The Australian **Immunisation Handbook** 7th Edition **2000**

The Australian Immunisation Handbook 7th Edition

NHMRC
National Health and Medical Research Council

IMMUNISATION

CONTACT DETAILS FOR COMMONWEALTH, STATE AND TERRITORY GOVERNMENT HEALTH AUTHORITIES

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South Australia	(08) 8226 7177
Tasmania	(03) 6233 3762 or 1800 671 738 (Tasmania only)
Victoria	(03) 9637 4144
Western Australia	(08) 9321 1312

For information on the Australian Childhood Immunisation Register or to request a child's immunisation history, contact the Health Insurance Commission on 1800 653 809 (free call), or visit the website at www.hic.gov.au.

What's new? - Changes introduced in this edition of the Handbook

See section 1.1

The Australian Standard Vaccination Schedule 2000–2002

AGE	VACCINE	
Birth	hepB[a]	
	Path 1[b]	**Path 2**[b]
2 months	DTPa-hepB and Hib and OPV	DTPa[c] and Hib (PRP-OMP)-hepB and OPV
4 months	DTPa-hepB and Hib and OPV	DTPa[c] and Hib (PRP-OMP)-hepB and OPV
6 months	DTPa-hepB and OPV	DTPa[c] and OPV
12 months	MMR and Hib	MMR and Hib (PRP-OMP)-hepB
18 months	DTPa	
4 years	DTPa and MMR and OPV	
10-13 years	hepB[d]	
1 month later	hepB[d]	
5 months after 2nd dose	hepB[d]	
15-19 years	Td	
	OPV	
Non-immune women who are post-partum or of child bearing age	MMR	
50 years	Td[e]	
50 years and over (Aboriginal and Torres Strait Islander people)	Pneumococcal vaccine (every 5 years) Influenza vaccine (every year)	
65 years and over	Pneumococcal vaccine (every 5 years) Influenza vaccine (every year)	

The Australian Standard Vaccination Schedule 2000–2002

The Australian Standard Vaccination Schedule shown here is that recommended by the National Health and Medical Research Council (NHMRC). In drawing up its recommendations the NHMRC has sought to reduce the number of injections given at each immunisation session through the use of new combination vaccines and to limit, as far as possible, the number of vaccine products that a practitioner would need to have available. For the immunisations at 2, 4, 6 and 12 months, two options for the use of combination vaccines which meet these criteria are recommended.

DISEASE	VACCINE	AVAILABLE PRODUCTS
Hepatitis B	hepB	Engerix-B™ or H-B VaxII™
Diphtheria, Tetanus, Pertussis	DTPa	Infanrix™ or Tripacel™
Diphtheria, Tetanus, Pertussis, Hepatitis B	DTPa-hepB	Infanrix-HepB™
Haemophilus Influenzae type B	Hib (PRP-OMP)	PedvaxHIB™
Haemophilus Influenzae type B, Hepatitis B	Hib (PRP-OMP)-hepB	Comvax™
Poliomyelitis	OPV	Polio Sabin™
Measles, Mumps, Rubella	MMR	MMRII® or Priorix™
Diphtheria, Tetanus	Td	ADT Vaccine™
Pneumococcal disease	Pneumococcal vaccine	Pneumovax23®
Influenza	Influenza vaccine	Fluarix™ or Fluvax® or Vaxigrip™ or Flurivin™

Notes

a. Hepatitis B vaccine should be given to all infants at birth and should not be delayed beyond 7 days after birth. Infants whose mothers are hepatitis B surface antigen positive (HBsAg+ve) should also be given hepatitis B immunoglobulin (HBIG) within 12 hours of birth.

b. When necessary the two paths may be interchanged with regard to their hepatitis B and Hib components. For example, when a child moves interstate, they may change from one path to the other (see part 1.8.1)

c. Wherever possible the same brand of DTPa should be used at 2, 4 and 6 months.

d. Adolescent hepatitis B vaccination is not necessary for those children who have previously received three doses of hepatitis B vaccine.

e. Td should be given at 50 years of age unless a Td booster dose has been documented in the previous 10 years.

Transition from the old to the new schedule

All babies born on or after 1 May 2000 should commence the new Australian Standard Vaccination Schedule. Because of logistics, funding and vaccine interchangeability issues, all children born before this date should commence or continue with the previous schedule.

Parent Advice Sheet

The following information can be photocopied and given to parents as post-vaccination advice.

Any injection may result in soreness, redness, itching, swelling or burning at an injection site for 1 to 2 days. Sometimes a small, hard lump may persist for some weeks or more. This is no cause for concern.

Common adverse events following immunisation and what to do about them

Common adverse events following DTP-containing vaccines

- usually mild and transient
- within 24 hours
- localised pain, redness and swelling at injection site
- low grade temperature (fever)
- being grizzly, unsettled and generally unhappy - may persist for 24 - 48 hours
- drowsiness

What to do

- give extra fluids to drink
- do not overdress the baby if hot
- give paracetamol to lower fever if needed

Common adverse events following MMR

- discomfort at injection site
- usually mild and transient

The following may occur 5 to 12 days after vaccination:

- low grade temperature (fever)
- faint rash (not infectious)
- head cold and/or runny nose
- cough and/or puffy eyes
- swelling of salivary glands

What to do

- give extra fluids to drink
- do not overdress the baby if hot
- give paracetamol to lower fever if needed

Common adverse events following Hib Vaccine

- usually mild and transient
- localised pain, redness and swelling at the injection site
- mild temperature (fever)

What to do

- give extra fluids to drink
- do not overdress the baby if hot
- give paracetamol to lower fever if needed

Possible common adverse events following Td

- usually mild and transient
- localised discomfort, redness and swelling at the injection site

What to do

- give paracetamol for pain or to lower fever if needed

If adverse events following immunisation are severe and persistent or if you are worried about your child, contact your doctor or hospital.

Possible common adverse events following OPV

- very rarely any adverse event
- occasionally, diarrhoea

What to do

- no treatment is usually needed

Possible common adverse events following influenza vaccine

- usually mild and transient
- low grade temperature (fever)
- occasional discomfort, redness and swelling at the injection site

What to do if discomfort at injection site

- give paracetamol to lower fever if needed

Possible common adverse events following hepatitis B vaccine

- very occasionally soreness, redness at the injection site
- low grade fever

What to do if fever

- give extra fluids to drink
- do not overdress the baby if hot

What to do if discomfort at injection site

- give paracetamol to lower fever if needed

Possible common adverse events following pneumococcal vaccine

- pain at the vaccine site
- low grade fever

What to do if fever

- give extra fluids to drink

What to do if discomfort at injection site

- give paracetamol to lower fever if needed

If adverse events following immunisation are severe and persistent or if you are worried about your child, contact your doctor or hospital.

Signs of anaphylaxis

- Skin signs, such as the rapid development of urticarial lesions (circumscribed, intensely itchy wheals with erythematous raised edges and pale, blanched centres).
- Signs of upper airway obstruction, such as hoarseness and stridor, resulting from angio-oedema of the hypopharynx, epiglottis and larynx.
- Indications of lower airway obstruction, such as subjective feelings of retrosternal tightness, and dyspnoea with audible expiratory wheeze from bronchospasm.
- Abdominal cramps and diarrhoea.
- Limpness and pallor, which are signs of severe anaphylaxis in children.
- Profound hypotension in association with tachycardia, and/or other signs of cardiovascular disturbance, such as sinus tachycardia or severe bradycardia.

Management of anaphylaxis

- If the patient is unconscious, lie him/her on the left side to keep the airway clear.
- Give adrenaline by deep intramuscular injection unless there is a strong central pulse and the patient's condition is good. See below for dosage. If there is no improvement in the patient's condition by 5 minutes, repeat doses should be given every 5 minutes until improvement occurs.
- If oxygen is available, administer it by face mask at a high flow rate.
- Send for professional assistance. Never leave the patient alone.
- If appropriate, begin cardiopulmonary resuscitation.
- All cases should be admitted to hospital for further observation and treatment.

Experienced practitioners may choose to use an oral airway if the appropriate size is available, but its use is not routinely recommended unless the patient is unconscious.

Injections of antihistamines or hydrocortisone are no longer considered to contribute to the emergency management of anaphylaxis, although hydrocortisone may be used for ongoing treatment of the patient.

Adrenaline dosage

The recommended dose of 1:1,000 adrenaline is 0.01 mg/kg body weight given by deep intramuscular injection. Adrenaline 1:1,000 contains 1 mg of adrenaline per mL. The following table lists the doses of 1:1,000 adrenaline to be used if the exact weight of the individual is not known.

Doses of 1:1,000 (one in one thousand) adrenaline for infants and children:

Less than 1 year	0.05-0.1 mL
1-2 years (approx. 10 kg)	0.1 mL
2-3 years (approx. 15 kg)	0.15 mL
4-6 years (approx. 20 kg)	0.2 mL
7-10 years (approx. 30 kg)	0.3 mL
11-12 years (approx. 40 kg)	0.4 mL
12 years and over	0.4-0.5 mL

The use of 1:1,000 adrenaline is recommended because it is universally available. A tuberculin syringe can be used to improve the accuracy of measurement when drawing up small doses.

Comparison of Effects of Vaccines and Diseases

DISEASE	EFFECTS OF DISEASE	SIDE EFFECTS OF VACCINATION
Diphtheria - contagious bacteria spread by droplets; causes severe throat and breathing difficulties.	About 1 in 15 patients dies. The bacteria release a toxin, which can produce nerve paralysis and heart failure.	DTPa vaccine - about 1 in 10 have local inflammation or fever. Serious adverse events are very rare, and much less common than DTPw.
Hepatitis B - contagious virus spread mainly by blood, sexual contact or from mother to newborn baby; causes acute hepatitis or chronic carriage.	About 1 in 3 chronic carriers will develop cirrhosis or liver cancer.	About 1 in 15 to 1 in 100 have pain and fever. Anaphylaxis occurs in about 1 in 600,000.
Hib - contagious bacteria spread by droplets; causes meningitis, epiglottitis (respiratory obstruction), septicaemia, osteomyelitis.	About 1 in 20 meningitis patients dies and 1 in 4 survivors has permanent brain or nerve damage. About 1 in 100 epiglottitis patients dies.	About 1 in 20 have discomfort or local inflammation. About 1 in 50 have fever.
Influenza - contagious virus spread by droplets; causes fever, muscle and joint pains, pneumonia.	Causes increased hospitalisation in the elderly. High-risk groups include the elderly, diabetics, alcoholics, etc.	About 1 in 10 have local reactions, Guillain-Barré syndrome occurs in in about 1 in 1 million.
Measles - highly infectious virus spread by droplets; causes fever, cough, rash.	1 in 25 children with measles develops pneumonia and 1 in 2,000 develops encephalitis (brain inflammation). For every 10 children who develop measles encephalitis, 1 dies and up to 4 have permanent brain damage. About 1 in 25,000 develops SSPE (brain degeneration), which is always fatal.	About 1 in 10 have discomfort, local inflammation or fever. About 1 in 100 develops a rash, which is noninfectious. 1 in 1 million recipients may develop encephalitis (inflammation of the brain).
Mumps - contagious virus spread by saliva; causes swollen neck glands, fever.	1 in 200 children develops encephalitis (brain inflammation). 1 in 5 males past puberty develops inflammation of the testicles. Occasionally mumps causes infertility or deafness.	1 in 100 recipients may develop swelling of the salivary glands. 1 in 3 million recipients develop mild encephalitis (inflammation of the brain).
Pertussis - contagious bacteria spread by droplets; causes whooping cough and vomiting, lasting up to 3 months.	About 1 in 200 whooping cough patients under the age of 6 months dies from pneumonia or brain damage.	As for DTPa vaccine (see diphtheria).
Polio - contagious virus spread by faeces and saliva; causes fever, headache, vomiting and may progress to paralysis.	About 1 in 20 hospitalised patients dies and 1 in 2 patients who survive is permanently paralysed.	Less than 1 in 100 recipients develop diarrhoea, headache, and/or muscle pains. 1 in 2.5 million recipients or close contacts develop paralysis.
Pneumococcus - bacteria spread by droplets; cause fever, pneumonia, septicaemia, meningitis.	About 1 in 10 meningitis patients dies.	Less than 1 in 20 have pain or local reactions.
Rubella - contagious virus spread by droplets; causes rash, fever, swollen glands, but causes severe malformations to babies of infected pregnant women.	About 5 in 10 patients develop a rash and painful swollen glands; 5 in 10 adolescents and adults have painful joints; 1 in 3,000 develops thrombocytopenia (bruising or bleeding); 1 in 6,000 develops inflammation of the brain; 9 in 10 babies infected during the first 10 weeks after conception will have a major congenital abnormality (such as deafness, blindness, brain damage or heart defects).	About 1 in 10 have discomfort, local inflammation, or fever. About 1 in 20 have swollen glands, stiff neck, or joint pains. About 1 in 100 have a rash, which is noninfectious. Thrombocytopenia (bruising or bleeding) occurs after a first dose of MMR at a rate of 1 in 30,500.
Tetanus - caused by toxin of bacteria in soil; causes painful muscle spasms, convulsions, lockjaw.	About 1 in 10 patients dies. The risk is greatest for the very young or old.	As for DTPa vaccine (see diphtheria).

The Australian Immunisation Handbook

7th Edition

IMMUNISE AUSTRALIA PROGRAM

NHMRC

National Health and Medical Research Council

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While every effort has been made to check dosage recommendations in this Handbook, it is still possible that errors have been missed. Furthermore, dosage recommendations are being continually revised and new adverse events recognised.

This Handbook is a general guide to appropriate practice, to be followed only subject to the clinician's judgement in each individual case. The Handbook is designed to provide information to assist decision-making and is based on the best information available at the date of compilation (29 February 2000).

Trade names used in this Handbook are for identification purposes only. Their use does not imply endorsement of any particular brand of drug or vaccine.

The objective of the National Health and Medical Research Council (NHMRC)is to advise the Australian community on the achievement and maintenance of the highest practicable standards of individual and public health and to foster research in the interests of improving those standards.

The Australian Technical Advisory Group on Immunisation (ATAGI) was established by the Minister for Health and Aged Care (formally Health and Family Services) in 1997 to provide expert technical and scientific advice on the Immunise Australia Program and to work cooperatively with the National Health and Medical Research Council on issues such as the revision of the Australian Standard Vaccination Schedule and the Australian Immunisation Handbook.

This handbook was published in conjunction with the National Immunisation Program, an initiative of the Commonwealth Department of Health and Aged Care. This Handbook is published about every two years, but changes to the schedule or to recommendations may occur more frequently. The Handbook will also be published at the following website: http://www.health.gov.au. Any changes or updates will be published on this website. This Handbook does not contain a full list of references for each chapter – the full references will be available on the electronic version.

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PREFACE

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PART 1 - VACCINATION PROCEDURES & THE STANDARD SCHEDULE

1.1 INTRODUCTION

The purpose of the Handbook is to give practitioners clear guidance about vaccination and to provide an accessible summary of the relevant data on vaccine-preventable infectious diseases in Australia.

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 bacterial and viral diseases. Smallpox has been eradicated, and poliomyelitis is close to global eradication.

As with most health care interventions, vaccination is not entirely risk-free, yet the currently available vaccines are safer than the risks of the diseases they prevent. The introduction of acellular pertussis-containing vaccines has significantly reduced the numbers of children affected by the common minor, but often distressing, side effects of vaccination. As a result of successful vaccination programs, deaths from tetanus, diphtheria, *Haemophilus influenzae* type b and measles are now extremely rare in Australia. Nevertheless, pertussis, measles and rubella still cause a great deal of disease and disability in Australia.

Vaccinating a child not only protects that child, but other children as well, by increasing the general level of immunity and minimising the spread of infection. It is vital that health care professionals take every available opportunity to vaccinate children and adults. It is also important that the public be made aware of the proven power of immunisation to save lives and prevent serious illness.

What's new? - Changes introduced in this edition of the Handbook

For those familiar with the previous edition of this Handbook, it is important to note that the 7th Edition introduces some changes to the recommended schedule and procedures for administering vaccines, as well as changes to the presentation of the Handbook.

Changes in the 7th edition

New vaccines

- The new combination vaccines diphtheria-tetanus-acellular pertussis-hepatitis B (DTPa-hepB) and *Haemophilus influenzae* type B (PRP-OMP)-hepatitis B (Hib(PRP-OMP)-hepB) have been registered for all 3 doses in the primary vaccination schedule. This provides the NHMRC with the opportunity to introduce universal infant hepatitis B vaccination, commencing at birth. Subsequent vaccine doses can now be given using these multivalent vaccines without adding a further injection into the schedule (see Part 1.8, page 39). Varicella zoster vaccines have now been registered for use in Australia (see Part 3.28, page 231).
- A number of new travel vaccines have been registered in Australia. These include an oral cholera vaccine (Part 3.3, page 88); a new yellow fever vaccine that can be stored at refrigerator temperature (Part 3.29, page 238); and a new Vi polysaccharide typhoid vaccine (Part 3.27, page 226).

Changes to the schedule

- There are two alternative schedules, designed because of the availability of two new combination vaccines, DTPa-hepB and Hib(PRP-OMP)-hepB; the only difference in antigens delivered is that the 4th dose of hepatitis B vaccine is given at 6 months if using DTPa-hepB, and at 12 months if using Hib(PRP-OMP)-hepB. See Part 1.8, page 39 for details.
- It is now recommended that all Australian children receive the same *Haemophilus influenzae* type b (Hib) vaccine (PRP-OMP). This change reduces the number of injections needed and reduces the complexity of the schedule (see Part 1.8, page 39).
- Universal hepatitis B vaccination commencing at birth can now be implemented (see Parts 1.8 and 3.8).
- Infants born to hepatitis B carrier mothers receive a birth dose of hepatitis B vaccine and hepatitis B immunoglobulin. They then receive the same schedule as other infants, with the next dose at 2 months (see Part 3.8, page 123).
- Pre-adolescent hepatitis B vaccination is now recommended at 10-13 years, instead of 10-16 years (see Part 3.8, page 120, 125).

- Booster doses of hepatitis B vaccine are no longer generally recommended, regardless of when and why the primary course was administered. Numerous studies have shown that immunity is long lasting (see Part 3.8, page 124).
- The second booster dose of DTPa is now recommended at 4 years, instead of 4-5 years (See Part 1.8, page 39).
- The second dose of MMR is now given at 4 years of age instead of 10-16 years (see Parts 1.8 and 3.12).
- Tetanus and diphtheria boosters are no longer recommended every 10 years. A tetanus booster is recommended at age 50 unless a booster dose has been documented within 10 years.
- Inactivated poliomyelitis vaccine (IPV) is an acceptable alternative to live, oral poliomyelitis vaccine (OPV) in the primary vaccination schedule and is interchangeable with OPV (see Part 3.18, page 191). However OPV will remain the publicly funded vaccine.
- Influenza vaccine is now recommended for children with cystic fibrosis, people with severe asthma and for pregnant women who will be in the 2nd or 3rd trimester of pregnancy during the influenza season (see Part 3.10, page 144).

Changes in procedures

- The routine use of paracetamol before or after vaccination is no longer recommended, unless a whole-cell pertussis containing vaccine (for example DTPw) is used.
- There are new recommendations on the documentation of the process of providing information to patients and obtaining valid consent (see part 1.3, page 14).
- MMR and OPV can be given together, and when not given on the same day, can be administered at any time before or after each other.
- Tepid sponging of children to reduce a fever of $<41^0$C is no longer routinely recommended, as there is no evidence to support the efficacy of this practice.
- The time limit for reporting adverse events following vaccination has been removed, as some adverse events occur years later (see Part 1.6, page 21).
- Changes in recommended dosage and administration of adrenaline for the management of anaphylaxis have been made (see Part 1.5, page 18).

Changes in the handbook

- Vaccines are now listed alphabetically
- A new section on vaccination for Aboriginal and Torres Strait Islander people has been added (see Part 2, page 68).
- If the recommendations of ATAGI differ from the product information for a particular vaccine, these differences are stated in a section titled "Conflict with product information".
- A new section on Anthrax has been added (see Part 3.1, page 74).
- The information on the transport and storage of vaccines (ie. the cold-chain) has been expanded and given more prominence within the Handbook (see blue pages, Part 1.12, page 54).
- New 'catch-up' schedules have been added for all vaccines in the Australian Standard Vaccination Schedule (see Part 1.9, page 43).
- The adverse events reporting information has been updated to reflect recent changes to the national reporting arrangements (see Part 1.6, page 21).
- The terminology 'vaccine adverse reactions' has been replaced by 'adverse events following immunisation'(AEFI), which is the terminology used by the World Health Organization.
- The information on the Australian Childhood Immunisation Register has been updated (see Part 1.4, page 15).

1.2 STANDARD VACCINATION PROCEDURES

The following vaccination procedure is recommended:

1. The resuscitation equipment, drugs and protocol necessary for the management of anaphylaxis must be available and checked prior to each vaccination session.
2. The vaccine refrigerator, and other 'cold-chain' components, must be maintained and monitored according to current recommendations. They should be checked prior to each working day.
3. Appropriate information about the risks and benefits of vaccination, and the risks of vaccine-preventable diseases, must be provided to, and discussed with, the person to be vaccinated, or that person's parent or guardian. This should be documented.
4. A pre-vaccination assessment, to determine the vaccinee's medical fitness for vaccination, must be undertaken. Any concern about the person's eligibility for vaccination must be discussed with a general practitioner (GP), paediatrician or public health physician with expertise in vaccination. If a person's health status or suitability for vaccination cannot be determined, vaccination should be deferred.
5. Following the provision of appropriate information, (see 3. above) and the pre-vaccination assessment (4. above), valid consent must be obtained from the person to be vaccinated, or from that person's parent or guardian. This should be documented.
6. The person to be vaccinated, or that person's parent or guardian, must be advised that the person should remain under observation in a designated place for 15 minutes after the vaccination.
7. The schedule, dose, route and technique of administration of the vaccines must be in accordance with the NHMRC guidelines. Note: each individual dose must be checked to see that the expiry date has not lapsed, and that there is no particulate matter or colour change in the vaccine.
8. Administer the vaccine(s). Also check the vaccination status of other family members and offer 'catch-up' vaccination where appropriate.
9. Needles, syringes and vaccine vials must be disposed of in accordance with standard infection control guidelines.
10. The parent or guardian of a child who has just been vaccinated must be advised on the management of the common adverse events that may occur after vaccination. It is important that they be given a

contact phone number in case a significant adverse event occurs within 24-48 hours of the vaccination.

11. Prior to departure, the person or the person's parent or guardian should be informed, preferably in writing, of the date of the next scheduled vaccination.
12. The details of the vaccination must be documented (i) on a record to be retained by the person, or the parent or guardian of the person; (ii) on the relevant clinical record and (iii) on an ACIR encounter form.
13. Any significant adverse event following immunisation should be promptly reported to the Adverse Drug Reactions Advisory Committee (ADRAC), or in some instances to the relevant State or Territory Health authorities (see Part 1.6, page 21).

Storage

Vaccines are biological products that lose their potency if they are not stored and transported correctly. Vaccines should be refrigerated at above 2°C and below 8°C. Except for BCG, OPV and freeze-dried MMR, no vaccines must ever be frozen. Diluent must never be frozen. Some vaccines (eg. BCG and reconstituted MMR) lose potency if exposed to light. Detailed guidelines on correct storage and transport are found at the end of Part 1, page 54.

Reconstitution

Storage conditions differ once vaccines have been reconstituted. Freeze-dried vaccines should be reconstituted with the diluent supplied with the vaccine and the reconstituted vaccines should be used within the recommended time period. Reconstituted vaccines should be checked for signs of deterioration, such as a change in colour or clarity. Reconstituted measles vaccine deteriorates rapidly at room temperature. A sterile 21-gauge needle should be used for reconstitution and a separate 23-gauge needle, 25 mm in length, should be used for administration of the vaccine. Diluent used for freeze-dried vaccines should be stored at between 2ºC to 8º C and must not be frozen. Alternatively diluent can be stored at room temperature.

Skin cleaning

When the skin is clean, there is no evidence that skin antisepsis is necessary. If the skin is to be cleaned, alcohol and other disinfecting agents must be allowed to evaporate before injection of vaccine, since they can inactivate live vaccine preparations.

Paracetamol to reduce adverse events

The routine use of paracetamol at the time of vaccination is no longer recommended. However, if whole cell pertussis (Pw) containing vaccines are used, paracetamol should be given orally to prevent common, minor adverse events such as fever and pain. It should be given 30 minutes prior to vaccination and 4 hourly thereafter, as required, to a maximum of 6 doses per 24 hours. Occasionally paracetamol may be indicated 7-10 days after the use of MMR. The dose is 15mg/kg of paracetamol liquid.

Route of administration

Almost all vaccines are given either by intramuscular (IM) or by deep subcutaneous (SC) injection. The major exceptions are OPV, oral typhoid and cholera vaccines, which are given orally, and BCG, which is given by intradermal injection. Although IM or deep SC injection can be used for most vaccines, the IM route is generally recommended.

Standard techniques, needle sizes, gauge and angles for injection of vaccines

Persons administering vaccines should observe standard occupational health and safety guidelines in order to minimise the risk of needlestick injury. A new, sterile, disposable syringe and needle should be used for each injection. Because of infection risks, ATAGI does not endorse the use of multidose vials. If multidose vials are used, a syringe or needle that has been used to inject a person should never come in contact with the vial. Disposable needles and syringes should be discarded in labelled, puncture-proof, spill-proof containers to prevent needlestick injury or re-use. Sharps containers must be kept out of the reach of children. Only sharps containers that meet Australian standards should be used. All persons injecting vaccines should be familiar with the NHMRC Infection Control Guidelines (April 1996).

Most vaccines should be injected deep into a muscle. The use of a short needle may lead to inadvertent SC injection and increase the risk of severe injection pain and local reactions (particularly with the alum-containing vaccines such as DTP). Always withdraw the plunger to ensure that vaccination does not occur directly into a blood vessel.

Intramuscular injections (needle length, gauge, angle and technique) for deltoid and anterolateral thigh

The standard needle for administering intramuscular (IM) vaccines is 23 gauge and 25 mm in length.*

*The exceptions are 1. Preterm babies 2 months or younger, or very small infants – use a 23 gauge 25mm or a 25 gauge 16mm needle; 2. IM injections in very obese adults, use 23 gauge 38mm needle.

The thigh or deltoid muscle should be bunched up to increase the muscle mass. The IM injection should then be administered at a 45 to 60º angle to the skin using a 25mm (23 gauge) needle. At this angle, a 25mm needle can be safely inserted to a depth of between 16-23 mm (skin to needle tip depth). The needle should be angled towards the knee when injecting into the anterolateral thigh, and towards the shoulder when injecting into the deltoid.

Inserting the needle at a 45 to 60 º angle results in less tissue resistance as the needle penetrates the muscle.

The 23g needle allows the vaccine to be injected slowly into the muscle rather than being forced in under high pressure, which can cause injection pain.

Subcutaneous and intradermal injections

The standard needle for administering vaccines by SC injection is a 25 gauge needle 16mm in length.

For very small babies under 2 months of age or pre-term infants: use a 27 gauge needle 12 mm in length for SC injections;

For intradermal injection of BCG vaccine, use a 26-27 gauge needle 10 mm in length. Intradermal injection technique requires special training.

Recommended sites for administering vaccines

Never give injections in the buttocks

The anterolateral thigh is the preferred site for vaccination in infants under 12 months of age. The deltoid region is the preferred site for vaccination in older children (those who have commenced walking) and adults.

Since the late 1980s, the World Health Organization has recommended the anterolateral aspect of the thigh as the preferred site for vaccination of infants. The vastus lateralis muscle is preferred for infants and children under 12 months, and has been demonstrated to be safe for vaccination of toddlers up to 18 months, but only if a 23 gauge needle, 25mm in length is used. The reasons for preferring the vastus lateralis muscle in infants under 12 months are as follows:

- it avoids the risk of sciatic nerve damage from gluteal injections. The risk of sciatic nerve damage from gluteal injections is greatest in infants because the position of the nerve is more variable;
- the deltoid in infants is not sufficiently bulky to absorb injections adequately;
- some vaccines (eg. hepatitis B vaccine) are less immunogenic if injected into the gluteal region;
- it avoids the risk of local reactions and chronic injection site nodules associated with inadvertent injection into the neurovascular bundle (which lies in the anteromedial thigh);
- it avoids the thicker layer of subcutaneous fat on the anterior thigh;
- the anterolateral thigh has a larger muscle mass than the gluteal region, and therefore has a reduced risk of severe local reactions.

Positioning of the child for injection, and location of injection sites for vaccination

It is important that infants and children do not move during the injection. However, excessive restraint can increase their fear and can result in increased muscle tension.

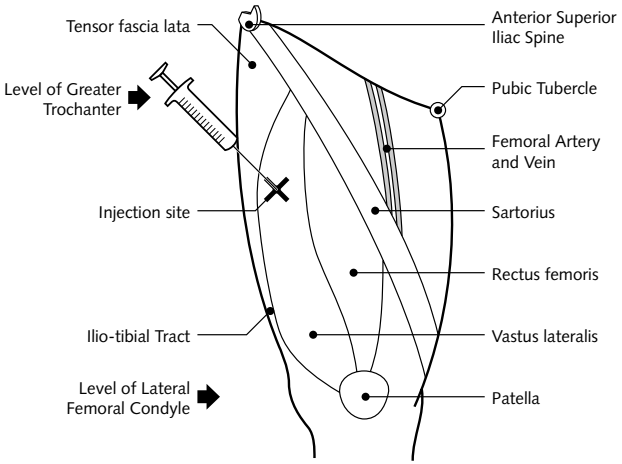
Make sure that the parent or caregiver feels comfortable about holding the infant for injections. Some will prefer not to be involved at all, and others do not even want to be present. These wishes must be respected. If the caregiver is helping to secure the infant, ensure that they understand what is expected of them and what will take place.

The anterolateral thigh - positioning of infants and location of injection site for IM injections

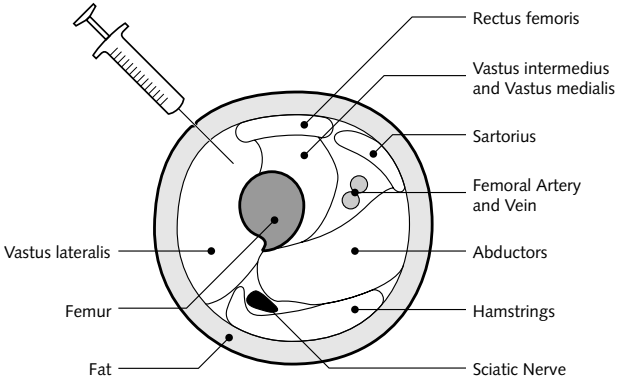
Vaccines should be injected into the junction of the upper and middle thirds of the vastus lateralis, which is the bulkiest part. The 25 mm length needle should be angled at 45 to 60 º to the skin, with the angle pointing down towards the knee. This ensures that the needle will pierce the skin a finger-width above (proximal to) the level of the junction of the upper and middle thirds of the muscle.

The infant can be held in the 'cuddle' or semi-recumbent position on the lap of the parent or caregiver. It is essential to undo the baby's napkin when locating the anatomical landmarks of the injection site, otherwise the vaccine may be given too low in the thigh. Alternatively, the infant can be positioned by being placed on his/her back on a table or bed. The forearm is placed across the infant's pelvis and the thigh is secured between the vaccinator's thumb and fingers. This position minimises delay between injections and makes the injection process easier.

1.2.1 Diagram of the muscles of the thigh showing the recommended injection site



1.2.2 Diagrammatic cross section of the thigh showing recommended injection site.



1.2.3 Photograph of an injection of vaccine into the thigh of an infant

(Note that the hand has been specialy positioned to show the angle of entry of the needle

Deltoid - positioning and location of injection site for IM injection

The most convenient way to position a child for a deltoid injection is for the child to sit sideways on the lap of the parent or caregiver. The arm to be injected is held close to the infant's body while the other arm is tucked behind the back of the parent or caregiver.

It is essential to expose the arm completely from shoulder to elbow when locating the deltoid site. Insufficient retraction of a shirt-sleeve may expose only the inferior portion of the deltoid. The best site is the middle of the muscle, which is halfway between the shoulder tip (acromion) and the muscle insertion at the middle of the humerus (deltoid tuberosity). The 25 mm long needle should be introduced at a 45 to 60 ^{o} angle pointing towards the shoulder. If the lower part of the deltoid is injected, there is a risk of radial nerve injury as the nerve winds forward and emerges from the triceps.

