothers develop primary VZV infection (chickenpox) from 7 or fewer days before delivery to 2 days after delivery. ZIG must be given, as the neonatal mortality without ZIG is up to 30% in this setting.1,7 ZIG must be given as early as possible in the incubation period.
- Neonates exposed to varicella in the 1st month of life, if the mother has no personal history of infection with VZV and is seronegative.27 ZIG should be given, due to the increased risk of severe varicella in newborns of seronegative women.
- Premature infants (born <28 weeks gestation or whose birth weight is <1000 g) exposed to VZV while still hospitalised should be given ZIG regardless of maternal history of varicella.
- Patients suffering from primary or acquired diseases associated with cellular immune deficiency, and those receiving immunosuppressive therapy.3,8

Note: If an immunocompromised VZV contact is shown to have recent evidence of detectable antibodies, it is not necessary to give ZIG, as its administration will not significantly increase varicella-zoster antibody titres in those who are already antibody positive. Note that varicella-zoster antibodies detected in patients who have been transfused or who have received intravenous immunoglobulin or ZIG in the previous 3 months may be passively acquired and transient.

The dose schedule recommended for ZIG administration is shown in Table 4.22.2.

<table>
<thead>
<tr>
<th>Weight of patient (kg)</th>
<th>Dose (IU)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0–10</td>
<td>200</td>
</tr>
<tr>
<td>11–30</td>
<td>400</td>
</tr>
<tr>
<td>&gt;30</td>
<td>600</td>
</tr>
</tbody>
</table>

A dose of ZIG may be repeated if a 2nd exposure occurs more than 3 weeks after the 1st dose of ZIG. However, testing for varicella antibodies is also recommended (refer above). NHIG can be used for the prevention of varicella if ZIG is unavailable (refer to Part 5 Passive immunisation (Handbook10-home-handbook10part5)). Persons receiving monthly high-dose intravenous NHIG are likely to be protected and probably do not require ZIG if the last dose of NHIG was given 3 weeks or less before exposure.

If VV is not contraindicated, it can be offered to non-immune age-eligible children and adults who have a significant exposure to varicella or HZ and wish to be protected against primary infection with VZV (refer to ‘Post-exposure vaccination’ in 4.22.7 Recommendations above).

Vaccination has the added benefit of reducing the likelihood of varicella infection, particularly moderate to severe disease, following exposure, and also provides long-term protection. Vaccination of exposed persons during outbreaks has also been shown to prevent further cases and to control outbreaks. If MMR vaccination is also indicated. MMRV vaccine can be used in children <14 years of age, although MMRV vaccine is not routinely recommended as the 1st dose of MMR-containing vaccine in children aged <4 years (refer to 4.22.7 Recommendations above).

Post-exposure vaccination should be administered within 5 days, and preferably within 3 days, after exposure.

### 4.22.13 Variations from product information

Varilrix and Varivax Refrigerated are registered for use as 2 doses of 0.5 mL (1–2 months apart) in adolescents ≥13 years of age and adults. The ATAGI instead recommends a single dose of varicella vaccine for children <14 years of age and 2 doses of varicella vaccine in those aged ≥14 years.

In adults and adolescents where 2 doses of varicella vaccine are required, the product information for Varilrix states that the 2nd dose should be given at least 6 weeks after the 1st dose. The ATAGI recommends instead that the 2nd dose may be given at least 4 weeks after the 1st dose.

The product information for both monovalent varicella vaccines and both MMRV vaccines recommends that women of child-bearing age should be advised not to become pregnant for 3 months after vaccination. The ATAGI instead recommends avoiding pregnancy for 28 days after vaccination.

The product information for Priorix-tetra and ProQuad states that persons with a history of anaphylactic or anaphylactoid reactions to egg should not be vaccinated. The ATAGI recommends instead that either Priorix-tetra or ProQuad can be given in this situation.

The product information for Priorix-tetra states that it should be given by SC injection. The ATAGI recommends that it may also be given by IM injection.

The product information for ProQuad states that the vaccine is indicated for vaccination in individuals 12 months through 12 years of age. The product information for Priorix-tetra states that this vaccine can be used in persons from 9 months of age. The ATAGI recommends instead that both MMRV vaccines can be given to persons up to 14 years of age. The ATAGI also recommends that MMRV vaccine should not be used routinely as the 1st dose of MMR-containing vaccine in children aged <4 years.

The product information for all varicella-containing vaccines states that salicylates should be avoided for 6 weeks after vaccination, as Reye syndrome has been reported following the use of salicylates during natural varicella infection. The ATAGI recommends instead that non-immune persons receiving long-term salicylate therapy can receive varicella-containing vaccine, as the benefit is likely to outweigh any possible risk of Reye syndrome occurring after vaccination.

The product information for Varilrix recommends delaying vaccination for 5 months after receipt of NHIG by IM injection or blood transfusion. The ATAGI recommends instead that varicella-containing vaccines should not be given for at least 6 months after receipt of immunoglobulin-containing blood products according to the intervals contained in Table 3.3.6 Recommended intervals between either immunoglobulins or blood products and MMR, MMRV or varicella vaccine (Handbook10-home~handbook10part3~handbook10-3-3#table-3-3-6).

The dosage of ZIG recommended in the product information differs from that in Table 4.22.2, which has been revised in order to minimise wastage of ZIG.

### References

A full reference list is available on the electronic Handbook or Immunise Australia website (http://www.immunise.health.gov.au).


4.23 Yellow fever

4.23.1 Virology
Yellow fever is a viral haemorrhagic fever caused by an RNA flavivirus. The virus is transmitted by mosquitoes (predominantly Aedes aegypti) through jungle (between non-human primates and mosquitoes) and urban (between humans and mosquitoes) zoonotic transmission cycles. In Africa, an intermediate transmission cycle exists between humans or non-human primates and Aedes species mosquitoes that breed in tree holes in savannah areas.1

4.23.2 Clinical features
The clinical spectrum of yellow fever varies from a non-specific febrile illness to fatal haemorrhagic fever.2 After an incubation period of 3 to 6 days, the disease begins abruptly with fever, prostration, myalgia and headache. The patient appears acutely ill with congestion of the conjunctivae; there is an intense viraemia during this 'period of infection', which lasts 3 to 4 days.2 This may be followed by the 'period of remission', in which the fever and symptoms settle over 24 to 48 hours, during which the virus is cleared by immune responses.6

Approximately 15 to 25% of patients may then relapse with a high fever, vomiting, epigastric pain, jaundice, renal failure and haemorrhage, referred to as 'the period of intoxication'.2 These complications can be severe, and reflect the viscerotropic nature of the yellow fever virus (its ability to infect the liver, heart and kidneys). The case-fatality rate varies widely, but can be more than 20% in local populations.5

4.23.3 Epidemiology
Yellow fever virus occurs in tropical and subtropical regions of Africa and South America where it is endemic and intermittently epidemic. The epidemiology of yellow fever is dynamic due to changes in climate, such as rainfall patterns, and human factors such as migration and air travel.1 West Africa has the highest burden of yellow fever disease, accounting for 90% of all yellow fever cases reported between 1985 and 2009. The remainder of cases occur in other regions of Africa and South America.4 In 2014, 21 cases of yellow fever, including 12 deaths, were reported to the World Health Organization (WHO) from three countries: the Democratic Republic of Congo, Brazil and Peru. In 2006, the WHO introduced the Yellow Fever Initiative with the aim to control and eliminate epidemic yellow fever in Africa by including yellow fever vaccine in routine childhood immunisation programs and implementing mass vaccination campaigns. In endemic areas where high vaccination coverage has been achieved, the occurrence of yellow fever outbreaks has decreased substantially. A similar approach has been taken in South America.5

The risk of susceptible travellers acquiring yellow fever varies considerably with season, location, duration of travel and utilisation of mosquito avoidance measures. There have been reported cases of yellow fever, all fatal, in unvaccinated travellers to Africa and South America.1 Updated information regarding yellow fever virus activity and/or risk in travel destinations should be sought from a reputable source prior to travel (for example, Health information for international travel (the 'Yellow book') published by the US Centers for Disease Control and Prevention, available at (www.cdc.gov/travel/yellowbook)).7

4.23.4 Vaccine

Yellow fever vaccine is a live, freeze-dried preparation of attenuated 17D strain yellow fever virus cultured in, and harvested from, embryonated chicken eggs. The vaccine does not contain antibiotics, preservatives or gelatin.

There are no studies that directly assess the efficacy of yellow fever vaccine. However, immunogenicity is used as a surrogate for protection, with thresholds for protective immunity defined as either log10 neutralisation index (LNI) >0.7, or a titre of >1:10 using plaque reduction neutralisation tests.8 Following a single dose of yellow fever vaccine, protective levels of neutralising antibodies are achieved in approximately 90% of healthy adult vaccine recipients by day 14, and in virtually all recipients by day 28.4 In children, the proportion of vaccine recipients who achieve protective yellow fever antibody levels following a single dose of vaccine is similar to that in adults.9,10 One randomised trial suggested lower seroconversion rates against yellow fever virus in children <2 years of age (70%); however, this was when yellow fever vaccine was co-administered with MMR vaccine.11 In comparison, 87% of children who received yellow fever and MMR vaccines separated by an interval of 30 days or more seroconverted. This study did not report on the proportion of participants with protective levels of neutralising antibodies based on commonly applied definitions.

Immunogenicity studies in individuals with underlying medical conditions are limited. Some data suggest that pregnant women and HIV-infected persons do not respond optimally to yellow fever vaccination. The proportion of recipients who achieved protective levels of neutralising antibodies was lower in women who received yellow fever vaccine in their third trimester of pregnancy (38.6%) than in non-pregnant women of child-bearing age and other adults (81.5–93.7%).12 However, a better response to the yellow fever vaccine was reported in a separate study of women vaccinated in their first trimester of pregnancy, suggesting that antibody response to vaccination in pregnant women may be dependent on length of gestation.13 Two studies reported lower rates of neutralising antibodies among HIV-infected persons compared with uninfected controls.14,15 Although some observational studies have reported seroconversion rates in HIV-infected persons similar to those reported in healthy adults (>90%), the number of participants in these studies was small and there were no healthy controls.16-18 When reported, CD4+ counts of HIV-infected subjects were >200 cells per µL. A number of studies found higher antibody titres were associated with higher CD4+ counts and lower HIV RNA levels.19,20

Data on the immunogenicity of yellow fever vaccine in persons who are immunocompromised, other than with HIV infection, is limited to a few small low quality studies and case reports.21,22 A reduced immune response to yellow fever vaccine has been reported among persons receiving immunosuppressive therapy for rheumatoid disease.23

Immunity to yellow fever virus following a single dose of yellow fever vaccine is expected to be life-long in the majority of healthy vaccine recipients. Protective levels of neutralising antibodies have been detected in 75 to 100% of healthy adults from endemic and non-endemic yellow fever areas when measured ≥10 years after primary immunisation (ranging from 10 to 69 years post vaccination).24,25 Although yellow fever disease has occurred in vaccine recipients, this has only been reported in persons living in highly endemic areas. A study from Brazil showed that among 459 persons with laboratory-confirmed yellow fever who reported previous vaccination, 432 (94%) had yellow fever ≥10 years after vaccination. This indicates probable secondary vaccine failure due to waning immunity, although primary vaccine failure (poor initial immune response) may also have contributed.26


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A booster dose of yellow fever vaccine has been shown to be effective in producing protective levels of yellow fever neutralising antibodies in those whose response to their primary vaccine dose was low or negative.28,29

4.23.5 Transport, storage and handling

Transport according to National vaccine storage guidelines: Strive for 5.30 Store at +2°C to +8°C. Do not freeze. Protect from light.

Stamaril must be reconstituted by adding the entire contents of the diluent syringe to the vial and shaking until the powder is completely dissolved. Reconstituted vaccine must be used within 1 hour.

4.23.6 Dosage and administration

The dose of yellow fever vaccine for children and adults is 0.5 mL, to be given by either IM or SC injection.

Co-administration with other vaccines

Inactivated vaccines and oral live vaccines relevant to travel (e.g. cholera, typhoid) can be given with, or at any time before or after, yellow fever vaccine.

If administration of both yellow fever and other parenteral live vaccines is indicated, the vaccines can be given either on the same day or at least 4 weeks apart. Studies of yellow fever vaccine administered at the same time as other live vaccines, including Japanese encephalitis,31 BCG and monovalent measles vaccines,32 have shown no impact on the immune response to any of the vaccine antigens. Although one Brazilian study suggested the co-administration of yellow fever and MMR vaccines results in lower seroconversion rates to the vaccine antigens than when the vaccines are administered at least 4 weeks apart (refer to 4.23.4 Vaccine above), further studies are required to determine the clinical significance of this finding. Yellow fever vaccine can be given at the same time as the Imojev Japanese encephalitis vaccine,31 using separate syringes and separate injection sites.

4.23.7 Recommendations

Children aged <9 months

Yellow fever vaccine is contraindicated in infants aged <9 months (refer to 4.23.9 Contraindications below).

Children aged ≥9 months and adults

Yellow fever vaccination can only be provided at Yellow Fever Vaccination Centres approved by the relevant state or territory health authorities (refer to ‘International travel requirements’ below).

A single dose of yellow fever vaccine is recommended for:

- persons ≥9 months of age travelling to, or living in, an area with a risk of yellow fever virus transmission. Information about the risk for specific destinations should be sought from a reputable source, such as the WHO33 or the Centers for Disease Control and Prevention,7 prior to travel.
- laboratory personnel who routinely work with yellow fever virus.

Vaccination is generally not recommended when travelling to an area where there is low potential for yellow fever virus exposure (i.e. no human yellow fever cases ever reported and evidence to suggest only low levels of yellow fever virus transmission in the past).

However, vaccination may be considered for travellers outside of the above groups under certain circumstances, for example, to meet specific countries’ vaccination requirements for travel (refer to ‘International travel requirements’ below).

Booster vaccination

In most individuals, a booster dose is not required as a single dose of yellow fever vaccine induces protective antibody levels that persist for many decades (refer to 4.23.4 Vaccine above).

A booster dose is recommended for those individuals who do not respond optimally to yellow fever vaccination (refer to 4.23.4 Vaccine above) if they are travelling to, or living in, an area with a risk of yellow fever virus transmission and 10 or more years have passed since their last dose. These individuals include:

- women who were pregnant when they received their initial dose of yellow fever vaccine, regardless of trimester
- persons who were infected with HIV when they received their initial dose of yellow fever vaccine (regardless of their degree of immunosuppression at the time).

A booster dose should also be considered for travellers outside of the above groups under certain circumstances, for example, to meet specific countries’ vaccination requirements for travel (refer to ‘International travel requirements’ below) or due to a higher risk of yellow fever virus infection (e.g. if living in a high-risk location for an extended period of time or travelling to an area with ongoing outbreaks).

Laboratory workers with ongoing exposure to yellow fever virus should have neutralising antibody titres measured if 10 years or more have passed since their last vaccine dose to determine if a protective antibody level has been maintained. If antibody titres cannot be measured, a booster dose should be administered every 10 years.

Individuals who received a haematopoietic stem cell transplant after a dose of yellow fever vaccine should receive an additional vaccine dose prior to the next time they will be at risk of yellow fever virus infection, irrespective of the period since their last dose. The additional dose should preferably be administered after a period of 24 months has elapsed following the transplant. If the patient has ongoing graft-versus-host disease or remains on immunosuppressive therapy, vaccination should be delayed until the patient is sufficiently immunocompetent. (Refer also to 3.3.3 Vaccination of immunocompromised persons, ‘Haematopoietic stem cell transplant recipients’.)