1.2.4 Photograph of an injection of vaccine into the upper arm of a child

Drawing up vaccines from ampoules

For vaccines that are either drawn up through a rubber bung, ampoule, or reconstituted, a new needle should be used for administration. Small air bubbles do not need to be extruded through the clean needle.

A needle or syringe that has been used to inject a person must never be used to draw up vaccine from a vial because of the risk of cross-contamination. Multi-dose vials should not be used, unless there is no alternative.

Administration of two or more vaccines on the same day

It is recommended that the scheduled injectable vaccines (eg. DTPa-hepB and Hib; or DTPa and Hib(PRP-OMP)-hepB) are given at the same time on the same day (eg. at two months of age). They should be given in different limbs and using separate syringes and needles. If three injectable vaccines are to be given on the same visit to an infant under 12 months, two injections can be administered in the same anterolateral thigh but the injection sites should be separated by at least 25mm, so that local reactions will not overlap.

Inactivated vaccines and live vaccines, particularly those in the childhood schedule, can be given during the same visit but in different limbs. For example, DTPa, Hib(PRP-OMP)-hepB, DTPa-hepB, MMR, Hib and polio vaccines can, if necessary for 'catch-up', be given on the same visit. More than one live virus vaccine may be given on the same day. Although MMR and OPV can be given at any time before or after each other, other live vaccine combinations (eg. MMR, BCG and varicella vaccine) that are not given simultaneously, must be separated by four weeks. In addition, there is a specific interaction between yellow fever and injectable cholera vaccines if given within 4 weeks of each other.

Practices which are not recommended.

- Varying from the recommended vaccination route and site can result in inadequate protection (eg. if hepatitis B vaccine is administered into the gluteal area) or can increase the risk of adverse events.(eg. if DTP vaccine is administered subcutaneously rather than intramuscularly).
- Administering smaller volumes than those recommended, for example 'split' or half-doses, may result in inadequate protection. 'Test' doses have the same likelihood of triggering major adverse events in susceptible individuals as do full doses, and therefore must not be given.
- Any vaccination using less than the standard dose, or a non-standard route or site of administration should not be counted as a valid vaccination, and the person should be re-vaccinated according to age with the appropriate 'catch-up' schedule.
- Larger than recommended doses can also be hazardous because they may cause excessive local or systemic concentrations of vaccines or other vaccine constituents, leading to severe reactions.
- Mixing vaccines with other vaccines, drugs or chemicals, is not recommended since no vaccine on the current schedule is registered to be used in this manner.
- Administering vaccines to an age group for which the vaccine is not registered is not recommended, and may increase the risk of an adverse event. For example, DTPa or DTPw vaccines are only registered for use in infants and children up to the 8th birthday.
- Different vaccines must not be mixed in the same syringe. Different vaccines given to a person on the same day should be injected at different sites (in different limbs where possible) using different syringes and needles.

1.3 CONSENT

Prior to vaccination, the individual to be vaccinated or the parent or guardian, should be given adequate information to make an informed decision. Extra information should be available if parents or the vaccinee request it.

The vaccine-provider should allow time for a discussion with the individual to ensure the issue of risk has been addressed. As with any medical intervention, the doctor/nurse should make a note in the clinical records that such a discussion has taken place prior to the person giving consent. A stamp or sticker, signed by the provider, is acceptable.

Valid consent is consent obtained after the parent or vaccinee is able to make an informed decision based on the risks and benefits of vaccination. The table on the back cover of this handbook is a summary of the effects of some vaccine preventable diseases so that they can be compared with the side effects of vaccines that are used to protect against these diseases. Valid consent should be obtained prior to each vaccination, after it has been established that there are no medical factors which contraindicate vaccination. It is preferable that printed information is available to supplement any verbal explanations. Translated material or interpreter services should be available for use by people from non-English speaking backgrounds.

In mass vaccination programs, such as those carried out at schools, the consent requirements are different from those that apply to the vaccination of individuals in general practice or at public immunisation clinics. In large-scale school programs, the parent or caregiver might not attend with the child on the day the vaccination is given. Vaccination in these circumstances should therefore proceed only after written consent from the parent or guardian has been obtained. Such consent should be based on information adequate to enable them to make an informed decision. In circumstances where the parent or guardian is in attendance, explicit verbal consent is required for vaccination, even when written consent has been given for previous vaccinations.

If a child is old enough to adequately understand the benefits and risks of the proposed vaccination, yet refuses the vaccination in spite of such understanding, their wish should be respected.

1.4 RECORDING OF VACCINATION

A permanent vaccination record should be established for each newborn infant and kept by the parent or guardian. Each vaccination provider should record all relevant vaccination information on this record. Parents and guardians should be urged to present the record every time their child is seen by a health professional.

The following items should be recorded in the child's Personal Health Record:

- details of the vaccine given, including the batch number and brand name;
- the name of the person providing the vaccination;
- the date of vaccination;
- the date the next vaccination is due.

The above information, as well as the fact that valid consent was given, must be documented in the clinical notes.

If the vaccine was not administered by the child's usual primary health care provider, reasonable attempts should be made to inform that provider of the vaccines given. All vaccination providers should have a system to recall individuals for subsequent recommended vaccinations.

The Australian Childhood Immunisation Register (ACIR)

The Australian Childhood Immunisation Register (ACIR) is a national database for recording details of vaccinations given to children under the age of seven who live in Australia. It is administered by the Health Insurance Commission (HIC) and provides a facility to assist health professionals increase childhood vaccination levels.

Children enrolled in Medicare are automatically included on the ACIR. Children not enrolled in Medicare will also be included when details of a vaccination are sent to the ACIR by a medical practitioner or other vaccination provider.

The ACIR provides an important means of accountability and evaluation of the childhood vaccination program. Since 1998, data held on the ACIR has been used to determine a family's entitlement to a number of Commonwealth Government benefits such as the Commonwealth Childcare Rebate, Childcare Assistance and the Maternity Immunisation Allowance. It is, therefore, important that vaccination data is submitted to the ACIR promptly.

Reporting to the ACIR.

Vaccination providers should send details of all vaccinations given to children under the age of seven to the ACIR. Vaccination providers receive a payment to cover the administrative process of providing vaccination information to the ACIR. Payment is made by electronic funds transfer (EFT).

The ACIR will request clarification from the provider for vaccination information which is either incomplete or where the vaccination is outside the NHMRC guidelines. This request is made either by telephone or through the payment statement sent each month to providers.

Vaccination details may be submitted using a paper form similar to the Medicare direct-bill form, or by sending data electronically. The Health Insurance Commission (HIC) must approve any software developed to send vaccination data to the ACIR. A list of software suppliers who have developed approved vaccination software may be obtained by calling the Electronic Data Interchange (EDI) Help Desk at the HIC on 1300 550 115 (local call cost). Paper forms can be ordered by calling 1800 653 809 (free call).

Vaccination providers in the Australian Capital Territory, Queensland and the Northern Territory currently sending data to the ACIR via their State or Territory health department should continue to do so. Vaccination providers in other States/Territories can send data directly to the ACIR via EDI or over the Internet, or by paper form.

A child's vaccination record can also be updated with vaccination details, where the vaccination was performed by another vaccination provider, by completing and sending an Immunisation History form to the HIC. The Immunisation History form does not generate a payment.

Child History Statement – replacing the Recall/Reminder Letters

The ACIR Recall/Reminder Scheme is currently being reviewed following a proposal to replace it with an immunisation History Statement. The Statement would advise parents about information recorded for their child on the ACIR, and would identify 'missing' information that prevents their child's record being assessed as 'up-to-date'.

The timetable for the History Statement is still to be determined.

Recording details of a deceased child

The ACIR should be notified of a deceased child to prevent an immunisation History Statement being sent to recently bereaved parents. Advice of a child's death can be provided by calling 1800 653 809 (free call), or by sending details on practice stationery. Details should include name, address, date of birth, Medicare number and date of death.

Ascertaining individual vaccination status

Parents can telephone the ACIR on 1800 653 809 (free call) for information about their child's vaccination status, regardless of where the child's vaccination was given in Australia. The information will be mailed to the address most recently recorded on the ACIR for that child.

Vaccination providers can also request a child's vaccination status. They will need the parent's consent to obtain this information.

Vaccination coverage and other reports

The ACIR is able to report on vaccination levels at a national, state and local level. These reports help to identify areas with low vaccination levels or assist in health planning programs.

Practices that are registered for the General Practice Immunisation Incentive program can receive quarterly reports on vaccination coverage for children within that practice. Details for individual children are available where the child is assessed as not fully vaccinated. These reports are a tool to assist practices to increase their practice's vaccination coverage.

The ACIR Internet Website

The ACIR Internet Website has recently been established and has two main parts, a general information area and a secure area. The Internet address for the ACIR is:

www1.hic.gov.au/general/acircirgacir

Any person with Internet access may view the ACIR site for general vaccination information and reports. The site also provides statistical data and examples of reports available on the secured area of the site.

Approved vaccination providers are able to access the secured area of the ACIR Internet site and obtain a range of statistical and identified reports. These reports are available, depending on the access level granted to the provider, and enable approved clients to view a child's

vaccination details, record vaccination information and access a range of other reports.

To register to access the secured area of the ACIR Internet site, providers should complete the online request form at www1.hic.gov.au/general/acircirgacir. Further information or assistance may be obtained by calling the ACIR Internet inquiry number on 1300 650 039 (local call).

1.5 IMMEDIATE ADVERSE EVENTS FOLLOWING IMMUNISATION

Observation after vaccination

Recipients of vaccines should remain under observation for a short interval to ensure that they do not experience an immediate adverse event. It is recommended that recipients remain in the vicinity of the place of vaccination for 15 minutes. In general, the more severe the reaction, the more rapid the onset. Most life-threatening adverse events begin within 10 minutes of vaccination.

The most important immediate reaction to vaccination is anaphylaxis. The incidence of true anaphylaxis to DTP-containing vaccines is only 1-3 cases per million vaccinations. In adults and older children, the most common adverse event is a syncopal episode (fainting), either immediately or soon after vaccination. Because of this, adults should be warned of the risk of driving or operating heavy machinery for an hour after vaccination. Hypotonic/hyporesponsive episodes in children do not usually occur immediately after vaccination. If such adverse events occur, they generally happen 4-24 hours after vaccination.

Children who have had a serious adverse event (other than a contraindication, such as anaphylaxis) to a vaccine may be subsequently vaccinated under close medical supervision. Check with the State or Territory health authority for more information.

Anaphylaxis

Anaphylaxis following routine vaccination is very rare, but can be fatal. Any health professional carrying out vaccination procedures must be able to distinguish between anaphylaxis, convulsions and fainting.

Fainting is relatively common after vaccination of adults and adolescents, but infants and babies rarely faint, and sudden loss of consciousness in children should be presumed to be an anaphylactic

reaction, particularly if a strong central pulse is absent. A strong central pulse (eg. carotid) persists during a faint or convulsion.

Signs of anaphylaxis

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

- skin signs, such as the rapid development of urticarial lesions (circumscribed, intensely itchy wheals with erythematous raised edges and pale, blanched centres);
- signs of upper airway obstruction, such as hoarseness and stridor, resulting from angio-oedema of the hypopharynx, epiglottis and larynx;
- indications of lower airway obstruction, such as subjective feelings of retrosternal tightness, and dyspnoea with audible expiratory wheeze from bronchospasm;
- abdominal cramps and diarrhoea;
- limpness and pallor, which are signs of severe anaphylaxis in children;
- profound hypotension in association with tachycardia, and/or other signs of cardiovascular disturbance, such as sinus tachycardia or severe bradycardia.

Management of anaphylaxis

Anaphylaxis occurs without warning, usually within 10 minutes of giving the vaccine. Adrenaline must always be immediately at hand whenever vaccination is given. All doctors and nurses responsible for vaccination must be familiar with the practical steps necessary to save life following an anaphylactic reaction.

Experienced practitioners may choose to use an oral airway if the appropriate size is available, but its use is not routinely recommended unless the patient is unconscious.

Injections of antihistamines or hydrocortisone are not recommended for

the emergency management of anaphylaxis, although hydrocortisone may be used for ongoing treatment.

Immediate availability and use of adrenaline is essential to successful management of anaphylaxis.

- If the patient is unconscious, lie him/her on the left side to keep the airway clear.
- Give adrenaline by deep intramuscular injection unless there is a strong central pulse and the patient's condition is good. See below for dosage. If there is no improvement in the patient's condition by 5 minutes, repeat doses should be given every 5 minutes until improvement occurs.
- If oxygen is available, administer it by face mask at a high flow rate.
- Send for professional assistance. Never leave the patient alone.
- If appropriate, begin cardiopulmonary resuscitation.
- All cases should be admitted to hospital for further observation and treatment.

Adrenaline dosage

The recommended dose of 1:1,000 adrenaline is 0.01 mg/kg body weight given by deep intramuscular injection. Adrenaline 1:1,000 contains 1 mg of adrenaline per mL. The following table lists the doses of 1:1,000 adrenaline to be used if the exact weight of the individual is not known.

Table 1.5.1: Doses of 1:1,000 (one in one thousand) adrenaline for infants and children

Doses of 1:1,000 (one in one thousand) adrenaline for infants and children:	
Less than 1 year	0.05-0.1 mL
1-2 years (approx. 10 kg)	0.1 mL
2-3 years (approx. 15 kg)	0.15 mL
4-6 years (approx. 20 kg)	0.2 mL
7-10 years (approx. 30 kg)	0.3 mL
11-12 years (approx. 40 kg)	0.4 mL
12 years and over	0.4-0.5 mL

The use of 1:1,000 adrenaline is recommended because it is universally available. A tuberculin syringe can be used to improve the accuracy of measurement when drawing up small doses.

An alternative approach to dealing with the problem of measurement of small volumes of adrenaline is to use 1:10,000 adrenaline in children up to 10 years of age.

Table 1.5.2: Doses of 1:10,000 (one in ten thousand) adrenaline for infants and children

Doses of 1:10,000 (one in ten thousand) adrenaline for infants and children:	
Less than 1 year	0.5-1 mL
1-2 years (approx. 10 kg)	1 mL
2-3 years (approx. 15 kg)	1.5 mL
4-6 years (approx. 20 kg)	2 mL
7-10 years (approx. 30 kg)	3 mL

If ampoules of 1:10,000 adrenaline are not available, a 1 mL ampoule of 1:1,000 adrenaline can be diluted with 9 mL of water for injection or normal saline. The dose of 1:10,000 adrenaline is 0.1 mL per kg (maximum 3 mL). If the weight of the child is in doubt, this can be roughly calculated on the basis of 0.3 mL per year of age (maximum 3 mL).

Doses of 1:1,000 (one in one thousand) adrenaline for adults 0.5 mL (0.5mg) repeated every 5 minutes as necessary until there is clinical improvement.

1.6 REPORTING ADVERSE EVENTS FOLLOWING IMMUNISATION (PREVIOUSLY KNOWN AS "VACCINE ADVERSE REACTIONS")

The term "vaccine adverse reaction" has been replaced by the World Health Organization recommended term, "adverse event following immunisation" (AEFI).

Before a vaccine is approved for supply in Australia, the manufacturer must demonstrate the quality, efficacy and safety of the product to the satisfaction of the Therapeutic Goods Administration of the Department of Health and Aged Care. In addition, the manufacturer is required to extensively test each lot ('batch') for quality, potency and safety prior to distribution.

Surveillance for adverse events following vaccination is an integral part of a national vaccination program. Through surveillance, it is hoped to

detect changes in the rates of known adverse events and also detect any adverse events which were previously undocumented or which result from incorrect vaccine delivery.

What is an adverse event following immunisation?

An adverse event is a serious, uncommon or unexpected event following immunisation. Such an event may be caused by the vaccine or may occur by chance after immunisation (ie. it would have occurred regardless of vaccination). Most vaccines have minor side effects (see table at the back of the book). Mild events such as fever or pain or redness at the site of injection commonly follow immunisation with some vaccines and should be anticipated.

Before vaccination the vaccine-provider should make sure that the individual to be vaccinated does not have a condition (or a history of a previous condition) which increases the risk of a severe adverse event, or is a contraindication to vaccination. One way to do this is to routinely inquire about such conditions.

Any serious or unexpected adverse event should be reported. Such a report does not imply causality. Parents and care-givers should be encouraged to notify doctors or nurses of adverse events following immunisation. The information provided may assist in identifying those children who should receive follow-up vaccination under close medical supervision.

Which adverse events should be reported?

> Notify any adverse event following vaccination in children or adults that you consider SERIOUS or UNEXPECTED, and possibly related to vaccination.

The following adverse events should be reported. Detailed definitions of the listed adverse events are available in Appendix 7. No time limit has been set, as some adverse events related to vaccination could occur many years later. The inclusion of conditions in the following list does not imply a causal association with vaccination. These conditions may occur coincidently following vacination. Providers should use clinical judgement and common sense in deciding which adverse events to report.

Abscess

Acute flaccid paralysis

- Allergic reaction
- Anaphylactoid reaction (acute hypersensitivity reaction)
- Anaphylaxis
- Arthralgia
- Arthritis
- Brachial neuritis
- Death
- Disseminated BCG
- Encephalopathy
- Encephalitis
- Fever - over 40.5º C
- Guillain-Barré Syndrome (GBS)
- Hypotensive –hyporesponsive episode (Shock, Collapse)
- Local reaction (severe)
- Lymphadenitis (includes suppurative lymphadenitis)
- Meningitis - diagnosis must be made by a physician
- Orchitis
- Osteitis
- Osteomyelitis
- Parotitis
- Rash (severe or unusual)
- Screaming (persistent)
- Seizure
- Sepsis
- Subacute sclerosing panencephalitis
- Thrombocytopenia
- Toxic-shock syndrome
- Vaccine associated paralytic poliomyelitis
- Other severe or unusual events

Medical practitioners or other health professionals are free to report any adverse events that concern them, but do not fit into any of the above categories. They should be reported under the category of 'other reactions' with a full description of the adverse event. This will enable new and unexpected adverse events following immunisation to be identified. In general, minor events do not need to be reported.

Common minor adverse events following immunisation

The following adverse events are frequent but not serious although they can be distressing for parents. These adverse events DO NOT contraindicate further vaccination, and do not need to be reported. Parents should be given advice on what to do about common reactions to vaccination (see Table on the back cover, 'Common adverse events following immunisation & what to do about them').

- Pertussis-containing vaccines (usually DTPw) frequently cause mild to moderate systemic and local effects, such as local swelling and redness, fever, crying and irritability. DTPa causes fewer adverse events than DTPw.
- Hib vaccine causes transient swelling and redness at the injection site in about 5% of infants.
- MMR vaccine may be followed about 7-10 days later by a fever lasting 2 or 3 days, malaise and/or rash. This is not infectious.
- Hepatitis B vaccine may cause transient, minor adverse events including soreness at the injection site (5%-15%), fever (2%-3% - usually low grade), nausea, dizziness, malaise, myalgia and arthralgia.
- Influenza vaccine may cause soreness at the vaccination site. Fever, malaise, and myalgia occur infrequently.
- Pneumococcal vaccine causes low grade fever or mild pain at the site of injection in about half the recipients.

How should adverse events following immunisation be reported?

The Adverse Drug Reactions Advisory Committee (ADRAC) receives reports on unexpected and serious adverse events for all medicines, including vaccines.

In New South Wales, Northern Territory, Queensland, and Western Australia adverse events following immunisation are notifiable. Therefore medical practitioners and other health professionals should report adverse events following immunisation directly to their respective State or Territory Health Department, who will notify ADRAC. In South Australia and the Australian Capital Territory adverse events are not notifiable, but should be reported to the respective State or Territory health department. Reports of adverse events in Victoria and Tasmania should be forwarded to ADRAC.

Table 1.6.1 Contact details for notification of adverse events

State/Territory	Report adverse events to:	Telephone number
NSW	State health department	Look under "Health" in the White Pages
WA	State health department	08-93211312
QLD	State health department	07-32341500
NT	Territory health department	08-8922 8044
SA[1]	State health department	08-8226 7177
ACT	Territory health department	02-6205 2300
Victoria	ADRAC	Use blue form[2]
Tasmania	ADRAC	Use blue form[2]

1. In SA, parents can also report adverse events by calling 1-300-364-100 (24 hours).
2. ADRAC's reply paid blue form has been modified and should be used for notifying adverse events following immunisation in Victoria and Tasmania.

Additional blue forms are available from:

The Secretary
Adverse Drug Reactions Advisory Committee
PO Box 100
Woden ACT 2606
Telephone: 02 6232 8386

ADRAC will forward copies of individual reports of adverse events following immunisation with vaccines in the Australian Standard Vaccination Schedule to those States and Territories which have programs for follow-up and give advice. In addition, reports from ADRAC and State and Territory Health Departments will be aggregated by the National Centre for Disease Control, Commonwealth Department of Health and Aged Care, and the aggregated information will be published in Communicable Diseases Intelligence (CDI).

1.7 SPECIAL RISK GROUPS

Children who have had a previous adverse event following immunisation

Children who have had a serious adverse event (other than a contraindication, such as anaphylaxis) to a vaccine may be subsequently vaccinated under close medical supervision. Check with the State or Territory health authority for more information.

Vaccination during pregnancy

Although the use of many vaccines during pregnancy is contraindicated on theoretical grounds, there is no convincing evidence that pregnancy, in itself, should constitute an absolute contraindication to the use of standard vaccines.

With the exceptions of smallpox vaccine and vaccines that may cause a high fever, there is no convincing evidence that the vaccines described in this handbook are harmful to the fetus if given during pregnancy. If a pregnant woman is likely to be at significant risk of a serious infection that can be prevented by vaccination, then the vaccine should be used. Conversely, if the risk of infection from a particular disease is not immediate and significant, then the relevant vaccine should not be used, or its use should be postponed until after the pregnancy. In some cases, the risk of exposure (and the need for vaccination) can be eliminated by changing travel plans.

Even though the risk of vaccines in pregnancy is generally low, the different sections in this book take the conservative position that the use of vaccines during pregnancy should be avoided since definitive studies on the level of risk have not been carried out. Live vaccines should be avoided unless the risk of disease is greater than the risk of the vaccine.

It is worth noting that fever may be a side-effect of some vaccines; this is significant because high temperatures in early pregnancy may affect the fetus.

MMR or rubella vaccine

Despite concerns that attenuated rubella vaccine virus might cause congenital abnormalities, rubella vaccine (monovalent or MMR) has been given to pregnant women (usually inadvertently) without harm to the fetus. Even though the rubella vaccine virus can infect the fetus if given in early pregnancy, there is no evidence that rubella vaccine causes

congenital rubella syndrome in infants born to susceptible mothers vaccinated during pregnancy. Rubella vaccination during pregnancy is not, by itself, an indication to terminate the pregnancy. All pregnant women should be tested for immunity to rubella, and susceptible women should be vaccinated immediately after delivery.

Poliomyelitis vaccine

OPV can be administered to pregnant women who are at substantial risk of exposure to poliomyelitis infection. An alternative is to give IPV, if the series of injections can be completed before the anticipated exposure.

Yellow fever vaccine

Pregnant women who must travel to an area where the risk of yellow fever is high should receive yellow fever vaccine.

Hepatitis B

Hepatitis B vaccine is recommended for pregnant women at risk of hepatitis B.

Immunoglobulins

There is no known risk to the fetus from passive immunisation of pregnant women with immunoglobulins.

Influenza

Influenza vaccine is considered safe in pregnancy. Influenza vaccine is recommended for pregnant women who have a risk factor for the complications of influenza, or who will be in the 2nd or 3rd trimester during the influenza season (see Part 3.10, page 144).

Contact between pregnant women and individuals who have recently received MMR or OPV

Although live viruses can be shed by individuals vaccinated with OPV, there is no evidence that there is any risk to the fetus if pregnant women are in contact with recently vaccinated individuals. MMR is not transmissible and is safe.

Breast feeding and vaccination

There is no evidence of risk to the breast-feeding baby if the mother is vaccinated with any of the live or inactivated vaccines described in this Handbook. Breast feeding does not adversely affect immunisation and is not a contraindication for the administration of any vaccine to the baby.

Preterm babies

Preterm babies should be vaccinated according to the recommended schedule, commencing at birth, provided they are well and that there are no other contraindications. Oral poliomyelitis virus vaccine, which might spread the live vaccine virus to other babies in the hospital, should not be given until the time of discharge. Alternatively, IPV (inactivated polio vaccine) can be used.

Vaccination of preterm infants should be commenced according to the standard schedule, without correction for prematurity, providing there are no contraindications. Preterm infants have a special need for protection. They have adequate antibody responses and do not have a higher incidence of adverse events.

Some preterm babies do not respond as well as term babies to hepatitis B vaccine and to the PRP-OMP Hib vaccine (PedvaxHIB).

For hepatitis B vaccination of babies less than 32 weeks gestation there are two alternative recommendations:

1. Give an extra dose of hepatitis B vaccine, with vaccination commencing at birth (a 0,2,4,6,12 month schedule). This option must be followed if the mother is a hepatitis B carrier (if this is the case, hepatitis B immunoglobulin must also be given at birth).

2. Delay vaccination until 2 months of age, and use a 4 dose (2,4,6,12 months) schedule.

Preterm babies whose mothers are hepatitis B positive should be vaccinated according to option (1) and should also be given hepatitis B immunoglobulin (see Part 3.8, page 123). Option (2) may be preferred for low risk babies, but there are no specific data in favour of this option.

When PRP-OMP Hib vaccine (PedvaxHIB) is used in an extremely preterm baby (<28 weeks or <1500g), an additional dose of vaccine should be given at 6 months of age (ie. doses should be given at 2, 4, 6, and 12 months of age).

Vaccination for those at special risk of infection

Some conditions increase the risk from infectious diseases. Children and adults with the following conditions should be vaccinated according to the standard schedule, and in some cases may require additional vaccines against other diseases. These conditions include the following: asthma, chronic lung disease, congenital heart disease, splenectomy,

Down's syndrome, HIV infection, babies born small for dates and babies born prematurely.

Vaccination of individuals with suppressed immunity due to disease or treatment

Live vaccines are usually contraindicated in immune-suppressed individuals.

Live vaccines should not be administered to the following individuals:

- patients receiving high-dose oral or injectable corticosteroids (in the case of children, this would include prednisolone 2 mg/kg per day for more than a week or 1 mg/kg/day for more than a month) or other immunosuppressive treatment, including general irradiation;
- those living with malignant conditions such as lymphoma, leukaemia, Hodgkin's disease or other tumours of the reticuloendothelial system, including those in remission who have received chemotherapy within the last 6 months (see below);
- patients with impaired immunological mechanisms, such as severe combined immunodeficiency, and patients who have had recent bone marrow or other organ transplants (see below).

In adults, daily doses of corticosteroids in excess of 60 mg of prednisolone (or equivalent) are associated with significant immunosuppression, although lower doses may be associated with some impairment of immune response. Under such circumstances, live vaccines (OPV, measles, mumps, rubella, yellow fever, BCG) should not be used. Inactivated vaccines are not dangerous to the recipient, but may not be effective.

Individuals with immunosuppression from disease or chemotherapy should not receive live virus vaccines until at least 6 months after chemotherapy has finished. Such patients should be given an injection of the appropriate preparation of immunoglobulin as soon as possible after exposure to measles or chickenpox.

For individuals treated with systemic corticosteroids at high dose, live vaccines (such as MMR, OPV, and BCG) should be postponed until at least 3 months after treatment has stopped. Children on lower daily doses of systemic corticosteroids for less than 2 weeks, and those on lower doses on alternate day regimens for longer periods, may be given live virus vaccines (such as MMR and OPV). Inactivated vaccines (such as pertussis and hepatitis A vaccines), modified toxins (such as

diphtheria and tetanus vaccines) and subunit vaccines (such as Hib and hepatitis B vaccines) can be given safely to patients receiving immunosuppressive therapy, but may be less effective.

Inactivated vaccines may be administered to immunosuppressed children and adults, although there are little available data on the efficacy of this practice and immunogenicity may be reduced. Children and adults who have received bone marrow transplants (see below) may require booster doses or revaccination depending on their serological and clinical status. Most paediatric oncology units in Australia have protocols for vaccination of such children when they are well and off major therapy

Oncology & transplant patients

Oncology patients, their siblings and household contacts

> Live vaccines such as oral polio vaccine (OPV), MMR and varicella must not be given to immunocompromised patients. OPV must not be given to the siblings or other household contacts of immunocompromised patients; inactivated polio vaccine (IPV) should be used instead.

During chemotherapy, and for 6 months afterwards, patients may receive inactivated vaccines (eg. DTPa, hepB) according to the normal schedule of vaccination. It should be remembered that patients are unlikely to mount a full immune response when they are on therapy.

Siblings of patients on chemotherapy should receive DTP, MMR, Hib and hepB as usual. IPV should be substituted for OPV during, and for 6 months after, chemotherapy. All varicella non-immune household contacts of oncology patients including those on chemotherapy but not those who have had a bone marrow transplant in the past 6 months or who are severely immunosuppressed or who have severe graft versus host disease, should be offered varicella vaccine (see Part 3.28, page 234). Should the vaccinee develop a varicella like rash following the vaccination, the oncology patient should be given zoster immune globulin (ZIG) although the possibility of transmission of the vaccine virus from a healthy vaccinee is extremely low.

At 6 months post-chemotherapy, if the patient is well, infection free, and there are no clinical concerns about their immune status, the following schedule of re-vaccination is recommended:

DTPa if less than 8 years (Td if >8 years), MMR, IPV, Hib (if less than 5 years old or prior splenectomy/hyposplenism) and hepB. These vaccines may be given without checking titres beforehand, and may be given together on one day. Measles and rubella antibody status should be checked 6-8 weeks after vaccination. Patients who have not seroconverted should be considered for a further dose of MMR.

IPV may be repeated 12 months later.

Any deviations from these guidelines should be discussed with the patient's oncologist.

Re-vaccination for bone marrow transplant (BMT) patients

Titres should be checked routinely in BMT patients, before and after vaccination. Inactivated vaccines should be given at 6 months post-BMT, so long as the patient has been off post-BMT immunosuppression for at least 3 months (ie. 6 months post-BMT for autologous BMT, 8-9 months post-BMT for allogeneic BMT).

Recommended schedule:

6 months post-BMT: IPV, DTP or Td, Hib, HepB

12 months post-BMT: IPV

15 months: MMR

Vaccination should be deferred for patients with chronic graft versus host disease or patients still receiving intravenous immunoglobulin.

Topical corticosteroids

Widespread use of potent topical corticosteroids (particularly when used in conjunction with occlusive dressings) for more than 2 weeks may give rise to immune suppression. In such cases, live vaccines should be withheld.

Inhaled corticosteroids

The use of inhaled steroids is not a contraindication to vaccination with either live or inactivated vaccines.

Vaccination of siblings and household contacts of immune suppressed individuals

Healthy siblings and close contacts of immune-suppressed children should be vaccinated against measles, mumps and rubella. There is no risk of transmission of the vaccine virus, and immunisation will ensure that these individuals have less chance of infecting their immune-

suppressed siblings. Varicella vaccine should also be given to healthy non-immune household contacts of immune suppressed individuals.

Because it contains a live (although attenuated) virus, OPV should not be given to immune suppressed individuals or their household contacts. IPV should be given instead.

Vaccination of recent recipients of normal human immunoglobulin

The immune response to virus vaccines (with the exception of yellow fever, rabies, and Japanese encephalitis vaccines) may be inhibited by normal human immunoglobulin. In general, live virus vaccines should be given 3 weeks before or 3 months after a dose of immunoglobulin. However, specialist advice should be sought if high-dose or intravenous immunoglobulins have been used.

In those about to travel, when time is short and there is significant risk of exposure to polio, the vaccine should be given even if immunoglobulin has been given at any time in the previous 3 months.

Vaccination of HIV-infected individuals

The vaccination of individuals infected with HIV presents a variety of problems. Firstly, the immune response to vaccines may be inadequate and, secondly, there is a risk that some live vaccines may themselves cause progressive infection. The degree of immunodeficiency induced by HIV varies from insignificant to profound, and this should be taken into account when considering a schedule of vaccination, as should the risk of acquisition of the infection one is trying to prevent. Although it may be logical to give higher or more frequent doses of vaccines to these patients, in most cases there are insufficient data to advocate such measures. Children with perinatally acquired HIV differ substantially from adults as immunisation and first exposure to vaccine antigens occurs after HIV infection, whereas for adults most vaccines are inducing a secondary immune response. HIV infected individuals of any age who are well controlled on combination antiretroviral therapy (undetected or low viral load with good preservation of CD4 lymphocyte count) are likely to respond well to vaccines.