International travel requirements

All those travelling to, or living in, countries with a risk of yellow fever virus transmission should be informed that the mosquito vectors of yellow fever usually bite during the day. They should be advised of the necessity for mosquito avoidance measures, even if vaccinated. These include the use of insect repellents, coils and sprays, the use of mosquito nets (preferably those that have been treated with an insecticide), and adequate screening of residential and work premises.

Under the International Health Regulations (2005) (IHR), many countries require travellers arriving from countries with a risk of yellow fever virus transmission to provide a valid International Certificate of Vaccination or Prophylaxis (ICVP) against yellow fever, or a valid letter of exemption, prior to entry. A country may require such documentation even for travellers who are only in transit through that country. This is because importation of the virus into these countries by an infected traveller could result in introduction and establishment of the virus in local Aedes aegypti mosquitoes. In 2014, the World Health Assembly of the WHO agreed to extend the validity of the ICVP from 10 years to the duration of the life of the vaccinated person, based on evidence demonstrating that a single dose of yellow fever vaccine provides protection for many decades in most individuals (refer to 4.23.4 Vaccine above). This change in the IHR took effect in June 2016 but yellow fever vaccination entry requirements for some countries may still vary.

It is recommended that the entry requirements for yellow fever vaccination for the countries a traveller intends to enter or transit through be confirmed prior to travel by contacting the country’s foreign missions in Australia.

Australia’s travel requirements

4.23.4 Immunocompromised

Yellow fever vaccine can be administered to HIV-infected persons who are at risk of yellow fever virus infection, providing they are not immunocompromised (refer to 3.3.3 HIV-infected persons). The risk of severe adverse events following yellow fever vaccine is greater in those aged ≥60 years than in younger adults. Therefore, HIV-infected persons should be advised of the necessity for mosquito avoidance measures (refer to 4.23.6 Adverse events). On follow-up of these infants, their neurological development was considered normal. Refer to 3.3 Groups with special vaccination requirements, Table 3.3.1 Recommendations for vaccination in pregnancy for more information.

4.23.8 Pregnancy and breastfeeding

Yellow fever vaccine is contraindicated in pregnant women, unless there is no evidence of any adverse outcomes. Therefore, women vaccinated in early pregnancy can be reassured that there is no evidence of risk to themselves and very low (if any) risk to the fetus. Administration of yellow fever vaccine to women who are breastfeeding infants aged <9 months should be avoided, except in situations where exposure to yellow fever virus cannot be avoided or postponed. Although extremely rare, there have been several case reports of transmission of the vaccine strain of yellow fever virus via breast milk resulting in probable vaccine-associated neurotropic disease in the infants (refer to 4.23.11 Adverse events below). On follow-up of these infants, their neurological development was considered normal. Refer to 3.3 Groups with special vaccination requirements, Table 3.3.1 Recommendations for vaccination in pregnancy for more information.

4.23.9 Contraindications

Any person with a true contraindication to yellow fever vaccine (refer to 4.23.9 Contraindications below) who intends to travel to countries with a risk of yellow fever virus transmission should obtain a dated and signed letter on letterhead stationery from an accredited Yellow Fever Vaccination Centre. The letter should clearly state the yellow fever vaccine is contraindicated on medical grounds and display the centre’s official stamp provided by the state or territory health professional. Medical exemption letters should be written for the current trip only. If exemption to yellow fever vaccine is required for any subsequent trips, a new medical exemption letter should be issued. The vaccination provider is also required to complete, stamp and sign the Medical Contraindications to Vaccination section of the ICVP. Patients with a history of any thymus disorder, including myasthenia gravis, thymoma, thymectomy and DiGeorge syndrome, or thymic damage from chemoradiotherapy or graft-versus-host disease, should not be given the yellow fever vaccine due to the increased risk of yellow fever vaccine-associated viscerotropic disease. There is a concern that immunocompromised individuals may not mount a sufficient immune response following vaccination and may be at risk of vaccine-related adverse events. However, there are few studies assessing yellow fever vaccine immunogenicity in these individuals (refer to 4.23.4 Vaccine above) and an association with serious adverse events has only been demonstrated for individuals with thymus disorders (refer to 4.23.11 Adverse events below).

Yellow fever vaccine can be given to certain persons infected with HIV who are at risk of yellow fever virus infection (refer to 4.23.10 Precautions below). Although extremely rare, there have been several case reports of transmission of the vaccine strain of yellow fever virus via breast milk resulting in probable vaccine-associated neurotropic disease in the infants (refer to 4.23.11 Adverse events below). On follow-up of these infants, their neurological development was considered normal. Refer to 3.3 Groups with special vaccination requirements, Table 3.3.1 Recommendations for vaccination in pregnancy for more information.

4.23.10 Precautions

Adults aged ≥60 years

The risk of severe adverse events following yellow fever vaccine is greater in those aged ≥60 years than in younger adults. Adults ≥60 years of age should be given yellow fever vaccine only if they intend to travel to endemic countries (as recommended above) and they have been informed about the (albeit very low) risks of developing a severe complication.

HIV-infected persons

Yellow fever vaccine can be administered to HIV-infected persons who are at risk of yellow fever virus infection, providing they are not immunocompromised (refer to 3.3.3 Vaccination of immunocompromised persons). Studies of yellow fever vaccine in small numbers of HIV-infected participants suggest a reduced immune response, but vaccination is well tolerated.

Between 1989 and March 2011, 113 cases of neurological adverse event following yellow fever vaccination were reported worldwide.\(^4\) YF-AND is more likely to occur in very young infants and the elderly. Of 23 cases of meningoencephalitis reported between 1945 and 2001, 16 (70%) were infants <9 months of age with the majority <4 months of age. Recommendations made in the 1960s against immunisation of infants aged <6 months led to a reduction in the number of reports.\(^4\) Although YF-AND is rare in adults overall, the risk among adults is greatest in persons >60 years of age.\(^39,41,51\)

### Vaccine-associated viscerotropic adverse events

Yellow fever vaccine-associated viscerotropic disease (YF-AVD) is a severe adverse event that is rarely fatal. YF-AND manifests as several distinct clinical syndromes, including meningoencephalitis (neurotropic disease), Guillain-Barré syndrome, acute disseminated encephalomyelitis and bulbapalsy.\(^47,48\) Between 1989 and March 2011, 113 cases of neurological adverse events following yellow fever vaccination were reported worldwide.\(^4\)

Vaccine-associated viscerotropic adverse events

Two risk factors have been identified for YF-AVD: older age and a history of thymus disease or thymectomy. A systematic review of YF-AVD among the elderly completed by the WHO found evidence to support an increased risk of YF-AVD among elderly travellers, though the risk among the elderly in endemic populations is undetermined.\(^43\) Four of the initial 27 reported cases of YF-AVD worldwide occurred in persons who had thymectomies performed for thymomas,\(^38\) a condition with a low prevalence in the general population.\(^38,53\)

A number of cases of YF-AVD have involved a history of autoimmune disease or diseases with potential autoimmune etiology. However, in a number of these cases, the individual also had another known risk factor. More information is needed to inform whether there is a greater risk of YF-AVD in persons with autoimmune disease.\(^54\)

### 4.23.12 Public health management of yellow fever

Yellow fever is a notifiable and quarantinable disease in all states and territories in Australia. Further instructions about the public health management of yellow fever, including management of cases of yellow fever and their contacts, should be obtained from state/territory public health authorities (refer to Appendix 1 Contact details for Australian, state and territory government health authorities and communicable disease control).

### 4.23.13 Variations from product information

The product information states that pregnancy is a contraindication to the yellow fever vaccine. The ATAGI recommends instead that pregnant women can be vaccinated where travel to an area with a risk of yellow fever virus transmission is unavoidable.

### References

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4.24.1 Virology

Varicella-zoster virus (VZV) is a DNA virus that is a member of the herpesvirus family. Primary infection with VZV is known as varicella or 'chickenpox'.1 Herpes zoster (HZ), or 'shingles', is caused by reactivation of latent VZV, which typically resides in the dorsal root or trigeminal nerve ganglia following primary infection.1

4.24.2 Clinical features

Reactivation of VZV causing HZ is thought to be particularly due to a decline in cellular immunity to the virus, and presents clinically as a unilateral vesicular rash in a dermatomal distribution in the majority of cases. A prodromal phase occurs 48 to 72 hours prior to the appearance of the lesions in 80% of cases.2 Associated symptoms may include headache, photophobia, malaise, and an itching, tingling or severe pain in the affected dermatome.3,4 In the majority of patients, HZ is an acute and self-limiting disease, with the rash lasting 10 to 15 days.1,3 However, complications can occur, especially with increasing age.

Post-herpetic neuralgia (PHN), the most frequent debilitating complication of HZ, is a neuropathic pain syndrome that persists or develops after the dermatomal rash has healed. PHN is most commonly defined as the persistence of pain for longer than 3 months after the onset of the rash (although definitions can vary by the period of persistent pain).5,6 Other complications may occur, depending on the site of reactivation. These include ophthalmic disease (such as keratitis and choriorretinitis), neurological complications (such as meningoencephalitis and myelitis), secondary bacterial skin infection, scarring and pneumonia.7 Rarely, disseminated HZ may develop, with widespread vesicular rash, and visceral, central nervous system and pulmonary involvement. Disseminated disease is more common in persons who are immunocompromised.4 Dermatomal pain without the appearance of rash is also documented (zoster sine herpete).

Antiviral therapy, if initiated within 3 days of the onset of HZ, has been shown to reduce the severity and duration of HZ and may reduce the risk of developing PHN.8-12 However, despite medical therapy, PHN may persist for years and can be refractory to treatment.13

4.24.3 Epidemiology

HZ occurs more commonly in persons of older age (particularly rising in incidence after the age of 50 years), with immunocompromise, and following a history of varicella in the 1st year of life. The lifetime risk of reactivation of VZV causing HZ is estimated to be approximately 20 to 30% and it affects half of those who live to 85 years.1,14-16 Second attacks of HZ occur in approximately 5% of immunocompetent persons, but are more frequent in persons who are immunocompromised.1,3,17,18 The rate of HZ cases reported annually in Australia, in all ages, is approximately 490 cases per 100 000 population, with estimates ranging from 330 to 830 per 100 000 population depending on data source. In comparison, approximately 1000 cases per 100 000 population are estimated to occur in persons aged ≥50 years.19-22 Among persons aged ≥250 years, HZ incidence rises with age from an estimated rate of 652 per 100 000 person-years in persons aged 50–59 years to 1450 per 100 000 person-years in persons aged 70–79 years.22 A similar incidence for HZ (1112 cases per 100 000 person-years) in persons ≥60 years of age has been estimated with active surveillance among unimmunised participants in the large efficacy study of zoster vaccine in the United States.23 Persons who are immunocompromised have an increased risk of HZ. For example, rates of HZ are up to 15 times higher in those who are immunocompromised due to HIV infection, and in the 1st year following haematopoietic stem cell transplantation (HSCT) up to 30% of patients may develop HZ.24

Overall, an estimated 13 to 26% of patients with HZ develop complications. Complications occur more frequently with increasing age and with immunocompromise.25,26 PHN is the most common complication of HZ but occurs very infrequently in children and young adults. In persons who develop HZ, PHN occurs in approximately 1 in 5 cases in those aged >80 years, compared with approximately 1 in 10 cases in those aged 50–59 years.22-26 The population-based incidence of PHN is 3 times higher in persons 70–79 years of age (235 per 100 000) than in persons 50–59 years of age (73 per 100 000).22

Modelling studies of the impact of universal childhood vaccination programs for varicella have predicted that a rise in the incidence of HZ could occur, based on the assumption that exposure to wild-type VZV circulating in the community boosts immunity.27 However, to date, multiple studies and surveillance data do not demonstrate any consistent changes in overall HZ incidence in the United States, which has a universal varicella vaccination program that commenced in 1995.28-30 Australian data show an increase in HZ GP consultation rates over time, commencing prior to varicella vaccine introduction, which is likely to be due to the increasing age of the population. Age-standardised HZ hospitalisation rates have not declined since introduction of varicella vaccine, and the use of zoster vaccine has not yet been extensive enough in any country to expect an impact on HZ epidemiology.31-33 In the United States, the incidence of HZ in children <10 years of age has declined, indicating that HZ rates are lower in varicella vaccine recipients.31

4.24.4 Vaccine

Zostavax is a live attenuated vaccine formulated from the same VZV vaccine strain (Oka/Merck) as the registered varicella (chickenpox) vaccine Varivax, but is of higher potency (on average, at least 14 times greater). The higher viral titre in Zostavax is required to elicit a boost in immune response in adults who usually remain seropositive to VZV following primary infection, but have declining cellular immunity with increasing age.36 Zostavax is used for the prevention of HZ in persons >50 years of age. It is important to note that the registered varicella vaccines are not indicated for use in preventing HZ in older people and Zostavax is not indicated for use in younger people who have not been previously immunised or infected with VZV. Zostavax is not indicated for use for therapeutic benefit during an acute HZ episode, nor for the treatment of PHN.

A single large, randomised, double-blind, placebo-controlled efficacy study of the frozen formulation of Zostavax (known as the ‘Shingles Prevention Study’ [SPS]) was conducted among 38 546 adults aged ≥60 years and demonstrated that Zostavax significantly reduced the likelihood of developing both HZ and PHN.23 Vaccination reduced the incidence of HZ by 51.3%, the incidence of PHN by 66.5%, and the burden of illness associated with HZ by 61.1% over a median of more than 3 years follow-up.23 The vaccine was more efficacious in reducing HZ in persons aged 60–69 years than in those aged 70–79 years (64% compared with 41% efficacy). However, efficacy against PHN was similar in both age groups.23 Efficacy against HZ in the ≥80 years age group was lower (18% and not statistically different to placebo). However, there were fewer participants of this age in the SPS.37 In those who developed HZ despite vaccination, the severity of pain associated with the episode was also reduced.38

Another randomised controlled study in >22 000 50–59-year olds demonstrated a reduction in the incidence of HZ after an average follow-up period of 1.3 years (range 0–2 years), with a vaccine efficacy for preventing HZ of 90.3%.39 In these clinical trials many participants were treated with antiviral and pain medication for their HZ, suggesting that the effect of the vaccine was in addition to any benefit obtained from medical therapy.23,26 Efficacy of a single dose of zoster vaccine appears to decline over time. Data from one short-term follow-up study of participants in the SPS showed a decline in vaccine efficacy; however, estimates remained statistically significant through to the fifth year post vaccination, with uncertain efficacy beyond that point.40,41 A longer-term study of SPS participants suggested that vaccine protection remained significant against HZ up to 8 years post vaccination; however, methodological limitations in that study limit interpretation of this result.42 The need for revaccination following a single dose of zoster vaccine has not yet been determined.
4.24.5 Transport, storage and handling

Transport according to National vaccine storage guidelines: Strive for 5. Store at +2°C to +8°C. Do not freeze. Protect from light.

Zostavax must be reconstituted by adding the entire contents of the diluent container to the vial and shaking until the powder is completely dissolved. Reconstituted vaccine must be used within 30 minutes.

4.24.6 Dosage and administration

The dose of Zostavax is 0.65 mL, to be given by SC injection.

Zostavax must never be given where varicella (chickenpox) vaccine is indicated. Zoster vaccine is only registered for use in adults ≥50 years of age.