Recommendations for use of specific vaccines in HIV-infected individuals.

- Diphtheria-tetanus-pertussis (DTP) containing vaccines - use the standard schedule.

- *Haemophilus influenzae* type b (Hib) vaccine - use the standard schedule.
- Poliomyelitis vaccines - live oral poliomyelitis vaccine has not proved harmful to asymptomatic HIV-infected children. Nevertheless, inactivated poliomyelitis vaccine (IPV) is preferred for such children because of increased risk of household contact with immunocompromised adults.
- Measles-mumps-rubella vaccine (MMR) - unless they are severely immunosuppressed, MMR should be routinely administered to HIV-infected children at 12 months of age. Table 1.7.1 shows age specific definitions of severe immunosuppression. Measles may cause severe disease in HIV-infected children. Severely immunocompromised children who are exposed to measles should therefore be given normal immunoglobulin (in a dose of 0.5 mL/kg), regardless of their vaccination status.

Table 1.7.1: Age specific CD4 count indicating severe immunosuppression in HIV infection

Age:	<12months	1-5 years	>=6Years
CD4 count:	<750	<500	<200
	($0.75x10^9$/l)	($0.50x10^9$/l)	($0.20x10^9$/l)

- Pneumococcal vaccine - pneumococcal disease, both respiratory and invasive, is a frequent cause of morbidity in HIV-infected children and adults. Pneumococcal polysaccharide vaccine is recommended for all HIV infected patients over the age of 2 years, although there is limited evidence of efficacy in this group.
- Influenza vaccine - because of potential morbidity from influenza, annual vaccination might be advisable in symptomatic HIV-infected adults and children, because benefit is likely to exceed risk.
- BCG vaccine - BCG must not be given to HIV-infected children or adults because of the risk of disseminated BCG infection.
- Hepatitis B vaccine - recombinant hepatitis B vaccines are safe to use, but the immunological response may be poor. HIV-positive individuals should receive twice the normal dosage (ie. double the normal volume of vaccine on 3 occasions or a standard dose of the increased strength dialysis formulation of vaccine on 3 occasions). Antibody level should be measured at the completion of the vaccination schedule. The indications for the use of hepatitis B vaccine are the same as for non-HIV-infected individuals.

A proportion of HIV-positive men who have sex with men may already have been exposed to the hepatitis B virus.

- Hepatitis A vaccine - the use of hepatitis A vaccine in HIV-infected individuals has not been evaluated, but there is no reason to believe that the vaccine would pose a risk and it should be given if indicated.
- Vaccinations for travel - live attenuated typhoid or yellow fever vaccines should not be given to HIV-infected individuals. Meningococcal, typhoid, cholera, and rabies vaccines are safe and can be used for the usual indications.

Vaccination for individuals with functional or anatomical asplenia

Individuals who have had their spleen removed or who have a non-functioning spleen are at increased lifelong risk of fulminant bacteraemia, most notably from pneumococcal and meningococcal infection.

All splenectomised individuals should receive pneumococcal and meningococcal vaccinations in addition to the vaccinations of the standard schedule. Repeat injections of pneumococcal and meningococcal vaccines should be given every 5 and 3 years respectively. In addition, *Haemophilus influenzae* type b (Hib) vaccination is recommended if the individual has close contact with children less than 5 years of age. In cases of elective splenectomy, the vaccinations should be given 2 weeks before the operation. Subsequent Hib boosters are not required.

Vaccination of children with sickle cell anaemia

Children with sickle cell anaemia should be vaccinated with Hib vaccine according to the infant schedule. These children should be given pneumococcal vaccine at 2 years of age, with repeat doses every 5 years thereafter. To further reduce the risk of pneumococcal disease, they should also be treated with daily prophylactic doses of penicillin V, commencing before the age of 4 months (penicillin V 125 mg b.d. rising to 250 mg b.d. when they reach 4 years of age, until 5 years of age).

Vaccination of those at occupational risk

Certain occupations are at increased risk for some vaccine preventable diseases. They include the following:

- Child care staff should be vaccinated against hepatitis A, measles, mumps, rubella and varicella. Two doses of MMR vaccine are required (see Part 3.12, page 156).

- Medical, nursing, other health professional and laboratory staff and medical, nursing and other health professional students should be vaccinated against infections they may encounter. These may include hepatitis B, hepatitis A, measles, mumps, rubella, influenza, varicella and tuberculosis. Two doses of MMR vaccine are required (see Part 3.12, page 156).
- Veterinarians, veterinary assistants and abattoir workers should be vaccinated against Q fever. Stockyard workers, shearers, animal transporters, laboratory workers handling veterinary specimens and many others exposed to cattle, sheep or goats or their products should be considered for vaccination against Q Fever.
- Microbiology staff should be vaccinated against hepatitis B. Some should also be vaccinated against pathogenic organisms with which they work, such as the agents causing Japanese encephalitis, hepatitis A, meningococcal infection, typhoid, Q fever, plague, rabies, Australian Bat Lyssavirus (ABL) and vaccinia.
- Sewerage workers should be vaccinated against hepatitis A.
- Police, members of the armed forces, and staff in institutions for custodial care and care of the intellectually handicapped may be at increased risk of hepatitis B, due to a high risk of significant contact with blood and body fluids. If such a risk is clearly present, they should be vaccinated.
- Those who come into contact with bats (both flying foxes and microbats) should be vaccinated against Australian Bat Lyssavirus (ABL) using rabies vaccine. These include managers of display or research colonies of bats, bat carers, researchers and students who handle the animals, wildlife officers and power line workers who frequently remove bats from power lines. Staff working in veterinary surgeries should also be vaccinated against ABL with rabies vaccine if they work with bats.

Vaccination of immigrants to Australia

Immigrants or visitors from foreign countries may be incompletely vaccinated and may, in addition, have unsatisfactory records of vaccination.

- If an immigrant child has no valid documentation of vaccination, the standard 'catch-up' schedule should be commenced. If the child is 12 months of age or older, the 1st doses of DTPa, hepB, OPV, MMR and Hib vaccine can be given at the same visit. For detailed 'catch-up' schedules, see part 1.9, page 43.

- If there is a valid record of vaccination, the history of prior doses should be taken into account when planning a vaccination series that complies with the Australian schedule.

Migrant women of child-bearing age need to be targeted for vaccination against rubella with MMR.

Vaccines for foreign travel

Vaccination for overseas travel is carried out to provide protection against certain infectious diseases that are endemic in overseas countries, and to fulfil quarantine requirements. It is important that persons intending to travel overseas are aware that vaccination plays only a limited role in the protection against travel infections, and they should be aware of other important strategies to protect themselves. Detailed information on vaccination for overseas travel can be obtained from a booklet issued by the World Health Organization (contact Hunter Publications, Reply Paid, RACGP, 70 Jolimont Street, Jolimont VIC 3002; telephone (03) 9417 5361) or travel vaccination centres.

The International Health Regulations of the World Health Organization permit countries to require a valid certificate of vaccination against yellow fever and cholera. However, since 1994, no country has officially required a cholera vaccination certificate for entry, even though the traveller may have visited a cholera-infected area. Currently, the only official overseas quarantine requirement is for yellow fever, and this requirement is exercised only by some countries.

Some countries, including Australia, require a valid certificate of vaccination against yellow fever in certain circumstances. Generally, individuals who have recently been in a yellow fever area are required to have a valid yellow fever vaccination certificate for entry. Travellers should check the requirements with the consulates of the countries they intend to visit.

All travellers should make sure that their standard vaccinations are up to date. It is particularly important that travellers are vaccinated against diphtheria and tetanus. For areas where poliomyelitis is still prevalent, travellers should be vaccinated with OPV. For areas where food hygiene is poor, travellers should be protected against hepatitis A and typhoid. The use of rabies vaccine, Japanese encephalitis vaccine, meningococcal vaccine, and BCG vaccine should be considered for travellers at high risk of the relevant infections. Not all travellers to countries or areas where

these diseases are endemic will be at risk, and vaccination may not be necessary. For example, visitors to Indonesia who stay at a major hotel in Bali for a few days do not require vaccination, but individuals who plan to spend many months in a village setting in a remote area of Java require a range of vaccinations. Cholera vaccination is not recommended for overseas travellers. Vaccination against plague is recommended for travellers at high risk.

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1.8 THE AUSTRALIAN STANDARD VACCINATION SCHEDULE

The Australian Standard Vaccination Schedule shown on the following two pages is that recommended by the National Health and Medical Research Council (NHMRC). In drawing up its recommendations, the NHMRC has sought to reduce the number of injections given at each vaccination session through the use of new combination vaccines and to limit, as far as possible, the number of vaccine products that a practitioner would need to have available. For the vaccinations at 2, 4, 6 and 12 months, two options for the use of combination vaccines which meet these criteria are recommended.

Table 1.8.1 - The Australian Standard Vaccination Schedule

AGE	VACCINE	
Birth	hepB[a]	
	Path 1[b]	**Path 2**[b]
2 months	DTPa-hepB and Hib and OPV	DTPa[c] and Hib (PRP-OMP)-hepB and OPV
4 months	DTPa-hepB and Hib and OPV	DTPa[c] and Hib (PRP-OMP)-hepB and OPV
6 months	DTPa-hepB and OPV	DTPa[c] and OPV
12 months	MMR and Hib	MMR and Hib (PRP-OMP)-hepB
18 months	DTPa	
4 years	DTPa and MMR and OPV	
10-13 years	hepB[d]	
1 month later	hepB[d]	
5 months after 2nd dose	hepB[d]	
15-19 years	Td	
	OPV	
Non-immune women who are post-partum or of child bearing age	MMR	
50 years	Td[e]	
50 years and over (Aboriginal and Torres Strait Islander people)	Pneumococcal vaccine (every 5 years) Influenza vaccine (every year)	
65 years and over	Pneumococcal vaccine (every 5 years) Influenza vaccine (every year)	

Notes

a. Hepatitis B vaccine should be given to all infants at birth and should not be delayed beyond 7 days after birth. Infants whose mothers are hepatitis B surface antigen positive (HBsAg+ve) should also be given hepatitis B immunoglobulin (HBIG) within 12 hours of birth.

b. When necessary the two paths may be interchanged with regard to their hepatitis B and Hib components. For example, when a child moves interstate, they may change from one path to the other (see part 1.8.1)

c Wherever possible the same brand of DTPa should be used at 2, 4 and 6 months.

d Adolescent hepatitis B vaccination is not necessary for those children who have previously received three doses of hepatitis B vaccine.

e Td should be given at 50 years of age unless a Td booster dose has been documented in the previous 10 years

DISEASE	VACCINE	AVAILABLE PRODUCTS
Hepatitis B	hepB	Engerix-B™ or H-B VaxII™
Diphtheria, Tetanus, Pertussis	DTPa	Infanrix™ or Tripacel™
Diphtheria, Tetanus, Pertussis, Hepatitis B	DTPa-hepB	Infanrix-HepB™
Haemophilus Influenzae type B	Hib (PRP-OMP)	PedvaxHIB™
Haemophilus Influenzae type B, Hepatitis B	Hib (PRP-OMP)-hepB	Comvax™
Poliomyelitis	OPV	Polio Sabin™
Measles, Mumps, Rubella	MMR	MMRII® or Priorix™
Diphtheria, Tetanus	Td	ADT Vaccine™
Pneumococcal disease	Pneumococcal vaccine	Pneumovax23®
Influenza	Influenza vaccine	Fluarix™ or Fluvax® or Vaxigrip™ or Flurivin™

Transition from the old to the new schedule

All babies born on or after 1 May 2000 should commence the new Australian Standard Vaccination Schedule. Because of logistics, funding and vaccine interchangeability issues, all children born before this date should commence or continue with the previous schedule.

1.8.1 GUIDELINES FOR ADMINISTERING SCHEDULE VACCINES

Precautions and contraindications relating to schedule vaccines

Children with minor illness (without an acute systemic illness and with a temperature below 38.5º C) may be vaccinated safely. Major illness or high fever might be confused with vaccine side effects and increase discomfort to the child. Therefore vaccination should be postponed for 2-3 days until the child is well. A return appointment for vaccination should be made at the time of deferral.

Severe adverse events which contraindicate further doses of DTP-containing vaccines (DTPw or DTPa)

- Encephalopathy within 7 days, defined as severe acute neurological illness with prolonged seizures and/or unconsciousness and/or focal signs, not due to another identified cause.
- Immediate severe allergic or anaphylactic reaction to vaccination with DTP.

  In these cases DT should be used for further vaccination. Although the pertussis component is the most likely cause of adverse events, further vaccination with diphtheria and tetanus vaccines should be undertaken under careful observation.

A simple febrile convulsion or pre-existing neurologic disease is not a contraindication to pertussis vaccine.

Severe adverse events which contraindicate other vaccines

True contraindications to other vaccines are extremely rare (see relevant chapters). An anaphylactic reaction to eggs does not contraindicate MMR vaccine.

Precautions and contraindications for immunocompromised people (including those with HIV/AIDS and other immunodeficiencies, and those receiving cytotoxics and corticosteroids)

Live vaccines are usually contraindicated in immune-suppressed individuals, including those with malignant disease or receiving chemotherapy. However, because immune-suppressed individuals are at risk of certain infections, the question of vaccination needs to be assessed by a specialist.

False contraindications to vaccination

The following conditions ARE NOT contraindications to any of the vaccines in the standard schedule:

- family history of any adverse events following immunisation;
- family history of convulsions;
- previous pertussis-like illness, measles, rubella or mumps infection;
- prematurity (vaccination should not be postponed);
- stable neurological conditions such as cerebral palsy and Down's syndrome;
- contact with an infectious disease;
- asthma, eczema, atopy, hay fever or `snuffles';
- treatment with antibiotics;
- treatment with locally acting (inhaled or low-dose topical) steroids;
- child's mother is pregnant;
- child being breast fed;
- history of jaundice after birth;
- low weight in an otherwise healthy child;
- over the age recommended in vaccination schedule;
- recent or imminent surgery;
- replacement corticosteroids.

Interchangeability of vaccines

In general, vaccines from different manufacturers that protect against the same disease (eg. Hepatitis B, Hib) may be administered interchangeably for an individual patient. However, until data supporting interchangeability of acellular pertussis-containing vaccines are available, vaccines from the same manufacturer should be used, whenever feasible, for the first 3 doses. If the previous acellular pertussis vaccine type is unknown or not available, vaccination should proceed with any registered product.

Disposal of infectious waste post-vaccination

It is important to dispose of infectious waste appropriately. Infectious waste, including sharps and plastic spoons used for OPV, must be disposed of immediately following administration of vaccine and at its point of use. Refer to your state or territory for management guidelines for the safe disposal of infectious waste or refer to the NHMRC guidelines.

1.9 'CATCH-UP' VACCINATION

Introduction

The objective of a 'catch-up' schedule is to complete a course of vaccination and provide adequate protection.

Every opportunity should be taken to check vaccination status and to provide missing doses. When infants and children have missed scheduled vaccine doses, a 'catch-up' schedule should be commenced.

The information and tables below are designed to assist in planning a 'catch-up' program based on the Australian Standard Vaccination Schedule.

If the vaccine-provider is uncertain about how to plan the 'catch-up' schedule, contact either a public health professional with vaccination expertise or a paediatrician.

Vaccination of children with inadequate vaccination records

The most important requirement for assessment of vaccination status is to have written documentation of vaccination, since verbal reports of alleged previous vaccination correlate poorly with actual immunity. However, vaccination providers are often faced with the problem of children with inadequate vaccination records.

Inadvertent additional vaccination with DTP, MMR, poliomyelitis and Hib vaccines is unlikely to cause serious adverse events.

All children lacking a convincing history of vaccination should be re-started on a full course of vaccination appropriate for their age.

Interrupted vaccine doses

If the recommended intervals between doses are exceeded, there is no need to recommence the schedule or give additional doses, because the immune response is not impaired by such delay.

If the process of administration of vaccine is interrupted, eg. by syringe-needle disconnection or vomiting of OPV, the whole dose should be repeated.

Issues to be considered when planning 'catch-up' vaccination

- Plan the 'catch-up' on the basis of documented evidence of previous vaccination.
- When commencing the recommended 'catch-up' vaccination schedule the interval between doses may be reduced or extended and the numbers of doses required will reduce with age. For example the 4th birthday is used as a marker for reduction in the number of doses of DTP-containing vaccine.
- As a child gets older the recommended vaccines change or they might need to be omitted from the schedule. For example DTP-containing vaccines are used up to the 8th birthday and then Td is used.
- For incomplete vaccination or overdue vaccinations, build on previous documented doses. Never start the schedule again, regardless of the interval (unless there are no written vaccination records).
- If more than one vaccine is overdue, it will often be appropriate to give all the vaccines at one visit (see Part 1.2, page 5). In such cases, the next visit should be scheduled for a time after the appropriate minimal interval (eg. normally 1-2 months between 1st and 2nd dose, and 2nd and 3rd doses of DTPa-hepB).
- Check rules on interchangeability of vaccines. Some vaccines and vaccine brands are not interchangeable.

Table 1.9.1: Minimum intervals between vaccine doses – A guide for planning 'catch-up' schedules

VACCINE	Minimum interval between doses			
	Dose 1 to 2	DOSES 2 to 3	DOSES 3 to 4	DOSES 4 to 5
DTPa, DTPa-hepB[1]	1 month	1 month	6 months	12 months
Td (ADT)	1 month	1 month	10 years	10 years
DT (CDT)	1 month	6 months	N/A	N/A
PRP-OMP (PedvaxHIB), Hib-(PRP-OMP)-hepB (Comvax)	1 month	2 months[2]	N/A	N/A
HbOC (HibTITER)	1 month	1 month	2 months[2]	N/A
PRP-T (Hiberix, Act-HIB)	1 month	1 month	2 months[2]	N/A
OPV	1 month	1 month	1 month	N/A
IPV[3]	1 month	1 month	1 month	N/A
MMR	1 month	N/A	N/A	N/A
Hepatitis B	1 month	2 months	N/A	N/A

(1) If possible, DTPa brands should not be used interchangeably for the 1st three doses. If this is not possible, vaccination should be completed with the available DTP brand. DTP containing vaccines can be interchanged for booster doses.

(2) Booster doses (3rd dose for PRP-OMP or 4th doses for HbOC or PRP-T) are given no earlier than 1st birthday and at least 2 months after previous dose.

(3) For unvaccinated adults at increased risk of exposure to poliovirus and who must use IPV, note that it takes 2-3 months before adequate protection is built up. Three doses of IPV should be administered at least 1 month apart before there is adequate protection.

'Catch-up' using DTP-containing vaccines

Some children received DT instead of DTP, and 'catch-up' for pertussis is requested or indicated. Monovalent pertussis vaccine is not available in Australia. This means that 'catch-up' vaccination against pertussis for children who have been fully vaccinated for age against diphtheria and tetanus with DT vaccine can only be given with DTPa. A total of 3 doses of DTPa can be given at least 1 month apart, up to a maximum of 6

doses of DT. In this situation, although good data for children under 8 years are not available, additional doses of DTPa may be more likely to be associated with large local reactions or fever. Parents should be informed of this possibility in balancing the benefits of protection against pertussis.

Children who are overdue for a DTP-containing vaccine but are under 8 years of age should be offered DTPa for 'catch-up''. Determine the child's current age and use their previous vaccination history (using documented information only) to plan the 'catch-up', building on previous doses. Do not repeat previous doses unless there are no records.

'Catch-up' for DTP vaccines for children under 8 years of age:

1. Complete the primary course by giving up to three doses of DTPa at 1 month intervals.
2. Give a booster dose at 18 months of age or 6 months after the third dose, whichever is later.
3. If the child is under 4 years of age at the time of the 4th dose then give a 5th dose at 4 years of age or 12 months after the 4th dose, whichever is later.

'Catch-up' using Td vaccine for children 8 years and over and for adults:

The minimum age for using Td (adult diphtheria and tetanus vaccine) or tetanus toxoid is 8 years of age.

Adolescents and adults who have not received the standard course of primary vaccination should receive, as a minimum, 3 doses of Td at least 1 month apart.

Two boosters are required at 10 year intervals.

If boosters are required this should be given as Td.

'Catch-up' for Hib vaccines (for children under 5 years of age)

Hib vaccines administered to children under 6 weeks of age are not effective.

Hib vaccines are used up to the 5th birthday. No Hib vaccines are recommended from 5 years onwards, except for patients with asplenia.

Table 1.9.2 Recommended 'catch-up' schedule when start of Hib vaccination has been delayed

Vaccine	Trade name and company	Age now 3-6 months	7-11 months	12-14 months	15-59 months
PRP-OMP (2), (3)	PedvaxHIB (Merck Sharp & Dohme) Comvax (CSL/Merck Sharp Dohme)	2 doses, 2 months apart, booster 12 months	2 doses, 2 months apart, booster 12 months and at least 2 months after previous dose	1 dose, booster at least 2 months after previous dose	Single dose (1)
HbOC (3) PRP-T (3)	HibTITER (Wyeth-Lederle) Hiberix (SmithKline Beecham) ActHIB (Pasteur Meriuex)	3 doses, 2 months apart, booster 18 months	2 doses, 2 months apart, booster 18 months	1 dose, booster 18 months	Single dose (1)

NOTES

1. When a booster is given after the age of 15 months, any of the 3 available conjugate Hib vaccines can be used.
2. Extremely preterm babies whose vaccination was started with PRP-OMP should be given an extra dose at 6 months
3. Use the same brand of Hib vaccine for the primary course

Table 1.9.3 Recommendations for Hib 'catch up' vaccination when doses have been delayed or missed

Age at presentation (months)	Previous vaccination history	Recommended regimen
7-11	1 dose	1 dose of Hib vaccine at 7-11 months, with booster at least 2 months later, at 12-15 months*
7-11	2 doses of PRP-OMP	Give 3rd dose of PRP-OMP at 12 months and at least 2 months after previous dose
7-11	2 doses of HbOC, PRP-T, unknown brand or mixture of vaccine brands	Give 3rd dose 1 or more months after 2nd dose, and 4th dose at 18 months*
12-14	2 doses before 12 months	A single dose of any registered Hib vaccine
12-14	1 dose before 12 months	2 additional doses of any registered Hib vaccine, separated by 2 months.
15-59	Any incomplete schedule	A single dose of any registered Hib vaccine.

* Where possible, the same brand of vaccine should be given for all doses. Do not delay vaccination.

'Catch-up' for hepatitis B vaccines

The 1st dose of hepatitis B vaccine can be given from birth onwards.

Paediatric formulations of monovalent hepatitis B vaccines can be used up to the 20th birthday. Adult formulations of monovalent hepatitis B vaccine are used from the 20th birthday.

Different brands of hepatitis B vaccine, including the hepatitis B component of multivalent vaccines such as DTPa-hepB and Hib(PRP-

OMP)-hepB, can be used interchangeably throughout the schedule.

A total of 3 doses is required to achieve adequate sero-protection when using either the adult or paediatric formulations. A minimum effective interval of 1 month is required between the 1st and 2nd doses of the schedule. A minimum interval of 2 months is recommended for adequate protection between the 2nd and 3rd doses. The optimal interval is 5 months between the 2nd and 3rd dose.

'Catch-up' for OPV or IPV

The 'catch-up' schedule for polio consists of 3 doses at least 1 month apart. IPV and OPV are interchangeable.

'Catch-up' for MMR vaccine

If no previous doses have been given, 'catch-up' for MMR consists of 2 doses, 1 month apart. If a single dose has been given more than a month earlier, give one dose.

1.10 PRE-VACCINATION QUESTIONNAIRE, PRE-VACCINATION ASSESSMENT, AND NOTES FOR PARENTS

This checklist can be copied and can be given to parents or guardians of children before they are vaccinated.

Pre-vaccination questionnaire

The checklist on the next page can be photocopied and given to parents just prior to vaccination. The pre-vaccination assessment chart that follows can be photocopied and displayed in the clinic for easy reference as a tool to help you assess the child's suitability to be vaccinated.

Pre vaccination checklist for parents or adult vaccinees

The following information is needed to assess the fitness of a person for vaccination. For vaccinees, the conditions listed below do not necessarily mean that you or your child cannot be vaccinated today, but please tell the doctor or nurse if any of the following apply:

The person to be vaccinated:

- is unwell today;
- has a disease which lowers immunity (eg. leukaemia, cancer, HIV/AIDS) or is having treatment which lowers immunity (eg. steroid medicines such as cortisone and prednisone, radiotherapy and chemotherapy);
- lives with someone who has a disease which lowers immunity, or lives with someone who is having treatment which lowers immunity;
- has had a severe reaction following any vaccine;
- has any severe allergies;
- has had a vaccine containing live viruses within the last month (eg. MMR, oral poliomyelitis or yellow fever), or an injection of immunoglobulin, or a whole blood transfusion within the last three months;
- is pregnant;
- has a medical condition affecting the brain or spinal cord;
- is living with someone who is not vaccinated.

Note: If you have any questions about this information or any other matter relating to vaccination, please ask the doctor or nurse before the vaccine is given.

Before any vaccination takes place, the nurse or doctor will ask you if:

- you have read this information;
- you understand this information;
- you need more information to decide whether to proceed.

The above conditions do not necessarily exclude a patient from being vaccinated, but they should be considered by the doctor or nurse giving the vaccination.

Did you bring your/your child's vaccination record card with you?

It is important for you to receive a personal record of you/your child's injections. If you don't have a record card, ask your doctor or nurse to give you one! Bring this record with you every time you bring your child for his/her injections. Make sure your doctor or nurse records all vaccinations on it. Your child may need this card to enter daycare, kindergarten or school.

Table 1.10.1 Pre-vaccination assessment of conditions that may preclude vaccines in the standard schedule – for use by doctor or nurse

Vaccine providers can use this chart as a quick guide to assess the patient prior to vaccination. Please refer the appropriate section about the specific vaccines within this Handbook for more detailed information.

Assessment	Defer vaccine until resolved condition (or discuss with the appropriate health professional)	Seek further advice (a)
Conditions		
Acute febrile illness (T >38.5°C)	All vaccines	N/A
Diarrhoea & vomiting	OPV	
Immunosuppressive illness	NA	OPV, MMR, R
Evolving neurological illness	NA	DTPa-hepB, DTPa or DTPw
Allergies to vaccine components		
Streptomycin (b)	NA	IPV
Neomycin(b)	NA	OPV, IPV, MMR, Influenza (Fluvax)
Polymyxin (b)	NA	IPV, Influenza (Fluvirin, Fluvax)
Gentamycin (b)	NA	Influenza (Fluvax)
Yeast (b)	NA	Hepatitis B vaccines
Gelatin	NA	MMR, JE
Egg protein	NA	Influenza, Q fever
Drugs		
Immunosuppressants	OPV, MMR, R	NA
Live vaccine within 4 weeks	Defer OPV for 4 weeks after oral typhoid vaccine	NA
Whole blood transfusion within 3 months	MMR, R	NA
Immunoglobulin within 3 months	MMR, R	NA

Other		
Previous very severe local and/or systemic adverse event (anaphylaxis)	NA	OPV, MMR, R, Hib, DTP-containing vaccines, DT, Td, T, hepB
Pregnancy	OPV, MMR, R	NA

Abbreviations

DTPa	diphtheria-tetanus-acellular pertussis vaccine
DTPa-hepB	diphtheria-tetanus-acellular pertussis-hepatitis B vaccine
DTPw	diphtheria-tetanus-whole cell pertussis vaccine
DT	combined diphtheria-tetanus vaccine
Td	adult diphtheria-tetanus vaccine
OPV	oral poliomyelitis vaccine
MMR	measles-mumps-rubella vaccine
R	rubella vaccine
Hib	Hib vaccine
T	tetanus vaccine
IPV	inactivated poliomyelitis vaccine
hepB	hepatitis B vaccine
NA	not applicable

Note:

(a) Seek further advice from a paediatrician or public health physician with expertise in vaccination; contact the Immunisation section within your State or Territory Heath authority or your local Public Health Unit

(b) Omit only if a patient has had an anaphylactic reaction to these substances (vaccines containing virus cultured in hens' eggs may be administered under appropriate medical supervision).

Advice to parents on common adverse events following immunisation

Many vaccine injections may result in soreness, redness, itching, swelling or burning at the injection site for 1 to 2 days. Sometimes a small, hard lump may persist for some weeks or longer. This is no cause for concern as it is an expected minor side effect of the vaccination. Paracetamol might be required to ease the pain.

See the back cover of the handbook for 'Common reactions to vaccination and what to do about them.' This table can be photocopied and given to parents as post-vaccination advice.

1.11 ADULT VACCINATION

A substantial proportion of vaccine preventable diseases now occur in older adolescents and adults. Persons who escaped natural infection as a child, or were not immunised against diphtheria, tetanus, measles, mumps, rubella and poliomyelitis, are at risk of these diseases and their complications. When outbreaks of measles occur, mortality and morbidity in adults may be high.

As well as ensuring that adults are protected against the diseases listed above, annual vaccination against influenza is recommended for all those 65 years of age and older, and for Aboriginal and Torres Strait Islander people 50 years and over. Vaccination against pneumococcal disease is recommended for all adults 65 years and over, and for Aboriginal and Torres Strait Islander people 50 years and over. See Table 1.8.1, The Australian Standard Vaccination Schedule for routinely recommended vaccines.

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1.12 TRANSPORT AND STORAGE OF VACCINES

The 'cold-chain' is the system of transporting and storing vaccines within the safe temperature range of between 2ºC to 8ºC from the place of manufacture to the point of administration. Maintenance of system requires that processes are in place to ensure that a potent vaccine reaches recipients.

The World Health Organization's Expanded Programme on Immunization (EPI) has developed detailed guidelines on the maintenance of an effective cold-chain. The guidelines here are based on the EPI recommendations, research and experience in Australia.

Safe vaccine storage when using a domestic refrigerator

'Frost free' rather than cyclic type domestic refrigerators are recommended for storage of vaccines. Cyclic type domestic refrigerators are not recommended because they produce wide fluctuations in the internal temperatures, with regular internal heating. The 'frost free' types of refrigerators do not have heating cycles but remain frost free with low levels of frequent warming temperatures.

Domestic refrigerators and many industrial refrigerators are designed only for the storage of food and drink and usually have several temperature zones to meet the requirements of different foods. They are not designed for the special temperature needs of vaccines. However, safe vaccine storage is possible in most refrigerators if the following procedures are adhered to:

- vaccine storage guidelines are followed;
- door openings are kept to a minimum;
- temperatures are checked and recorded daily;
- one person should be given responsibility for adjusting the refrigerator control (it is important that other staff are also trained to ensure continuous monitoring);
- defrosting is done regularly and ice is not allowed to build up.

The refrigerator to be used should be dedicated to vaccine storage whenever possible. **Do not store food or drink in vaccine refrigerators**. Vaccines should only be stored on the middle and upper shelves in normal domestic refrigerators. If using a bar fridge, the middle shelf should be used, as vaccines stored near the evaporation plate or on the top shelf of a bar fridge can be inadvertently frozen. The lower shelves,

drawers and the door of normal domestic refrigerators become to warm (above 10ºC) if the refrigerator is opened frequently.

Do not crowd the vaccines by overfilling the refrigerator; allow room for the cold air to circulate within the refrigerator. Fill the lower drawers and the door with plastic bottles filled with salt water. This helps to stabilise the temperatures within the refrigerator. Allow space between the bottles for good air circulation. Add enough salt to make the water undrinkable (about 1-2 tablespoons per litre).

If a dedicated vaccine fridge is not available, store the vaccines in a (pre-cooled) Styrofoam container with lid closed and place in the middle of the refrigerator. Ensure the vaccines inside the container are monitored and place a label on the outside stating "Vaccines–Keep refrigerated".

When preparing ice packs or freezer blocks for transport, cool the thawed ice packs on the lower shelf of the refrigerator during the day before placing in the freezer. Place cooled ice packs in the freezer at the end of the day for freezing overnight. Allow a minimum of 2 days for complete freezing before using the blocks for transporting vaccines. Do not stack ice packs on top of each other in the freezer. Set them on their edge and allow space between them.

Maintaining and monitoring refrigerator temperatures

Refrigerators used for vaccines should have a minimum/maximum thermometer placed on a middle shelf and temperatures should be checked and recorded daily. The most cost effective minimum/maximum thermometer is a digital type with a probe.

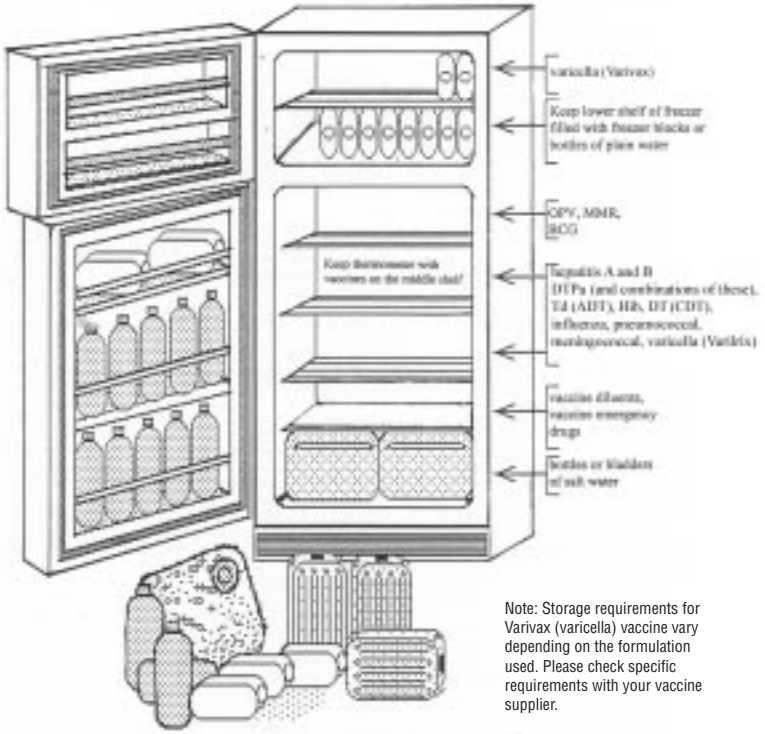
If using a digital thermometer with a probe, the probe should be placed directly in contact with the vaccine vial. Do not put the probe into fluid. The recommendation of keeping the vaccine storage temp at between 2ºC to 8ºC is based on air, not fluid temperatures.

The refrigerator temperature should be read around the same time each day, preferably in the middle of the day. One person only should be responsible for adjusting the refrigerator to maintain the temperature in the recommended range of 2ºC to 8ºC.

The door should be kept closed as much as possible. Refrigerators used for vaccine storage should have an uninterrupted power supply and door openings should be kept to a minimum.

During a power failure of 4 hours or less, the refrigerator door should be left closed. If the power fails for more than 4 hours, store vaccines in a

Fig 1.12.1 Thermal lag modification and storage patterns in a domestic refridgerator



Note: Storage requirements for Varivax (varicella) vaccine vary depending on the formulation used. Please check specific requirements with your vaccine supplier.

Keep vaccines in trays on the safe upper shelves.

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

Illustrating the modification and storage patterns required for safe vaccine storage in a Domestic rerigerator.

Diagram courtesy of Ms Nan Miller, Territory Health Services.

pre-cooled, insulated container with ice packs to keep them cool (see section 'Transporting vaccines in insulated containers' for more information).

Maintenance of the vaccine refrigerator

Refrigerator breakdowns should be repaired immediately. The door seals should be in good condition so that the door closes securely. Refrigerators that are not 'frost free' should be defrosted regularly to prevent ice build-up. Ice build-up can reduce the efficiency and performance of a refrigerator.

During defrosting or cleaning of the refrigerator, move the vaccines to a second refrigerator. This temporary storage refrigerator must also be monitored to ensure the correct temperature is maintained. Alternatively the vaccines can be stored in a pre-cooled insulated container with ice packs or ice until the normal vaccine refrigerator is ready for use again. There is more information in the section called 'Transporting vaccines in insulated containers'.

Unpacking vaccines after transport

Do not remove vaccines from their packaging regardless of their bulkiness. Removal from original packaging exposes vaccines to room temperature and/or lighting. Check cold-chain monitors when the vaccines arrive to ensure they have not been exposed to temperatures above 8ºC or below 0ºC.

If cold-chain monitors (CCM) have not been included, check that the ice packs are still partially frozen; if they are completely thawed, the vaccines have not been kept sufficiently cold and may not be effective. Do not discard any vaccines until you discuss the necessary actions with your State/Territory vaccine distribution centre, vaccine supplier, hospital pharmacy or local public health unit.

Cold-chain monitors (CCM)[1]

Cold-chain monitors (CCM) include time-temperature (heat monitors) and freeze monitors. The CCM should accompany all vaccines during any long distance vaccine transport. A minimum/maximum thermometer is an acceptable alternative for monitoring temperature inside cold boxes during transport to outreach settings.

1. These CCM have been tested extensively by the World Health Organisation in developing countries but have not been tested under all Australian conditions.

The CCM should not be removed from the (cold box) container until all vaccines have been removed for use or stored[1]. The index on the time-temperature or freeze monitor (or alternatively, the minimum/maximum thermometer if working in an outreach setting) should be checked when a vaccine is removed from the cold box. Any changes should be recorded. If possible, the CCM that arrived with the vaccines should remain with a portion of the vaccines during storage in the refrigerator until the vaccines have been used or discarded.

Always contact the State/Territory Vaccine Distribution Centre, vaccine supplier, hospital pharmacy or the local public health unit for more information if required.

Time-temperature monitors (for monitoring exposure to heat over time):

These CCM work by showing colour change on an indicator strip when the temperature reaches or exceeds a set threshold. The indicator strip should be attached to a card on which instructions for use are printed, in accordance with World Health Organization (WHO) format.

There is a one time-temperature monitor available that has two separate temperature thresholds:

- The Monitor Mark™ (Model 10N/34AA) manufactured by 3M; with +10ºC, irreversible colour change (14 days to full scale colour change at +12ºC); plus 34ºC, irreversible colour change (3 hours to full scale colour change at 37ºC).

If an equivalent monitor to this one recommended by the WHO becomes available in Australia, it should also be considered for use.

One vaccine manufacturer/distributor uses an in-house time-temperature monitor "Bulls Eye"™ . This is a heat-sensitive monitor and the manufacturer claims that it changes colour from "satisfactory" to "unsatisfactory" at 30 hours at 21^{0}C, and 10 days at 12^{0}C. It is more heat sensitive than the Monitor Mark™ and this might mean that if the monitor activates, vaccines could be discarded even though they are still potent. If the Bulls Eye™ monitors activate, vaccine providers should always seek advice from their State/Territory Vaccine Distribution Centre before vaccines are discarded. There is currently not sufficient evidence to assess the manufacturer's claims about this monitor's performance under various temperature conditions.

Freeze indicators:

Freeze indicators work by a colour spot change at threshold temperature at or below freezing. There are different models available in Australia made by different manufacturers:

- Freeze Watch™ (freeze) indicator (Berlinger or 3M). There are two models available: one is set to activate at 0°C and the other activates at -5°C. The model that activates at 0°C is recommended for use in Australia.
- ColdMarkTM (freeze) indicator (IntroTech™). There are two models available: one is set to activate at 0°C and the other activates at -3°C. The model that activates at 0°C is recommended for use in Australia.

Procedures to be observed when using vaccines

Vaccines should remain in the refrigerator until they are required and all unused vaccines should be immediately returned to the refrigerator. BCG vaccine that has been taken in and out of refrigeration during a clinic session should be discarded at the end of the clinic day.

OPV will not lose potency if it is quickly thawed and then refrozen. The freeze-thaw cycle can occur until the vial is empty as long as the vaccine is stored in a freezer capable of achieving temperatures below -20ºC. Most domestic refrigerators (with freezer compartments) are not capable of achieving this temperature. A minimum/maximum thermometer can be used to check the freezer temperature.

It is now recommended that opened multidose vials of OPV can be used in subsequent sessions if the following three conditions are met:

- the expiry date has not passed;
- the cold-chain is maintained (between 2°C to 8°C);
- the vaccine has not been taken away from the health centre (eg. outreach immunisation setting).

Transporting vaccines in insulated containers

Refrigerated transport is the best way to distribute vaccines from the central (usually state) vaccine centre to the door of the immunisation service provider (clinic or surgery). This transport should include appropriate temperature control and monitoring equipment. When this is not feasible, other methods can be used to achieve an effective cold chain.

Containers specifically designed for transporting vaccines should be

used if available. If such a container is not available, the following guidelines for packing vaccine for transport in an insulated container should be observed.

- Before packing ice packs with vaccines, remove the ice packs from the freezer at least 30 minutes prior to packing and allow them to 'sweat'. This increases the temperature of the ice packs and reduces the risk of freezing vaccines.
- Place vaccines (and time-temperature monitors and freeze monitor as required) in a small Styrofoam container ('six-pack' container). Close the lid and secure with tape. Pack the small Styrofoam container inside a larger insulated container (a 'cooler' such as the 'Esky™') and surround it with ice packs. Close and secure the lid of the large container. The vaccines must not be in direct contact with the ice packs because of the risk of freezing.
- If the vaccines are not packed using the above technique, an alternative method is to pack the vaccines inside a pre-cooled cold box (eg. Esky ™). Place the ice packs on top of the vaccines, ensuring they are separated from the vaccines by a layer of polystyrene foam, shredded paper or bubble-wrap plastic. Ensure the vaccines, CCM, ice packs and 'filler' material are packed to ensure they do not move around during transport. Vaccines must be packed in such a way as to ensure the ice packs do not come into direct contact with the vaccines or CCM, and the cold air can circulate freely around the vaccine.
- Remove vaccines only as they are required, making sure the lids are replaced on the lids of both small and large containers each time (if this is the method of transport). If the time-temperature monitors and/or freeze indicators (or alternatively, the min/max thermometer in an outreach situation) are used, they should be checked before administering the vaccine. If the time-temperature monitor indicates that vaccine is being subjected to temperatures above 10ºC while being transported, use more freezer blocks to reduce and maintain the internal temperature at the correct level.

Stability of vaccines at different temperatures

High temperatures affect all vaccines whereas freezing damages others. In Australia, freezing has been shown to be the major cause of vaccine damage in both tropical and temperate areas. If concerned about loss of vaccine potency, contact your state or territory immunisation coordinator.

NOTE: The following vaccines are unstable at room temperature and must not be exposed to light:

- BCG (Bacille Calmette-Guérin)vaccine;
- Reconstituted measles-mumps-rubella (MMR) vaccine; and
- Oral Polio Vaccine (OPV).

Do not freeze:

- Diphtheria-tetanus-pertussis containing vaccines;
- Haemophilus influenzae type b (exception PRP-T);
- Hepatitis B;
- Hepatitis A;
- Influenza;
- Pneumococcal;
- Meningococcal;
- All reconstituted vaccines;
- All combinations of these vaccines; and
- Vaccine diluents.

Note: Several other less frequently used vaccines (eg. rabies, typhoid, and yellow fever) are also damaged by freezing.

Table 1.12.1 Stability of some standard vaccines at different temperatures

Stability at different storage temperature (1)					
Vaccine (2)	**< 0°C**	**2°C to 8°C**	**22°C to 25°C**	**35°C to 37°C**	**over 37°C**
Diphtheria, tetanus and pertussis-containing vaccines (acellular and whole cell pertussis components). Includes DTPa, DTPa-hepB, DT (DT & Td), DTPw-containing vaccines)	DTPa-containing vaccines: Do not freeze. As little as 24 hours at < 0°C or > 25°C may cause antigens to fall from suspension and be very difficult to resuspend DTPw-containing vaccines: Freezing can reduce potency. Freezing point of tetanus is between -5°C to -10°C. Freezing point of pertussis is not known. Vaccine loses significant potency when stored at -5°C to -10°C. Frozen vaccine can still remain as a liquid. Discard these vaccines if freeze monitor has been activated or vaccines have been exposed to temperatures of 0°C or below.	Store at 2°C to 8°C for 18 to 24 months in spite of continuous slow decrease in potency of the pertussis component.	The DT components are stable for 4, possibly 6 months; the limiting factor is the pertussis component. Some vaccines containing pertussis are only stable for only 2 weeks at this temperature.	The DT components are stable for weeks but the stability of the pertussis component varies with different vaccines. Some pertussis-containing vaccines lose 50% of potency during storage for one week.	DT components: stable for 2 weeks at 45°C; At 53°C, loss of potency after few days. At 60-65°C, loss of potency after few hours. Pertussis component: about 10% loss of potency per day at 45°C; rapid loss in potency is stored at 5°C. Pertussis component is the limiting factor.

Stability at different storage temperature (1)					
Vaccine (2)	< 0°C	2°C to 8°C	22°C to 25°C	35°C to 37°C	over 37°C
Hib-containing vaccines (eg. PRP-OMP, HbOC, PRP-T, Hib (PRP-OMP)-hepB See below for Act-Hib (PRP-T)	Do not freeze. The precise freezing point is not established. Manufacturers state freezing temperature of HbOC is -1.0°C. Discard if freeze monitor has been activated or vaccine has been exposed to temperature of 0°C or below Freeze-dried PRP-T can be frozen	Store at between 2°C to 8°C	Stable for at least 24 months when stored at 25°C	Information not available	Information not available
Act-HIB	Do not freeze	Store for up to 3 years at 2°C to 8°C	Stable for up to 24 months at 25°C	Stable for up to 12 months at 37°C	Information not available
Oral Polio Vaccine (OPV) (Unopened vials)	May be frozen. Can be stored for up to 2 years if kept at −20°C. This is difficult to achieve in domestic refrigerators.	Can be stored for between 6-12 months. Do not exceed 8°C	Unstable: 50% loss of potency after 3 weeks exposure to this temperature	Very unstable: loss of potency after 1 to 3 days at this temperature	Very unstable at 41°C: 50% loss of potency after 1 day; Complete loss of potency after 1−3 hours at 50°C
Oral Polio Vaccine (OPV) (opened vials)	May be stored frozen for up to 2 years at −20°C. This is difficult to achieve in domestic refrigerators. The freeze-thaw-refreeze cycle can recur until the vial is empty. Discard on expiry	Opened vials can be stored at 2°C to 8°C between use, if expiry date has not passed. Discard any unused vaccine if it has been transported outside the clinic/surgery (eg. outreach)	Stable for at least 1 week when stored at 20°C to 25°C	Information not available	Remains potent for 24 hours.
Inactivated Polio Vaccine (IPV)	Do not freeze. Discard if freeze monitor has been activated or vaccine has been exposed to temperature of 0°C or below	Store for up to 2 years between 2°C to 8°C	Loses significant potency after 20 days	Destroyed after 20 days	Information not available

Stability at different storage temperature (1)					
Vaccine (2)	**< 0°C**	**2°C to 8°C**	**22°C to 25°C**	**35°C to 37°C**	**over 37°C**
Measles, Mumps, Rubella (MMR) (Freeze-dried vaccine)	May be stored in freezer at 0°C or below. Protect from light, which may inactivate virus. Diluent (3) Store at room temperature, or between 2° to 8°C; do not freeze	Safe storage for 2 years at 2°C to 8°C. Diluent (3) Store at room-temperature, or between 2°C to 8°C; do not freeze	Retains satisfactory potency for 1 month	Retains satisfactory potency for at least 1 week	50% loss of potency after 2 to 3 days at 4°C: 80% loss of potency after 1 day at 54°C
Measles, Mumps, Rubella (MMR) (Reconstituted with diluent)	Do not freeze. (Do not store at or under 0°C) Protect from light	Can be stored at between 2°C to 8°C. Protect from light, which may inactivate the vaccine virus Should be used in one vaccination session (-8 hours) if kept cool and protected from sunlight. If not, discard after 1 hour	Unstable: 50% loss of potency after 1 hour, 70% loss after 3 hours Protect from light	Very unstable: titre may be below acceptable level after 2 to 7 hours Protect from light	Inactivation within 1 hour (NHMRC 1997)
Hepatitis B vaccine	Do not freeze. (Do not store at or below 0°C). Freezing point −0.5°C and vaccine is destroyed at this temperature. Discard if freeze monitor has been activated or vaccine has been exposed to temperature of 0°C or below	Retains satisfactory potency for 2 years	Retains satisfactory potency for 30 days	Stable for 1 week	Stable for 3 days
Hepatitis A vaccine	Do not freeze Discard if freeze monitor has been activated or vaccine has been exposed to temperature of 0°C or below	Store at between 2°C to 8°C for many months.	Stable for 15 months	Stable for 15 months	Information not available

Stability at different storage temperature (1)					
Vaccine (2)	< 0°C	2°C to 8°C	22°C to 25°C	35°C to 37°C	over 37°C
Influenza vaccine	Do not freeze Discard if freeze monitor has been activated or vaccine has been exposed to temperature of 0°C or below	Store at between 2°C to 8°C	Not available	Not available	Not available
Pneumococcal vaccin	Do not freeze Discard if freeze monitor has been activated or vaccine has been exposed to temperature of 0°C or below	Store at between 2°C to 8°C	Not available	Not available	Not available
Varicella vaccines: Varilrix	May be stored in freezer	Store at between 2°C to 8°C. Can be stored for 24 months from the date of manufacture if stored at 2°C to 8°C	Not available	Not available	Not available
Varivax	Store at -15°C or below in a freezer which has a separate sealed freezer door, and that reliably maintains temperatures below -15°C; administer vaccine immediately after reconstitution; discard if not used within 30 minutes.	Highly unstable - loses potency	Highly unstable - loses potency	Highly unstable - loses potency	Highly unstable - loses potency

Stability at different storage temperature (1)					
Vaccine (2)	**< 0°C**	**2°C to 8°C**	**22°C to 25°C**	**35°C to 37°C**	**over 37°C**
BCG (freeze-dried form)	Can be stored at up to -20°C. Do not expose to light (ultraviolet and/or fluorescent) Diluent (3) Store at room temperature, or between 2°C to 8°C; do not freeze	Safe storage for 12 months. Do not expose to light (ultraviolet and/or fluorescent) Diluent (3) Do not freeze; store at between 2°C to 8°C or room temperature	Stability varies. Some BCG vaccine may lose 25% to 40% of original potency after 2 months Do not expose to light (ultraviolet and/or fluorescent) Diluent (3) Do not freeze; store at between 2°C to 8°C or room temperature.	Loses potency rapidly. Store for only 2-3 weeks. Do not expose to light (ultraviolet and/or fluorescent) Diluent Do not freeze; store at between 2°C to 8°C or room temperature.	Rapid loss of potency. Up to 73% of potency at 3 days. Do not expose to light (ultraviolet and/or fluorescent) Diluent Do not freeze; store at between 2°C to 8°C or room temperature.
BCG (Reconstituted with diluent)	DO NOT FREEZE	Very unstable. Protect form all forms of light (inactivates vaccine). Keep at between 2°C to 8°C when vial is not in used. Discard all unused vaccine at the end of the vaccination session (6 hours)	Very unstable. Protect from all forms of light (inactivates vaccine). Keep at between 2°C to 8°C when vial is not be used.	Very unstable. Protect from all forms of light (inactivates vaccine). Keep at between 2°C to 8°C when vial is not be used.	Very unstable. Protect from all forms of light (inactivates vaccine). Keep at between 2°C to 8°C when vial is not be used.

1. For thermostability information on other vaccines not listed in this table, refer to the specific chapter in this Handbook
2. The vaccines that are most unstable at room temperature are OPV, reconstituted MMR vaccine, and reconstituted BCG vaccine. OPV, reconstituted BCG, and reconstituted MMR vaccines must be protected from exposure to light.
3. DO NOT FREEZE DILUENT AS THIS MAY CAUSE UNDETECTABLE CRACKS IN THE AMPOULE LEADING TO CONTAMINATION

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PART 2 - VACCINATION FOR ABORIGINAL AND TORRES STRAIT ISLANDER PEOPLE

Introduction

Aboriginal and Torres Strait Islander people experience a much greater burden of infectious diseases than do other Australians. Although much of this excess burden is borne by indigenous children, indigenous adults also experience very high rates of infections such as pneumonia. Some of these infections are vaccine-preventable.

The diseases and the vaccines

(i) Children.

Apart from BCG, which is recommended for some indigenous infants at birth, the Standard Vaccination Schedule is now the same for all Australian children. Indigenous Australians are at increased risk of acquiring tuberculosis. Although there is uncertainty about the efficacy of BCG in preventing pulmonary tuberculosis, it seems to be particularly protective against disseminated forms of the disease. BCG is recommended for indigenous neonates in 'regions of high incidence'. It is usually administered to eligible infants by hospital staff (ie. midwives) soon after delivery.

Serological surveys carried out before hepatitis B vaccines became widely available indicated that although there was considerable variation between communities, the prevalence of markers of hepatitis B virus (HBV) infection and HBV carriage was very high in many indigenous communities.

A small percentage of indigenous children have a suboptimal response to recombinant hepatitis B vaccine. The cause of this suboptimal response is unlikely to be related to vaccine 'cold-chain' failure, but may be determined by inherited mechanisms. Regardless, there has been a marked decline in the prevalence of markers of HBV infection and carriage in indigenous children since the introduction of hepatitis B vaccine. It has also been shown that the majority of indigenous children who were vaccinated in infancy still have vaccine-induced immunological memory at 5-6 years of age, indicating that they do not require a booster dose at school entry.

Indigenous children in north Australia (and probably elsewhere) have a suboptimal response to OPV. This has also been observed in children in developing countries, where it has been attributed to 'a complex array of

factors related to the vaccine, host and environment'. It is fortunate that the disease has been eradicated from Australia because there is no simple solution to the suboptimal response. Nevertheless any indigenous child with an acute flaccid paralysis should immediately be investigated to exclude poliomyelitis.

Prior to the introduction of an effective *Haemophilus influenzae* type b (Hib) vaccine, not only was the incidence of invasive Hib disease very high in indigenous children, but also it occurred at a younger age than that in non-indigenous children.

A vaccine to prevent Hib disease in indigenous children needed to be immunogenic when administered early in infancy. For reasons that are not entirely clear the vaccine known by the abbreviation PRP-OMP (PedvaxHIB) is more immunogenic at 2 months of age than the other conjugated Hib vaccines. PRP-OMP was included as the preferred Hib vaccine for indigenous children in the Australian Standard Vaccination Schedule in 1993. Since then there has been a dramatic decline of Hib disease in indigenous Australian children.

The crowded living circumstances experienced by many indigenous families probably place their children at increased risk of complicated and severe measles, and therefore high uptake of measles vaccine is particularly important for these children. Until recently measles vaccine (as MMR) was given to indigenous children in the Northern Territory (NT) at 9 months of age, but the recommended age for MMR for all children in the NT is now 12 months of age. Indigenous children have a similar immune response to measles vaccine administered at 12 months of age to that seen in other Australian children.

(ii) Adults

Indigenous adults experience considerably greater mortality and morbidity from pneumonia and invasive pneumococcal disease than do other Australian adults. In Western Australia, for example, Aboriginal adults aged 25-54 years have at least a 30-fold greater risk of hospitalisation from pneumonia than other adults, and this excess risk is even apparent among Aboriginal adults living in the Perth and Fremantle metropolitan area. In central Australia, Aboriginal adults aged 15-59 years have a 20-fold greater incidence of invasive pneumococcal disease than non-Aboriginal adults. This incidence is the highest ever reported, being only closely matched by that in indigenous adults in North America.

Because of flaws in the studies, the efficacy of the pneumococcal polysaccharide vaccine in either the elderly or adults with pre-existing medical conditions has never been satisfactorily defined in randomised controlled trials. However, with one exception, case-control studies consistently demonstrate that the vaccine is 50-80% effective in preventing invasive pneumococcal disease in older adults, most of whom have underlying conditions. On the other hand, randomised controlled trials have clearly shown that pneumococcal vaccine is very effective (80-90%) in protecting healthy young adults.

A study in far north Queensland has demonstrated that the NHMRC recommendations for pneumococcal vaccination are appropriate for indigenous adults. It is very important that the vaccine be offered to indigenous adults still in relatively good health, before the chronic or severe complications of any pre-existing conditions develop. In particular, the vaccine should be offered to young men who have begun to consume hazardous amounts of alcohol, and to recently diagnosed diabetics.

Polysaccharide vaccines such as the pneumococcal vaccine do not induce immunological memory. It is recognised that pneumococcal antibodies decline to prevaccination levels within five years of vaccination, but it is uncertain whether the vaccine's efficacy also wanes with time. In the United States, 'revaccination once is recommended for persons ... at highest risk for serious pneumococcal infection'. Indigenous Australian adults are at an extremely high-risk, and until evidence becomes available to the contrary, revaccination is recommended every five years.

Revaccination at intervals of five years or more is associated with a modestly increased risk of local (injection site) reactions, but nevertheless the benefits of revaccination out-weigh concerns about the adverse events. It is inevitable that on occasion indigenous adults will be inadvertently revaccinated at intervals less than the recommended five-yearly interval. The available evidence suggests that the risk of serious adverse events following 'early' revaccination (for example after a 3- or 4- year interval) with the pneumococcal polysaccharide vaccine is probably negligible.

(iii) Other vaccines

The first ever outbreak of Japanese encephalitis (JE) in Australia occurred in the remote outer islands of the Torres Strait in 1995. JE vaccine was first offered to the residents of these islands in late 1995, and

since then the vaccine has been integrated into the childhood vaccination schedule commencing at 12 months of age (see JE vaccine section). Should the risk of JE become evident, through on-going surveillance, it may be necessary to implement JE vaccination in indigenous communities on the mainland.

On occasion, it is necessary to use the meningococcal vaccine to control outbreaks of invasive meningococcal disease in indigenous communities. Guidelines for the control of meningococcal disease in Aboriginal and Torres Strait Islander communities have been published elsewhere.

Although hepatitis A is 'hyperendemic' in many Aboriginal communities in the Northern Territory, with the majority (90%) of children being infected by five years of age, this is not necessarily the situation in indigenous communities elsewhere in Australia. With improvements in living environments, water supply and waste disposal there is an upward shift in the age of infection with hepatitis A. This means that the infection occurs at an age when clinical symptoms are more obvious, and paradoxically the disease becomes a more visible and an apparently more common public health problem.

Thus in north Queensland, for example, the mean age of indigenous cases of hepatitis A is 12.6 years. For this reason, and because there have been several deaths from hepatitis A in indigenous children in the region, hepatitis A vaccination has been offered to indigenous children in north Queensland since early 1999.

Although Aboriginal children in central Australia have an extremely high incidence of invasive pneumococcal diseases such as pneumonia, septicaemia and meningitis, indigenous children elsewhere in the country are also at an increased risk. Although the pneumococcal polysaccharide vaccine is not appropriate for young children, the technology used to develop the very effective conjugate Hib vaccines has been used to develop conjugate pneumococcal vaccines that may be suitable for young indigenous children. A recent clinical trial in California showed that a 7-valent conjugate pneumococcal vaccine was highly (100%) effective in preventing invasive pneumococcal disease after administration from 2 months of age. There is an urgent need for such vaccines for young indigenous children. It is possible that these vaccines may prevent otitis media as well as invasive pneumococcal disease.

Vaccine service delivery for indigenous Australians

Vaccination is a fundamental aspect of primary health care services not only for indigenous children but also for indigenous adults. The primary goal for childhood vaccination in Australia is that 90% of all children should be fully vaccinated by their second birthday by the year 2000. This should be the goal for service providers for indigenous children; it has been proposed that 80% of 'at-risk' indigenous adults should receive influenza and pneumococcal vaccines as recommended by NHMRC.

A strong commitment is required for optimal vaccination coverage of indigenous children, particularly those in rural towns or urban settings. There is a need for relevant and appropriate information for the parents of indigenous children and there is a need for high quality training for the service providers, in particular for indigenous health workers. Close attention must be given to the vaccine 'cold-chain', to ensure that vaccines are not inadvertently frozen. The true indications and false contraindications for vaccination must be clearly understood.

> The National Aboriginal Health Strategy states that children must be 'free from infection (eg. colds, fever, bronchitis)', otherwise 'vaccination must be postponed'. This is NOT correct: colds, fever (unless ≥38.5ºC), and bronchitis are NOT indications to postpone vaccination; children with colds, fever <38.5ºC and bronchitis should be vaccinated.

All vaccination providers should have a system to recall indigenous people for subsequent vaccinations. Information about under-vaccinated children should be freely shared between service providers, particularly in urban settings. Innovative strategies, such as an outreach vaccination service, offering home vaccination where appropriate, must be attempted and maintained if successful.

Similar strategies are required for successful vaccination programs for indigenous adults. Again innovative strategies will be necessary to reach those at high risk, such as the homeless and those with alcohol problems. Vaccination clinics should be established for those in alcohol rehabilitation programmes and in correctional centres.

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PART 3 VACCINES

3.1 ANTHRAX

Bacteriology

Anthrax is a zoonotic disease of both wild and domestic animals, primarily herbivores. Animals generally ingest spores of the causative organism, *Bacillus anthracis* (*B. anthracis*), while grazing on infected land or as a result of eating contaminated meat. Virulent bacteria then rapidly cause fulminant clinical disease in infected animals. Extremely durable spores are produced when organisms in the carcass are exposed to air.

Clinical features

Anthrax infection in man may take one of four forms. Most frequent is the cutaneous form. The gastrointestinal, meningeal and respiratory forms of anthrax are far less common. The cutaneous form of the disease starts as a small papule, which develops into a characteristic painless skin ulcer (eschar) which may be surrounded by significant edema. Patients are generally toxic and there may be local lymphadenitis. Ten to twenty percent of persons contracting cutaneous anthrax will die if not treated. With appropriate treatment, mortality should be less than 1%. High mortality rates are associated with pulmonary, meningeal or gastrointestinal anthrax infection in man. Anthracitic meningitis may occur as a complication of any of the forms of disease, but may also occur de novo.

Epidemiology

Human anthrax is currently found throughout the world but is concentrated in the Middle East, parts of Europe, Africa and Asia. In less developed countries, disease occurs as a result of human contact with infected domestic animals or infected animal products. Occupational anthrax, once seen amongst European and American agricultural workers and tanners who contracted the disease after exposure to hides of animals contaminated by the spores, is now extremely rare. Recently there has been public concern that anthrax may be used as a biological weapon by either military or terrorist groups. Indeed the biggest epidemic of human inhalation anthrax this century occurred in 1979 after the accidental release of spores from a Russian military research facility.

A variety of strategies are used to prevent infection with anthrax spores. These include education of machine operators, control of potentially infected dust, the disinfection of potentially contaminated surfaces and the use of personal protective equipment including masks. Areas of land heavily contaminated with anthrax spores have been quarantined.

Management

Suspected cases of anthrax are most effectively treated with penicillin, in combination with active immunisation. Tetracycline, erythromycin or ciprofloxacin may be used as alternatives, particularly to treat penicillin-resistant organisms. Suspected cases should be isolated.

Vaccines

At present there are two vaccines against anthrax available in Australia, one manufactured by the Michigan Department of Public Health, and the other by the Defence Evaluation Research Agency, CBD Porton Down, in the United Kingdom. While neither is registered in Australia for general use, they may be released for use after authorisation by the Therapeutic Goods Administration.

The protective component in both vaccines is thought to be protective antigen (PA). Small, variable amounts of lethal factor (LF) and edema factor (EF) may enhance the protective efficacy of some vaccine lots.

Both the UK and USA vaccines consist of alum-precipitated cell-free filtrate of killed bacilli (sometimes called supernatant particles). The US vaccine is adsorbed onto aluminium-hydroxide.

While there are few comparative studies on the subject of vaccination against anthrax these studies show that killed anthrax vaccines are safe and efficacious when used in humans. There may also be a case for the use of tetracycline or ciprofloxacin chemoprophylaxis to partially protect individuals should they be inadvertently exposed to anthrax.

Transport, storage and handling

Transport in an insulated container as detailed in Part 1.12, page 59. Do not freeze or store vaccine in direct contact with ice packs. Both anthrax vaccines should be stored in a refrigerator at 2ºC to 8ºC. They must not be frozen.

Dosage and administration

The UK vaccine is administered in 0.5 mL doses at 0,3, 6 and 32 weeks. A booster dose should be given yearly. The US vaccine is administered

subcutaneously in 0.5 mL doses at 0,2 and 4 weeks followed by boosters at 6,12 and 18 months. Thereafter at risk individuals are recommended to have annual booster doses. A number of studies suggest greater than 90% production of protective antibodies after the third dose of anthrax vaccine.

Recommendations

Anthrax vaccine should be administered to persons exposed to a high risk of the disease. These include workers handling infected animals or exposed to imported, infected animal products. The incidence and severity of side effects from the vaccine, although perhaps variable from batch to batch, is low. No comment can be made on the comparison of effectiveness of the two vaccines as no study has compared them directly. The two vaccines are not inter-changeable.