Co-administration with other vaccines

Zostavax can be given at the same time as influenza vaccine, using separate syringes and injection sites.

Zostavax can be given at the same time as pneumococcal polysaccharide vaccine (Pneumovax 23; 23vPPV) reported no effect on the immunogenicity of Pneumovax 23 but suggested that the immunogenicity of Zostavax (indicated by VZV antibody levels) was reduced when the vaccines were administered simultaneously compared with administration 4 weeks apart. However, VZV antibody levels have not been shown to directly correlate with clinical protection and a large observational study from the United States reported that concomitant administration of Zostavax and 23vPPV did not affect the effectiveness of Zostavax against HZ.

4.24.7 Recommendations

Zoster vaccine recommendations are based on the risk of HZ and PHN in relation to vaccine efficacy, as above. It is important to review a person’s medical history and medication use prior to vaccination as zoster vaccine is contraindicated in persons who are immuno compromised (refer to 4.24.9 Contraindications and 4.24.10 Precautions).

Adults aged ≥70 years

A single dose of zoster vaccine is recommended for adults aged ≥70 years who have not previously received a dose of zoster vaccine.

Routine vaccination of persons aged 70–79 years is expected to obtain the greatest benefits against HZ and its complications. Although the vaccine efficacy against HZ is lower in this age group compared with younger ages, persons ≥70 years of age experience a greater risk of disease. (Refer also to 4.24.3 Epidemiology and 4.24.4 Vaccine above.)

In persons aged ≥80 years vaccination is less efficacious but may still provide some clinical benefit to the vaccinated individual (refer to 4.24.4 Vaccine above).

Adults aged 60–69 years

A single dose of zoster vaccine is recommended for adults aged 60–69 years who have not previously received a dose of zoster vaccine.

In this age group the incidence of both HZ and PHN is high and the efficacy of the vaccine has been demonstrated; however, the exact duration of vaccine efficacy is not known and it is possible that protection following a single vaccine dose wanes with time (refer to 4.24.4 Vaccine above). The need for revaccination is not yet determined.

Adults aged 50–59 years

Routine use of zoster vaccine in persons aged 50–59 years is not recommended.

Although the incidence of HZ in persons 50–59 years of age is higher than in younger age groups, the likelihood of developing PHN and other complications of HZ is lower in this age group than in those ≥60 years of age.

Persons aged 50–59 years who wish to protect themselves against HZ can be vaccinated; however, the exact duration of vaccine efficacy is not known and it is possible that protection following a single dose wanes with time (refer to 4.24.4 Vaccine above). The need for revaccination is not yet determined.

Persons aged <50 years

Zoster vaccination is not recommended for use in persons <50 years of age and is not registered for use in this age group. There have been very limited studies of the safety and immunogenicity of zoster vaccine in this age group (refer to 4.24.4 Vaccine above).

Persons with a history of a previous episode of HZ

Persons with a history of a previous episode of HZ can be given zoster vaccine. It is possible that a history of previous zoster may be inaccurate or a mistaken diagnosis. In addition, the risk of a repeat episode of zoster has been estimated at approximately 5% in immunocompetent persons. Persons with a history of HZ were excluded from the SPS, so no data on the efficacy of the vaccine in those with a history of HZ is available. The safety and immunogenicity of zoster vaccine in persons with a history of HZ has been studied in one small clinical trial; the vaccine was well tolerated and immunogenic. Injection site reactions were more common in vaccine recipients than in placebo recipients, but similar to vaccine recipients in the SPS. Systemic adverse events were similar between groups. The length of time following an episode of HZ after which it would be reasonable to vaccinate has not been established. However, it is suggested that the vaccine could be given at least 1 year after the episode of HZ.

Persons previously vaccinated with varicella vaccine

Household contacts of persons who are immunocompromised

Vaccination is recommended for persons ≥50 years of age who are household contacts of a person who is, or is expected to become, immunocompromised. Based on evidence that the rate of VZV-like rashes after vaccination is extremely low, it is unlikely that transmission of vaccine-associated virus to a susceptible contact would occur.\(^{23}\) If a vaccinated person develops a varicella- or zoster-like rash, they should cover the rash and avoid contact with persons who are immunocompromised for the duration of the rash. The efficacy of the HZ vaccine is less than 100%, and rashes in vaccinated persons may be due to reactivation of wild-type VZV. If household contacts (<50 years of age) of a person who is immunocompromised have not been previously vaccinated with VZV or immunised with varicella vaccine, they should receive varicella vaccine (refer to 4.22 Varicella\(\text{(Handbook10-home\text{-handbook10part4\text{-handbook10-4-22})}\)).

Serological testing before and after zoster vaccination

Neither history of previous varicella infection nor evidence of prior immunity to VZV is required prior to the routine administration of the zoster vaccine (with the exception of certain immunocompromised persons, refer below). Most older people in Australia are seropositive to VZV due to previous primary varicella infection. Limited data from small studies of the administration of high-dose VZV-containing vaccine (comparable to Zostavax) to healthy VZV seronegative adults, compared with previously infected adults, suggest that the vaccine was well tolerated and immunogenic in seronegative persons, although the incidence of self-limited injection site reactions may be slightly higher.\(^{54,55}\) If a healthy adult eligible for zoster vaccine has laboratory evidence of a lack of immunity to VZV, and does not have a history of age-appropriate varicella vaccination, they may be vaccinated with either 2 doses of varicella vaccine, rather than zoster vaccine (preferred; refer to 4.22 Varicella\(\text{(Handbook10-home\text{-handbook10part4\text{-handbook10-4-22})}\)) or 1 dose of zoster vaccine as an alternative.

Serological testing prior to zoster vaccination is recommended if vaccination is being considered for persons with asymptomatic HIV infection or persons anticipating future significant immunocompromise (refer to 4.24.10 Precautions ‘Persons with HIV infection’ and ‘Persons anticipating future significant immunocompromise’ below). Persons in these categories who have negative VZV IgG should generally not be given Zostavax.

Laboratory testing to check for an immune response after zoster vaccination is not recommended. Zoster vaccine boosts both humoral (IgG) and cellular immune responses; however, confirmation of such immune responses is neither necessary nor predictive of protection against the development of zoster.

### 4.24.8 Pregnancy and breastfeeding

VZV-containing vaccines are contraindicated in pregnant women, although women of child-bearing age are not eligible for zoster vaccination. Pregnancy should be avoided for 28 days after vaccination (refer to 4.22 Varicella\(\text{(Handbook10-home\text{-handbook10part4\text{-handbook10-4-22})}\}).

A non-immune pregnant household contact is not a contraindication to zoster vaccination.

Refer to 3.3 Groups with special vaccination requirements, Table 3.3.1 Recommendations for vaccination in pregnancy\(\text{(Handbook10-home\text{-handbook10part3\text{-handbook10-3-3\text{-table-3-3-1}}\})}\) for more information.

### 4.24.9 Contraindications

Anaphylaxis to vaccine components

Zoster vaccine is contraindicated in persons who have had:

- anaphylaxis following a previous dose of any VZV-containing vaccine
- anaphylaxis following any vaccine component.

Persons who are immunocompromised

In persons who are or have recently been immunocompromised, the safety of administering zoster vaccine should always be considered on a case-by-case basis (refer also to 4.24.11 Adverse events below). If there is uncertainty around the level of immunocompromise and when vaccine administration may be safe, vaccination should be withheld and expert advice sought from the treating physician and/or an immunisation specialist.

Live attenuated zoster vaccine is contraindicated in persons with current or recent severe immunocompromise due to either a primary or acquired medical condition, or due to medical treatment. This includes persons receiving high-dose systemic immunosuppressive therapy, such as chemotherapy, radiation therapy, oral corticosteroids (≥20 mg per day of prednisone equivalent dose for ≥14 days), or biologic or targeted synthetic disease modifying anti-therapeutic drugs (sDMARDs or tsDMARDs); persons suffering from malignant conditions of the reticuloendothelial system (such as lymphoma, leukaemia, Hodgkin’s disease, even if not receiving active treatment); persons with AIDS or symptomatic HIV infection; and any person with similar immunocompromise due to a disease or treatment (refer to Table 4.24.1 Recommendations for use of zoster vaccine in persons on immunosuppressive therapy and 3.3.3 Vaccination of immunocompromised persons\(\text{(Handbook10-home\text{-handbook10part3\text{-handbook10-3-383-3-3})\)).}\)

Persons with less severe immunocompromise than described above (e.g. those on low-dose corticosteroids or selected conventional synthetic DMARDs (csDMARDs), or with asymptomatic HIV infection) may be considered for vaccination on a case-by-case basis after seeking appropriate specialist advice (refer to 4.24.10 Precautions below and 3.3 Groups with special vaccination requirements). For example, zoster vaccine can be given to patients receiving certain csDMARDs in low doses (i.e. methotrexate ≤0.4 mg/kg per week, azathioprine ≤3.0 mg/kg per day or mercaptopurine ≤1.5 mg/kg per day), either on their own or in combination with low-dose corticosteroids (<20 mg per day of prednisone equivalent dose).\(^{55,56}\) At these doses, it is likely that the level of immunocompromise is not severe. In addition, most adults >50 years of age have had previous wild-type VZV infection, and thus have immune memory to VZV, which also mitigates any risk of vaccine virus replication. However, if the extent of immunocompromise is unclear seek expert advice prior to vaccination. Serological confirmation of previous VZV infection prior to vaccination may also be appropriate in certain patients receiving immunosuppressive therapy (refer to 4.24.7 Recommendations, ‘Serological testing before and after zoster vaccination’ above). Persons whose treatment with high-dose systemic immunosuppressive therapy has ceased may be vaccinated if an appropriate time interval has passed (refer to Table 4.24.1 Recommendations for use of zoster vaccine in persons on immunosuppressive therapy and 3.3.3 Vaccination of immunocompromised persons).

<table>
<thead>
<tr>
<th>Treatment regimen</th>
<th>Immunosuppressive therapy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Therapy for less than 14 days</td>
<td>High-dose corticosteroid monotherapy (≥20 mg per day of prednisone or equivalent)</td>
</tr>
<tr>
<td>Therapy for 14 days or longer</td>
<td>csDMARDs</td>
</tr>
<tr>
<td>Azathioprine</td>
<td>&gt;3.0 mg/kg per day</td>
</tr>
<tr>
<td>6-mercaptopurine</td>
<td>&gt;1.5 mg/kg per day</td>
</tr>
<tr>
<td>Methotrexate</td>
<td>&gt;0.4 mg/kg per week</td>
</tr>
<tr>
<td>Immune 1 month prior to treatment initiation OR at least 1 month after treatment cessation</td>
<td>Immune 1 month prior to treatment initiation OR at least 1 month after treatment cessation</td>
</tr>
</tbody>
</table>

Table 4.24.1: Recommendations for use of zoster vaccine in persons on immunosuppressive therapy

Management of immunocompromised persons who inadvertently receive zoster vaccine

If an immunocompromised person is inadvertently vaccinated with zoster vaccine, they should be promptly assessed and appropriate management discussed with an infectious diseases and/or immunisation expert. The relevant state or territory health authority and the TGA should be notified. (For mechanisms for reporting to the TGA, refer to 2.3.2 Adverse events following immunisation(Handbook10-home-handbook10part2-handbook10-2-3#2-3-2)).

It is important to establish the person’s degree of immunocompromise and risk of vaccine-associated adverse effects. Management of the patient may include the need for specific clinical investigations (including, but not limited to, VZV testing from any rash or other affected sites) and/or pre-emptive or therapeutic use of antiviral medication.

4.24.10 Precautions

Persons with HIV infection

Vaccination with zoster vaccine is not recommended for persons with AIDS or symptomatic HIV infection (refer to 3.3.3 Vaccination of immunocompromised persons(Handbook10-home-handbook10part3-handbook10-3-3#3-3)). Table 3.3.4 Categories of immunocompromise in HIV-infected persons, based on age-specific CD4+ counts and percentage of total lymphocytes(Handbook10-home-handbook10part3-handbook10-3-3#3-3-3)) or significant immunocompromise due to other diseases and/or treatment (refer to 4.24.9 Contraindications above).

Persons with asymptomatic HIV infection who are on antiretroviral therapy and who have a very low or undetectable viral load and CD4+ count ≥500 per µL can be vaccinated. Where there is a strong indication to vaccinate, some experts suggest a CD4+ count of 500 per µL is safe.76 Expert advice should be sought from the treating physician and/or an immunisation specialist. (Refer also to 3.3.3 Vaccination of immunocompromised persons(Handbook10-home-handbook10part3-handbook10-3-3#3-3-3), ‘HIV-infected persons’). Serological confirmation of previous VZV infection is recommended prior to vaccination (refer to 2.4.7 Recommendations, ‘Serological testing before and after zoster vaccination’ above).

Although asymptomatic HIV-infected persons are likely to have a higher relative risk of developing HZ in the future,24 it is possible that both the efficacy and the safety of zoster vaccination may be reduced in such recipients, as compared with uninfected persons.

Persons anticipating future significant immunocompromise

Immunocompetent persons who anticipate future alteration of their immune status because of an existing illness can be given zoster vaccine on a case-by-case basis after seeking appropriate specialist advice.37 This may include persons with conditions such as anticipated solid organ transplantation, solid tumours that will require future chemotherapy or radiation therapy, and inflammatory diseases (e.g. rheumatoid arthritis, systemic lupus erythematosus, inflammatory bowel disease, psoriasis) who, at the time, may have minimal alteration to their immune system, but can anticipate significant immunocompromise in the future due to their disease and/or treatment. Since these persons are at high risk of developing zoster in the future, vaccination at least 1 month prior to the onset of immunocompromise may be appropriate (after seeking specialist advice).37 Serological confirmation of previous VZV infection is recommended prior to vaccination (refer to 4.24.7 Recommendations, ‘Serological testing before and after zoster vaccination’ above).

Vaccination before or after immunoglobulin or blood product administration

Zoster vaccine can be given at any time before or after administration of immunoglobulin or any antibody-containing blood product. This is because zoster vaccine is indicated in persons who, because of their age, are assumed to have had a previous VZV infection and, therefore, already have serum antibody levels comparable to those found in blood products. (Refer also to 3.3.4 Vaccination of recent recipients of normal human immunoglobulin and other(Handbook10-home-handbook10part3-handbook10-3-3#3-3-4), ‘Blood products’)

Persons receiving long-term aspirin or salicylate therapy

Persons receiving long-term salicylate therapy (aspirin) can be vaccinated if indicated. There have been no reports of an association between Reye syndrome and varicella vaccination, and it is unlikely that vaccination of a previously VZV-infected older person with zoster vaccine carries any risk of Reye syndrome.

Persons receiving antiviral medication

It is possible that the use of antiviral agents with anti-VZV activity, such as acyclovir, famciclovir or valaciclovir, may interfere with the replication of the Zostavax live attenuated virus. Persons on such antiviral medication should cease treatment no less than 24 hours prior to vaccination and for at least 14 days after vaccination.37,36

4.24.11 Adverse events

Injection site reactions (including erythema, pain, swelling and/or itch at the injection site) occurred in approximately half of clinical trial participants given Zostavax, irrespective of a previous history of HZ (refer also to 4.24.4 Vaccine above).

Varicella-like rashes at the injection site occurred rarely, in 0.1% of recipients; however, they were more common than in placebo recipients. Varicella-like rashes that were not localised to the injection site were also rare, and did not occur more often in vaccine compared with placebo recipients (0.1% in both groups). In the clinical trials in which rashes were analysed by PCR for VZV, the majority were due to wild-type virus; only 2 subjects were found to have rashes due to the Oka/Merck VZV vaccine strain (refer also to 4.24.4 Vaccine above).