Adverse events and precautions

- Local reactions including induration, erythema larger than 5cm in diameter, edema, pruritis and tenderness may occur in the first 1-2 days after vaccination and generally disappear by day 3.
- Very rare adverse events include edema extending from the vaccination site to the elbow or forearm, and a small, painless nodule that may persist for weeks.
- Systemic adverse events are characterized by mild myalgia, headache, and mild to moderate malaise, which lasts 1-2 days.
- There are no reported longterm sequelae of local or systemic adverse events following anthrax vaccination.
- Although anthrax vaccination has been linked to the so-called "Gulf War syndrome", there is no objective data to support this contention.

Contraindications

People who have recovered from a cutaneous infection with anthrax may have severe local reactions if vaccinated with anthrax vaccine.

Use in pregnancy

Information not available.

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3.2 AUSTRALIAN BAT LYSSAVIRUS INFECTION AND RABIES

Virology

Rabies virus and Australian Bat Lyssavirus (ABL) are members of the family Rhabdoviridae, genus Lyssavirus. There are seven known genotypes within the genus Lyssavirus; ABL (genotype 7) is more closely related to rabies virus (genotype 1) than any of the other five genotypes.

Clinical features

Only two human cases of ABL infection have ever been recognised; for the purposes of this Section it will be assumed that ABL infection has the same clinical features as rabies. Rabies is an almost invariably fatal encephalitis. The usual incubation period is 20-90 days; prolonged incubation periods of several years duration, although rare, have been reported. Typically, in the prodromal phase of the disease, which lasts up to 10 days, the patient may experience non specific symptoms such as anorexia, cough, fever, headache, myalgia, nausea, sore throat, tiredness and vomiting. Paraesthesiae and/or fasciculations at or near the site of the wound are present in 50-80% of patients at this stage. Anxiety, agitation and apprehension may also occur.

In the encephalitic phase, objective signs of nervous system involvement include aerophobia, hydrophobia, bizarre behaviour, disorientation and hyperactivity. Signs of autonomic instability such as hypersalivation, hyperthermia and hyperventilation may occur. The neurological status of the patient deteriorates over a period of up to 12 days, and the patient either dies abruptly from cardiac or respiratory arrest, or lapses into a coma.

Epidemiology

Rabies is endemic throughout much of Africa, Asia, the Americas and Europe, where the virus is maintained in certain species of mammals. Australia, New Zealand and Papua New Guinea are free of endemic rabies. Human rabies characteristically follows a bite from a rabid animal, most frequently a dog, but in some parts of the world other animals, such as jackals and bats, are important sources of exposure. In countries where rabies vaccination of domestic animals is widespread (North America and Europe), wild animals such as raccoons and foxes are important reservoirs.

Cases of rabies after animal scratches or the licking of open wounds are extremely rare. Cases have been recorded after exposure to aerosols in a laboratory and in caves infested with rabid bats, and eight cases have been reported following corneal transplants from donors who died with undiagnosed rabies.

In Australia, two cases of a fatal rabies-like illness caused by ABL have been reported, one in 1996 and the other in 1998. Both patients had been bitten by bats. Evidence of ABL infection has since been identified in all four species of Australian fruit bats (flying foxes) and in two species of Australian insectivorous bats. It should therefore be assumed that all Australian bats have the potential to carry this lyssavirus.

Rabies vaccine

- Merieux Inactivated Rabies Vaccine® - CSL/Pasteur Merieux Connaught (beta-propiolactone inactivated human diploid cell cultured Wistar rabies virus (strain PM/W1381503-3M); each 1.0 mL dose contains at least 2.5 IU viral antigens, neomycin 100-150 µg, and up to 70mg of human serum albumin. Presentation is a 1.0 mL single dose vial of lyophilised vaccine with 1.0 mL distilled water as diluent.

Rabies immunoglobulin

Imogam Rabies® - Pasteur Merieux Connaught (Human rabies immunoglobulin; each 1.0mL contains IgG class human rabies antibodies with a minimum titre of 150 IU, glycine 22.5mg and sodium chloride 1mg. Supplied in 2 mL and 10 mL vials).

Transport, storage and handling

Transport in an insulated container as detailed in Part 1.12, page 59. Do not freeze or store vaccine in direct contact with ice packs. Do not freeze diluent. If vaccine has been exposed to temperature less than 0ºC, do not use. Check expiry date on vial or container before storage. To

reconstitute the vaccine, use only the diluent supplied and shake gently. The normal colour is pinkish due to phenol red.

Dosage and administration

Pre-exposure prophylaxis for all ages consists of a total of 3 intramuscular or deep subcutaneous injections of 1 mL of rabies vaccine, the 2nd given 7 days after the first, and the 3rd given 28 days after the first.

Inadvertent prolongation of the intervals does not impair the response. Doses should be given in the deltoid area, as rabies neutralising antibody 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.

Recommendations

As mentioned above ABL is genetically very closely related to rabies virus; rabies vaccine and immunoglobulin have been shown to be protective against ABL in laboratory animals. Vaccination of humans against rabies or ABL is recommended for people at special risk (eg. veterinarians), and for those who have possibly been exposed to these viruses.

For post-exposure treatment, rabies vaccine and immunoglobulin are available without charge from State and Territory health authorities (see Appendix 1 for contact phone numbers). For pre-exposure prophylaxis, the vaccine can be obtained from CSL Ltd. Costs of pre-exposure prophylaxis have to be met by the individual or their employer.

Pre-exposure prophylaxis for rabies and Australian Bat Lyssavirus

The rationale for pre-exposure prophylaxis is that (i) vaccination may provide protection to people with inapparent exposure to rabies or ABL, (ii) it may protect people whose post-exposure treatment may be delayed, and (iii) it simplifies post-exposure management. Patients should be advised that the main reason for pre-exposure prophylaxis is to prime the immune system for a secondary response, and that if a possible rabies or ABL exposure occurs, booster doses of vaccine may still be required.

Pre-exposure prophylaxis is strongly recommended for expatriates and travellers who will be spending prolonged periods (ie. more than a month) in rural areas of rabies endemic areas. Although rabies is endemic in much of Africa, Asia, the Americas and Europe, some countries and regions of the world are considered to be rabies-free. The

World Health Organization (WHO) maintains data on rabies infected countries, the most recent of which can be accessed at its web site http://www.who.int/. A list of rabies-free countries as in 1997 can be found at the end of this section.

Pre-exposure prophylaxis for all ages consists of a total of 3 intramuscular or deep subcutaneous injections of 1 mL of rabies vaccine, the 2nd given 7 days after the first, and the 3rd given 28 days after the first.

Pre-exposure prophylaxis with rabies vaccine is recommended for people in Australia liable to receive bites or scratches from bats (this includes bat handlers, veterinarians, wildlife officers and others who come into direct contact with bats). The same regimen is used for ABL as that for rabies.

Rabies vaccine is not approved for administration by the intradermal route in Australia.

Because the antibody response is satisfactory after the pre-exposure prophylaxis regimen, routine serological testing to confirm seroconversion is not necessary except for people who are immunosuppressed. Immunosupressed people who are at risk of exposure to rabies or ABL should be vaccinated and their antibody titres checked.

Booster doses of rabies vaccine should be considered for vaccinated people who have ongoing exposure to either rabies or ABL. People who work with live lyssaviruses in research laboratories are at risk of inapparent exposure, and should have rabies antibody titres measured every 6 months. If the titre is inadequate, they should have a booster dose. Other laboratory workers who perform rabies or ABL diagnostic tests, those who are those exposed to potentially rabid animals in endemic countries and those with occupational exposures to bats in Australia, should have rabies antibody titres measured every two years. If the titre is inadequate, they should have a booster dose. Alternatively a booster dose may be offered every two years without determining antibody titre.

Post-exposure treatment for rabies and Australian Bat Lyssavirus exposures (see Table 3.2.1)

An assessment must be made immediately of the potential risk of transmission of rabies after exposure to a possibly infected animal. Dogs and monkeys comprise the usual exposures in Asia, Africa and Central

and South America, but exposures to other animals must also be assessed for potential rabies transmission. A list of rabies-free countries can be found at the end of this section. Because the rabies status of any country may change, advice should be sought from State and Territory health authorities before advising against rabies post-exposure treatment (PET).

The essential components of PET are prompt local treatment and, for people who have not previously been vaccinated, administration of rabies immunoglobulin (RIG) and rabies vaccine. For PET of previously vaccinated people, see immediately following Table 3.2.1. PET of a patient presenting after possible rabies exposure should be commenced as soon as possible; treatment should not be withheld even if there is a considerable delay in recognising exposure. Unless the animal has been tested and found to be negative for rabies, the course should be completed irrespective of the clinical outcome in the animal.

Immediate and thorough washing of all bite wounds and scratches with soap and water, and the use of a virucidal preparation such as povidone-iodine solution, is an important measure in the prevention of rabies and ABL infection. In experimental animals, simple cleansing with these agents has been shown to reduce markedly the likelihood of rabies.

Consideration should be given at this stage of wound management to the possibility of tetanus and other wound infections, and appropriate measures taken. Primary suture of a bite from a potentially rabid animal should be avoided. They should be cleaned, debrided and well infiltrated with RIG (see below). Secondary suture, if necessary, should be performed after 1-2 weeks, when it can be assumed that the patient has circulating neutralising antibodies.

Rabies has occurred in people who have received PET rabies vaccine without RIG. Therefore PET should always include administration of RIG at the same time as the first dose of rabies vaccine, the only exceptions being people with documented evidence of either completion of the pre-exposure prophylaxis regimen or adequate rabies antibody titres. These people should receive vaccine only.

PET should be considered whenever a bite, scratch or mucous membrane exposure (to saliva)from any Australian bat has occurred. Any wound inflicted by a bat must be washed thoroughly as described above. Note that exposure to bat urine or faeces, or to a bat that has been dead for more than 4 hours does not warrant PET. In the case of possible exposure to ABL, PET is the same as for rabies, except that if it is

commenced more than one year after exposure, consideration may be given to omitting the RIG. Advice should be sought from State or Territory health authorities in this circumstance.

Where PET for ABL is indicated, the bat should, if possible without placing other persons at risk of exposure, be kept and arrangements made immediately for testing by the relevant state veterinary or health authority. PET can be withheld if the result (concerning the bat's ABL status) will be available within 48 hours of the exposure; if the result will not be available within 48 hours PET should be commenced immediately. Advice on the availability of RIG and rabies vaccine may be obtained from local public health authorities. Contact details are given in Appendix 1.

Use of rabies vaccine in PET

PET for presumed exposure to either rabies virus or ABL consists of (i) a total of 5 doses of 1.0 mL of rabies vaccines given intramuscularly or deep subcutaneously, and (ii) RIG (see below). The first dose of vaccine is given immediately (day 0), and subsequent doses are given on days 3, 7, 14, and 28. In adults and children the vaccine should be administered into the deltoid area, as administration in other sites may result in reduced neutralising antibody titres. In infants less than 12 months of age, administration into the anterolateral aspect of the thigh is recommended.

Serological testing to measure response is unnecessary except in unusual circumstances, such as when the patient is known to be immunocompromised. In such cases, the antibody titre should be measured two weeks after the dose given at 28 days and a further dose given if the titre is inadequate.

Use of rabies immunoglobulin in PET

RIG should be administered at the beginning of PET, the only exceptions being people with documented evidence of either completion of the pre-exposure prophylaxis regimen or adequate rabies antibody titres. These people should receive vaccine only.

A single dose of RIG is given to provide localised anti-rabies antibody protection whilst the patient responds to the rabies vaccine. It should be given at the same time as the 1st post-exposure dose of vaccine (day 0). If not given with the 1st vaccine dose, it may be given up to day 7, but should not be given any later in the course of the vaccination program. From day 8 onwards, an antibody response to rabies vaccine is presumed to have occurred.

The dose of RIG for all age groups is 20 IU per kg body mass. RIG should be infiltrated in and around all wounds using as much of the calculated dose as possible, and the remainder administered intramuscularly. If the wounds are severe and the calculated volume of RIG is inadequate for complete infiltration (eg. extensive bites in a young child), the RIG should be diluted in saline to make up an adequate volume for the careful infiltration of all wounds. If the wound has healed, the RIG should be administered in the vicinity of the healed wound (eg. around a scar).

Many bat bites occur on fingertips making the infiltration of RIG difficult. However, there has been a documented case of rabies that occurred in a child with a fingertip bite which was not infiltrated with RIG; all the calculated volume of RIG was injected into the buttock. Therefore, an attempt must be made to infiltrate as much RIG as possible into fingertip bites.

Because there is a theoretical risk that RIG may suppress the patient's response to rabies vaccine, no more than the recommended dose should be given.

Table 3.2.1: Summary of rabies and Australian Bat Lyssavirus post-exposure treatment (PET) for non-immune individuals

	Immediate (Day 0)	Follow-up doses
Local treatment	Wound cleansing is vital	
Rabies vaccine	1.0 mL	1.0 mL on days 3, 7, 14, 28
Rabies immunoglobulin (150 IU/mL)	20 IU/KG - no later than 7 days after rabies vaccine started	Do not give later than day 7

Post-exposure treatment of previously vaccinated people

People who have either completed a recommended course of pre-exposure prophylaxis, or previous PET, or who have documented rabies neutralising antibodies, require a modified PET regimen if potentially exposed to either rabies virus or ABL. Local wound cleansing as described above must be carried out, and a total of 2 doses of rabies vaccine (1.0 mL each) should be given intramuscularly on day 0 and on

day 3. RIG is not necessary in these cases. This modified regimen should be used regardless of the time interval since the pre-exposure prophylaxis, and should be used for every subsequent exposure.

In cases where the vaccination status is uncertain because the documentation of a full course of rabies vaccine is not available, the standard PET regimen (RIG plus 5 doses of rabies vaccine) should be administered.

People who have inadvertently received intradermal pre-exposure prophylaxis, and who are subsequently exposed, should be given the standard PET regimen (RIG plus 5 doses of rabies vaccine).

PET commenced overseas

Australians who are exposed to a potentially rabid animal while travelling abroad may be given PET whilst abroad with vaccines that are not available in Australia.

The Thai Red Cross Rabies Committee considers that the following 'first' and 'second' generation tissue culture vaccines are comparable in potency and safety, and clinically interchangeable:

- human diploid cell vaccines (eg. Imovax® Rabies),
- purified chick embryo cell vaccines (eg. Rabipur®),
- purified vero cell vaccine (Verorab®),
- purified duck embryo vaccine (Lyssavac N®), and
- rhesus lung cell vaccine (Rabies Vaccine Adsorbed),

Therefore, if a person has received one of the above vaccines abroad, the standard PET regimen should be completed in Australia with the locally available human diploid cell rabies vaccine. If the PET was started overseas with one of the above vaccines but RIG was not given, and the person presents in Australia within 7 days of commencing PET, RIG should be given immediately. If the person presents in Australia after 8 days then RIG should be withheld.

If PET was started abroad using either a primary hamster kidney cell culture vaccine (in widespread use in China) or a nerve tissue vaccine (eg. sheep brain vaccine), the standard PET regimen (RIG plus 5 doses of human diploid cell rabies vaccine) should be commenced in Australia as soon as possible. The full regimen of 5 doses of vaccine should be administered, regardless of how many doses of the above (sub-optimal) vaccines were received overseas.

Adverse events and precautions

In a large (1770 volunteers) study the following adverse events were reported following the administration of human diploid cell culture rabies vaccine: sore arm (15-25%), headache (5-8%), malaise, nausea or both (2-5%) and allergic oedema (0.1%). In another study of post-exposure vaccination, 21% had local reactions, 3.6% had fever, 7% had headache and 5% had nausea. These reactions are not more frequent in children.

Anaphylactic reactions are rare (approximately 1 per 10,000 vaccinations) following administration of human diploid cell culture rabies vaccines. However, allergic reactions occur in approximately 6% of people receiving booster doses of some of the human diploid cell vaccines. The reactions typically occur 2-21 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 3-propiolactone-altered human albumin in the implicated vaccines. NB: Merieux Inactivated Rabies Vaccine® contains human albumin.

Although five cases of central nervous system disease, including three cases of neurologic illness resembling Guillain-Barré syndrome, have been reported among the millions of individuals given human diploid cell culture rabies vaccines, this rate is too low to be certainly related to the vaccination.

Management of adverse events

Once initiated, rabies prophylaxis should not be interrupted or discontinued because of local reactions or mild systemic reactions. Such reactions can usually be managed with either aspirin or paracetamol.

Because rabies and ABL infection are lethal diseases, the recommended vaccination regimens, in particular the PET 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 rabies or ABL infection must be carefully considered before deciding to discontinue vaccination.

Contraindications

There are no contraindications to PET in a person with a presumed exposure to either rabies or ABL. Pre-exposure vaccination is

contraindicated in persons with anaphylactic sensitivity to neomycin or any other component of rabies vaccine.

Use of steroids and immunosuppressive agents

Corticosteroids and immunosuppressive agents can interfere with the development of active immunity, and therefore if possible should not be administered during PET. A person who either has an immunosuppressing illness or is taking immunosuppressant medications should have their rabies antibodies titre checked two weeks after completion of the vaccination regimen.

Use in Pregnancy

Pregnancy is never a contraindication to rabies vaccination. Follow-up of 202 Thai women vaccinated during pregnancy did not show either increased medical complications or birth defects.

Conflict with product information

The product information of the rabies vaccine states that it may be given either subcutaneously into the infraspinous fossa or intramuscularly into the buttock. Neither of these sites is recommended for use in Australia, in particular the buttock should never be used.

Rabies vaccine is not registered for either pre-exposure or post-exposure prophylaxis against ABL.

The product information recommends a routine 6th dose at 90 days in the PET regimen. This dose is not considered necessary on a routine basis but should be offered to an immunosuppressed person without adequate antibodies following the standard regimen. It also recommends a pre-exposure booster after a year; boosters are usually recommended in Australia after 2 years (see above).

Rabies-free countries

The following countries and areas were reported to be rabies free by WHO in 1997:

Africa – Cape Verde, Lesotho, Libyan Arab Jamahiriya, Mauritius, Réunion, Seychelles.

Americas – Antigua and Barbuda, Bahamas, Barbados, Jamaica, Montserrat, Saint Kitts And Nevis, Saint Lucia, Uruguay.

Asia – Armenia, Bahrain, Brunei Darussalam, Cyprus, Hong Kong, Japan, Kuwait, Malaysia (Sabah and Sarawak), Maldives, Qatar, Singapore, United Arab Emirates.

Europe – Albania, Andorra, Finland, Gibraltar, Greece, Iceland, Ireland, Isle of Man, Italy, Jersey (Channel Islands), Malta, Norway (except Svalbards Islands), Portugal, Spain (except Mellila), Sweden, United Kingdom.

Oceania – Australia, Cook Islands, Fiji, French Polynesia, Guam, Kiribati, New Caledonia, New Zealand, Palau, Papua New Guinea, Samoa, Solomon Islands, Tonga, Vanuatu

NB: In July 1998, the Indonesian Ministry of Health informed WHO that Bali remained free of rabies. Therefore PET following exposure to either dogs or monkeys in Bali, unlike most other areas of Southeast Asia, is not warranted.

Current WHO literature (Weekly Epidemiological Record) and the WHO web site, (http://www.who.int/) should be consulted for updates to this list.

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3.3 CHOLERA

Bacteriology

Cholera is caused by enterotoxin producing *Vibrio cholerae* of the sero group 01 and 0139. Sero group 01 includes two biotypes – classical and El Tor – each of which includes organisms of Inaba, Ogawa and Hikojima serotypes. Free living organisms may multiply in marine waters and have been discovered in some rivers on the Queensland coast.

Clinical Features

Cholera is characterised by sudden onset of painless, profuse watery diarrhoea. Dehydration, metabolic acidosis and hypotension may soon follow. If untreated, more than half of the severe cases will die. Mild cases also occur, as does sub-clinical infection.

Epidemiology

The 0-6 annual cases of cholera in Australia almost always occur in individuals who have been infected in endemic areas of Asia, Africa, the Middle East, South America or parts of Oceania. In 1977 a locally acquired case led to the discovery of *V. cholerae* in some rivers of the Queensland coast. Because of this, health workers should be aware that sporadic cases of cholera may rarely follow unhygienic use of river water. The disease is usually transmitted via food and water contaminated with human excreta. Shellfish obtained from contaminated waters have also been responsible for outbreaks.

As the incubation period of the disease may extend up to five days, surveillance of household contacts or those exposed to a possible common source should be maintained for five days from the date of last exposure. Stool cultures may be taken from close contacts if required and food handlers should not be allowed to return to work until symptoms have ceased. Contacts should also be advised to maintain high standards of personal hygiene to avoid becoming infected.

Cases should be reported immediately to the public health authorities.

Vaccines

- Cholera vaccine - CSL (heat-killed injectable suspension of the Inaba and Ogawa serotypes of classical V. cholerae, serotype O1 + phenol 0.5% as a preservative). This is a heat-killed preserved suspension of V. cholerae. The vaccine is not effective against V. cholerae 0139. In

well designed clinical trials in Bangladesh and the Philippines the efficacy of cholera vaccination was 57% in the first seven months, 51% in the first year as a whole and 47% in year two. In the third year following vaccination there was no effect in under 5 year olds, but the vaccine was still protective in over 5 year olds (efficacy 57%). This vaccine is not recommended for use in Australia.

Orochol – CSL (live recombinant oral vaccine consisting of attenuated CVD103-HgR based on *V. cholerae* 01 Classical Inaba strain 569b). A single dose of one double chambered sachet contains 2-10x10^8 live V. cholera CVD 103-HgR bacteria + lactose + aspartame + sucrose amino acid mixture + ascorbic acid + sodium bicarbonate.

Trials of the safety and immunogenicity of the vaccine have been carried out in Thailand, Indonesia, Chile, Peru and Switzerland. No trial of efficacy of live oral vaccines in endemic areas has yet been completed although a large trial in Indonesia is in progress. Review of data available to date from the Indonesian trial suggests that the oral vaccines demonstrate greater efficacy especially in the third year after vaccination but the differences are not statistically significant. Orochol will not provide protection against 0139 V. cholerae.

Transport, storage and handling

Transport in an insulated container with approved freeze monitor, and time-temperature monitor. Do not freeze or store vaccine in direct contact with ice packs. If vaccine has been exposed to temperature less than 0ºC, do not use. Store in refrigerator at between 2ºC to 8ºC. Check expiry date on vial or container before storage. Rotate stock so that shortest date vaccines are used first. Protect from light.

Dosage and administration

Oral cholera vaccine (Orachol) is administered orally in a single dose and boosters are currently recommended every 6 months. It should not be administered to children under two years of age. The vaccine should not be given to anyone on antimicrobials and should be given one hour before a meal. The concomitant administration of chloroquine has been shown to decrease immune response to the vaccine and should therefore not be administered sooner than one week after vaccination. Yellow fever vaccination and OPV may be administered at the same time as Orochol. However, there should be an interval of at least eight hours between administration of oral cholera and typhoid vaccines. Orochol is prepared for administration by emptying the contents of the sachet into 100mL of cold or lukewarm water and stirring vigorously for 5-10 seconds. It should not be suspended in milk, juice or carbonated drinks.

Recommendations

Cholera vaccine is not recommended for use in Australia. Despite the endemicity of cholera in some countries often visited by Australians, routine use of the vaccine is not recommended as the risk is very low. Careful and sensible selection of food and water is of far greater importance to the traveller than the vaccine. The World Health Organization no longer recommends use of the vaccine, and vaccination against cholera is no longer an official requirement for entry into any foreign country.

Adverse events and precautions

No serious adverse events have been reported from live attenuated vaccine.

Contraindications

Do not use the vaccines in individuals with known hypersensitivity to a previous dose.

Injectable vaccine is not recommended for infants under six months of age. Oral vaccine is not recommended for children under 2 years of age.

Use in Pregnancy

There is no evidence of risk to the fetus, and cholera vaccine may be given to pregnant and lactating women.

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3.4 CYTOMEGALOVIRUS

Virology

Cytomegalovirus (CMV) is a double stranded DNA herpes virus, which causes characteristic intranuclear and cytoplasmic inclusion bodies.

Clinical features

CMV is usually asymptomatic in normal hosts. It may occasionally cause a mononucleosis syndrome. It can cause congenital abnormalities following primary or reactivation infection in mothers. Congenital CMV is characterised by petechiae, hepatosplenomegaly and jaundice. Microcephaly, cerebral calcification and prematurity may also occur. In adults, severe CMV infection, including retinitis, colitis and pneumonitis, is seen in immunocompromised hosts, particularly those with HIV infection or following organ transplant.

Epidemiology

CMV has a world-wide distribution, and is spread by repeated or prolonged intimate exposure. The virus is present in milk, saliva, faeces and urine. Once infected, an individual probably carries the infection for life, most commonly in latent form.

Vaccine

There is no CMV vaccine registered in Australia.

CMV immunoglobulin

CMV immunoglobulin is indicated for the prevention and treatment of CMV infection in certain individuals at high risk of CMV infection. The product contains no antibacterial agent, and so it must be used immediately after opening. Any unused portion must be discarded. If the solution has been frozen, it must not be used. If the use of CMV immunoglobulin is contemplated, detailed protocols for administration and management of adverse events should be consulted.

- CMV immunoglobulin (human) - CSL (6% solution of immunoglobulin prepared from human plasma containing high levels of antibody to CMV + maltose 10%; no antiseptic; 30 mL bottle for intravenous injection).

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3.5 DIPHTHERIA

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 to produce an adherent pseudomembrane. Systemically, the toxin acts on cells of the myocardium, nervous system and adrenals.

Clinical Features

The incubation period is 2-5 days. The disease is communicable for up to 4 weeks, but carriers may shed organisms for longer. Spread is by droplets or by direct contact with sores or with articles soiled by infected persons. The disease primarily affects the upper respiratory tract, but the skin can be involved. It is characterised by an inflammatory exudate which forms a greyish or green membrane in the upper respiratory tract and which can cause acute severe respiratory obstruction. Diphtheria toxin can cause neuropathy and cardiomyopathy, which may be fatal. The introduction of diphtheria antitoxin in the 1890s reduced the death rate to about 10%, but the mortality has not been further reduced by the use of antibiotics and other modern treatments. Effective protection against diphtheria is achieved by active immunisation with diphtheria vaccine.

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 disappearance. Diphtheria has been almost eradicated from Australia, but sporadic cases continue to occur in unvaccinated individuals. There is now little possibility of acquiring natural immunity, and no opportunity to boost declining immunity with subclinical infection. A high vaccination rate must therefore be

maintained to protect the population from resurgence of the disease. An increase in the incidence of infections from toxigenic strains could follow introduction of cases or carriers from overseas, or from local emergence of a virulent strain.

The risk of diphtheria outbreaks in a population with inadequate immunity is demonstrated by the 1990s epidemic of diphtheria in the newly independent States of the former Soviet Union. In 1995 alone, there were over 50,000 cases reported, and from 1991-1996 there were over 140,000 cases and over 4000 deaths. Cases also occurred in neighbouring European countries and in visitors to the area. The major cause of the epidemic was decreasing vaccination rates. Waning vaccine-induced immunity in adults has recently been demonstrated in the United Kingdom, where more than 50% of blood donors aged 50-59 years had antitoxin levels below the minimum protective level (<0.01 IU/mL). These reports emphasise the importance of maintaining high levels of diphtheria immunity in the entire population. In Australia, the NHMRC recommended routine adult boosting with Td vaccine in 1984, but it is likely that many adults are still not fully protected. Public health authorities may, in some circumstances, decide to test the level of diphtheria immunity in individuals. Serological methods for testing diphtheria immunity are available in specialist laboratories.

Special features

Contacts and carriers

A case of diphtheria is of considerable public health importance. A doctor treating a suspected case should ensure that the case is officially notified and should seek advice from the State or regional public health authorities on further management. The following section gives an outline of the usual strategies adopted.

Contacts of a diphtheria case, or carriers of a toxigenic strain, should be given a complete course or a booster dose of vaccination, according to their age and vaccination history.

- Unvaccinated child contacts who have not reached their 8th birthday - give 3 injections of diphtheria vaccine (monovalent diphtheria vaccine, DTPa, or DT) at 1-2 monthly intervals. The opportunity should be taken to 'catch-up' with all other vaccinations at this time.
- Unvaccinated child contacts who have passed their 8th birthday, and adult contacts - give 3 injections of adult diphtheria-tetanus (Td vaccine at 1 monthly intervals).

- Vaccinated child contacts who have not reached their 8th birthday - give 1 booster injection of diphtheria vaccine (as monovalent diphtheria vaccine, DTPa, or DT).
- Vaccinated child contacts who have passed their 8th birthday, and adult contacts - give 1 booster injection of adult diphtheria-tetanus vaccine (Td).

All contacts of a case of diphtheria should also be given a prophylactic course of 7 days of oral erythromycin or a single dose of IM penicillin. The patient with diphtheria should also receive a primary course of vaccinations when they have recovered.

Diphtheria antitoxin

In cases of suspected clinical diphtheria, diphtheria antitoxin should be given immediately, rather than waiting for bacteriological confirmation of the disease. Penicillin should also be given at this stage.

Diphtheria antitoxin from horse serum is used because sera of sufficient titre are not available from humans. Due to the presence of foreign protein, diphtheria antitoxin may provoke acute severe allergic reactions or serum sickness. Consequently, a test dose should be administered to exclude hypersensitivity. If there is evidence of hypersensitivity, it may be necessary to administer diphtheria antitoxin under corticosteroid, adrenaline, and antihistamine cover. The therapeutic dose of antitoxin will depend on the clinical condition of the patient, and may be given either intramuscularly or diluted for administration in an intravenous infusion.

- Diphtheria antitoxin - CSL (diphtheria antitoxin 10,000 U).

Vaccine

A variety of formulations of diphtheria vaccine are available in Australia.

Diphtheria together with acellular pertussis-containing vaccines

- Infanrix-hepB (Diphtheria-tetanus-acellular pertussis adsorbed-hepatitis B) - SmithKline Beecham (diphtheria toxoid 25 Lf, tetanus toxoid 10 Lf, pertussis toxoid 25µg, pertussis filamentous haemagglutinin 25µg, pertactin 8µg, hepatitis B surface antigen 10µg; adsorbed to aluminium hydroxide 0.5 mg, aluminium phosphate 0.2 mg, polysorbate 80 <100µg, polysorbate 20 < 5µg; preservative - phenoxyethanol 2.5µg; formaldehyde < 1µg; 0.5 mL dose).

- Infanrix (diphtheria-tetanus-acellular pertussis adsorbed) - SmithKline Beecham (diphtheria toxoid >25 Lf, tetanus toxoid 10 Lf, pertussis toxoid 25 µg; pertussis filamentous haemagglutinin 25µg, pertactin 8µg; adsorbed on to aluminium hydroxide; phenoxyethanol as preservative; 0.5 mL dose).
- Tripacel (diphtheria-tetanus-acellular pertussis adsorbed) - CSL/Pasteur Merieux Connaught (diphtheria toxoid LFL equal or > 30 IU, tetanus toxoid LFL equal or > 40IU, pertussis toxoid 10 µg, pertussis filamentous haemagglutinin 5µg, pertussis fimbriae 2+3 5µg, pertactin 3µg; 1.5µg aluminium phosphate as an adjuvant, and 3.4µg phenoxyethanol as a preservative; 0.5 mL dose).

Diphtheria together with whole cell pertussis (DTPw) containing vaccines

- Triple Antigen (diphtheria-tetanus-pertussis adsorbed) - CSL (diphtheria toxoid 30 IU, tetanus toxoid 60 IU, killed B. pertussis <20,000 million per 0.5 mL, adsorbed on to aluminium phosphate; thiomersal 0.01% w/v; 0.5 mL dose).

Adsorbed diphtheria tetanus vaccine - DT (paediatric formulation) and Td (adult formulation)

- Diphtheria tetanus vaccine (CDT) - CSL (diphtheria toxoid 30 Lf and tetanus toxoid 6 Lf per 0.5 mL adsorbed on to aluminium phosphate; thiomersal 0.01% w/v).
- Diphtheria tetanus vaccine (ADT) - CSL (diphtheria toxoid 2 Lf and tetanus toxoid 6 Lf per 0.5 mL adsorbed on to aluminium phosphate; thiomersal 0.01% w/v).