Fever >38.5°C was not seen more commonly in vaccine recipients, and occurred in <0.1% of subjects overall.

Systemic symptoms were reported in vaccine recipients more commonly than in placebo recipients (Zostavax 6.3% versus placebo 4.9%), with the most frequently reported systemic symptoms being headache36 and fatigue.72

Post-marketing surveillance in the United States in a cohort of almost 200 000 adults who received the zoster vaccine found no increased risk for a number of potential adverse events occurring after vaccination (such as cerebrovascular events, encephalitis, etc.), but did find a 2-fold increased risk in the 1st week after vaccination for events coded as ‘allergic reactions’, of
4.24.12 Variations from product information

The product information for Zostavax states that the vaccine can be administered concurrently with inactivated influenza vaccine but not with 23vPPV. The ATAGI instead recommends that Zostavax may be administered concurrently with other vaccines (including 23vPPV).

The product information for Zostavax states that the safety and efficacy of Zostavax have not been established in adults with known HIV infection, with or without evidence of immunocompromise. The ATAGI recommends instead that Zostavax may be administered to HIV-infected persons without immunocompromise, and following confirmation of pre-existing immunity to VZV.

References


20. Machintry CR, Chu CP, Burgess MA. Use of hospitalization and pharmaceutical prescribing data to compare the prevacccination burden of varicella and herpes zoster in Australia. Epidemiology and Infection 2003;131:675-82.
42. Tseng HF, Smith N, Sy LS, Jacobsen SJ. Evaluation of the incidence of herpes zoster after concomitant administration of zoster vaccine and polysaccharide pneumococcal vaccine.
Part 5 Passive Immunisation

5.1 Passive immunisation using immunoglobulin preparations

Immunoglobulin preparations are used to provide passive immunisation, that is, the direct administration of antibodies to a non-immune person to provide immediate protection against infection or disease.

Immunoglobulin infusions are also indicated for some immunocompromised persons who are antibody-deficient. In addition, immunoglobulins are also used in the treatment of a number of specific immune-mediated conditions in order to modulate the disease course. For further information regarding the use of intravenous immunoglobulin, refer to Criteria for the clinical use of intravenous immunoglobulin in Australia [see http://www.nba.gov.au/ivig/index.html]1.

There are two types of immunoglobulin:

- normal human immunoglobulin
- specific immunoglobulins.

Normal human immunoglobulin (NHIG) is derived from the pooled plasma of blood donors. It contains antibody to microbial agents that are prevalent in the general population.

Specific immunoglobulin preparations are obtained from pooled blood donations from patients convalescing from the relevant infection, donors recently vaccinated with the relevant vaccine, or those who, on screening, have been found to have sufficiently high antibody concentrations. These blood-derived specific immunoglobulins therefore contain concentrations of antibody to an individual organism or toxin at a higher titre than would be present in normal immunoglobulin.

Donors of blood used for the production of NHIG and specific immunoglobulin products are screened, and the products are treated to minimise the risk of the immunoglobulin preparations containing HIV, hepatitis A, hepatitis B or hepatitis C viruses, or parvovirus. Two dedicated pathogen inactivation steps are incorporated into the manufacturing process. A pasteurisation step is usually used during manufacture. The risk of prion transmission remains theoretical (see Resident risk estimates for transfusion-transmissible infections [http://www.transfusion.com.au/adverse_events/risks/estimates] for further details).

## 5.1.1 Availability of immunoglobulins

CSL Limited supplies NHIG for IM use both directly to hospitals and to the Australian Red Cross Blood Service. Rabies immunoglobulin, tetanus immunoglobulin and botulism antitoxin can only be obtained by application to state/territory health authorities. Respiratory syncytial virus (RSV) monoclonal antibody (Synagis; Abbott Australia) is available commercially.

Other specific immunoglobulins (for hepatitis B, cytomegalovirus, tetanus and varicella-zoster), which are derived from Australian donated plasma, can be obtained only from the Australian Red Cross Blood Service medical officer. The Australian Red Cross Blood Service supplies these products free of charge.

The Blood Service can be contacted by telephone nationally on 13 14 95; callers will then be connected to the relevant state or territory Australian Red Cross Blood Service branch.

### Individual state or territory contact numbers:

- Australian Capital Territory - 02 6206 6024
- New South Wales - 1300 478 348
- Northern Territory - 08 8928 5116
- Queensland - 07 3838 9010
- South Australia - 08 8422 1201
- Tasmania - 03 6230 6209
- Victoria - 03 9694 0200
- Western Australia - 08 9421 2869

## 5.1.2 Transport, storage and handling

Store all immunoglobulins at +2°C to +8°C. Do not freeze. Protect from light.

## 5.1.3 Normal human immunoglobulin for intramuscular use

Normal human immunoglobulin (NHIG) is prepared by plasma fractionation of blood collected from volunteer donors by the Australian Red Cross Blood Service. It is a sterile solution of immunoglobulin, mainly IgG, and contains those antibodies commonly present in adult human blood. In Australia, NHIG is supplied as a 16% solution and made available through the Australian Red Cross Blood Service.

### Recommended route

NHIG should be given by deep IM injection, using an appropriately sized needle. The NHIG should be introduced slowly into the muscle, to reduce pain. This product contains 160 mg/mL immunoglobulin (mainly IgG) prepared from Australian blood donations. Supplied in 2 mL and 5 mL vials. Also contains glycine.

### Administration

NHIG should be given by deep IM injection, using an appropriately sized needle. The NHIG should be introduced slowly into the muscle, to reduce pain. This product must not be administered intravenously because of possible severe adverse events, and hence an attempt to draw back on the syringe after IM insertion of the needle should be made in order to ensure that the needle is not in a small vessel. A special product for IV use (NHIG [intravenous]) has been developed for patients requiring large doses of immunoglobulin. For further information regarding the use of intravenous immunoglobulins, refer to Criteria for the clinical use of intravenous immunoglobulin in Australia.¹

### Recommendations

Immunoglobulin preparations may be given to susceptible persons, as either pre-exposure or post-exposure prophylaxis, against specific infections. Normal pooled immunoglobulin contains sufficiently high antibody concentrations to be effective against hepatitis A and measles. Both hepatitis A and measles are notifiable diseases and further instructions about their management and the need for immunoglobulin can be found in national guidelines [http://www.health.gov.au/cdrn/筹资] and obtained from state/territory public health authorities (see Appendix 1 [Handbook10-home~handbook10-tools~handbook10-appendices~handbook10-appendix1]). Contact details for Australian, state and territory government health authorities and communicable disease control). The duration of effect of NHIG is dose-related. It is estimated that protection is maintained for 3 to 4 weeks with standard recommended doses of NHIG.

### Prevention of hepatitis A

Hepatitis A vaccination (see 4.4 Hepatitis A [Handbook10-home~handbook10-part4~handbook10-4-4]) is recommended in preference to NHIG for post-exposure hepatitis A prophylaxis in persons ≥12 months of age who are immunocompetent.


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Prevention of measles

Measles vaccination (see 4.9 Measles (Handbook10-home-handbook10part4-handbook10-4-9)) within 72 hours of case contact is recommended in preference to NHIG for post-exposure measles prophylaxis in many instances (see Table 4.9.2 (Handbook10-home-handbook10part4-handbook10-4-9#table-4-9-2)) in 4.9 Measles (Handbook10-home-handbook10part4-handbook10-4-9)).

NHIG contains sufficiently high levels of antibody against measles to be able to prevent or ameliorate infection in susceptible persons. It should be given as soon as possible and within 7 days of exposure. Active protection, against measles particularly, may be required if the exposed person has an underlying immunological disorder (HIV/AIDS, immunosuppressive therapy), or to control an outbreak of measles among non-immunised persons, for example, in a childcare centre. The use of NHIG should be considered in HIV-positive persons exposed to a patient with measles.

Immune deficiency

Patients with abnormal antibody production (primary hypogammaglobulinaemia, multiple myeloma, chronic lymphoblastic leukaemia) usually receive therapy with the IV preparation of normal human immunoglobulin (NHIG [intravenous]). However, in some cases, NHIG is given by IM injection. The aim of therapy is to maintain serum IgG levels above 6 g/L. Some patients may receive the IM (160 mg/mL) preparation subcutaneously. For further information regarding the use of intravenous immunoglobulins, refer to Criteria for the clinical use of intravenous immunoglobulin in Australia.¹

¹Note: Skin tests with NHIG should not be undertaken. The intradermal injection of concentrated immunoglobulin causes a localised area of inflammation, which can be misinterpreted as a positive allergic reaction. True allergic responses to NHIG given by IM injection are extremely rare.

5.1.4 Specific immunoglobulins

Specific immunoglobulins are used to protect against specific microbial agents such as hepatitis B, rabies and varicella-zoster viruses, and tetanus. Further instructions about the management of these diseases and the need for immunoglobulin should be obtained from state/territory public health authorities (see Appendix 1 (Handbook10-home-handbook10tools-handbook10-appendices-handbook10-appendix1)). Contact details for Australian state and territory government health authorities and communicable disease control, and the national guidelines for management of disease from rables and other lyssaviruses, including Australian bat lyssavirus (http://www.health.gov.au/internet/main/publishing.nsf/Content/cdna-song-abvl-rabies.htm).

Specific immunoglobulins for botulism and cytomegalovirus (CMV) and a monoclonal antibody preparation for respiratory syncytial virus (RSV) are available as described below. Potential interactions, adverse events and storage requirements for these specific immunoglobulins are similar to those for NHIG (IM).

Hepatitis B specific immunoglobulin

Hepatitis B specific immunoglobulin (HBIG) is prepared from plasma donated through routine blood bank collection. Stocks of HBIG are very limited, and use should be strictly reserved for those who are at high risk, such as babies born to mothers with chronic hepatitis B infection and non-immune persons who are exposed through occupational exposure to the blood of unidentified persons, or to persons who are chronically infected with hepatitis B or whose hepatitis status cannot be ascertained in time.⁴ Requests for HBIG should be directed to the Australian Red Cross Blood Service in your state/territory (see 5.1.1 Availability of immunoglobulins above).

See 4.5.4.5.7 Recommendations (Handbook10-home-handbook10part4-handbook10-4-5#Handbook10-home-handbook10part4-handbook10-4-5#p-11), for more information.

Rabies specific immunoglobulin

Rabies specific immunoglobulin (HRIG) is prepared from the plasma of hyperimmunised human donors. HRIG is only administered in persons who have not received a previous course of rabies vaccine. HRIG is also administered as part of the post-exposure prophylaxis used following potential Australian bat lyssavirus or other lyssavirus exposures in previously unvaccinated persons.⁵

A single dose of HRIG is given to provide localised anti-rabies antibody protection while the patient responds to the rabies vaccine. It should be given at the same time as the first post-exposure dose of vaccine (day 0). If not given with the 1st vaccine dose, it may be given up to day 7. From day 8 onwards, an antibody response to rabies vaccine is presumed to have occurred.

The dose of HRIG is based on body mass and should be infiltrated in and around all wounds, using as much of the calculated HRIG dose as possible. The remainder of the HRIG dose should be administered intramuscularly at a site away from the injection site of rabies vaccine.

See 4.16 Rabies and other lyssaviruses (including Australian bat lyssavirus) (Handbook10-home-handbook10part4-handbook10-4-16), for more information.

Varicella-zoster specific immunoglobulin

Zoster immunoglobulin (ZIG) is highly efficacious, but is often in short supply. Normal high-titre zoster immunoglobulin is available from the Australian Red Cross Blood Service on a restricted basis for the prevention of varicella in high-risk subjects who report a significant exposure to varicella or herpes zoster. If ZIG is unavailable, large doses of NHIG can be given intramuscularly. This does not necessarily prevent varicella, but it lessens the severity of the disease. ZIG has no proven use in the treatment of established varicella or zoster infection. ZIG must be given early in the incubation period (within 96 hours of exposure), but may have some efficacy if administered out to as late as 10 days post exposure. ZIG is able to prevent or ameliorate varicella in infants <1 month of age, in children who are being treated with immunosuppressive therapy, and in pregnant women.⁶,⁷ Patients suffering from primary or acquired diseases associated with cellular immune deficiency and those receiving immunosuppressive therapy should be tested for varicella-zoster antibodies following contact with a person with confirmed varicella. However, this should not delay ZIG administration, preferably within 96 hours and up to 10 days after initial exposure.⁸

See 4.22 Varicella (Handbook10-home-handbook10part4-handbook10-4-22), for more information.

Botulism antitoxin

An equine antitoxin (derived from horses) has long been used in the treatment of adult botulism, but has not been shown to be effective in infant botulism.⁹ Equine antitoxin is manufactured by pharmaceutical companies such as Chiron. Use in Australia is governed by the Therapeutic Goods Administration’s Special Access Scheme and physicians wishing to access this product should initially contact the relevant state/territory health authority (see Appendix 1 (Handbook10-home-handbook10tools-handbook10-appendices-handbook10-appendix1)). Contact details for Australian, state and territory government health authorities and communicable disease control. Hypersensitivity, presenting as fever, serum sickness or anaphylaxis, may follow the use of equine antitoxin. Skin testing followed by appropriate dosing should be administered according to the manufacturer’s instructions.

An intravenous botulinum antitoxin, produced in the United States (BabyBIG); its sponsor is the Californian Department of Health Services), significantly reduces the duration of mechanical ventilation and hospitalisation in infant’s with botulism.¹⁰ This product has been administered to Australian children with infant botulism.¹¹ It is not currently registered in Australia, but is registered by the United States Food and Drug Authority. Access to this product should be sought through the TGA’s Special Access Scheme.

Cytomegalovirus immunoglobulin

Cytomegalovirus (CMV) immunoglobulin is indicated for the prevention of CMV infection in immunocompromised persons at high risk of severe CMV disease, such as after bone marrow and renal transplants.¹² The treatment of established CMV infection and disease is primarily with antivirals, such as ganciclovir or valganciclovir, and there is contradictory evidence whether the addition of CMV immunoglobulin improves outcome.¹²,¹³


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Respiratory syncytial virus monoclonal antibodies

A humanised mouse monoclonal antibody to respiratory syncytial virus (RSV) produced by cultured cells, palivizumab, is registered in Australia for prevention of serious lower respiratory tract disease caused by RSV in children at high risk of RSV disease. There is no consensus regarding the use of palivizumab in Australia. This product is given by IM injection each month to children at high risk of severe RSV disease, during the seasonal period of exposure to RSV. Palivizumab has been found to reduce the absolute risk of hospitalisation from about 10% to about 5% for babies born prematurely, for babies with chronic neonatal lung disease, and also for babies with hyodynamically significant congenital heart disease, particularly when complicated by large left-to-right shunts leading to pulmonary hypertension. It has not been shown to reduce the incidence of more severe outcomes, such as the need for ventilation, nor has it been shown to reduce mortality. There are currently a number of clinical trials assessing a recombinant humanised antibody, motavizumab.

The dose of palivizumab is 15 mg/kg once a month, to be given by IM injection, preferably in the anterolateral thigh. Where possible, the 1st dose should be administered before commencement of the RSV season.

Tetanus immunoglobulin

**Tetanus immunoglobulin (human) for intramuscular use**

Tetanus immunoglobulin (TIG) should be used for passive protection of persons who have sustained a tetanus-prone wound, where the person has not previously received 3 or more doses of a tetanus toxoid-containing vaccine or where there is doubt about their tetanus vaccination status. In persons who have a humoral immune deficiency, TIG should be provided after a tetanus-prone injury, regardless of the time since their last dose of tetanus-containing vaccine. TIG provides immediate protection that lasts for a period of 3 to 4 weeks. For wounds not categorised as tetanus-prone, such as clean cuts, TIG is unnecessary. Detailed information on appropriate tetanus prophylaxis measures in wound management, including use of TIG, are outlined in Table 4.19 (Handbook10-home-handbook10-part4-handbook10-4-19table-4-19-1) in 4.19. Tetanus (Handbook10-home-handbook10-part4-handbook10-4-19).

The recommended dose for TIG is 250 IU, to be given by IM injection as soon as practicable after the injury. If more than 24 hours have elapsed, 500 IU should be given. Because of its viscosity, TIG should be given to adults using a 21 gauge needle. For children, it can be given slowly using a 23 gauge needle. A tetanus toxoid-containing vaccine should be given at the same time in the opposite limb with a separate syringe, and arrangements should be made to complete the full course of tetanus toxoid-containing vaccinations. Details for accessing TIG should be obtained from the Australian Red Cross Blood Service (see 5.1.1 Availability of immunoglobulins above).

**Tetanus immunoglobulin (human) for intravenous use**

Tetanus immunoglobulin for IV use (TIVG) is used in the management of clinical tetanus. The recommended dose is 4000 IU, to be given by slow intravenous infusion. Detailed protocols for administration of this product and management of adverse events should be consulted if its use is contemplated. Requests for TIVG should be directed to the Australian Red Cross Blood Service in your state/territory (see 5.1.1 Availability of immunoglobulins above).

Diphtheria antitoxin

Diphtheria antitoxin is prepared by immunising horses against the toxin produced by Corynebacterium diphtheriae.

Advice should be sought with respect to diphtheria antitoxin access and dosage, and special arrangements made if hypersensitivity is suspected; this can be coordinated through the relevant state/territory health authority (see Appendix 1 (Handbook10-home-handbook10-tools-handbook10-appendices-handbook10-appendix1) Contact details for Australian, state and territory government health authorities and communicable disease control).

5.1.5 Potential interaction with vaccines

Live attenuated viral vaccines

Live attenuated viral vaccines can interfere with the response to certain live attenuated viral vaccines by preventing vaccine virus replication after administration. Therefore, administration of live attenuated viral vaccines, such as measles and varicella vaccines (but not rotavirus, zoster or yellow fever vaccines), should be deferred, dependent on the clinical status of the patient, for at least 3 months after the IM administration of NHIG, and for at least 8 months after the administration of inactivated NHIG. For detailed information on recommended intervals, see 3.3 (Handbook10-home-handbook10-part3-handbook10-3-3) Groups with special vaccination requirements, Table 3.3.6 (Handbook10-home-handbook10-part3-handbook10-3-3-6) Recommended intervals between either immunoglobulins or blood products and MMR, MMRV, varicella or varicella vaccination. For the same reason, if vaccination has occurred, administration of immunoglobulin products should be deferred if possible until at least 3 weeks after a measles-containing or varicella-containing vaccine has been given, unless it is essential that immunoglobulin be administered. However, Rh (D) immunoglobulin (anti-D) does not interfere with the antibody response to MMR- or varicella-containing vaccines and the two may be given at the same time in different sites with separate syringes or at any time in relation to each other (see 3.3 Groups with special vaccination requirements).

Inactivated vaccines

Inactivated vaccines, such as tetanus, hepatitis B or rabies, may be administered concurrently with immunoglobulin preparations, or at any time before or after receipt of immunoglobulin, using separate syringes and separate injection sites. This usually would occur when there has been actual or possible acute exposure to one of these infectious agents.

5.1.6 Use in pregnancy

Refer to 3.3 Groups with special vaccination requirements (Handbook10-home-handbook10-part3-handbook10-3-3), Table 3.3.1 (Handbook10-home-handbook10-part3-handbook10-3-3-1) Recommendations for vaccination in pregnancy for more information.

5.1.7 Contraindications

Hypersensitivity reactions to immunoglobulin preparations occur rarely but may be more common in patients receiving repeated injections. Intramuscular immunoglobulins should not be administered to persons who have severe thrombocytopenia or any coagulation disorder that would contraindicate intramuscular injections.

5.1.8 Adverse events and precautions

Refer to using separate syringes and separate injection sites. This usually would occur when there has been actual or possible acute exposure to one of these infectious agents.

Inactivated vaccines, such as tetanus, hepatitis B or rabies, may be administered concurrently with immunoglobulin preparations, or at any time before or after receipt of immunoglobulin,

Immunoglobulin products should be deferred if possible until at least 3 weeks after a measles-containing or varicella-containing vaccine has been given, unless it is essential that immunoglobulin be administered. However, Rh (D) immunoglobulin (anti-D) does not interfere with the antibody response to MMR- or varicella-containing vaccines and the two may be given at the same time in different sites with separate syringes or at any time in relation to each other (see 3.3 Groups with special vaccination requirements).
Anaphylaxis following an injection of NHIG is very rare, but has been reported. Anaphylaxis is more likely to occur if NHIG for IM use is inadvertently given intravenously.

Local tenderness, erythema and muscle stiffness at the site of injection may occur within minutes to hours after injection. Systemic adverse events such as mild pyrexia, malaise, drowsiness, urticaria and angioedema are uncommon, occurring in fewer than 1% of recipients. Skin lesions, headache, dizziness, nausea, general hypersensitivity reactions and convulsions may occur rarely.

References

Appendices

- Appendix 1: Contact details for Australian, state and territory government health authorities and communicable disease control
  (Handbook10-home-handbook10-tools-handbook10-appendices-handbook10-appendix1)
  (Handbook10-home-handbook10-tools-handbook10-appendices-handbook10-appendix2)
- Appendix 3: Components of vaccines used in the National Immunisation Program
  (Handbook10-home-handbook10-tools-handbook10-appendices-handbook10-appendix3)
- Appendix 4: Commonly asked questions about vaccination
  (Handbook10-home-handbook10-tools-handbook10-appendices-handbook10-appendix4)
- Appendix 5: Glossary of technical terms
  (Handbook10-home-handbook10-tools-handbook10-appendices-handbook10-appendix5)
- Appendix 6: Commonly used abbreviations
  (Handbook10-home-handbook10-tools-handbook10-appendices-handbook10-appendix6)
- Appendix 7: Overview of vaccine availability in Australia
# Appendix 1: Contact details for Australian, state and territory government health authorities and communicable disease control

PDF printable version of Appendix 1: Contact details for Australian, state and territory government health authorities and communicable disease control of the 10th edition of the Handbook (PDF 89 KB)/7491D3986306F818CA257D4D0024FBD/8File/Appendix-1-Contact-details.pdf

## Australian Government health authorities

<table>
<thead>
<tr>
<th>Australian Government Department of Health (<a href="http://www.immunise.health.gov.au">http://www.immunise.health.gov.au</a>)</th>
<th>02 6289 1555</th>
</tr>
</thead>
<tbody>
<tr>
<td>Freecall: 1800 671 811</td>
<td></td>
</tr>
</tbody>
</table>

Australian Childhood Immunisation Register enquiries (ACIR)†
| ACIR email (mailto:acir@humanservices.gov.au)                                   |              |

## State and territory government health authorities

### Australian Capital Territory

<table>
<thead>
<tr>
<th>02 6205 2300</th>
</tr>
</thead>
<tbody>
<tr>
<td>Immunisation Enquiry Line</td>
</tr>
</tbody>
</table>

### New South Wales

| 1300 066 055 |
| (to connect to your local Public Health Unit) |

### Northern Territory

| 08 8922 8044 |
| Centre for Disease Control |

### Queensland

| 13 HEALTH (13 4325 84) |
| Contact your local Public Health Unit |

### South Australia (http://www.sahealth.sa.gov.au/)

| 1300 232 272 (8.30 am to 5.00 pm) |
| CDCB Email (mailto:CDCB@health.sa.gov.au) |

### Tasmania

| 03 6222 7666 or 1800 671 738 |


| 1300 882 008 |
| Email (mailto:immunisation@health.vic.gov.au) |

### Western Australia

| 08 9388 4868 |
| 08 9328 0553 (after hours Infectious Diseases Emergency) |
| CDC Email (mailto:cdc@health.wa.gov.au) |

## Contact details for communicable disease control

### Australian Capital Territory

| 24-hour Communicable Disease Control Section: |
| 02 6205 2155 |

### New South Wales

| 1300 066 055 |
| (for connection to Public Health Unit) |

### Northern Territory

| 8.30 am to 5.00 pm: 08 8922 8044 Centre for Disease Control |
| (After hours Royal Darwin Hospital 08 8922 8888 for CDC on-call doctor) |

### Queensland

| Contact your local Public/Population Health Unit, phone number listed in the White Pages |

### South Australia

| 24 hour general enquiries line: 1300 232 272 |

### Tasmania

| 24 hour hotline: 1800 671 738 |

### Victoria

| 24 hour contact number: 1300 651 160 |

### Western Australia

| Perth Metropolitan area: |
| 08 9388 4852 |
| After hours/Emergency: 08 9328 0533 |
| Outside Perth Metropolitan area: |
| Contact regional Population Health Unit |

* See also state/territory and Therapeutic Goods Administration (TGA) contact details for reporting AEFI in Table 2.3.3 Contact information for notification of adverse events following immunisation in 2.3.2 Adverse events following immunisation.

† For more information on other registers, see 2.3.4 Immunisation registers in 2.3.2 Adverse events following immunisation.


For each Handbook chapter, broad literature searches were conducted for the years since the last Handbook searches were performed, using up to 24 databases, listed in Table A2.1. The purpose of these searches was to ensure that NCIRS technical writers and ATAGI members had access to all relevant information from the latest medical literature to allow identification of important issues related to the updating of all Handbook chapters. In addition, since writing of the 9th edition of the Handbook, Selected Dissemination Information (SDI) searches were established to enable the ongoing collection of new relevant items on the search topics. This process used the same search strategies as previously described, which allowed consideration and inclusion of papers published since publication of the 9th edition Handbook.

Table A2.1: Electronic databases searched for the 10th edition

<table>
<thead>
<tr>
<th>Electronic database</th>
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<tr>
<td>MEDLINE</td>
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<tr>
<td>Cochrane Library – including Cochrane Database of Systematic Reviews, Database of Abstracts of Reviews of Effects, the Cochrane Central Register of Controlled Trials (CENTRAL), Methods Studies, the Health Technology Assessment Database, the NHS Economic Evaluation Database</td>
<td>2006–2011</td>
</tr>
<tr>
<td>Cumulated Index Nursing &amp; Allied Health Literature (CINAHL) (when required)</td>
<td>2006–2011</td>
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<tr>
<td>Clinical Evidence</td>
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<td>EMBASE</td>
<td>2006–2011</td>
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</tbody>
</table>

Searches were conducted using the electronic databases detailed in Table A2.1, with the search period from 2006 to October 2011, in order to retrieve items published since the searches completed for the 9th edition of the Handbook. The scope of the searches was broad, to ensure maximum retrieval and minimise the exclusion of items of interest. Previous Handbook searches were examined to determine the scope required for the new searches, and similar search strategies were employed to ensure consistency of information retrieval, taking into account new terms added to the databases.

Various search methods were tested, including ‘explode’ and ‘focus’ options. ‘Exploded’ terms retrieve citations containing the term being searched and all the narrower related terms in the database. ‘Focus’ searches retrieve citations that have the search term as the major focus of the item. In the trial searches, some items of interest were missed using the ‘focus’ method, thus ‘exploded’ searches were utilised. All subheadings assigned to the subject headings were generally included. In general, the search strategy consisted of the disease topic and relevant vaccine terms, used in combination with the terms immunisation/immunisation programs. Boolean operators AND, OR and NOT were used as appropriate. To ensure relevant and accurate retrieval, thesaurus terms (the controlled vocabulary terms used in the database) were used whenever possible. Keyword searching was used in the absence of an appropriate thesaurus term or if the database did not have thesaurus terms. To facilitate relevant retrieval and to limit what, in some instances, are very large search result sets, the following limits were applied to the disease topic searches:

- Publication year – searches were generally limited to items published from 2006–2011.
- Language – searches were limited to items in English.
- Human – items discussing only animals were removed.
- In vitro – items discussing only in vitro studies were removed.
- Abstracts – search results restricted to items containing abstracts.

The search limits were slightly modified for some of the searches. For example, the Australian-specific searches did not have search results limited to abstract only, to ensure that all Australian items were retrieved.

The ATAGI and NCIRS technical writers also identified, where possible, focused clinical questions for each of the Handbook chapters, in advance of conducting literature searches. Specific searches were conducted for these questions, both using the databases and time periods above, but also using additional databases, longer time periods and other strategies, such as clinical trial registries and handsearching, as necessary.
Appendix 3: Components of vaccines used in the National Immunisation Program

Please note that vaccine manufacture is subject to ongoing refinement and change. Therefore, the information in Table A3.1 may change. This information was current as of early 2017 and has been sourced from the product information (PI) of each vaccine listed. The Therapeutic Goods Administration (http://www.tga.gov.au) provides the most current versions of the PI and Consumer Medicines Information (CMI) documents for vaccines (and other medicines).

For vaccines not listed in the National Immunisation Program (NIP), please refer to individual product information leaflet as supplied with the vaccine, or the Handbook chapter pertinent to that vaccine.

None of the vaccines listed on the NIP contains thiomersal.

Table A3.1: Components of vaccines used in the National Immunisation Program

<table>
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<th>Vaccine brand</th>
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<tr>
<td>Albumin/serum</td>
<td>Avaxim</td>
<td>Hepatitis A (HAV)</td>
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<tr>
<td></td>
<td>M-M-R II</td>
<td>Measles-mumps-rubella (MMR)</td>
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<td>ProQuad</td>
<td>Measles-mumps-rubella-varicella (MMRV)</td>
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<td>Quadracel</td>
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<td>Vaqta</td>
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<td>H-B-Vax II</td>
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<td>Diphtheria-tetanus-acellular pertussis-hepatitis B-inactivated poliomyelitis- <em>Haemophilus influenzae</em> type b (DTPa-hepB-IPV-Hib)</td>
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</tbody>
</table>

* If the person to be vaccinated has had an anaphylactic reaction to any of the vaccine components, administration of that vaccine may be contraindicated. Specialist advice should be sought to identify the component and to review if the person can be vaccinated in future.

† Please also refer to Appendix 4 Commonly asked questions about vaccination (Handbook10-home~handbook10-tools~handbook10-appendices~handbook10-appendix4) for more specific information about these various constituents.
Appendix 4: Commonly asked questions about vaccination

This appendix contains information for providers to refer to when responding to questions and concerns about immunisation. It covers general questions on adult and childhood vaccination, including contraindications and precautions. In addition, a discussion on some of the more recent concerns about vaccination is included, covering issues relating to vaccine safety, vaccine content, immunisation as a possible cause of some illnesses of uncertain origin, and the need for vaccination.

This appendix is divided into six sections:

- General questions
- Questions about contraindications and precautions
- Questions about vaccine safety
- Questions about vaccine content
- Questions about the need for immunisation
- Further information about vaccination

A.4.1 General questions

How does vaccination work?