Adsorbed diphtheria vaccine

- Diphtheria vaccine, adsorbed - CSL (purified diphtheria toxoid 30 Lf per 0.5 mL adsorbed on to aluminium phosphate; thiomersal 0.01% w/v).
- Diphtheria vaccine, adsorbed (Diluted for adult use) - CSL (purified diphtheria toxoid 2 Lf per 0.5 mL adsorbed on to aluminium phosphate; thiomersal 0.01% w/v).

Diphtheria vaccination stimulates the production of antitoxin, which protects against the toxin. The immunogen is prepared by treating a cell-free purified preparation of toxin with formaldehyde, thereby converting it into the innocuous diphtheria toxoid. The toxoid is usually adsorbed on to an adjuvant, either aluminium phosphate or aluminium

hydroxide, to increase its immunogenicity. Antigens from Bordetella pertussis also act as an effective adjuvant.

Transport, storage and handling

Transport in an insulated container with approved freeze monitor, and time-temperature monitor. Observe the national guidelines for packing vaccines in insulated containers. Do not freeze or store vaccine in direct contact with ice packs. If vaccine has been exposed to temperature less than 0ºC, do not use. Store in refrigerator at between 2ºC to 8ºC. Check expiry date on vial or container before storage. Rotate stock so that shortest date vaccines are used first.

Dosage and administration

Diphtheria-containing vaccines should be given in a different limb from other concurrently administered vaccines. Accurate recording of the sites of injection of concurrently administered vaccines allows any local reactions to be attributed to the appropriate antigen or antigens. Unless a combination vaccine containing DTPa and Hib is used, it is a good strategy to routinely give DTPa-containing vaccines on the right side and Hib on the left side. Note that the adult formulations of diphtheria-containing vaccines provide a much smaller dose of diphtheria toxoid than the children's formulation (2 Lf versus 30 Lf).

Do not mix DTP-containing vaccines and other vaccines in the same syringe.

Recommendations

Diphtheria vaccination is part of the standard childhood vaccination schedule (see Table 1.2). Primary vaccination is achieved with 3 doses of a diphtheria toxoid-containing vaccine at 2 monthly intervals, with boosters at 18 months and 4 years. Prior to the 8th birthday, DTP-containing vaccines should be given. After the 8th birthday Td should be given (see 'catch-up' schedule, Part 1.9, page 43). The change to Td (low dose diphtheria toxoid) after the 8th birthday is related to the reduced tolerance of older children and adults to diphtheria toxoid. For details on the management of children who have missed some doses of the standard childhood vaccination schedule, see 'catch-up' schedule, Part 1.9, page 43.

Older individuals who have not received diphtheria vaccination are also likely to have missed tetanus vaccination. Those who have not reached their 8th birthday should receive 3 injections of DTP-containing vaccines(or DT) at intervals of 1-2 months, and those individuals who

have passed their 8th birthday should receive 3 doses of Td at intervals of 1 month followed by 2 booster doses at 10 yearly intervals.

> It was previously recommended by NHMRC that adults be given a booster, usually as Td, at 10-year intervals. This is no longer recommended routinely for people who have had a full primary course of three diphtheria-containing vaccines and at least two boosters. Immunity following such a course is long lasting.

Diphtheria can be a significant risk for travellers to some countries (particularly SE Asia, the Russian federation, the Ukraine, Baltic countries or Eastern European countries), so all international travellers to these regions should ensure that their Td vaccination is current.

Adverse events and precautions

Diphtheria vaccine is most commonly given in combination with tetanus and pertussis vaccines (DTP), and adverse events may be due to any of the components. Rarely, diphtheria vaccine may cause transient fever, headache, malaise, and local reactions at the injection site.

As with all suspected adverse events to vaccines, severe adverse events following diphtheria vaccine should be reported as set out in Part 1.6, page 21.

Contraindications

In individuals who have a history of a previous adverse event, the risk of further diphtheria vaccine doses must be assessed in relation to the potential benefit.

Use in pregnancy

Diphtheria toxoid is safe in pregnancy and lactation.

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3.6 HAEMOPHILUS INFLUENZAE TYPE b (Hib)

Bacteriology

Haemophilus influenzae is a Gram negative cocco-bacillus, which has fastidious growth requirements in the laboratory. Strains isolated from respiratory tract specimens such as sputum and middle ear or sinus fluid are usually strains without a capsule, also known as nontypable (NT). Although six capsular types (a to f) have been described, before the introduction of Hib vaccine, almost all *Haemophilus influenzae* isolates from sterile sites (blood, cerebrospinal fluid, joint or pleural fluid) were of one capsular type – type b (Hib). Prior to 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 less than 2 years of age are unable to mount an antibody response to the type b capsular polysaccharide, even following invasive disease.

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. Hib is rarely isolated from the blood without a focal infection such as the above being evident or subsequently developing. 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. Septic arthritis and cellulitis present with local signs related to the involved joint or skin, and pneumonia due to Hib with respiratory distress and often pleural effusion. There are no specific clinical features of any of these infections due to Hib which 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.

Epidemiology

Pre Hib vaccination

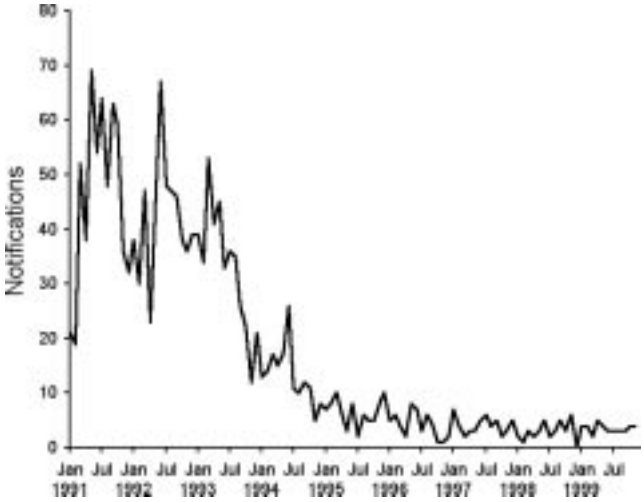
Before the introduction of routine Hib vaccination in 1993, there were at least 500 cases of Hib disease in Australian children under 6 years of age every year. Hib meningitis accounted for approximately 60% of all invasive Hib disease, with most cases occurring in children under the age of 18 months. Hib epiglottitis usually occurred in children over the age of 18 months. Other manifestations such as cellulitis, septic arthritis, and pneumonia occurred at a similar age to meningitis.

The incidence of Hib disease in Australian Aboriginal children, especially those in remote rural areas, was considerably higher than in non-Aboriginal children. Most importantly, the onset of Hib disease in Aboriginal children was at a much younger age, with a peak incidence at 4 months compared with 6-11 months for non-Aboriginal children; it was due mostly to meningitis, with epiglottitis being rare. In both Aboriginal and non-Aboriginal children, the case fatality rate for Hib meningitis was approximately 5%, and up to 15% of the survivors had neurological sequelae such as deafness and intellectual impairment. In Australia, there were about 10-15 deaths each year from Hib infection, and 20-40% of the survivors were left with permanent neurological damage, making Hib disease comparable in importance to measles or poliomyelitis before vaccination.

Post Hib vaccination

Since Hib vaccines were included in the routine vaccination schedule in 1993, there has been a reduction of >90% in notified cases of Hib disease from 502 in 1992 to 35 in 1998 (see Fig 3.6.1). This reduction has been particularly marked in indigenous children. Similar impressive reductions in Hib disease have been seen in other countries with routine childhood vaccination. There has been no evidence of a shift in Hib cases to older age groups or to other capsular types in Australia or elsewhere. As Hib vaccination coverage has increased, a higher proportion of Hib cases will have received one or more doses of Hib vaccine. Similarly, with Hib disease now rare overall, cases of epiglottitis can no longer be assumed to be due to Hib unless there is some supporting laboratory evidence, such as isolation from blood culture or epiglottic swab or detection of Hib antigen in urine. Indeed, all sterile site isolates of *Haemophilus influenzae* from immunised children should be confirmed as type b by a reference laboratory before vaccine failure is assumed.

3.6.1 *Haemophilus influenzae* type b notifications in children under the age of 5 years, Australia, 1991 to 1999



Special situations

Management of contacts of a child with invasive Hib disease

Rifampicin chemoprophylaxis is no longer indicated unless the household contains one or more infants under 7 months of age (regardless of vaccination status), or a child aged 7 months to 5 years who is inadequately vaccinated according to the Hib schedule. In this case, all persons in the household should receive rifampicin prophylaxis following a case of invasive Hib disease in any household member. The recommended dose is 20 mg/kg as a single daily dose (maximum daily dose 600 mg) for 4 days. Neonates (<1 month of age) should receive 10 mg/kg daily for 4 days.

Natural infection does not always result in immunity to Hib disease. Any inadequately vaccinated children who have had Hib disease should receive age-appropriate Hib vaccination as soon as possible (see Table 1.9.2 above). Similarly, if the case child attends a child care facility for more than 18 hours a week, and other children under 24 months of age in this facility are in close contact, rifampicin chemoprophylaxis should also be given to all contacts (including staff) if any of the close contacts are inadequately vaccinated.

Contraindications, side effects and drug interactions of Rifampicin are complicated. Decisions about use and advice about contraindications, dosing and supply of rifampicin should always be made in collaboration with the local public health authorities.

Preterm babies

Extremely preterm babies (<28 weeks or <1500g) should be vaccinated with PRP-OMP and should be given an extra dose at 6 months, resulting in a 4-dose schedule at 2,4,6 and 12 months (see Part 1.7, page 28).

Splenectomy

Hib is an uncommon cause of post splenectomy sepsis in adults and children. Children over 2 years of age who have received all scheduled doses of Hib vaccine do not require a booster dose following splenectomy. A single dose of Hib vaccine is recommended for other individuals (unvaccinated or incompletely for age) of any age who have close contact with children less than 5 years of age. The vaccine should be given two weeks before splenectomy. Subsequent booster doses of Hib vaccine are not required. (For other immunisations recommended for asplenic or splenectomised persons, see Part 1.9, page 46)

Vaccines

The first generation Hib vaccines, consisting of purified polysaccharide (PRP) from the Hib capsule, were not effective in children under the age of 18 months. However, the 2nd generation Hib vaccines, which consist of PRP chemically linked ('conjugated') to a variety of carrier proteins, have been shown to be not only immunogenic but also highly effective (over 95%) in protecting young children from invasive Hib disease. The carrier protein used in a conjugate Hib vaccine ensures a good antibody response to the Hib capsular polysaccharide, but there is no significant antibody response to the carrier protein.

- PedvaxHIB (liquid) – CSL/Merck, Sharpe & Dohme (PRP-OMP; purified capsular polysaccharide of the Ross Haemophilus influenzae type b strain 7.5µg conjugated to meningococcal protein 125µg; (liquid formulation with borax 35µg; aluminium hydroxide containing 225µg aluminium; 0.9% sodium chloride). Liquid PedvaxHIB will replace the lyophilised vaccine in 2000.
- PedvaxHIB (lyophilised) - CSL/Merck, Sharp & Dohme (PRP-OMP; purified capsular polysaccharide of the Ross Haemophilus

influenzae type b strain 15µg conjugated to meningococcal protein 250µg; lyophilised powder + diluent (0.9% sodium chloride, aluminium hydroxide containing 225µg of aluminium); thiomersal 0.005% as preservative.

- HibTITER - Wyeth-Lederle (HbOC; purified capsular polysaccharide of the Eagan Haemophilus influenzae type b strain 10µg conjugated to diphtheria CRM-197 protein - a non-toxic variant of diphtheria toxin - 25µg in 0.9% sodium chloride).
- Hiberix - Smith Kline Beecham (PRP-T; purified capsular polysaccharide of the Eagan Haemophilus influenzae type b strain 20,732, 10µg conjugated to 30µg tetanus toxoid a white lyophilised pellet for reconstitution with 0.9% saline.
- ActHib - Pasteur Merieux (PRP-T; purified capsular polysaccharide of the Haemophilus influenzae type b bacterial strain 10µg conjugated to 18-30µg tetanus toxoid; lyophilised powder for reconstitution with 0.5 mL diluent; contains buffer and sucrose.
- Comvax (OMP Hib- Hepatitis B)– CSL/Merck Sharp Dohme (PRP-OMP; purified capsular polysaccharide of the Ross Haemophilus influenzae type b strain 7.5µg conjugated to meningococcal protein 125µg; hepatitis B surface antigen 5µg; aluminium hydroxide containing 225µg aluminium; 0.9% sodium chloride)

Interchangeability of Hib vaccines

It is recommended that the same conjugate vaccine be used to complete the course. However, if necessary, after the first dose, any Hib vaccine may be used to complete the primary course. Only two doses of PRP-OMP are required for primary vaccination, but if any doses of another Hib vaccine are given, a total of 3 doses is required. This means that if the previous Hib vaccine type is unknown for any doses or the same vaccine type is unavailable, the primary course can be completed with a total of 3 doses of any combination of registered Hib vaccines. For booster doses and in children over 15 months of age, regardless of previous Hib vaccinations, a single dose of any registered Hib vaccine is sufficient for protection. Details of 'catch-up' schedules are given in Part 1.9, page 43.

Transport, Storage and handling

Transport in an insulated container with approved freeze monitor, and time-temperature monitor. Observe the national guidelines for packing vaccines in insulated containers. Do not freeze or store vaccine in direct contact with ice packs. If vaccine has been exposed to temperature less

than 0ºC, do not use. Conjugate Hib vaccines should be stored at 2ºC to 8ºC; they must NOT be frozen.

Dosage and administration

The dose of Hib vaccine is 0.5 mL. It should be given by intramuscular injection, in a different limb from other concurrently administered vaccines. Unless a combination vaccine containing DTPa and Hib is used, it is a good strategy to routinely give DTP on the right side and Hib on the left side. Conjugate Hib vaccines may be administered on the same day as any of the other standard childhood vaccines (DTPa, OPV, MMR, and hepatitis B).

Conjugate Hib vaccines may be given at the same time as any other vaccine(s) but at a separate site.

> Hib vaccines should not be mixed with another vaccine in the same syringe.

Recommendations

Hib vaccine is recommended for all infants from 2 months of age. PRP-OMP is the recommended vaccine for all Australian children, and should be given at 2 and 4 months, followed by a booster at 12 months of age. PRP-OMP is preferred because it is suitable for all children and requires fewer doses to complete primary immunisation. Children who have commenced vaccination with an alternative Hib vaccine should complete the course with that vaccine. However, if the same vaccine is not available or the vaccine type is unknown, any licensed Hib vaccine may be used as outlined above. Vaccines other than PRP-OMP require a booster at 15 months or older. All available Hib vaccines offer equivalent protection.

Hib vaccination is important for all children, but is particularly important for the following children who are at higher risk:

Aboriginal and Torres Strait Islander children under 5 years of age;

Children under 5 years of age who attend day care;

Children under 5 years after splenectomy or with functional asplenia;

Children under 24 months of age who have developed invasive Hib disease (these children do not always acquire protective immunity following Hib disease, but they usually respond well to conjugate Hib vaccines).

Hib vaccine in older persons with asplenia who are contact with children under the age of 5 years.

Adverse events and precautions

Swelling and redness at the injection site following the 1st dose has been reported in up to 5% of cases. These reactions usually appear within 3-4 hours and resolve completely within 24 hours. The incidence of these reactions declines with subsequent doses, so it is recommended that the course of vaccination be completed despite the occurrence of such reactions.

As Hib vaccine is given at the same time as DTP vaccine, it can be difficult to link a generalised adverse event to any specific antigen. However, when Hib is given simultaneously with DTPw, the incidence of generalised adverse events is no greater than when DTPw is given alone.

As with all suspected adverse events following vaccines, severe adverse events following Haemophilus influenzae type b vaccine should be reported as set out in Part 1.6, page 21.

Contraindications

If the child is suffering from any acute illness, vaccination should be postponed until the child has recovered. Minor infections, without fever or systemic upset, are not reasons to postpone vaccination.

Rarely, severe local or generalised adverse events temporally related to Hib vaccine may occur, but will be difficult to differentiate from those due to other concomitantly administered vaccines, especially DTP. Many States have special advisory clinics for children who have suffered suspected adverse events. A scheduled vaccination should not be withheld without consultation with a paediatrician or public health physician with expertise in vaccination.

Hib vaccine is not indicated for persons over 5 years of age, unless they are asplenic.

Conflict with product information

The product information for Hib vaccines recommends the vaccine for children aged 2 months to 5 years. ATAGI recommends Hib vaccine in older persons with asplenia who are contact with children under the age of 5 years.

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3.7 HEPATITIS A

Virology

Hepatitis A is an acute infection of the liver caused by the hepatitis A virus (HAV), which used to be classified as an enterovirus but is now classified as a hepatovirus. The virus survives well in the environment. 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.

Clinical features

The incubation period of hepatitis A is 15-50 days, with a mean of about 30 days. HAV is excreted in faeces for up to two weeks before the onset of illness and for at least one week afterwards. Patients with hepatitis A should, therefore, be considered as being infectious for a week after the onset of jaundice.

In young children HAV usually causes either an asymptomatic infection or a very mild illness without jaundice. Patients with symptomatic illness typically have a 4-10 day prodrome 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, 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 fulminant hepatitis, albeit very rarely. Hepatitis A does not cause chronic liver disease.

The diagnosis 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 3-6 months after the acute illness. False negative IgM results are extremely rare but there are occasional false positives in patients with rheumatoid arthritis. Serum anti-HAV IgG indicates past infection and therefore immunity, and probably persists for life.

Epidemiology

HAV is predominantly transmitted by the faecal-oral route. The infecting dose is unknown, but because HAV is transmitted so readily by person to person contact, it is presumed to be low.

The epidemiology of hepatitis A is closely linked to social and environmental circumstances. Globally, three patterns of hepatitis A are recognised:

i) In regions with poor environmental sanitation and hygiene, HAV infection is 'highly' endemic. It is virtually a universal infection early in life (<5 years of age), at an age when most of the infections are asymptomatic. Consequently hepatitis A is an 'invisible' public health issue with few reported cases. This pattern exists in many of the poorer developing countries, and also in Aboriginal communities in the Northern Territory.

ii) A pattern of 'intermediate' endemicity is seen in regions with transitional economies and recent improvements in environmental circumstances. Many children escape infection in early childhood, but nevertheless still become infected later in childhood or during adolescence when symptomatic disease is likely. Therefore paradoxically, whereas the rate of infection is declining the 'visibility' of hepatitis A, and therefore the public health concern, is increasing. This pattern exists in some parts of southeast Asia, and in the indigenous communities of north Queensland.

iii) In industrialised countries with high standards of hygiene and sanitation the pattern is of 'low' endemicity. Because they have not been previously exposed to HAV, many adults are susceptible and can readily acquire hepatitis A when, for example, they travel to regions of high endemicity. This situation pertains to much of Australia.

Within Australia, three broad patterns of hepatitis A occur:

a) Large, slowly evolving community-wide outbreaks. These occur at intervals of 5 or more years and are particularly difficult to control. They tend to affect low socioeconomic areas, and young children play a substantial role in their propagation.

   Certain gatherings or groups of people are prone to be affected by HAV. They are susceptible to intense transmission among themselves, and are able to serve as a potential source for transmission to the broader community. The intensifying effect of these settings is particularly evident during community-wide outbreaks. These settings include:

- child day-care centres and pre-schools,
- communities of men who have sex with men,
- schools and residential facilities for the intellectually disabled, and
- communities of injecting drug users.

b) Sporadic cases of hepatitis A. Although some of these cases are acquired during travel to developing countries and to indigenous communities, most do not have either an obvious risk factor or an apparent link to other cases. It is probable that unrecognised infection in young children contributes to a substantial proportion of these cases.

c) Point-source outbreaks from contaminated food or water, or an infected food-handler. Bivalve shellfish are well recognised elsewhere as causing outbreaks of hepatitis A. Shellfish harvested from faecally contaminated waters may contain concentrated HAV, which can remain viable for many days. Light steaming of bivalves to open the shells is insufficient to inactivate HAV. However point-source outbreaks of hepatitis A, even from contaminated shellfish, appear to be very uncommon in Australia.

Vaccines

Four hepatitis A vaccines, and two combined hepatitis A/hepatitis B vaccines, are registered for use in Australia:

- Havrix 1440 - SmithKline Beecham (formaldehyde inactivated hepatitis A virus (HM175 strain) adsorbed onto aluminium hydroxide; each 1.0mL dose contains 1440 enzyme linked immunosorbent assay (ELISA) units of viral antigens, aluminium 0.5mg as aluminium hydroxide, 0.5% w/v 2-phenoxyethanol and a trace amount of neomycin sulphate).
- Havrix Junior - SmithKline Beecham (formaldehyde inactivated hepatitis A virus (HM175 strain) adsorbed onto aluminium hydroxide; each 0.5mL dose contains 720 ELISA units of viral antigens, aluminium 0.25mg as aluminium hydroxide, 0.5% w/v 2-phenoxyethanol and a trace amount of neomycin sulphate).
- Vaqta Adult formulation – CSL/Merck Sharp & Dohme (formaldehyde inactivated hepatitis A virus (CR326F strain) adsorbed onto aluminium hydroxide; each 1.0mL dose contains approximately 50 units (U) of hepatitis A virus protein, aluminium 0.45mg as aluminium hydroxide and borax 70µg).
- Vaqta Paediatric/Adolescent formulation – CSL/Merck Sharp & Dohme (formaldehyde inactivated hepatitis A virus (CR326F strain) adsorbed onto aluminium hydroxide; each 0.5mL dose contains approximately 25 units (U) of hepatitis A virus protein, aluminium 0.225mg as aluminium hydroxide and borax 35µg).

- Twinrix Adult - SmithKline Beecham (formaldehyde inactivated hepatitis A virus (HM175 strain) and recombinant hepatitis B vaccine adsorbed onto aluminium adjuvant; each 1.0mL dose contains 720 ELISA units of HAV antigens, 20µg recombinant DNA hepatitis B surface antigen protein, aluminium 0.45mg as aluminium phosphate and aluminium hydroxide, 0.5% w/v 2-phenoxyethanol and a trace amount of neomycin sulphate).
- Twinrix Junior - SmithKline Beecham (formaldehyde inactivated hepatitis A virus (HM175 strain) and recombinant hepatitis B vaccine adsorbed onto aluminium adjuvant; each 0.5mL dose contains 360 ELISA units of HAV antigens, 10µg recombinant DNA hepatitis B surface antigen protein, aluminium 0.225mg as aluminium phosphate and aluminium hydroxide, 0.5% w/v 2-phenoxyethanol and a trace amount of neomycin sulphate).

The inactivated hepatitis A vaccines are prepared from HAV harvested from human diploid cell culture, which is then purified by ultrafiltration and chromatography, inactivated by formaldehyde, and then adsorbed onto aluminium hydroxide adjuvant. The HM175 strain vaccines contain a preservative, 2-phenoxyethanol. The vaccines contain minute amounts of residual formaldehyde.

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. Also, the two manufacturers use slightly different production methods and quantify the HAV antigen content in their respective vaccines differently. To date few comparisons between the 'equivalent' vaccines of the different manufacturers have been made, and there is not yet enough evidence to indicate that they are inter-changeable.

The inactivated hepatitis A vaccines induce HAV antibodies (anti-HAV) at titres many fold greater than that provided by the recommended dose of normal human immunoglobulin. Although the vaccines are highly immunogenic (see below), the titres are usually below the detection limits of the routinely available commercial tests for anti-HAV. Therefore testing to assess immunity following vaccination against hepatitis A is neither necessary nor appropriate.

Anti-HAV levels considered protective were induced in 88% and 98% of adults within two and four weeks respectively of a single dose of the 1440 ELISA U HM175 strain vaccine; most of the vaccinees had neutralising antibody. Similar responses (100%) have been observed following administration of the 50 U CR326F vaccine. The inactivated

hepatitis A vaccines are also highly immunogenic in children; >95% of children and adolescents have protective levels of anti-HAV one month after the administration of either the 720 ELISA U HM175 strain vaccine or the 25 U CR326F strain vaccine.

A clinical trial in the United States in the early 1990's determined that the 25 U CR326F strain vaccine, administered to seronegative children 2-16 years of age, had a protective efficacy of 100% after a single dose. A very large clinical trial conducted in Thailand, again in the early 1990's, determined that three doses of the 360 ELISA U HM175 strain vaccine, administered to children 1-16 years of age in a 0, 1 and 12 months schedule, had a protective efficacy of 95%. The protective efficacy after the first two doses (0, 1 months) was 94%; following the third dose 12 months later the efficacy was 100%.

The duration of immunity following vaccination is not certain but mathematical models based upon the observed decline in antibodies suggest that protection persists for at least 20 years. If the vaccines induce immunological memory, capable of mounting an anamnestic response upon subsequent exposure to HAV, the protection could be lifelong.

Transport, storage and handling

Transport in an insulated container with approved freeze monitor, and time-temperature monitor. Do not freeze or store vaccine in direct contact with ice packs. If vaccine has been exposed to temperature less than 0ºC, do not use. Store in refrigerator at 2ºC to 8ºC. The vaccine retains potency after being exposed to 37ºC for one week. Check expiry date on vial or container before storage. Rotate stock so that shortest date vaccines are used first.

Dosage and administration

The vaccine should not be diluted or mixed with other vaccines. Shake the vial vigorously before withdrawing dose and inject vaccine as soon as possible. The vaccine assumes a slightly opaque appearance once in suspension. The dose is 1 mL for adults and 0.5 mL for children from 2 years up to either 15 or 17 years (see Table 3.7.1) given by deep intramuscular injection.

Recommendations

The inactivated hepatitis A vaccines are administered by the intramuscular route. The recommended schedules for use in Australia are given in Table 3.7.1.

Table 3.7.1: Recommended dosages and schedules of the inactivated hepatitis A vaccines.

Vaccine	Vaccinees age (yrs)	Dose (HAV antigen)	Volume per dose (mL)	Vaccination schedule (months)
Havrix® Junior	2-15	720 ELISA U	0.5	0, 6-12
Havrix® 1440	>15	1440 ELISA U	1.0	0, 6-12
Vaqta® Paediatric/ Adolescent	2-17	25 U	0.5	0, 6-18
Vaqta® Adult	>17	50 U	1.0	0, 6
Twinrix® Junior	1-15	360 ELISA U	0.5	0, 1, 6
Twinrix® Adult	>15	720 ELISA U	1.0	0, 1, 6

To avoid the expense of unnecessary vaccination, it is recommended that the following be screened for pre-existing immunity to hepatitis A:

- those born prior to 1950;
- those who spent their early childhood in endemic areas, including in indigenous Australian communities; and
- those with an unexplained previous episode of hepatitis or jaundice.

If, upon screening, a person has either total hepatitis A antibodies or anti-HAV IgG, he/she has presumably had prior, perhaps unrecognised, HAV infection, and can be assumed to be immune, therefore not needing hepatitis A vaccination.

a) Travellers to endemic areas

Hepatitis A is the most frequent vaccine-preventable disease to affect travellers, and travel to endemic areas remains one of the leading risk factors for sporadic hepatitis A in Australia.

Hepatitis A vaccine is strongly recommended for all travellers to 'moderate' and 'high' endemicity countries, which essentially means to all developing countries. 'Travellers' includes 'up-market' business

travellers, particularly those undertaking regular visits to endemic countries, as well as backpackers undertaking prolonged travel 'on the road'. It also includes expatriates, diplomats, aid workers and missionaries living abroad, and military personnel who may have to be deployed overseas at very short notice.

A single dose of vaccine provides protective levels of anti-HAV for at least a year, but the second dose is recommended to prolong the protection much longer. A single dose can be assumed to provide adequate protection if administered within 2 weeks of departure and some authorities believe that vaccine alone can be administered up to the day of departure. However, further studies are required before this can be assumed to be adequate; for the traveller who is leaving within two weeks, hepatitis A vaccine as well as normal human immunoglobulin (NIGH) (Table 3.7.2) are recommended for optimal protection. It is well recognised that the concomitant administration of NIGH and hepatitis A vaccine results in lower anti-HAV titres than when the vaccine is administered alone. However, the titres are nevertheless still very high, and the lower response is not considered to be of any adverse consequence.

The administration of other vaccines relevant to international travel, either simultaneously with or within a month of the inactivated hepatitis A vaccines does not appear to affect the immune response to the latter. In particular, the simultaneous administration (in separate syringes) of hepatitis A and Vi capsular polysaccharide typhoid vaccine results in immune responses virtually the same as when the vaccines are administered alone.

b) Visitors to rural and remote indigenous communities

As mentioned above, hepatitis A is endemic in many rural and remote indigenous Australian communities. Therefore hepatitis A vaccination is recommended for all non-indigenous people who either reside on or make frequent visits to remote indigenous communities. Most of these people either live in or visit the communities for work-related purposes, and include teachers, police, storekeepers and legal personnel. If screening indicates that they are susceptible, indigenous people from urban environments who are similarly employed should also be vaccinated.

c) Child day-care and pre-school personnel

Occupationally acquired hepatitis A is a common occurrence among, and certainly the most frequent vaccine-preventable disease to affect day-care and pre-school personnel. The asymptomatic nature of the

infection in young children, their lack of control over their bowel motions, their lack of attention to good personal hygiene and the need for adult supervision of their toileting needs all contribute to this increased risk. Vaccination against hepatitis A is strongly recommended for these staff, and must be considered as a standard 'workplace health and safety' practice.

d) The intellectually disabled and their carers

Because the intellectually disabled may have suboptimal personal hygiene and because they may require assistance with their toileting needs, hepatitis A vaccination is recommended for them and their carers. The vaccination of carers is particularly important in facilities where they may be responsible for several intellectually disabled people, such as in special schools and residential facilities.

e) Health care providers

Although they do occur, nosocomial outbreaks of hepatitis A are uncommon in Australia. However there are numerous case reports of hospital-acquired hepatitis A among paediatric nurses, particularly those caring for ill indigenous children. Even though standard precautions should be utilised at all times, hepatitis A vaccination is recommended for:

- nursing and medical staff in paediatric wards, intensive care units and emergency departments that provide for substantial populations of indigenous children; and
- nursing and medical staff on rural and remote indigenous communities.

f) Sewage workers

Although there are no Australian data, studies from such disparate societies as Singapore and England indicate that sewage workers are at increased risk of occupationally-acquired hepatitis A. Therefore vaccination of sewage workers against hepatitis A is recommended and should be considered as a standard 'workplace health and safety' practice.

g) Men who have sex with men

The hepatitis A vaccine should be offered to all men who have sex with men. The vaccine can be delivered at services such as primary care and specialty clinics, STD clinics and at HIV counselling and testing services. Oral-anal and digital-rectal sexual practices place men who have sex with men at an increased risk of hepatitis A.

h) Injecting drug users

It is possible that HAV could be transmitted either in contaminated blood in shared syringes, or in contaminated drugs (that have been carried in condoms concealed in the rectum). However, it is more plausible that the generally poor personal hygiene and inadequate living conditions are the underlying circumstances contributing to the increased risk of hepatitis A in injecting drug users. Services that provide for injecting drug users should offer hepatitis A vaccine to their clients.

i) Patients with chronic liver disease

Although it would seem obvious that another hepatic insult might be particularly severe in patients with pre-existing chronic liver disease, there is not consistent support for this argument in the literature. For example, some studies report severe hepatitis A in those with chronic liver disease from hepatitis B infection, whereas others find no such severity. A similar inconsistency exists for chronic liver disease from hepatitis C infection. Until this dichotomy can be clarified it would be prudent to recommend hepatitis A vaccine for patients with chronic liver disease of any aetiology.

j) Haemophiliacs who may receive pooled plasma concentrates

Because viraemia occurs in those incubating the infection, asymptomatic blood donors on rare occasions have been the source of HAV infection transmitted by transfusion. There have also reports, albeit rare, of HAV transmission via clotting factor concentrates that were prepared using a solvent-detergent method of viral inactivation.

HAV transmission via either blood transfusion or receipt of clotting factor concentrates has not been recognised in Australia. The preparation of clotting factor concentrates used in Australia involves either heat treatment or filtration procedures that are designed to either inactivate or remove viruses. Neither the Australian Red Cross Blood Service nor the Haematology Society of Australia has a policy on hepatitis A vaccination for patients who receive either blood or blood products. However the Medical Advisory Panel of the Haemophilia Foundation of Australia recommends hepatitis A vaccination 'for haemophiliacs who are likely to receive pooled plasma concentrates'.

k) Food handlers

The food industry workforce is very large, with a rapid turnover of personnel in some sectors, and point source outbreaks of hepatitis A caused by infected food-handlers are rare in Australia. Therefore it is

neither feasible nor necessary to vaccinate food-handlers against hepatitis A.

NB. the prior recommendation, that 'vaccination of food handlers should be encouraged', is rescinded.

The combined hepatitis A/hepatitis B vaccines

The immunogenicity and reactogenicity profiles of the combined hepatitis A/hepatitis B vaccines are similar to those when the vaccines are administered separately. Virtually all recipients of the combination vaccines are immune to HAV, and at least 90% are immune to hepatitis B, after the first two doses.

The combined hepatitis A/hepatitis B vaccines should be considered for those at risk of acquiring both infections including:

- expatriates and longterm visitors to developing countries;
- at-risk health care workers and medical and nursing students;
- men who have sex with men; and
- injecting drug users.

Management of hepatitis A

a) Following all cases

Normal human immunoglobulin (NIGH) should be administered to close contacts of all cases of hepatitis A. 'Close contacts' are those who have had contact with a case during the two weeks before up until one week after the onset of jaundice, and usually includes only household and/or sexual contacts. The NIGH should be given within two weeks of the exposure in the doses given in Table 3.7.2; NIGH may not be effective if given >2 weeks after the exposure.

Table 3.7.2: Recommended doses of normal human immunoglobulin (NIGH) to be given as a single intramuscular injection for short-term (up to 3 months) prophylaxis.

Weight	Dose NIGH
Under 25 kg	0.5 mL
25 – 50 kg	1.0 mL
Over 50 kg	2.0 mL

If a person with hepatitis A is a food-handler by occupation, NIGH should be administered to the other food-handlers employed in the same food establishment. A review of food-handling procedures in the establishment should be undertaken and the staff reminded of standard food and personal hygiene practices. A food handler with hepatitis A should be excluded from work until one week after the onset of jaundice.

Although a recent clinical trial in Italy demonstrated that hepatitis A vaccine was ~80% effective in preventing secondary infection among household contacts of sporadic cases of hepatitis A, the trial did not involve the use of NIGH. Because only NIGH can offer immediate protection, the use of vaccine alone is not recommended for the management of contacts of cases of hepatitis A unless either there is a shortage of NIGH. If the contact with a case took place more than 2 weeks previously, then vaccine could be used, but there is no evidence it will be effective. As mentioned above, hepatitis A vaccine can be administered at the same time as NIGH.

(b) Cases associated with either a child day-care centre or pre-school

When a single case of hepatitis A is associated with either a day-care centre or pre-school (ie. the case is an attendee child, a staff member or a household contact of an attendee child), NIGH should be administered to any unvaccinated staff members. The staff and parents should be reminded of standard hygiene practices. The case should be excluded from the facility until one week after the onset of jaundice (or the onset of other symptoms if a child does not have jaundice).

Although a single case of hepatitis A probably does not justify the mass use of NIGH, two or more cases (associated with a day-care or pre-school facility) that occur in different households is strongly suggestive that transmission of HAV is occurring within the facility. NIGH should then be offered to all staff and attendee children at the facility. (Attempts to rationalise the use of NIGH and administer it to specific cohorts of children at the facility may not be effective in stopping the transmission of HAV).

NB: The administration of measles-mumps-rubella vaccine must be delayed for three months after the administration of NIGH.

c) Outbreaks of hepatitis A

Although personal hygiene is invariably promoted during outbreaks of hepatitis A, there is very little evidence that this is effective. However, under certain circumstances outbreaks of hepatitis A are amenable to control using either NIGH or hepatitis A vaccine.

There is good evidence that the prompt and liberal administration of NIGH interrupts outbreaks of hepatitis A in well-defined communities such as child day-care centres, schools and hospitals, and in closed communities such as religious communities. There is increasing evidence that hepatitis A vaccination can also interrupt outbreaks in well-defined communities such as tertiary education settings and rural communities, and in closed communities such as religious communities. However neither NIGH nor hepatitis A vaccine have been demonstrated to effectively interrupt transmission of HAV in large community-wide outbreaks. This may be because these interventions have been implemented too late and with inadequate coverage.

Therefore as soon as an outbreak of hepatitis A is recognised as occurring in either a well-defined or closed community NIGH should be administered to all those considered at risk. Hepatitis A vaccine should be considered as an alternative to NIGH in those communities, such as indigenous communities, that are likely to experience further outbreaks in the future. During community-wide outbreaks, the emphasis should be on ensuring that NIGH is administered to the close contacts (ie. household and sexual contacts) of cases, and to maintain surveillance for hepatitis A occurring within those settings capable of intensifying the transmission of HAV.

Adverse events and precautions

The most frequent adverse event following the hepatitis A vaccines is mild local pain – probably caused by the aluminium hydroxide adjuvant – which is of a short duration. About 50% of adult recipients of either the 1440 ELISA U HM175 strain vaccine or the 50 U CR326F vaccine reported local soreness at the injection site, 14% reported headache and ~5% malaise or fatigue. About 20% and 5% of children who received the 720 ELISA U HM175 strain vaccine and the 25 U CR326F vaccine respectively experienced soreness at the injection site, and 6% and <1% respectively experienced fever.

The hepatitis A vaccines do not affect liver enzyme levels. Although, upon rare occasion, serious adverse events such as Guillain-Barré syndrome and autoimmune haemolytic anaemia may follow hepatitis A vaccination, there is to date no evidence of a causal relationship.

Hepatitis A vaccines should not be administered to anyone with an anaphylactic sensitivity to any of the vaccine components.

Contraindications

Hypersensitivity to any component of the vaccine is a contraindication.

Use in pregnancy

Pregnancy is not a contradiction to hepatitis A vaccination but pregnant women should only be vaccinated if there is a substantial risk of exposure to HAV.

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3.8 HEPATITIS B

Virology

Hepatitis B virus contains a partially double stranded DNA. The outer surface of the virus is a glycolipid which contains the hepatitis B surface antigen (HBsAg); the other important antigenic components are the hepatitis B core-antigen (HBcAg), and the hepatitis Be antigen (HBeAg). HBcAg is not detectable in serum, but can be detected in liver tissue in people with acute or chronic hepatitis B infection. Antibodies developed to HBsAg (anti-HBs) indicate immunity, whereas persistence of HBeAg and HBsAg denote infectivity, which is greater if HBeAg is positive.

Clinical features

In adults, the infection frequently causes symptomatic acute hepatitis (approximately 50%), but in young children, particularly those under one year of age, infection is usually asymptomatic. The incubation

period is 45 to 180 days and the period of communicability extends from several weeks before the onset of acute illness to usually the end of the period of acute illness. Acute illness is 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, arthralgia, skin rashes, arthritis and the passage of dark coloured urine and light coloured stools. During recovery, malaise and fatigue may persist for many weeks. Fulminant hepatitis occurs approximately in 1% of acute cases.

Following acute infection, 1% to 12% of those infected as adults and up to 90% of those infected post-partum as neonates remain persistently infected for many years. Such virus carriers may be a potential source of infection to others and have a significantly increased risk of chronic hepatitis and primary liver cancer later in life. Carriers are identified by the longterm presence (greater than six months) of circulating HBsAg.

Persons with chronic infection usually remain asymptomatic and may not be aware that they are infected, although they are capable of transmitting the disease. Most of the serious complications associated with hepatitis B infection, however, occur in persons in whom chronic infection continues. Chronic active hepatitis develops in over 25% of carriers and 15-25% of such persons will die prematurely of cirrhosis or hepatocellular carcinoma.

Epidemiology

Carrier rates differ in different parts of the world and may be quite variable within countries. Carrier rates vary from 0.1% to 0.2% among caucasians in the United States, Northern Europe and Australia; 1% - 5% in the Mediterranean countries, parts of Eastern Europe, USSR, China, Africa, Central and South America; and greater than 10% in some Australian Aboriginal, Central African, and South-East Asian populations. First generation immigrants usually retain the carrier rate of their country of origin, but subsequent generations show a declining carrier rate irrespective of vaccination. Australian Aboriginal infection and carrier rates also vary between place of residence. A study in WA in 1989 showed that carrier rates were 3% - 5% in the South West of the State with 7% - 9% carrier rates in rural areas and infection rates varying from 35% to 75%.

Notification of hepatitis B to the National Notifiable Diseases Surveillance System began in 1993 and a peak of 328 cases was notified in 1994. The number of notifications has since decreased gradually to 226 cases in 1998.

Transmission of hepatitis B may result from inoculation or mucosal contact with blood or sexual secretions from an individual with active infection (HBsAg positive) ie acute infection or chronic carrier. Saliva may also contain levels of virus which are likely to be infective only if injected directly into tissue.

Routes of transmission include:

- Sharing injecting equipment, (such as occurs in injecting drug use).
- Needlestick injury, and other types of parenteral inoculation.
- Sexual intercourse (heterosexual or homosexual, although the latter has a higher risk).
- Transmission from infected mother to neonate (vertical transmission), usually at or around the time of birth;
- Child-to-child (horizontal) transmission, usually through contact between open sores or wounds.
- Breast feeding.

Transmission by inadvertent parenteral inoculation such as by toothbrush, razor etc. through close personal contact in households in which a carrier resides is a low but significant risk.

Screening of blood and organ donors has virtually eliminated the risk of transmission of hepatitis B through blood transfusion and organ transplants.

The initial strategy for the control of hepatitis B in Australia commenced in 1988, targeting groups at particular risk for vaccination at birth. In addition to vaccine, hepatitis B immunoglobulin (HBIG) was given if the mother was a hepatitis B carrier. As it became obvious that not all carrier mothers were being detected by focussing only on specific groups, vaccination needed to be offered to all new born infants.

In 1996, the NHMRC recommended a universal hepatitis B vaccination program for infants and adolescents. The infant program will be implemented as part of the new standard schedule with multivalent vaccines containing hepatitis B that have now been registered in Australia. The adolescent program commenced in 1997, with most States targeting one birth cohort at age 10-13 years. The adolescent program will continue until those immunised for hepatitis B in the childhood program reach adolescence.

Vaccines

- Engerix B – SmithKline Beecham (recombinant DNA hepatitis B vaccine; adult and paediatric formulations contain hepatitis B surface antigen 20µg per ml, adsorbed onto 0.5 mg per mL aluminum hydroxide; thiomersal 0.005% - adult 1 mL monodose dose vials; paediatric 0.5 mL monodose vials). The paediatric formulation is registered for use in children up to the 20th birthday, if full compliance with the schedule can be guaranteed.
- HBVax II – CSL/Merck Sharpe and Dohme (recombinant DNA hepatitis B vaccine; adult and paediatric formulations contain hepatitis B surface antigen 10µg per mL adsorbed onto 0.5 mg per mL aluminium hydroxide; thiomersal 0.005% - adult 1 mL monodose vials; paediatric 0.5 mL monodose vials). A dialysis formulation containing hepatitis B surface antigen 40µg per mL in one mL vials is also available. The paediatric formulation is registered for use in children and adolescents up to the 20th birthday.
- Infanrix-hepB (Diphtheria-tetanus-acellular pertussis adsorbed-hepatitis B) - SmithKline Beecham (diphtheria toxoid 25 Lf, tetanus toxoid 10 Lf, pertussis toxoid 25µg, pertussis filamentous haemagglutinin 25µg, pertactin 8µg, hepatitis B surface antigen 10µg; adsorbed to aluminium hydroxide 0.5 mg, aluminium phosphate 0.2 mg, polysorbate 80 <100µg, polysorbate 20 < 5µg; preservative - phenoxyethanol 2.5µg; formaldehyde < 1µg; 0.5 mL dose)
- Comvax– CSL/Merck Sharp Dohme (OMP Hib-Hepatitis B containing PRP-OMP; purified capsular polysaccharide of the Ross Haemophilus influenzae type b strain 7.5µg conjugated to meningococcal protein 125µg; hepatitis B surface antigen 5µg; aluminium hydroxide containing 225µg aluminium; 0.9% sodium chloride; 0.5 mL dose)
- Twinrix Adult - SmithKline Beecham (formaldehyde inactivated hepatitis A virus (HM175 strain) and recombinant hepatitis B vaccine adsorbed onto aluminium adjuvant; each 1.0mL dose contains 720 ELISA units of HAV antigens, 20µg recombinant DNA hepatitis B surface antigen protein, aluminium 0.45mg as aluminium phosphate and aluminium hydroxide, 0.5% w/v 2-phenoxyethanol and a trace amount of neomycin sulphate). This vaccine is registered for use in individuals aged 15 years and over.
- Twinrix Junior - SmithKline Beecham (formaldehyde inactivated hepatitis A virus (HM175 strain) and recombinant hepatitis B vaccine

adsorbed onto aluminium adjuvant; each 0.5mL dose contains 360 ELISA units of HAV antigens, 10µg recombinant DNA hepatitis B surface antigen protein, aluminium 0.225mg as aluminium phosphate and aluminium hydroxide, 0.5% w/v 2-phenoxyethanol and a trace amount of neomycin sulphate). This vaccine is registered for children aged between 1 and 14 years of age.

The vaccines are prepared using recombinant technology and are non-infectious sub-unit vaccines where the active constituents are derived from genetically engineered Saccharomyces cerevisiae yeast cells, which carry the hepatitis B surface antigen gene. For monovalent vaccines, purification of the HBsAg protein by physical chemical methods is followed by adsorption onto aluminium hydroxide and the addition of thiomersal 0.005% as a preservative. The two monovalent vaccines have given almost identical results in clinical trials. Thiomersal-free vaccines will become available in 2000.

Transport, storage and handling

Transport in an insulated container with an approved freeze monitor. Choose a model that activates at 0ºC. Also include a time-temperature monitor. Do not freeze or store vaccine in direct contact with ice-packs. Freezing destroys the potency of the vaccine. The vaccine should be stored at 2ºC to 8ºC. If vaccine has been exposed to temperatures below 0ºC, contact your state immunisation coordinator. Both monovalent vaccines are white, slightly opalescent liquids. Any visible change in the product, such as an amorphous flocculate or a granular precipitate, may indicate incorrect storage conditions and consequent reduction in vaccine immunogenicity. Do not use vaccine with these changes. Check expiry date on vial or container before use. Rotate stock so that the shortest dated vaccines are used first.

Dosage and administration

The vaccine should be administered by deep intramuscular injection into the deltoid muscle in adults and older children, and into the antero-lateral aspect of the thigh in neonates and infants under 12 months of age.

For children and younger adolescents who have already commenced the primary schedule (for age cut-off times see the recommendations for the various vaccines), a total of three doses of 0.5 mL is recommended. The optimal interval is one month between the first and second doses and a third dose at five months after the second dose. The use of longer time intervals between doses does not impair immunogenicity of hepatitis B

vaccine. The minimum interval between the second and third doses is 2 months.

For adults and older adolescents a full course of hepatitis B vaccine consists of three doses of 1 mL. There should be an interval of one to two months between the first and second dose with a third dose at two to five months after the second dose (this schedule applies to both Engerix B and HBVax II). This induces protective levels of neutralising antibody against hepatitis B virus in over 90% of young adults. The frequency of seroconversion increases progressively from approximately 35% after the first injection to over 90% after the third injection. There is evidence of immunity (anti-HBsAg antibody) in most vaccinated subjects after administration of two doses of the three-dose vaccine regime. However, the third dose is necessary to increase the percentage of responders and provides longer protection.

In dialysis patients, HIV infected and other immunocompromised individuals a larger than usual dose (1 mL of normal adult formulation in each arm on each occasion or a single dose of dialysis formulation vaccine on each occasion) at each date is recommended to increase the likelihood of seroconversion.

Using Different Vaccine Formulations in the same Course

In some circumstances the formulation (brand of vaccine) that was used for previous doses is not known or is not available when a person returns for further hepatitis B vaccination. There is no reason to believe that the use of a different brand will not be satisfactory in such circumstances, even though switching of brands is not recommended.

Recommendations

Primary Vaccination

A birth dose of hepatitis B vaccine, followed by doses given in multivalent vaccines at 2, 4 and either 6 or 12 months, is now recommended for all children.

Preterm babies (<32 weeks gestation) should either be vaccinated at birth and given an extra booster (using a 0, 2, 4, 6, 12 month schedule) or hepatitis B vaccine should be delayed until the baby is 2 months old, using a 2, 4, 6 and 12 month schedule. Until a thiomersal-free monovalent hepatitis B vaccine is available, the latter option is preferred for preterm babies whose mothers are hepatitis B negative. For preterm or term babies of carrier mothers, a birth dose of vaccine and hepatitis B immunoglobulin must be given.

The multivalent vaccines DTPa-hepB and Hib(PRP-OMP)-hepB may be used as recommended in the schedule for primary vaccination following a monovalent dose of hepatitis B vaccine given at birth. If the monovalent dose at birth is missed, vaccination against hepatitis B should be continued with a multivalent vaccine, following the routine schedule.

The combined hepatitis A and B vaccine is indicated for active immunisation against hepatitis A and hepatitis B virus infection. The paediatric combined hepatitis A and B vaccine is indicated in subjects aged 1–14 years whereas the adult vaccine is indicated in subjects 15 years and over. These combinations may be used as required and generally are recommended for travellers proceeding to high endemic countries for hepatitis A, and where the risk of hepatitis B may be considered significant.

Accelerated schedule

In circumstances where more rapid protection is required (eg. contacts of hepatitis B carriers and vaccination of travellers), only one product, Engerix B, is registered for use in an accelerated schedule. The accelerated schedule for adults using Engerix B is 0, 7 and 21 days with a booster at 12 months.

Booster doses

There is good evidence that a completed primary course of hepatitis B vaccination provides long lasting protection in immunocompetent individuals, so booster doses are not recommended. This applies to adults, children and all subgroups (such as health care workers).

However, booster doses are recommended for immunosuppressed individuals, for people living with HIV infection or with renal failure. The time for boosting should be decided by regular monitoring of hepatitis B antibody levels at six to twelve monthly intervals.

Serological confirmation of post-vaccination immunity

Post-vaccination serological testing, three months after the third dose of hepatitis B, is recommended for persons in the following categories:

- those at occupational risk (eg. health care workers whose work involves exposure to blood and body fluids);
- those at risk of severe or complicated disease (eg. the immunocompromised, and persons with pre-existing liver disease not related to hepatitis B);

- those in whom a poor response to hepatitis B vaccination is expected (eg. haemodialysis patients).

If adequate anti-HBs levels are not reached following the third dose, the possibility of HBsAg carriage should be investigated. Those who are HBsAg negative and do not respond should be offered further doses of vaccine. This can be given as either a 4th double dose or a further 3 doses at monthly intervals with testing 2 weeks after each additional dose. Persistent non-responders should be informed about the need for hepatitis B immunoglobulin (HBIG) within 48 hours of parenteral exposure to HBV.

Management of infants born to hepatitis B carrier mothers

Routine antenatal screening for HBsAg is essential for correct implementation of the strategy to minimise carriage in high-risk families. Infants born to HBsAg positive mothers should be given HBIG 100 international units (0.5 mL intramuscularly) after physiological stabilisation, and preferably within 12 hours of birth. The efficacy of HBIG decreases markedly if treatment is delayed beyond 48 hours. They should also be vaccinated with the first dose of monovalent hepatitis B vaccine at the same time as HBIG is given but in the opposite thigh. This regime results in seroconversion rates of over 90% in neonates. These rates are unaffected by concurrent administration of HBIG to infants born to HBsAg positive mothers. If this is not possible, vaccination should not be delayed beyond 7 days after birth. Three subsequent doses of a multivalent vaccine should be given at 2,4 and either 6 or 12 months according to the instructions for the particular vaccine, so that the infant is given a total of four doses of hepatitis B containing vaccines.

Universal pre-adolescent vaccination against hepatitis B

Vaccination for all pre-adolescents aged 10 to 13 years either at the end of primary school or the beginning of secondary school commenced in Australia in 1998. Not all States or Territories implemented the program in schools, depending instead on provision of the vaccination through general practice and routine clinics. Pre-adolescent vaccination at age 10-13 years is still recommended, but is not necessary for children who have received a primary course of hepatitis B vaccine.

Other groups for whom hepatitis B vaccination is recommended

Household contacts (other than sexual partners) of acute and chronic hepatitis B carriers

There is a low, but definite, risk of transmission from a patient with acute hepatitis B. This risk is reduced if domestic items capable of causing skin penetration (such as combs, nail brushes, tooth brushes and razors), are not shared. Cutlery, crockery and other household items are decontaminated by ordinary washing in hot water and detergent.

The risk of contacts acquiring hepatitis B infection varies according to the HBeAg status of the carrier, and with cultural and socio-economic factors. However, it should be recognised that in many situations, a number of family members will have been exposed by the time the risk is recognised. Testing before planned vaccination is recommended for such families as well as members of families who have migrated from high prevalence countries.

Those at sexual risk

Susceptible (anti-HBs negative) sexual partners of patients with acute hepatitis B have an increased risk of infection and should be offered post-exposure hepatitis B immunoglobulin HBIG and hepatitis B vaccination; both should be initiated as soon as possible. Susceptible (anti-HBs negative) partners of carriers also have a substantial risk of infection (particularly if the carrier is HBeAg positive) and should be offered vaccination. Hepatitis B is a relatively common problem in clients of STD (sexually transmitted disease) clinics and vaccination should be offered to susceptible individuals at the time of first attendance, and followed up until three doses of monovalent vaccine have been administered.

Sexually active men who have sex with men should be vaccinated regardless of their age or the duration of their homosexual activities, unless they are already anti-HBs positive or have serological evidence of past or continuing infection. HIV positive individuals should receive twice the normal dosage (ie. double the normal volume of vaccine on three occasions or a standard dose of the increased strength dialysis formulation vaccine on three occasions). The combined hepatitis A and B vaccine may be appropriate for men who have sex with men, if they are not immune to either disease, as they are at risk for both.

Injecting drug users

Any users of injectable drugs who have not been infected should be vaccinated. HIV positive injecting drug users should receive twice the normal dosage or a standard dose of the double strength dialysis formulation of vaccine.

Haemodialysis patients

There is a risk of exposure to hepatitis B virus in haemodialysis units. Vaccination is recommended for susceptible patients, preferably before enrollment into the program. Such patients should receive twice the normal dose (ie. double the normal volume) of vaccine. An alternative is to use the double strength dialysis formulation of vaccine on three occasions.

Recipients of certain blood products

Screening of all blood donors for HBsAg has greatly decreased the incidence of transfusion related hepatitis B virus infection, but patients with clotting disorders who receive blood product concentrates may have an elevated risk of hepatitis B virus infection. Vaccination is recommended for these persons and should be initiated at the time their specific clotting disorder is identified.

Individuals with chronic liver disease and/or hepatitis C

Hepatitis B vaccination is recommended for those in this category who are HBsAg negative as the health of such individuals may be severely affected by a superimposed hepatitis B infection.

Residents and staff of facilities for persons with intellectual disabilities

The risk of transmission of hepatitis B virus in these settings is increased by exposure to blood and contact to skin lesions and other infective secretions. Hepatitis B virus markers are commonly found in individuals in such facilities, especially those of larger institutions. It has not been recognised to be a major problem where such individuals are housed in smaller groups in small facilities. Vaccination of staff and susceptible residents should be considered in both residential and non-residential care of persons with intellectual disabilities.

Inmates and staff of long term correctional facilities

Inmates are at risk of hepatitis B because of the prevalence of homosexual intercourse, injecting drug use and amateur tattooing in some correctional facilities. Managers of the correctional facilities should

consider offering screening and vaccination to inmates. Vaccination of staff should be maintained as for health care workers.

Health care workers and embalmers

The risk to the worker depends on:

- the HBsAg carrier rate among the population;
- the degree of exposure to blood and body fluids;
- the thoroughness with which precautions to avoid blood and body fluid exposure are practiced.

The risk differs considerably from setting-to-setting in different parts of Australia, but it is recommended that all staff directly involved in patient care, embalming or in the handling of human blood or tissue be vaccinated.

Individuals adopting children from overseas

These children should be tested for hepatitis B, and if HBSAg positive, members of the adoptive family should be vaccinated.

Others in whom vaccination might be justified

Police, members of the armed forces and emergency services staff may be at increased risk of hepatitis B, depending on the duties to which they are assigned. If they are at risk they should be vaccinated.

Hepatitis B vaccination should be considered for long term travellers to high endemic areas, but short term tourists or business travellers are at very little risk of hepatitis B, provided they avoid exposure through sexual contact, injecting drug use, tattooing and body piercing. However, vaccination is indicated for those residing for some time in high prevalence countries and expecting personal contact with local residents.

The question of vaccination of classroom contacts of acute and chronic hepatitis B cases and carriers in Australia is difficult to resolve, because studies in different countries provide conflicting evidence about the risk to classroom contacts of carriers. What is known is that the risk in Australian schools is very low indeed, substantially less than in the household situation. Vaccination of classroom contacts is seldom indicated, and should only be contemplated after identification of the source of infection in the index case, or in the case of an outbreak of hepatitis B. If the need for hepatitis B vaccination is raised, the assessment of risk should be the responsibility of the local public health authority.

Staff of child day care centres will normally be at minimal risk of hepatitis B. If advice on risk is sought, the inquiry should be directed to the local public health authority.

Contact sports generally carry a very low risk of hepatitis B infection. Although the risk is very low vaccination should not be discouraged.

Use of the combination hepatitis A/hepatitis B vaccine

The combined hepatitis A/hepatitis B vaccines should be considered for those at risk of acquiring both infections including:

- expatriates and longterm visitors to developing countries;
- at-risk health care workers and medical and nursing students;
- men who have sex with men and
- injecting drug users.

Post-exposure prophylaxis for Hepatitis B

Following significant exposure (percutaneous, ocular, or mucous membrane) to blood or potentially blood-contaminated secretions, the source of the blood should be tested as soon as possible for HBsAg, and a blood sample taken from the recipient for anti-HBs testing, unless a recent satisfactory anti-HBs result is on record. If the recipient is anti-HBs-negative, and the source is HBsAg-positive or cannot be identified and tested rapidly, a single dose of HBIG (400 IU for adults and 100 IU for children and young adolescents) should be given within 72 hours. Hepatitis B vaccine should be given intramuscularly into the deltoid or anterolateral thigh as soon as possible, but within seven days of exposure. The second dose should be given one to two months after the first and the third dose six months after the first dose.

In most instances, it is advisable to offer a course of hepatitis B vaccine to the non-immune health care worker sustaining non-HBV needlestick injury, since the injury itself is evidence that they work in an area with a significant risk of exposure.

Table 3.8.1 Post-exposure prophylaxis against hepatitis B virus for non-immune individuals

Type of Exposure	Hepatitis B Immunoglobulin		Vaccine	
Perinatal (exposure of babies during and after birth)	100 IU by IM injection	Within 12 hours of birth, preferably immediately after birth	0.5 ml by IM injection	Immediately after birth (preferably within 24 hours and no later than 7 days)[a], then repeat at 2, 4 and either 6 or 12 months.
Percutaneous (needlestick)	400 IU by IM injection	Single dose within 72 hours	0.5 or 1ml by IM injection depending on age [b]	Within 7 days[b] repeat at 1-2 months and 5 months after 2nd dose.
Sexual	400 IU by IM injection	Within 14 days of sexual contact	0.5 or 1ml by IM injection depending on age[b]	Within 14 days[b] repeat at 1-2 months and 5 months after 2nd dose.

a. The 1st dose can be given at the same time as the hepatitis B immunoglobulin dose, but should be administered at a separate site.

b. For children and younger adolescents, use the 0.5ml IM dose recommended by the manufacturers

Adverse events and precautions

Side-effects are transient and minor, and include soreness at the injection site (5-15%), fever (2-3% - usually low grade), nausea, dizziness, malaise, myalgia and arthralgia. Fever can be expected in 0.6-3.7% of neonates immunised with hepatitis B vaccine.

Anaphylaxis has been reported extremely rarely in adults. Although various adverse events (demyelinating diseases, Guillain-Barre syndrome, arthritis, and sudden infant death syndrome) have been reported, there is no evidence of a causal relationship with hepatitis B vaccination.

There have been a few reports of generalised febrile reactions attributed to yeast allergy, and exceptional instances of periarteritis nodosum have been reported.

Contraindications

- Effect of Vaccination on Carriers

The vaccine produces neither therapeutic effects or adverse events in hepatitis B virus carriers.

- Vaccination of Immune Persons

Vaccination of individuals who have antibodies against hepatitis B virus from a previous infection is not necessary, but will not cause adverse events. Such individuals may have a post-vaccination increase in their levels of antibody to HBsAg (anti-HBs). Passively acquired antibody, whether from hepatitis B immunoglobulin administration or from the transplacental route will not interfere with active immunisation provided different sites are used for injection.

Use in pregnancy

The safety of hepatitis B vaccine for the developing fetus has not yet been confirmed by a large scale trial. However, hepatitis B vaccine consists of non-infectious HBsAg particles produced in yeast, so the risk to the fetus from the vaccine should be negligible. On the other hand, hepatitis B virus infection in a pregnant woman may result in severe disease for the mother and chronic infection for the newborn. Pregnancy should not be considered a contraindication to the use of this vaccine for persons for whom it would otherwise be indicated.

Conflict with Product Information

Booster doses are not recommended immunocompetent persons. The product information suggests that individuals at special risk should receive boosters five yearly.

HEPATITIS B IMMUNOGLOBULIN

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 antibody to HBsAg. As stocks of HBIG are very limited, use should be strictly reserved for those who are at serious risk, such as babies born to hepatitis B carrier mothers and health care workers who are exposed to the blood of HBsAg-positive individuals through needlestick injury. Requests should be directed to the Director of the Australian Red Cross Blood Service in the State or Territory.

Babies born to hepatitis B carrier mothers

Infants born to HBsAg-positive mothers require 100 IU HBIG on the day of birth to provide immediate passive protection. Active vaccination against hepatitis B should be commenced at the same time.

HBIG is not recommended for infants born to HBsAg-negative mothers in families from high prevalence ethnic groups because there is epidemiological evidence that exposure from non-maternal sources is rare in the 1st year of life; vaccination alone will suffice in these cases.

- Hepatitis B immunoglobulin - CSL (immunoglobulin prepared from human plasma containing high levels of antibody to surface antigen of the hepatitis B virus 100 IU and 400 IU ampoules).

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3.9 IMMUNOGLOBULIN PREPARATIONS

Introduction

Passive immunity results from the injection of human immunoglobulin. The protection afforded is immediate, and the length of protection is dose related, lasting usually for only a few weeks. There are two types of immunoglobulin, normal and specific.

- Normal immunoglobulin (human) (NIGH)

  This is derived from the pooled plasma of blood donors. It contains antibody to viruses which are prevalent in the general population.

- Specific immunoglobulins

  These products are used to protect individuals against specific viruses such as cytomegalovirus, hepatitis B, rabies, Australian Bat Lyssavirus, tetanus, and varicella/zoster infections. Each of the specific immunoglobulins is dealt with under the relevant disease.

Although not an infection, Rh(D) haemolytic disease can be prevented by a specific immunoglobulin and that product is considered under "Rhesus disease of the newborn".

To date, most have been obtained from pooled blood of patients convalescing from the relevant infection, donors recently vaccinated with the relevant vaccine or those who on screening are found to have sufficiently high antibody levels. 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.

The first monoclonal antibody against an organism, respiratory syncytial virus (RSV), has now been registered in Australia. Such products are not derived from blood donations.

Adverse events and storage requirements for specific immunoglobulins are similar to those for normal immunoglobulin (human), and are therefore not listed under each specific immunoglobulin.

NIGH and specific immunoglobulin products are screened and treated to ensure that they do not contain HIV, HBV, or HCV. NIGH has a pasteurisation step added to its method of manufacture to further reduce any risk. The risk of prion transmission remains theoretical.

Potential interaction with vaccines

Live attenuated virus vaccines:

- Passively acquired antibody can interfere with the response to live, attenuated virus vaccines. Therefore, administration of live attenuated vaccines such as measles should be deferred until approximately three months after passive immunisation. Immunoglobulins should not be administered for at least two weeks after a vaccine has been given.

Inactivated vaccines:

- Inactivated vaccines (eg tetanus or hepatitis B) may be administered concurrently with passive antibody, using separate syringes and separate injection sites to induce passive/active immunity.

Availability of immunoglobulins (Human), (NIGH)

CSL supplies normal immunoglobulin for IM use.

Rabies immunoglobulin can only be obtained upon application from State or Territory health authorities. Sandoglobulin NIGH for intravenous use and RSV monoclonal antibody Palivizumab (Synagis: Abbott Australia) are available commercially.