When a healthy person becomes infected with a virus or bacteria (also known as a pathogen), for example, the measles virus, the body recognises the virus as an invader, produces antibodies that eventually destroy the virus, and recovery occurs. If contact with the measles virus occurs again in the future, the body’s immune system ‘remembers’ the measles virus and produces an increase in antibodies to destroy this pathogen.

Vaccination is the process that is used to stimulate the body’s immune system in the same way as the real pathogen or disease would, but without causing the symptoms of the disease. Most vaccines provide the body with ‘memory’ so that an individual does not get the disease if exposed to it (refer to 1.5 Fundamentals of immunisation).

Vaccination conveys immunity to diseases by a process called active immunity, which can be achieved by administration of either inactivated (i.e. not live) or live attenuated pathogens or their products. Live vaccines are attenuated, or weakened, by growing the organism through serial culturing or (passaging) steps in various tissue culture media. Inactivation is usually done using heat or formalin (sometimes both). Inactivated vaccines may include the whole pathogen (such as oral cholera vaccine), the toxin produced by the pathogen (such as tetanus and diphtheria vaccines), or specific antigens (such as Haemophilus influenzae type b [Hib], meningococcal and pneumococcal vaccines). In some cases, the antigen is conjugated (i.e. chemically linked) with proteins to facilitate the immune response. Inactivated viral vaccines may include whole viruses (such as inactivated poliomyelitis vaccine [IPV] and hepatitis A vaccines) or specific antigens (such as influenza and hepatitis B vaccines). Live attenuated viral vaccines include measles-mumps-rubella (MMR), varicella and yellow fever vaccines.

Immunity can also be acquired passively by the administration of immunoglobulins, which are the same as antibodies (refer to 1.5 Fundamentals of immunisation).

A randomised control trial has shown that a single booster dose in adults achieves high levels of protection against pertussis. However, the few studies which look at how long immunity lasts following a single booster dose suggest a decline out to 10 years (refer to 4.12 Pertussis[Handbook10-home-handbook10part4-handbook10-4-12]).

A single dose of dTpa is recommended for the following groups, unless contraindicated or if they have already received a previous dose of dTpa in the last 10 years (or shorter intervals where specifically indicated, refer to 4.12 Pertussis[Handbook10-home-handbook10part4-handbook10-4-12]).

Are steroids a contraindication to vaccination?

Yes. Persons with a neurological disease are often at increased risk of complications from diseases like measles, influenza and whooping cough, as they can be more prone to respiratory

Febrile seizures, a relatively common response to fever in all young children, can occur at a low rate following immunisation. A history of febrile seizure of any cause is not a reason to avoid

Stable neurological conditions (such as epilepsy) are not a reason to avoid giving any vaccines, including pertussis (whooping cough) (refer to Should persons with epilepsy be vaccinated?

A child or adult with a minor illness (without systemic illness and with a temperature <38.5°C) may be safely vaccinated. People, including infants, toddlers and teenagers with minor coughs

Should a person with an intercurrent illness be vaccinated?

A child or adult with a minor illness (without systemic illness and with a temperature <38.5°C) may be safely vaccinated. People, including infants, toddlers and teenagers with minor coughs

Can someone who has had whooping cough (pertussis) still be vaccinated?

Vaccination with pertussis vaccine in children, adolescents or adults who have had laboratory-confirmed pertussis infection is safe and is necessary, as natural immunity does not confer life-

What are the precautions to vaccination?

In general, persons with impaired immunity or on immunosuppressive therapy, or pregnant women, should not be given live vaccines. However, any general concerns that the person to be

Should persons with a neurological disease or conditions receive the normal vaccination schedule?

Yes. Persons with a neurological disease are often at increased risk of complications from diseases like measles, influenza and whooping cough, as they can be more prone to respiratory

Are steroids a contraindication to vaccination?
Inactivated vaccines, for example, DTPa-hepB-IPV or hepatitis B, may be less effective in this group, but are not contraindicated. Therapy with inhaled steroids is not a contraindication to vaccination.

Should vaccines be given to persons who have problems with their immune systems?

Persons who are immunocompromised (from either a disease or medical treatment) should generally not be given live viral vaccines such as MMR, MRV, varicella, zoster or rotavirus vaccines (refer to 4.9 Measles/Hibvaccine10-handbook10-part4-handbook10-and handbook10-part4-handbook10-2-4). Influenza (Handbook10-handbook10-part4-handbook10-2-4 and 4.17 Rotavirus (Handbook10-handbook10-part4-handbook10-2-4)).

HIV-infected persons may be given MMR, varicella and zoster vaccines, provided they do not have severe immunocompromise (refer to 3.3 Groups with special vaccination requirements (Handbook10-handbook10-part3-handbook10-3-3) and Table 3.3.4 Categories of immunocompromise in HIV-infected persons, based on age-specific CD4 counts and percentage of total lymphocytes(Handbook10-handbook10-part3-handbook10-3-3-3-4)). The close contacts of persons who are immunocompromised can be given live viral vaccines, except oral polio vaccine, which is no longer used in Australia.

The rash seen in a small percentage of MMR vaccine recipients, usually between 5 and 12 days after vaccination, is not infectious. Non-immune household contacts of persons who are immunocompromised should receive varicella vaccine. There is an almost negligible risk of transmitting varicella vaccine virus from a vaccine-related vesicular rash to contacts. However, vaccine-related rash occurs in 3% to 5% of vaccinated persons, either locally at the injection site or generalised, with a median of only 25 lesions. This small infection risk of the very virulent attenuated vaccine strain is far outweighed by the high risk of non-immune contacts catching wild varicella infection and transmitting the virus to the immunocompromised household member via respiratory droplets or from the large number of skin lesions that occur with wild varicella infection (a median of 300 to 500 lesions).

Live viral vaccines can be given to persons with leukaemia and other malignancies at least 3 months after they have completed chemotherapy, provided there are no concerns about their immune status. Such measures would normally be carried out under the supervision of the person’s oncologist (refer to 3.3.3 Vaccination of immunocompromised persons (Handbook10-handbook10-part3-handbook10-3-3-3-3)).

What vaccines should someone with HIV infection receive?

Persons with HIV (Human Immunodeficiency Virus) infection, especially children, should have all routine inactivated vaccines on the National Immunisation Program schedule. Varicella vaccine is contraindicated in persons with HIV who are significantly immunocompromised, as it can cause disseminated varicella infection. However, it may be considered for asymptomatic or mildly symptomatic HIV-infected children, after weighing up the potential risks and benefits. This should be discussed with the child’s specialist. MMR vaccine can be given to children with HIV, depending on their CD4 counts (refer to ‘Should vaccines be given to persons who have problems with their immune systems?’ above). Persons with HIV infection should also be vaccinated against pneumococcal disease (refer to 4.13 Pneumococcal disease (Handbook10-handbook10-part4-handbook10-4-13)). Influenza vaccine is also recommended for HIV-infected persons. They should not be given BCG, due to the risk of disseminated infection. More detailed information on the use of vaccines in persons with HIV is included in 3.3.3 Vaccination of immunocompromised persons (Handbook10-handbook10-part3-handbook10-3-3-3-3). Should chronically ill persons be vaccinated?

In general, persons with chronic diseases should be vaccinated as a matter of priority, because they are often more at risk from complications from vaccine-preventable diseases. Annual influenza vaccine is highly recommended for chronically ill persons and their household contacts.

Care is needed with the use of live attenuated viral vaccines in situations where the person’s illness, or its treatment, may result in impaired immunity. Advice may need to be sought on these patients to clarify the safety of live viral vaccine doses.

Should children or household contacts be vaccinated while the child’s mother is pregnant?

There is no problem with giving routine vaccinations to a child, or others, living in the same household with a pregnant woman. MMR vaccine viruses are not transmissible. Administration of varicella vaccine to household contacts of non-immune pregnant women is safe. Transmission of varicella vaccine virus is very rare. There is an almost negligible risk of transmitting varicella vaccine virus from a vaccine-related vesicular rash to contacts. However, vaccine-related rash occurs in 3% to 5% of vaccinated persons, either locally at the injection site or generalised, with a median of only 25 lesions. Furthermore, vaccinating the child of a pregnant mother will reduce the risk of her being infected by her offspring with the more virulent wild virus strain if she is not immune (refer to 3.3.2 Vaccination of women who are planning pregnancy, pregnant or breastfeeding, and preterm infants (Handbook10-handbook10-part3-handbook10-3-3-3-2)).

Should persons with allergies be vaccinated? What precautions are required for atopic or egg-sensitive children or adults?

Depending on the allergy identified, often there may not be a contraindication to vaccination. Specialist medical advice should always be sought in order to determine which vaccinations can be safely given. For example, a history of an allergy to antibiotics most commonly relates to β-lactam, or related antibiotics, and is not a contraindication to vaccines that contain neomycin, polymyxin B or gentamicin. Previous reactions to neomycin that only involved the skin are not considered a risk factor for a severe allergic reaction or anaphylaxis to vaccines manufactured with neomycin, since there are only trace amounts of this antibiotic in the final product (refer to 3.3.1 Vaccination of persons who have had an adverse event following immunisation (Handbook10-handbook10-part3-handbook10-3-3-3-3)). For other allergies, refer to Appendix 3, Components of vaccines used in the National Immunisation Program (Handbook10-handbook10-part3-handbook10-3-3-3-3-3).

For other allergies, refer to Appendix 3, Components of vaccines used in the National Immunisation Program (Handbook10-handbook10-part3-handbook10-3-3-3-3-3).

Persons with egg allergies can receive MMR vaccines because the measles and mumps components of MMR vaccine do not contain sufficient amounts of egg ovalbumin to contraindicate MMR vaccination of people with egg allergy (even anaphylaxis). (Refer to 3.3.1 Vaccination of persons who have had an adverse event following immunisation and 4.9 Measles (Handbook10-handbook10-part3-handbook10-3-3-3-3-3)). A simple dislike of eggs, or having diarrhoea or stomach pains after eating eggs, are not reasons to avoid MMR vaccination, and no special precautions are required in these circumstances. These persons can also have all other routine vaccines without special precautions.

A history of anaphylaxis or allergy to egg had previously been considered an absolute contraindication to influenza vaccination, but there have now been a number of studies indicating that the majority of such persons can be safely vaccinated.4,5 Given that there is still a small risk of anaphylaxis, it is essential that such persons are vaccinated in facilities with staff able to recognise and treat anaphylaxis. (Refer also to 4.7 Influenza (Handbook10-handbook10-part3-handbook10-4-13)).

Yellow fever. Q fever and one of the available rabies vaccines contain a higher amount of egg albumin than is present in the currently available influenza vaccines. Persons with egg allergy requiring vaccination with either yellow fever, rabies or Q fever vaccines, should seek specialist immunisation advice from their state or territory health department. Refer also to relevant chapters of this Handbook.

Families with questions about allergies and vaccines are encouraged to discuss this with their immunisation service provider and, where necessary, seek referral to an immunologist to have any questions promptly answered to avoid unnecessary delays of vaccine doses or referral to a specialist immunisation clinic. Information on specialist immunisation clinics is available from your local state or territory health department. (Refer to Appendix 1 (Handbook10-handbook10-part3-handbook10-3-3-3-3-3). For further details.)

A4.3 Questions about vaccine safety

thiomersal. The aromatic ether alcohol, 2-phenoxyethanol, is used as a preservative in many vaccines, and also as a preservative in cosmetics. It is used in vaccines as an alternative preservative to other environmental sources may be more difficult to eliminate. Particularly those of very low birth weight, with repeated doses of thiomersal-containing vaccines might have resulted in levels of mercury above the recommended guidelines. Individuals with very low body weight are usually more susceptible to toxic effects from a certain intake of mercury. Thus, the possibility existed that vaccination of newborn babies, other environmental sources are also possible sources of mercury. Vaccines used in the past, such as DTP, contained only 25 µg of thiomersal per dose.

A4.4 Questions about vaccine content

Refer also to Table A3.1 Components of vaccines used in the National Immunisation Program in Appendix 3 (Handbook10-home~handbook10-tools~handbook10-appendices~handbook10-appendix3#table-a-3-1). Refer also to the product information (PI) or the consumer medicines information (CMI) for individual vaccines; both are available from the TGA website (http://www.tga.gov.au).

Preservatives

Preservatives are used to prevent fungal and or bacterial contamination of the vaccine. They include thiomersal, phenoxethanol and phenol. Thiomersal (or thimerosal) is a compound that is partly composed of a form of mercury called ethylmercury. It has been used in very small amounts in vaccines for about 60 years to prevent bacterial and fungal contamination of vaccines. In the past, the small amount of thiomersal in vaccines was one of several potential sources of mercury. Diet (such as some seafood) and other environmental sources are also possible sources of mercury. Vaccines used in the past, such as DTP, contained only 25 µg of thiomersal per dose.

Mercury causes a toxic effect after it reaches a certain level in the body. Whether or not it reaches a toxic level depends on the amount of mercury consumed and the person’s body weight; individuals with very low body weight are usually more susceptible to toxic effects from a certain intake of mercury. Thus, the possibility existed that vaccination of newborn babies, particularly those of very low birth weight, with repeated doses of thiomersal-containing vaccines might have resulted in levels of mercury above the recommended guidelines. Thiomersal was removed from vaccines in response to the above theoretical concern and to reduce total exposure to mercury in babies and young children in a world where other environmental sources may be more difficult to eliminate.

Currently, all vaccines on the NIP for children and adolescents are free of thiomersal. Phenoxethanol

The aromatic ether alcohol, 2-phenoxethanol, is used as a preservative in many vaccines, and also as a preservative in cosmetics. It is used in vaccines as an alternative preservative to thiomersal.

Phenol

Phenol is an aromatic alcohol used as a preservative in a few vaccines.


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Adjuvants are compounds used to enhance the immune response to vaccination and include various aluminium salts, such as aluminium hydroxide, aluminium phosphate and potassium aluminium sulphate (alum). A review of all available studies of aluminium-containing diphtheria, tetanus and pertussis vaccines (either alone or in combination) found no evidence that aluminium salts in vaccines cause any serious or long-term adverse events.  

Aluminium  
A small amount of aluminium salts has been added to some vaccines for about 60 years. Aluminium acts as an adjuvant, which improves the protective response to vaccination by keeping antigens near the injection site so they can be readily accessed by cells responsible for inducing an immune response. The use of aluminium in vaccines means that, for a given immune response, less antigen is needed per dose of vaccine, and a lower number of total doses are required. Although aluminium-containing vaccines have been associated with local reactions and, less often, with the development of subcutaneous nodules at the injection site, other studies have reported fewer reactions with aluminium-adsorbed vaccines than with unadsorbed vaccines. Concerns about the longer-term effects of aluminium in vaccines arose after some studies suggested a link between aluminium in the water supply and Alzheimer’s disease, but this link has never been substantiated. The amount of aluminium in vaccines is very small and the intake from vaccines is far less than that received from diet or medications such as some antacids.  

Additives  
Additives are used to stabilise vaccines in adverse conditions (temperature extremes of heat and freeze drying) and to prevent the vaccine components adhering to the side of the vial. Examples of additives include:  

- lactose and sucrose (both sugars)  
- sorbitol and mannitol (both sugar alcohols)  
- polysorbate 80, made from sorbitol and oleic acid (an omega fatty acid)  
- glycine and monosodium glutamate or MSG (both are amino acids or salts of amino acids)  
- gelatin, which is partially hydrolysed collagen, usually of bovine or porcine origin.  

Some members of the Islamic and Jewish faiths may object to vaccination, arguing that vaccines can contain pork products. However, scholars of the Islamic Organization for Medical Sciences have determined that the transformation of pork products into gelatin will sufficiently alter them, thus making it permissible for observant Muslims to receive vaccines, even if the vaccines contain porcine gelatin. Likewise, leaders of the Jewish faith have also indicated that pork-derived additives to medicines are permitted. Further information may be obtained from the following websites: Vaccine Safety (http://www.vaccinesafety.edu/Porcine-vaccineavoidal.htm) (www.vaccinesafety.edu/Porcine-vaccineavoidal.htm) and Immunisation Action Coalition (http://www.immunize.org/search?coаксn=PORCINE%20&ie=UTF-8&qa=porcine&as=Search) (www.immunize.org/concerns/porcine.pdf)  

- human serum albumin (protein).  

Manufacturing residuals  
Manufacturing residuals are residual quantities of reagents used in the manufacturing process of individual vaccines. They include antibiotics (such as neomycin or polymyxin), inactivating agents (e.g. formaldehyde) as well as cellular residuals (egg and yeast proteins), traces of which may be present in the final vaccine. Antibiotics are used during the manufacturing process to ensure that bacterial contamination does not occur; traces of these antibiotics may remain in the final vaccine. Inactivating agents are used to ensure that the bacterial toxin or viral components of the vaccine are not harmful, but will result in an immune response. Cellular residuals are minimised by extensive filtering. However, trace amounts may be present in the final product. The most commonly found residual is formaldehyde.  

Formaldehyde  
Formaldehyde is used during the manufacture of many vaccines. For example, with tetanus vaccines, formaldehyde is used to detoxify the tetanus toxin produced. The non-toxic protein, which becomes the active ingredient of the vaccine, is further purified to remove contaminants and any excess (unreacted or unbound) formaldehyde. The current standard applicable to vaccines for human use in Australia is less than 0.02% w/v of free formaldehyde. The maximum amount of free formaldehyde detected by the Therapeutic Goods Administration during testing of vaccines registered in Australia has been 0.004% w/v, which is well below the standard limit.  

Other ingredients and information about manufacturing  
Vaccines also may be made up in sterile water or sterile saline (salt-water). Some viruses used in vaccines require the use of ‘cell lines’ in which to grow the vaccine virus. The cell lines are not included as a component of the vaccine. Some of these cell lines (called human diploid cell lines – WI-38 and MRC-5) were originally derived from human fetal tissue in the 1960s. These cell lines have been growing under laboratory conditions for more than 40 years, and there has been no further fetal tissue obtained since the 1960s. The vaccines manufactured using viruses that were grown in these cell lines include rubella vaccine and MMR vaccine, hepatitis A vaccines, varicella vaccines, rabies vaccine and oral polio (Sabin) vaccine (no longer available in Australia). Many of these vaccines prevent severe disease in unborn babies and infants, including, most notably, rubella, which causes congenital rubella syndrome.  

A4.5 Questions about the need for immunisation  
Isn’t natural immunity better than immunity from vaccination?  
While vaccine-induced immunity may diminish with time without boosters (vaccine or contact with wild-type infection), ‘natural’ immunity, acquired by catching the disease, is usually life-long, with the exception of pertussis. The problem is that the wild or ‘natural’ disease has a higher risk of serious illness and occasionally death. Children or adults can be revaccinated (with some, but not all, vaccines) if their immunity from the vaccine falls to a low level or if previous research has shown that a booster vaccination is required for long-term protection. It is important to remember that vaccines are many times safer than the diseases they prevent.  

Diseases like measles, polio and diphtheria have already disappeared from most parts of Australia. Why do we need to keep vaccinating children against these diseases?  
Although these diseases are much less common now, they still exist. The potential problem of disease escalation is kept in check by routine vaccination programs. In countries where vaccination rates have declined, vaccine-preventable diseases have sometimes reappeared. For example, Holland has one of the highest rates of fully vaccinated people in the world. However, in the early 1990s, there was a large outbreak of polio among a group of Dutch people who belonged to a religious group that objected to vaccination. While many of these people suffered severe complications like paralysis, polio did not spread into the rest of the Dutch community. This was due to the high rate of vaccination against polio, which protected the rest of the Dutch community.  

There have been recent outbreaks of whooping cough, measles and rubella in Australia, and a number of children have died. Cases of tetanus and diphtheria, although rare, still occur. Thus, even though these diseases are much less common now than in the past, it is necessary to continue to protect Australian children, so that the diseases cannot re-emerge to cause large epidemics and deaths.  

Also, many of the diseases against which we vaccinate our children are still common in other areas of the world. For example, measles still occur in many Asian countries, where many people take holidays or travel for business. Therefore, it is possible for non-immune individuals to acquire measles overseas, and, with the speed of air travel, arrive home and be able to pass measles onto those around them if they are unprotected. Measles is highly infectious and can infect others for several hours after an infected person has left a room. Vaccination, while not 100% effective, can considerably minimise a person’s chance of catching a disease. The more people who are vaccinated, the less chance there is that a disease, such as measles, will spread widely in the community. This is referred to as herd immunity.  

Why do some children get the disease despite being vaccinated?  
This is possible because a small proportion of those who are vaccinated will remain susceptible to the disease. However, in the cases in which illness does occur in vaccinated individuals, the illness is usually much less severe than in those who were not vaccinated. The protection provided by the same vaccine to different individuals can differ. For example, if 100 children are vaccinated, the disease may still occur in 1 child. However, if the disease occurred in 100 unvaccinated children, the disease will often be less severe in vaccinated children.
Children are vaccinated with a full schedule of pertussis-containing vaccines, but even so, disease is often less severe in these vaccinated children. To put it another way, if you do not vaccinate 100 children with MMR vaccine, and the children are exposed to measles, all of them will catch the disease with a risk of high rates of complications like pneumonia or encephalitis. The reason why fewer children become infected than these figures suggest is due to the high vaccine coverage rates in the community. If there are high coverage rates, there is less chance of contact with the infection and, although some children may be susceptible, they have a low chance of contact with the infection (this situation is also called ‘herd immunity’).

What about homeopathic ‘immunisation’?

Homeopathic ‘immunisation’ has not been proved to give protection against infectious diseases: only conventional vaccination produces a measurable immune response. The Council of the Faculty of Homeopathy, London, issued a statement in 1993, which reads: ‘The Faculty of Homeopathy, London, strongly supports the conventional vaccination program and has stated that vaccination should be carried out in the normal way, using the conventional tested and proved vaccines, in the absence of medical contraindications’.

A4.6 Further information about vaccination

More information about vaccination can be found in the following publications produced by the Australian Government Department of Health:

- Understanding childhood immunisation
- Immunisation myths and realities – responding to arguments against immunisation: a guide for providers.

The following two websites include further publications, fact sheets, etc. and are recommended for both immunisation service providers and the general public:

- Immunise Australia website (http://www.immunise.health.gov.au)
- The National Centre for Immunisation Research and Surveillance of Vaccine Preventable Diseases (NCIRS) website (http://www.ncirs.edu.au/)

Also, check with your local state or territory Public Health Unit or local council, maternal child health nurse or public health vaccination clinic for more information (refer to Appendix 1 Contact details for Australian, state and territory government health authorities and communicable disease control).

References

Appendix 5: Glossary of technical terms

PDF printable version of Appendix 5: Glossary of technical terms of the 10th edition of the Handbook (PDF 91 KB) (DA653078B03190FDCA257D4D00254A81/$File/Appendix-5-Glossary.pdf)

A B C D E F G H I J K L M N O P Q R S T U V W X Y Z

A B

Adjuvant

a preparation added to a vaccine to improve the immune response to that vaccine

Adverse event following immunisation (AEFI)

an unwanted reaction following administration of a vaccine, which may or may not be caused by the vaccine; adverse events may be at the site of injection, or may be a general illness or a general allergic reaction

Anaphylaxis

a sudden and severe allergic reaction, which results in a serious fall in blood pressure and/or respiratory obstruction and may cause unconsciousness and death if not treated immediately

Attenuation

the process of modifying a virus or bacteria to reduce its virulence (disease-inducing ability) while retaining its ability to induce a strong immune response (immunogenicity)

Bacteria

microorganisms that are smaller than a blood cell, but bigger than a virus; examples of bacterial infections are diphtheria, tetanus, pertussis, Hib and tuberculosis

Brachial neuritis

pain in the arm, causing persisting weakness of the limb on the side of vaccination

C D

Chronically infected

formerly referred to as a ‘carrier’; a person who has an infection that, although not necessarily causing symptoms, may still be active and may spread to others; chronic infection may last for years; examples of infections that can result in chronically infected states are hepatitis B and typhoid

Conjugate

some bacterial vaccines (e.g. Hib, meningococcal and pneumococcal conjugate vaccines) are made from the chemical linking (conjugation) of a tiny amount of the ‘sugar’ (correctly known as the polysaccharide) that makes up the cell coat of the bacteria with a protein molecule, in order to improve the immune response to the vaccine

Contraindication

a reason why a vaccine or drug must not be given

Corticosteroid

a drug used to reduce inflammation and other immune responses

DT

a vaccine that protects against diphtheria and tetanus. The acronym DT, using capital letters, signifies the child formulation of diphtheria and tetanus-containing vaccine, and denotes the substantially larger amounts of diphtheria toxoid in this formulation than in the adolescent/adult formulation.

dT

reduced antigen content formulation of diphtheria-tetanus vaccine, which contains substantially lower concentrations of diphtheria toxoid, and approximately half the tetanus antigen content, than the child formulation (which is signified by using capital letters DT). This vaccine is most commonly administered to adolescents/adults.

DTP/DTPa/DTPw

a vaccine that protects against diphtheria, tetanus and pertussis (whooping cough). The DTP used in Australia and many other industrialised countries is DTPa, which contains anacellular pertussis component made of refined pertussis extracts instead of inactivated whole pertussis bacteria (DTPw). The acronym DTPa, using capital letters, signifies child formulations of diphtheria, tetanus and acellular pertussis-containing vaccines, and denotes the substantially larger amounts of diphtheria toxoid and pertussis antigens in these formulations than in the adolescent/adult formulations.

dTpa

reduced antigen content formulation of diphtheria-tetanus-acellular pertussis vaccine, which contains substantially lower concentrations of diphtheria toxoid and pertussis antigens, and approximately half the tetanus antigen content, than the child formulations (which are signified by using all capital letters [DTPa]). This vaccine is most commonly administered to adolescents/adults.

E F

Effectiveness

the extent to which a vaccine produces a benefit in a defined population in uncontrolled or routine circumstances

Efficacy

the extent to which a vaccine produces a benefit in a defined population in controlled or ideal circumstances, for example, in a randomised controlled trial

Encephalitis

inflammation of the brain

Encephalopathy
a general term to describe a variety of illnesses that affect the brain, including encephalitis

Endemic
endemic infections are present all the time in a community

Enzootic
enzootic infections are present all the time in animals of a specific geographic area

Epidemic
epidemic infections are those that spread rapidly in a community; measles and influenza viruses are common causes of epidemics in Australia; small epidemics are often called outbreaks

Extensive limb swelling
swelling of the limb, with or without redness, which:
- extends from the joint above to the joint below the injection site, or beyond a joint (above or below the injection site), or
- results in the circumference of the limb being twice the normal size.

Febrile
related to a fever, as in febrile illness and febrile convulsions

G H I
Hepatitis
an inflammation of the liver; can be caused by viral infections

Hypotonic-hyporesponsive episode (shock, collapse)
the sudden onset of pallor or cyanosis, limpness (muscle hypotonia), and reduced responsiveness or unresponsiveness occurring after vaccination, where no other cause is evident, such as a vasovagal episode or anaphylaxis. The episode usually occurs 1 to 48 hours after vaccination and resolves spontaneously.

Immunisation
the process of inducing immunity to an infectious agent by administering a vaccine

Immunity
the ability of the body to fight off certain infections; immunity can result from natural ('wild') infections or from vaccination

Immunogenicity
the ability (or the degree) to which a particular substance, in this context a vaccine, may provoke an immune response

Immunoglobulin
a protein extract from blood, sometimes called ‘antibody’, that fights off infection; injection of immunoglobulins provides temporary immunity against certain infections

Incubation period
after a person is infected with bacteria or viruses, it often takes days or weeks for the infection to cause an obvious illness; the time between exposure to the infectious agent and development of the disease is called the incubation period

Infection
an infection occurs when bacteria or viruses invade the body; if the body cannot fight the infection, it may cause an illness

Intradermal (ID) injection
an injection into the surface layers of the skin; this is used for the administration of bacille Calmette-Guérin (BCG), the tuberculosis vaccine

Intramuscular (IM) injection
an injection into the muscle; vaccines are usually injected into a muscle of the upper outer thigh, or a muscle in the upper arm

Intussusception
when one portion of the bowel telescopes into the next portion of bowel, resulting in a blockage

Invasive disease
this term is often used when talking about pneumococcal or meningococcal disease. This term means that the bacteria (or germs) have been found in the blood, spinal fluid or another part of the body that would normally be sterile (or germ free).

J K L
Jaundice
yellow skin colour that may result from severe hepatitis

M N O

P Q R S
Pandemic influenza
a global epidemic that results when a new strain of influenza virus appears in the human population. It causes more severe disease in the population because there is little immunity to this new strain.

Paracetamol
a medicine that helps reduce fever; it may be given to minimise fevers following vaccination

Pertussis
whooping cough, an illness caused by a bacterium, *Bordetella pertussis*

Polysaccharide
a group of complex carbohydrates (sugars), which make up the cell coating present in some bacteria

Polyvalent vaccine
a combination vaccine that protects against more than one disease; examples are DTPa and MMR

Rotavirus
a virus that is a common cause of diarrhoea (and often vomiting as well) in young children. The diarrhoea can be severe in very young children, such that they may need intravenous fluids (i.e. through a vein in the arm) in hospital.

Rubella
a viral illness, sometimes also known as German measles

Seizure
a witnessed sudden loss of consciousness and generalised, tonic, clonic, tonic-clonic, or atonic motor manifestations.

Types of seizures include:
- febrile seizures; with fever >38.5°C
- afebrile seizures; without fever
- syncopal seizures; a syncope/vasovagal episode followed by seizure(s).

Subcutaneous (SC) injection
an injection into the tissue between the skin and the underlying muscle

Syncope
see vasovagal episode

T U V
Thrombocytopenia
platelet count <50 x 10^9/L

Transverse myelitis
a brief but intense attack of inflammation (swelling) in the spinal cord that damages myelin

Vaccination
the administration of a vaccine; if vaccination is successful, it results in immunity

Vaccine
a product often made from extracts of killed viruses or bacteria, or from live weakened strains of viruses or bacteria; the vaccine is capable of stimulating an immune response that protects against natural ('wild') infection

Varicella
chickenpox, an infection caused by the varicella-zoster virus

Vasovagal episode (syncope, faint)
episode of pallor and unresponsiveness or reduced responsiveness or feeling light-headed AND occurring while vaccine is being administered or shortly after (usually within 5 minutes) AND bradycardia AND resolution of symptoms with a change in position (supine position or head between knees or limbs elevated)

Virus
a tiny living organism, smaller than a bacterium, that can cause infections; measles, rubella, mumps, polio, influenza and hepatitis B are examples of viruses

W X Y Z
Zoster
an abbreviation for herpes zoster infection (also known as shingles); a painful rash and illness, caused by the varicella-zoster (chickenpox) virus
### Appendix 6: Commonly used abbreviations

PDF printable version of Appendix 6: Commonly used abbreviations of the 10th edition of the Handbook (PDF 44 KB)

<table>
<thead>
<tr>
<th>Abbreviation</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>ABLV</td>
<td>Australian bat lyssavirus</td>
</tr>
<tr>
<td>ACIR</td>
<td>Australian Childhood Immunisation Register</td>
</tr>
<tr>
<td>ACT</td>
<td>Australian Capital Territory</td>
</tr>
<tr>
<td>ADRS</td>
<td>Adverse Drug Reactions System</td>
</tr>
<tr>
<td>AEfi</td>
<td>adverse event following immunisation</td>
</tr>
<tr>
<td>AIDS</td>
<td>acquired immunodeficiency syndrome</td>
</tr>
<tr>
<td>anti-HBe</td>
<td>antibody to hepatitis B e antigen</td>
</tr>
<tr>
<td>anti-HBc</td>
<td>antibody to hepatitis B core antigen</td>
</tr>
<tr>
<td>anti-HBs</td>
<td>antibody to hepatitis B surface antigen</td>
</tr>
<tr>
<td>AOM</td>
<td>acute otitis media</td>
</tr>
<tr>
<td>ASCIA</td>
<td>Australasian Society of Clinical Immunology and Allergy</td>
</tr>
<tr>
<td>ATAGI</td>
<td>Australian Technical Advisory Group on Immunisation</td>
</tr>
<tr>
<td>BCG</td>
<td>bacille Calmette-Guérin</td>
</tr>
<tr>
<td>CCID</td>
<td>cell culture infectious dose 50%</td>
</tr>
<tr>
<td>CDNA</td>
<td>Communicable Diseases Network Australia</td>
</tr>
<tr>
<td>CI</td>
<td>confidence interval</td>
</tr>
<tr>
<td>CIN</td>
<td>cervical intraepithelial neoplasia</td>
</tr>
<tr>
<td>CRS</td>
<td>congenital rubella syndrome</td>
</tr>
<tr>
<td>CSF</td>
<td>cerebrospinal fluid</td>
</tr>
<tr>
<td>DNA</td>
<td>deoxyribonucleic acid</td>
</tr>
<tr>
<td>DT</td>
<td>diphtheria-tetanus vaccine for use in children</td>
</tr>
<tr>
<td>DTPa</td>
<td>diphtheria-tetanus-acellular pertussis vaccine</td>
</tr>
<tr>
<td>dTpa</td>
<td>diphtheria-tetanus-acellular pertussis vaccine, reduced antigen content formulation</td>
</tr>
<tr>
<td>DTPw</td>
<td>diphtheria-tetanus-whole-cell pertussis vaccine</td>
</tr>
<tr>
<td>EIA</td>
<td>enzyme immunoassay</td>
</tr>
<tr>
<td>ELISA</td>
<td>enzyme-linked immunosorbent assay</td>
</tr>
<tr>
<td>FHA</td>
<td>filamentous haemagglutinin</td>
</tr>
<tr>
<td>FIM</td>
<td>fimbriae (pertussis)</td>
</tr>
<tr>
<td>GBS</td>
<td>Guillain-Barré syndrome</td>
</tr>
<tr>
<td>GP</td>
<td>general practitioner</td>
</tr>
<tr>
<td>GVHD</td>
<td>graft-versus-host disease</td>
</tr>
<tr>
<td>HAV</td>
<td>hepatitis A virus</td>
</tr>
<tr>
<td>HBcAg</td>
<td>hepatitis B core antigen</td>
</tr>
<tr>
<td>HBeAg</td>
<td>hepatitis B e antigen</td>
</tr>
<tr>
<td>HBIG</td>
<td>hepatitis B immunoglobulin</td>
</tr>
<tr>
<td>HBsAg</td>
<td>hepatitis B surface antigen</td>
</tr>
<tr>
<td>HBV</td>
<td>hepatitis B virus</td>
</tr>
<tr>
<td>HCW</td>
<td>healthcare worker</td>
</tr>
<tr>
<td>HDCV</td>
<td>human diploid cell vaccine (rabies)</td>
</tr>
<tr>
<td>HepA</td>
<td>hepatitis A vaccine</td>
</tr>
<tr>
<td>HepB</td>
<td>hepatitis B vaccine</td>
</tr>
<tr>
<td>HHE</td>
<td>hypotonic-hyporesponsive episode</td>
</tr>
<tr>
<td>Hib</td>
<td>Haemophilus influenzae type b</td>
</tr>
<tr>
<td>Hib-MenCCV</td>
<td>Haemophilus influenzae type b-meningococcal C conjugate vaccine</td>
</tr>
<tr>
<td>HIV</td>
<td>human immunodeficiency virus</td>
</tr>
<tr>
<td>HPV</td>
<td>human papillomavirus</td>
</tr>
<tr>
<td>2vHPV</td>
<td>bivalent HPV vaccine</td>
</tr>
<tr>
<td>4vHPV</td>
<td>quadrivalent HPV vaccine</td>
</tr>
<tr>
<td>HRIG</td>
<td>human rabies immunoglobulin</td>
</tr>
<tr>
<td>HSCT</td>
<td>haematopoietic stem cell transplant</td>
</tr>
<tr>
<td>HZ</td>
<td>herpes zoster</td>
</tr>
<tr>
<td>ID</td>
<td>intradermal</td>
</tr>
<tr>
<td>IgA/G/M</td>
<td>immunoglobulin A/G/M</td>
</tr>
<tr>
<td>IM</td>
<td>intramuscular</td>
</tr>
<tr>
<td>IPD</td>
<td>invasive pneumococcal disease</td>
</tr>
<tr>
<td>IPV</td>
<td>inactivated poliovirus vaccine</td>
</tr>
<tr>
<td>IS</td>
<td>intussusception</td>
</tr>
<tr>
<td>ITP</td>
<td>idiopathic thrombocytopenia purpura</td>
</tr>
<tr>
<td>IU</td>
<td>international units</td>
</tr>
<tr>
<td>IV</td>
<td>intravenous</td>
</tr>
<tr>
<td>JE</td>
<td>Japanese encephalitis</td>
</tr>
<tr>
<td>LT-ETEC</td>
<td>heat-labile toxin producing enterotoxigenic Escherichia coli</td>
</tr>
<tr>
<td>MenCCV</td>
<td>meningococcal serogroup C conjugate vaccine</td>
</tr>
<tr>
<td>4vMenCV</td>
<td>quadrivalent meningococcal conjugate vaccine</td>
</tr>
<tr>
<td>4vMenPV</td>
<td>quadrivalent meningococcal polysaccharide vaccine</td>
</tr>
<tr>
<td>MMR</td>
<td>measles-mumps-rubella</td>
</tr>
<tr>
<td>MMRV</td>
<td>measles-mumps-rubella-varicella</td>
</tr>
<tr>
<td>NCIRS</td>
<td>National Centre for Immunisation Research and Surveillance of Vaccine Preventable Diseases</td>
</tr>
<tr>
<td>NHG</td>
<td>normal human immunoglobulin</td>
</tr>
<tr>
<td>NHMRC</td>
<td>National Health and Medical Research Council</td>
</tr>
<tr>
<td>NHVPR</td>
<td>National HPV Vaccination Program Register</td>
</tr>
<tr>
<td>NIP</td>
<td>National Immunisation Program</td>
</tr>
<tr>
<td>NSW</td>
<td>New South Wales</td>
</tr>
<tr>
<td>NT</td>
<td>Northern Territory</td>
</tr>
</tbody>
</table>
- OMP outer membrane protein
- OPV oral poliomyelitis vaccine
- PCECV purified chick embryo cell vaccine (rabies)
- PCR polymerase chain reaction
- 7vPCV 7-valent pneumococcal conjugate vaccine
- 10vPCV 10-valent pneumococcal conjugate vaccine
- 13vPCV 13-valent pneumococcal conjugate vaccine
- PEP post-exposure prophylaxis
- pH1N1 pandemic influenza A(H1N1)pdm09
- PHN post-herpetic neuralgia
- PI product information
- PreP pre-exposure prophylaxis
- 23vPPV 23-valent pneumococcal polysaccharide vaccine
- PRN pertactin
- PRP polyribosylribitol phosphate
- PRP-OMP PRP conjugated to the outer membrane protein of Neisseria meningitidis
- PRP-T PRP conjugated to tetanus toxoid
- PT pertussis toxoid
- Qld Queensland
- RCT randomised controlled trial
- RIG rabies immunoglobulin
- RNA ribonucleic acid
- SA South Australia
- SC subcutaneous
- SCID severe combined immunodeficiency
- SIDS sudden infant death syndrome
- SOT solid organ transplant
- SSPE subacute sclerosing panencephalitis
- Tas Tasmania
- TB tuberculosis
- TCID_{50} tissue culture infectious dose 50%
- TGA Therapeutic Goods Administration
- TIG tetanus immunoglobulin
- TST tuberculin skin test
- Vic Victoria
- VLP virus-like particle
- VNA (rabies) virus neutralising antibody
- VPD vaccine-preventable disease
- VV varicella vaccine
- VZV varicella-zoster virus
- WA Western Australia
- WHO World Health Organization
- ZIG zoster immunoglobulin
Table A7.1: Key dates when vaccines first came into widespread use in Australia

<table>
<thead>
<tr>
<th>Year</th>
<th>Vaccine</th>
</tr>
</thead>
<tbody>
<tr>
<td>1945</td>
<td>Tetanus toxoid</td>
</tr>
<tr>
<td>1953</td>
<td>Diphtheria-tetanus-pertussis, whole-cell (DTPw)</td>
</tr>
<tr>
<td>1956</td>
<td>Poliomyelitis (Salk) (inactivated poliomyelitis vaccine [IPV])</td>
</tr>
<tr>
<td>1966</td>
<td>Poliomyelitis (Sabin) (live attenuated oral poliomyelitis vaccine [OPV])</td>
</tr>
<tr>
<td>1970</td>
<td>Measles</td>
</tr>
<tr>
<td>1971</td>
<td>Rubella</td>
</tr>
<tr>
<td>1975</td>
<td>Child diphtheria-tetanus (CDT)</td>
</tr>
<tr>
<td>1982</td>
<td>Adult diphtheria-tetanus (ADT)</td>
</tr>
<tr>
<td>1982</td>
<td>Measles-mumps</td>
</tr>
<tr>
<td>1982</td>
<td>Hepatitis B (hepB) (serum-derived vaccine)</td>
</tr>
<tr>
<td>1987</td>
<td>Hepatitis B (recombinant vaccine)</td>
</tr>
<tr>
<td>1989</td>
<td>Measles-mumps-rubella (MMR)</td>
</tr>
<tr>
<td>1993</td>
<td>Haemophilus influenzae type b</td>
</tr>
<tr>
<td>1994</td>
<td>Hepatitis A</td>
</tr>
<tr>
<td>1997</td>
<td>Diphtheria-tetanus-pertussis, acellular (DTPa)</td>
</tr>
<tr>
<td>1999</td>
<td>Influenza</td>
</tr>
<tr>
<td>1999</td>
<td>23-valent pneumococcal polysaccharide (23vPPV)</td>
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<tr>
<td>2000</td>
<td>DTPa-hepB</td>
</tr>
<tr>
<td>2000</td>
<td>Hib(PRP-OMP)-hepB</td>
</tr>
<tr>
<td>2001</td>
<td>7-valent pneumococcal conjugate (7vPCV)</td>
</tr>
<tr>
<td>2003</td>
<td>Varicella</td>
</tr>
<tr>
<td>2003</td>
<td>Meningococcal C conjugate</td>
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<tr>
<td>2004</td>
<td>Diphtheria-tetanus-pertussis, acellular; reduced antigen content formulations (dTpa and dTpa-IPV)</td>
</tr>
<tr>
<td>2005</td>
<td>Pentavalent and hexavalent combination DTPa vaccines (DTPa-hepB-IPV-Hib; DTPa-IPV; DTPa-hepB-IPV; DTPa-IPV-Hib)</td>
</tr>
<tr>
<td>2007</td>
<td>Human papillomavirus (HPV)</td>
</tr>
<tr>
<td>2007</td>
<td>Rotavirus</td>
</tr>
<tr>
<td>2009</td>
<td>10-valent pneumococcal conjugate (10vPCV)</td>
</tr>
<tr>
<td>2011</td>
<td>13-valent pneumococcal conjugate (13vPCV)</td>
</tr>
<tr>
<td>2013</td>
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- Immunise Australia Program (http://www.immunise.health.gov.au)
- National Health and Medical Research Council (NHMRC) (http://www.nhmrc.gov.au/)
Response to Public Consultation Submissions for the August 2016 Update of the Handbook

The Australian Technical Advisory Group on Immunisation (ATAGI) made updates to some chapters of the 10th edition of The Australian Immunisation Handbook (the Handbook) in August 2016, in which there are new recommendations or changes to existing clinical advice.

Prior to completion of the August 2016 update of the Handbook, the ATAGI sought public consultation over a four-week period during January 2016 to February 2016 on the Yellow fever chapter, as this was a Category II update. The ATAGI reviewed all public comments received and where possible incorporated them into the Handbook. An electronic version of the response to public consultation submissions is available below.

- Response to Public Consultation Submissions for the August 2016 Update of the Handbook (PDF 677 KB)
- Response to Public Consultation Submissions for the August 2016 Update of the Handbook (Word 74 KB)
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Publication Approval

These guidelines were approved by the Chief Executive Officer (CEO) of the National Health and Medical Research Council (NHMRC) on 25/01/2013 (with subsequent amendments approved by the CEO on 19/12/2013, 27/03/2015, 22/06/2015, 21/03/2016, 01/08/2016, 17/02/2017 and 01/08/2017), under Section 14A of the National Health and Medical Research Council Act 1992. In approving these guidelines the NHMRC considers that they meet the NHMRC standard for clinical practice guidelines. This approval is valid for a period of five years.

NHMRC is satisfied that they are based on the systematic identification and synthesis of the best available scientific evidence and make clear recommendations for health professionals practising in an Australian health care setting.

This publication reflects the views of the authors and not necessarily the views of the Australian Government.

Disclaimer
While every effort has been made to check drug dosage recommendations in this Handbook, it is still possible that errors have been missed. Furthermore, dosage recommendations are continually being revised and new adverse events recognised.

Trade names used in this publication are for identification purposes only. Their use does not imply endorsement of any particular brand of drug or vaccine. This Handbook is a general guide to appropriate practice subject to clinician’s judgement in each individual case. It is designed to provide information to assist decision making using the best information available at date of National Health and Medical Research Council approval (25 January 2013, with subsequent amendments approved by the CEO on 19/12/2013, 27/03/2015, 22/06/2015, 21/03/2016, 01/08/2016 and 17/02/2017). The Australian Government Department of Health does not accept any liability for any injury, loss or damage incurred by use of or reliance on the information.

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The ATAGI
The Australian Technical Advisory Group on Immunisation (ATAGI) was established by the then Minister for Health and Family Services in 1998 to provide expert technical and scientific advice on the Immunise Australia Program and to work cooperatively with the NHMRC on issues such as the The Australian Immunisation Handbook.

The Handbook
This Handbook is updated on a regular basis and changes to the recommendations or schedule may occur between publications. The Handbook and any changes between publications are available on the Immunisation website(http://www.immunise.health.gov.au/internet/immunise/publishing.nsf/Content/Handbook10-home).

Tenth Edition 2017 update

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