The specific immunoglobulins and the CSL NIGH for intravenous (IV) use, which are derived from Australian donated plasma, can only be obtained from the Australian Red Cross Blood Service with the permission of the State Director. The State Directors can be contacted by telephone (ACT 02 6206 6006; NSW 02 9229 4444; QLD 07 3835 1333; SA 08 8422 1200; NT 08 8941 1555 TAS 03 6230 6230 VIC 03 9694 0111; WA 08 9325 3333). The Australian Red Cross Blood Service supplies these products free of charge.

Transport, storage and handling

All immunoglobulins must be protected from light and stored in a refrigerator at 2ºC to 8ºC. They must not be frozen.

Normal Immunoglobulin (Human) (NIGH)–IM (intramuscular) use

Normal immunoglobulin (human) (NIGH) is prepared by plasma fractionation of blood collected from voluntary donors by the Australian Red Cross Blood Service. It is a sterile solution of immunoglobulins and contains those antibodies commonly present in adult human blood. In Australia, NIGH is supplied as a 16% solution; in the United States, as a 16.5% solution; but in the United Kingdom, as a 10% solution. NIGH and other immunoglobulin products are screened and treated to ensure that they do not contain HIV, HBV, or HCV.

- Normal immunoglobulin (human) (NIGH)- CSL (16% solution of IgG fraction of pooled normal human plasma 2 mL and 5 mL vials for intramuscular injection).

Dosage and administration

NIGH should be given by deep intramuscular injection using a large (19 or 20) gauge needle. The NIGH should be introduced slowly into the muscle to reduce pain.

This product should NOT be administered intravenously because of possible adverse events. A special product for intravenous use (normal

immunoglobulin (human, intravenous)) has been developed for patients requiring large doses of immunoglobulin (see page 138).

For information on the dose of IM NIGH for specific conditions such as hepatitis A and measles please refer to the specific chapters on these diseases in this Handbook.

Recommendations

- Passive immunisation

Immunoglobulin preparations may be given to susceptible individuals as either pre-exposure or post-exposure prophylaxis against specific infections. Normal pooled immunoglobulin contains sufficiently high antibody levels to be effective against hepatitis A and measles.

- Prevention of hepatitis A (see also Part 3.7, page 115)

NIGH contains sufficiently high levels of antibody against hepatitis A to be able to prevent or ameliorate infection in susceptible individuals.

NIGH is very effective in controlling the spread of a common source outbreak of hepatitis A in either a family or community setting. Hepatitis A vaccine is strongly preferred for the protection of travellers, but NIGH can be used in circumstances where there is insufficient time (<2 weeks) to ensure a protective response from hepatitis A vaccine, or if the vaccine is scarce. If NIGH is used, hepatitis A vaccine should also be given.

- Prevention of measles (see also Part 3.12, page 162)

NIGH contains sufficiently high level of antibody against measles to be able to prevent or ameliorate infection in susceptible individuals. Protection against measles may be required if the exposed individual has an underlying immunological disorder (AIDS, immunosuppressive therapy) or to control an outbreak of measles among non-immunised individuals, eg. in a child-care centre. The use of NIGH should be considered in HIV-positive persons exposed to a patient with measles.

- Prevention of chickenpox (varicella) (see also part 3.28, page 237)

Chickenpox should be prevented or made less severe in infants under 1 month of age, in children who are being treated with immunosuppressive therapy, and in pregnant women. Zoster immunoglobulin (ZIG) is recommended for non-immune HIV-positive persons within 10 days of exposure to clinical cases of chickenpox. If zoster immunoglobulin is unavailable, large doses of normal immunoglobulin can be used. This does not necessarily prevent

chickenpox, but it lessens the severity of the disease. The dose of NIGH is 0.4 to 1.0 mL of immunoglobulin per kg body weight.

- Immune deficiency

Patients with abnormal antibody production (primary hypogammaglobulinaemia, multiple myeloma, chronic lymphoblastic leukaemia) are usually treated with normal immunoglobulin (human, intravenous) (see below). However, in some cases, NIGH is given by intramuscular injection. The intramuscular dose of NIGH is 0.6-0.9 mL/kg every 2-4 weeks. The intention is to maintain serum IgG levels above 4.0 g/L.

Duration of effect

The duration of effect of immunoglobulins is dose related. It is estimated that protection will be maintained for 3-4 weeks with standard doses of normal immunoglobulin.

Skin testing with immunoglobulin

Skin tests with normal immunoglobulin (human) 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 human immunoglobulin given in the prescribed intramuscular manner are extremely rare.

Adverse events and precautions

Local tenderness and muscle stiffness at the site of injection sometimes occurs and may persist for several hours after injection.

Systemic adverse events such as urticaria and angio-oedema may occur. Sometimes the recipient may develop erythema or low grade fever.

Anaphylactic reactions following an injection of human immunoglobulin are rare, but have been reported. Anaphylaxis is more likely to occur if normal immunoglobulin is inadvertently given intravenously. In highly allergic individuals, repeated injections may lead to anaphylactic shock.

Contraindications

Hypersensitivity reactions occur rarely but may be more common in patients receiving repeated injections. NIGH should not be given to individuals with selective IgA deficiency.

Normal Immunoglobulin (Human) (NIGH)–IV (intravenous) use

Normal Immunoglobulin (human, intravenous) is usually abbreviated as NIGH (intravenous). Two NIGH (intravenous) products are registered in Australia:

- Intragam – CSL Ltd is a 6% solution of immunoglobulin G (IgG) prepared by CSL Ltd from Australian blood donations and made available through the Australian Red Cross Blood Service. It contains negligible amounts of IgM and IgA. It is supplied as 3g in 50mL and 12g in 200mL bottle (for intravenous use).
- Sandoglobulin – Novartis is human immunoglobulin (at least 90% 1gG) for intravenous use derived from overseas pooled voluntary donations of venous plasma from sources acceptable to the TGA. It is supplied as a preservative-free lyophilised powder for reconstitution as 3g (with sucrose 5g) and 6g (with sucrose 10g) vials.

Dosage and administration

The infusion should be commenced slowly and the rate gradually increased.

Patients should be closely observed for the duration of the infusion. The patient's pulse, blood pressure and respiration rate are recorded at 15 minute intervals and the temperature every hour. All of these observations should also be made and recorded prior to the commencement of the infusion.

The dose for replacement therapy in immune deficiency is 0.4 to 0.6 g/kg every 3-4 weeks. In Kawasaki disease, a single dose of 2g/kg, given over at least 6 to 8 hours is recommended, repeated once if fever fails to resolve within 48 hours.

Recommendations

- antibody deficiency

NIGH (intravenous) is indicated for patients with antibody deficiency syndromes requiring large monthly doses of immunoglobulin. NIGH (intravenous) produces higher serum levels of IgG than the standard (intramuscular) preparation.

- Kawasaki disease

In clinical studies, NIGH (intravenous) has been found to be effective in the acute phase of Kawasaki disease, as it reduces the risk of coronary artery involvement.

- other

NIGH (intravenous) has been used in the management of immune thrombocytopenia, Guillain-Barré syndrome, chronic inflammatory demyelinating polyneuropathy, post-transfusional purpura, and in patients with bacterial infections associated with secondary immunodeficiency.

(Note: Some recommendations in this section are not included in the current registered indications for either Intragam or Sandoglobulin).

Adverse events and precautions

Adverse events consist of shivering, chest and back pains and moderate pyrexia. Severe headache attributed to aseptic meningitis has also been observed with IV NIGH. This can be ameliorated by slowing the infusion or by mixing the 6% preparation with four volumes of normal saline prior to administration. There have been isolated reports of renal dysfunction and acute renal failure following the administration of intravenous immunoglobulin. To date, anaphylactic shock has not been experienced with NIGH (intravenous). Subjects with IgA deficiency have an increased risk of severe adverse events following NIGH (intravenous).

Contraindications

Individuals who are known to have had an anaphylactic or severe systemic response to normal human immunoglobulin. Individuals with the selective IgA deficiencies should not receive Sandoglobulin or any immune globulin preparation.

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3.10 INFLUENZA

Virology

Influenza is an orthomyxovirus, classified as type A, B or C, based on antigenic characteristics of the nucleoproteins and matrix proteins. Influenza A and B are clinically important in humans. Influenza A is further subtyped on the basis of surface haemagglutinin (H) and neuraminidase (N) antigens. Influenza A is capable of major antigenic shifts, which can result in pandemics. Minor antigenic drifts are more common, and can result in epidemics.

Clinical features

Influenza viruses cause major epidemics of respiratory disease. Influenza is characterised by abrupt onset of fever, myalgia, headache, sore throat and acute cough, and can cause extreme malaise lasting several days.

Primary viral pneumonia occurs rarely, but secondary bacterial pneumonia frequently complicates influenza in individuals 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.

Epidemiology

In most years, minor or major epidemics of type A or type B influenza occur. Epidemics usually occur during the winter months. During

epidemics, there is a rise in mortality among the elderly and people with chronic diseases, with increased morbidity and hospitalisation for pneumonia and exacerbation of chronic diseases. Every 10-30 years, new subtypes of influenza A emerge and cause pandemics in which a quarter or more of the population may be affected over a short period.

Vaccines

- Fluvax - CSL (inactivated influenza vaccine. 0.5 mL pre-filled syringe).
- Vaxigrip - CSL/Pasteur Merieux (inactivated influenza vaccine. 0.5 mL pre-filled syringe).
- Fluarix – SmithKline Beecham (inactivated influenza vaccine. 0.5 mL pre-filled syringe).
- Fluvirin – Medeva/Ebos Health & Science (inactivated influenza vaccine. 0.5 mL pre-filled syringe).

The influenza vaccines available in Australia are split virion or purified antigen vaccines prepared from virus which has been grown in the allantoic cavity of embryonated eggs, purified by zonal centrifugation, disrupted by a detergent or solvent-detergent process and inactivated with beta-propiolactone (Fluvax and Fluvirin) or formaldehyde (Vaxigrip and Fluarix). The final product contains 15mg of the surface haemagglutinins of each of the component strains recommended annually by the Australian Influenza Vaccine Committee. Each of the vaccines contains thiomersal 0.01% w/v as a preservative.

The formulation of influenza vaccine is reviewed annually so that changes in the composition can be made to adjust to antigenic shifts and antigenic drift. The effectiveness of influenza vaccine 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 in circulation. When the antigenic match between vaccine and circulating viruses is close, influenza vaccine is 70%-90% effective in healthy persons younger than age 65 years. Among elderly persons living outside nursing homes or similar chronic-care facilities, influenza vaccine is 30%-70% effective in preventing all hospitalisation for pneumonia and influenza. Among elderly persons residing in nursing homes, influenza vaccine is most effective in preventing severe illness, secondary complications, and deaths. In this population, the vaccine can be 50%-60% effective in preventing hospitalisation or pneumonia and 80% effective in preventing death, even though the effectiveness in preventing influenza illness may be lower. Currently available influenza vaccines confer protection for about a year. Low levels of protection may persist

for a further year, if the prevalent strain remains the same or undergoes only minor antigenic drift. To provide continuing protection, annual vaccination with vaccine containing the most recent strains is necessary.

Transport, storage and handling

Transport in an insulated container with approved freeze and time-temperature monitor. Do not freeze or store vaccine in direct contact with ice packs. If vaccine has been exposed to temperature less than 0ºC, do not use. Store in refrigerator at 2ºC to 8ºC. Check expiry date on vial or container before storage. Rotate stock so that shortest date vaccines are used first. At the end of each year, vaccine should be appropriately discarded to avoid inadvertently using a product with incorrect formulation for the following year.

Dosage and administration

Shake the vial vigorously before withdrawing dose and inject vaccine as soon as possible. Influenza vaccine is administered by a deep subcutaneous injection in the deltoid muscle for adults and children and the anterolateral aspect of the thigh for infants.

Table 3.10.1 Recommended doses of influenza vaccine

Age	Dose	Number of doses
6 months - 2 years	0.125mL	1 or 2*
2- 6 years	0.25mL	1 or 2*
6 - 9 years	0.5mL	1 or 2*
>9 years	0.5mL	1

*Two doses at least one month apart are recommended for children aged under 9 years who are receiving influenza vaccine for the first time.

NB: the influenza vaccines available in Australia are not packed in syringes graduated for measurement of recommended paediatric doses. Options for measuring doses are to use a ruler or template to judge the needed volume. Excess vaccine is expelled from the syringe and the remaining volume injected. All of the product information documents have some differences from table 3.10.1. Fluvirin does not have a dose recommendation below 4 years of age. The dosage recommendations for Fluvax and Vaxigrip start at 3 months of age. Recommended upper age limits for a second dose vary.

Timing

Vaccination is best undertaken in autumn, in anticipation of winter outbreaks of influenza. However, vaccination can be given as early as February. In autumn the opportunities to provide influenza vaccination

to persons at increased risk should not be missed when they present for routine care. Vaccination can still be offered to adults and children even after influenza virus activity is documented in a community, as protection is achieved within days.

Influenza vaccine can be administered concurrently with other vaccines, including pneumococcal vaccine and all the scheduled childhood vaccines.

The administration of inactivated influenza vaccine to individuals at risk of complications of infection is the single most important measure in preventing or attenuating influenza infection and preventing mortality during epidemics. After vaccination, nearly all vaccinated adults develop antibody titres that are likely to protect them against the strains of virus represented in the vaccine. In addition, the individual is protected against many related variants. Infants, the very elderly, and patients with impaired immunity may develop lower post-vaccination antibody titres. Under these circumstances, influenza vaccine may be more effective in preventing lower respiratory tract involvement or other complications of influenza than in preventing infection.

Recommendations

1. General

Influenza vaccine should be given routinely on an annual basis to individuals 65 years of age and older. The vaccine is funded by the Commonwealth Government for this age group. The risk to the elderly is greatest if they also have chronic cardiac or lung disease, and is increased for residents of nursing homes and other chronic care facilities. Annual influenza vaccination is recommended for Aboriginal and Torres Strait Island adults aged 50 years and above, because of the greatly increased risk of premature death from respiratory disease.

Doctors should administer influenza vaccine to any person who wishes to reduce the likelihood of becoming ill with influenza. Vaccine can be administered to children as young as 6 months, however there is an increased risk of minor adverse events in children under 5 years of age. Persons who provide essential community services should be considered for vaccination to minimise disruption of essential activities during influenza outbreaks.

2. Individuals who are at increased risk of influenza-related complications

Annual vaccination is recommended for these groups:

- All adults aged 65 years and over.
- All Aboriginal and Torres Strait Island adults ≥50 years.
- Adults and children (≥6 months old) with chronic disorders of the pulmonary or circulatory systems. This includes children with congenital heart disease and cystic fibrosis. Influenza vaccine is not routinely recommended for persons with asthma, as there is insufficient randomised controlled trial evidence that annual immunisation is beneficial at the population level. However, annual influenza immunisation is recommended for severe asthmatics, such as those requiring frequent hospitalisations.
- Adults and children (≥6 months) with other chronic illness requiring regular medical follow-up or hospitalisation in the preceding year. This includes diabetes mellitus (and other chronic metabolic diseases), renal dysfunction, haemoglobinopathies, or immunosuppression (including immunosuppression caused by medication).
- Residents of nursing homes and other longterm care facilities.
- Children and teenagers (6 months to 18 years) on longterm aspirin therapy who therefore may be at risk of developing Reye syndrome after influenza.

3. Those who can transmit influenza to persons at increased risk

Annual vaccination is recommended for health care providers, staff of nursing homes and longterm care facilities, providers of home care to persons at high risk (eg. nurses, volunteer workers), household members (including children ≥6 months old) of persons in increased-risk groups.

4. Use of influenza vaccine in other groups

Workplace

Mass vaccination of individuals in particular industries or worksites cannot usually be justified on public health grounds. However, the cost effectiveness of influenza vaccination in industry varies from year to year, depending on the intensity of the epidemics.

Pregnant women

Influenza vaccine is safe for pregnant women. Pregnant women who fall into one of the above risk categories should be vaccinated. In addition, there is evidence from a number of studies that pregnant women, particularly during the second and third trimester, are at increased risk of influenza-associated complications. The US Centers for Disease

Control estimates that an average of 1-2 hospitalisations among pregnant women could be prevented for every 1,000 pregnant women immunised. It is therefore recommended that all women who will be in the second or third trimester of pregnancy during the influenza season be vaccinated **in advance**, so that they will be protected during that period.

Persons infected with HIV

Persons infected with HIV may develop serious illness and be at increased risk of complications if infected with influenza. Whilst patients with advanced HIV disease and low CD4 T-lymphocyte counts may not develop protective antibody titres, there is evidence that for those with minimal symptoms and high CD4 T-lymphocyte counts protective antibody titres are obtained after influenza vaccination. For these reasons influenza vaccination is recommended for HIV infected persons.

Travellers

The risk of influenza is elevated in travellers in large tourist groups. Such groups often consist of a high proportion of elderly persons as well as people from other parts of the world where influenza is circulating. Due to the short incubation period, exposure to influenza may result in illness whilst travelling. Any person in one of the risk groups in Table 3.10.2 should be vaccinated prior to travel. In addition, any person wishing to reduce the chance of becoming infected with influenza, particularly those in large tourist groups or travelling to the Northern Hemisphere from October to March, should consider influenza vaccination prior to departure.

Persons who are vaccinated with the previous season's vaccine before travel should be revaccinated in the autumn with the current vaccine.

Pandemics

At the time of a pandemic, the priority groups and the timing of vaccination may be quite different from those during inter-pandemic periods. In addition, the number of vaccine doses required to confer protection and the optimal time for vaccination may differ. The Australian Influenza Pandemic Planning Committee is developing guidelines for vaccine use and will advise health authorities regarding priority groups, dosing schedules and timing of vaccination should a pandemic occur.

Adverse events and precautions

- Soreness at the vaccination site.
- Fever, malaise, and myalgia occur infrequently. These adverse events may commence within a few hours of vaccination and may last for 1 to 2 days. In children under the age of 5 years these adverse events may be more pronounced. Symptoms post-vaccination may mimic influenza infection, but the current influenza vaccine does not contain live virus and cannot cause influenza.
- Immediate adverse events (such as hives, angio-oedema, asthma, or systemic anaphylaxis) are a rare consequence of influenza vaccination. They probably represent an allergic response to a residual component of the manufacturing process, most likely egg protein. Persons with a history of anaphylaxis after eating eggs or a history of allergic response following occupational exposure to egg protein should not be given influenza vaccine.
- Evidence from the US indicates that Guillain-Barré syndrome (GBS) is rarely associated with influenza vaccination although a causal relationship has not been established. Even with an estimated excess risk of 1 to 2 cases per million persons vaccinated, this risk is still substantially smaller than the risk of severe influenza illness and its complications.

Contraindications

- Individuals with anaphylactic hypersensitivity to eggs should not be given influenza vaccine. This includes persons who, on ingestion of eggs, develop swelling of the lips or tongue or experience acute respiratory distress or collapse.
- Individuals with hypersensitivity to any of the product components should not be vaccinated.
- Individuals with an acute febrile illness (fever >38.5 0C) should not be vaccinated until their symptoms have abated. However, minor illness with or without fever should not contraindicate the use of influenza vaccine.
- Patients with a history of Guillain-Barre Syndrome (GBS) with an onset related in time to influenza vaccination may be at increased risk of again developing GBS if given influenza vaccine. The risk should be weighed against the benefits to the individual patient of influenza vaccination. Because patients with a history of GBS have an increased likelihood of again developing the syndrome, the chance of them coincidentally developing the syndrome following influenza

vaccination may be higher than in individuals with no history of GBS.

Conflict with product information

The product information states that influenza vaccine confers protection for 6-12 months. The literature suggests that protection is for 12 months or more. The product information lists allergy to chicken feathers and some food proteins as a contraindication.

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3.11 JAPANESE ENCEPHALITIS

Virology

Japanese encephalitis (JE) is caused by a mosquito-borne flavivirus.

Clinical features

The disease is an acute neurological syndrome characterised by headache, fever, convulsions, focal neurological signs, depressed level of consciousness and coma. It has a high case-fatality rate and there is a high prevalence of neurological sequelae in those who survive the acute illness. It is recognised, however, that most infections are asymptomatic;

published estimates of the symptomatic to asymptomatic infection ratio vary from 1:25 to 1:300.

Epidemiology

JE is a significant public health problem in many parts of Asia including the Indian subcontinent, Southeast Asia and China. In recent years however the disease has extended beyond it's traditionally recognised boundaries with, for example, an outbreak occurring in the Torres Strait, north Australia, in 1995.

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 so-called 'amplifying' hosts but not within other large vertebrates such as horses and man. Indeed, man is 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.

There are two recognised epidemiological patterns of JE. In the temperate or subtropical regions of Asia (northern Thailand, northern Vietnam, Korea, Japan, Taiwan, China, Nepal and northern India) the disease occurs in epidemics during the summer or wet season months. In the tropical regions (most of Southeast Asia, Sri Lanka, southern India) the disease is endemic, occurring throughout the year.

In some countries (Japan, the Republic of Korea, some provinces of China) the incidence of JE has declined considerably in recent decades, and it has been eradicated from Singapore. Vaccination, changes in pig husbandry, a reduction in land utilised for rice farming and improved socioeconomic circumstances have all contributed to these changes. However elsewhere in Asia there are an estimated 50,000 cases with 10,000 deaths annually.

In early 1995 three cases of JE, two of them fatal, occurred on Badu island in the Torres Strait. Subsequent serological surveys showed that JE virus activity was widespread in many other remote 'outer' islands of the Torres Strait (Figure 3.11.1) at or about that time. The 1995 outbreak is the first known incursion of JE into Australia.

Surveillance using sentinel pigs showed further incursions of JE, on the island of Saibai, in the Torres Strait in the wet season of 1996 and again in 1997. The surveillance did not detect JE virus activity in any other outer islands in these years.

In early 1998, however, a further case of JE occurred in an unvaccinated

3.11.1 Map of outer islands of the Torres Strait

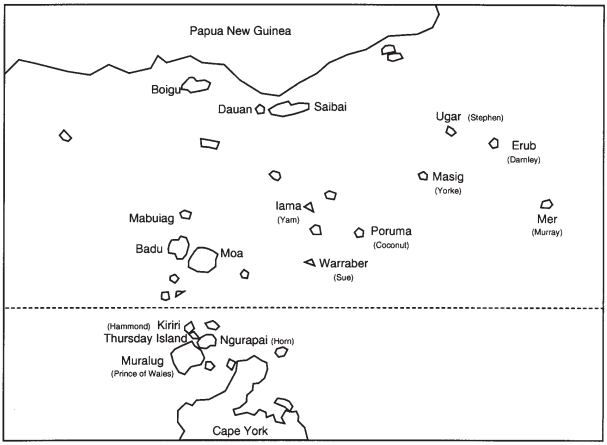

Figure 1. The Torres Strait. The outer islands are north of the arbitrary dotted line.

Badu island resident, and the first ever mainland case of JE occurred in a person working on the west coast of Cape York, nearly 300 km south of Weipa. Furthermore, the sentinel at the northern-most tip of Cape York showed, for the first time, clear evidence of JE virus activity. There have therefore been, to date, five cases of JE acquired in Australia.

Vaccine

- JE-VAX - Japanese encephalitis vaccine inactivated - CSL/Biken (formalin inactivated Japanese encephalitis virus + thiomersal 0.007%; each 1.0mL dose contains gelatin approx. 500µg, formaldehyde <100µg, and mouse brain serum protein <50ng).

JE vaccine is an inactivated mouse brain-derived vaccine manufactured in Japan. It is prepared by inoculating mice intracerebrally with Nakayama strain JE virus; the harvested virus is then inactivated with formaldehyde and purified by ultra-centrifugation. No myelin basic protein can be detected at the threshold of the assay (<2ng/mL).

A clinical trial in Thailand in the early 1980's determined that two doses of the inactivated mouse brain-derived vaccine, administered to children seven days apart, had a protective efficacy of 91%. However, immunogenicity studies have demonstrated that three doses of the vaccine are required to ensure adequate immunity in vaccinees from JE non-endemic areas.

Transport, storage and handling

Un-constituted (lyophilised or freeze-dried) vaccine should be transported in an insulated container with approved freeze monitor, and time-temperature monitor. Do not freeze Japanese encephalitis vaccine or store vaccine in direct contact with ice packs. If vaccine has been exposed to temperature less than 0ºC, do not use.

Store vaccine and diluent in refrigerator at 2ºC to 8ºC. Do not freeze diluent. Check expiry date on vial or container before storage. Rotate stock so that shortest date vaccines are used first. Reconstituted vaccine should be stored at between 2ºC to 8ºC and used within 8 hours. Any unused vaccine should be discarded at the end of a session.

Dosage and administration

The volume injected is 0.5 mL for 1 – 3 year old children and 1.0 mL for all those including adults over 3 years of age. For those people from non-endemic regions including Australia, a 3 dose regime (ie days 0, 7 and 28) over a month is required. A single booster doses are required at 3 yearly intervals. The dose is given by subcutaneous injection.

Recommendations

a) Travellers

Although the risk of travellers in Asia acquiring JE is extremely low, there have been instances of even short-term travellers developing the disease. Therefore all travellers to Asia (and other tropical regions) must be fully aware of the need to take appropriate measures to avoid mosquito bites.

The risk of JE to travellers to Asia is determined by the season of travel, the regions visited, the duration of travel, the extent of outdoors activity and the extent to which mosquito-avoidance measures are taken. Clearly the risk is greater during prolonged travel to rural areas of Asia during the wet season; it is probably negligible during short business trips to urban areas.

Therefore JE vaccination is recommended for

(i) travellers spending one month or more in rural areas of Asia, particularly if the travel is during the wet season, and/or there is considerable outdoor activity and/or the standard of accommodation is suboptimal, and

(ii) for all other travellers spending a year or more in Asia (except for Singapore), even if much of the stay is in urban areas.

NB: With the exceptions of Bali, Singapore, Hong Kong and Japan, rabies is endemic throughout Asia. Bearing in mind these exceptions, travellers eligible for JE vaccine are almost certainly also eligible for (pre-exposure) rabies vaccine. Because neither vaccine is a live vaccine, and because the same regimen is used for both vaccines (days 0, 7 and 28), they should be given at the same time but in different limbs.

b) Residents of Far North Queensland

There have been incursions of JE virus into the outer islands of the Torres Strait (see figure 3.11.1) every wet season (December-May) since first being recognised since 1995. From the dates of onset of symptoms of the four JE cases in the Torres Strait, and from a review of the sentinel pig surveillance information, it is clear that the period of risk is greatest from February–March and probably negligible during the dry season (June to November inclusive).

A large JE vaccination campaign took place in the outer islands in late 1995/early 1996. Since then JE vaccination has been integrated into the routine vaccination schedule for children resident on the outer islands, with the first dose being given simultaneously with MMR at 12 months of age. A booster JE campaign took place in the outer islands in late 1998, three years after the initial campaign.

JE vaccination is currently recommended for

(i) all residents (over one year of age) of the outer islands in the Torres Strait, and

(ii) all 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).

NB. The period of greatest risk is from February to March and the vaccination course should be completed before February. Those arriving in the outer islands late in the wet season (ie. in May) have arrived 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 only visiting the inner islands, including Thursday Island) do not need the vaccine.

Extensive serological surveys undertaken in 1998 showed no evidence of JE transmission to residents of communities either on the west coast or the northern-most tip of Cape York and there has not been any evidence of on-going transmission. At this time there is **no** recommendation to administer JE vaccine to either residents of, or visitors to, Cape York.

c) Laboratory personnel

Laboratory-acquired JE has occurred, principally in research settings where concentrated virus preparations were being handled. JE vaccination is recommended for all research laboratory personnel who potentially might be exposed to the virus.

Adverse events and precautions

Local reactions and minor systemic reactions are common following vaccination against JE. About 20% experience tenderness, redness and/or swelling at the injection site, and 10% experience systemic reactions such as fever, headache, being 'off-colour', chills, dizziness, aching muscles, nausea and/or vomiting.

Hypersensitivity (allergic) reactions occur in about 0.5% (ie. 1 in 200) vaccinees. These adverse events include urticaria that is often widely distributed over the body, angioedema of the limbs, face and throat and generalised pruritis (sometimes without a rash). In the early 1990's, apparently severe allergic reactions to the inactivated mouse brain-derived JE vaccine were reported from several industrialised countries, including Australia. In a few cases, upper airway swelling with respiratory distress and hypotension occurred; some had to be hospitalised.

An important feature of the hypersensitivity reactions to JE vaccine is they may be delayed for several days, in some cases up to 10 days, after vaccine administration. The risk of these delayed adverse events seems to be increased after the first and second doses, and they appear to be more likely to occur in those with a history of allergic reactions, especially urticaria. Although the pathogenesis of the more severe hypersensitivity reactions remains uncertain, there is some evidence that gelatin, added to stabilise the vaccine, may be the provoking agent. Vaccinees should remain within ready access to medical care for 10 days following vaccination.

In recent years, several cases of acute encephalomyelitis temporally linked to the administration of the inactivated mouse brain-derived JE vaccine have been reported. Three such cases, two fatal, have recently been reported from the Republic of Korea; their cause remains unknown.

The inactivated mouse brain-derived JE vaccine is contraindicated in those less than one year of age, and those who have had a significant allergic reaction, such as generalised urticaria, to a previous dose. A past history of 'allergy' to bee stings, medications, foods etc. must be seriously considered and may also be a contraindication to vaccination.

There are few data on the safety and efficacy of JE vaccine in immunocompromised people. A small study undertaken in Thailand has documented that HIV-infected infants respond less well to two doses of JE vaccine than do non-infected infants; the response to further doses was not studied.

Use in pregnancy

Although JE vaccine might pose a theoretical risk to the developing fetus, no adverse outcomes of pregnancy have ever been attributed to vaccination against JE. Because JE virus infection during the first and second trimester is also associated with miscarriage, only pregnant women at risk of acquiring JE should be offered JE vaccine.

Conflict with product information

The product information states that definite recommendations cannot be given on the timing of booster doses and that a booster dose…may be given after two years. However, although the data are limited, they do suggest that neutralising antibody persists for at least three years following a three-dose primary series.

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3.12 MEASLES

Virology

Measles is a paramyxovirus, genus Morbillivirus. It is an RNA virus with six structural proteins, three complexed to the RNA 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. Measles virus has a short survival time (<2 hours) in air, and is rapidly inactivated by heat, light and acidic pH.

Clinical features

Measles is a highly infectious, acute viral illness. The infection is spread by respiratory droplets. The incubation period is 10-14 days. The prodrome, lasting 2-4 days, is characterised by fever, followed by cough, coryza and conjunctivitis. The rash follows, typically beginning on the face and upper neck, and then becoming generalised. Measles is often a severe disease, frequently complicated by otitis media (2.5%) and bronchopneumonia (4%). Acute encephalitis occurs in 2-10/10,000 reported cases. Measles encephalitis has a mortality of 10-15%, and 15-40% of survivors of this complication have permanent brain damage. Subacute sclerosing panencephalitis (SSPE) is a late complication of measles in about 1/25,000 cases. SSPE causes progressive brain damage and is always fatal. Complications from measles are more common and more severe in chronically ill and very young children. This is particularly true in developing countries. Measles is highly infectious from the beginning of the prodromal (3–5 days before the rash appears) period for as many as 4 days after the appearance of the rash.

Epidemiology

In the 19 years from 1976 to 1995, measles caused more deaths in Australia (98) than diphtheria (4), tetanus (52), pertussis (21), and poliomyelitis (4) combined. Although vaccination rates have improved, the uptake of measles vaccine in Australia has not yet reached optimal levels. In 1999, the Australian Childhood Immunisation Register recorded that 88% of children aged 2 years had been vaccinated for measles, but this is considered to be an underestimate of vaccine coverage. Following the Measles Control Campaign (which resulted in 1.7 million primary school children being vaccinated),a national serosurvey in the first quarter of 1999 showed that 89% of children aged 2-6 years, 94% of those aged 6-11 years and 91% of those aged 12-18 years, were immune to measles.

The effectiveness of measles vaccine has been established in the United States. In 1963, before the vaccine was registered, there were 400,000 cases reported each year. In 1994 the countries of the WHO Region of the Americas established the goal of eliminating measles in the Region by the year 2000. However, in 1997 there was a resurgence, especially in Brazil (20 000 confirmed cases). In the USA there were only 138 confirmed cases in 1997, and there is continued progress towards elimination in the Region.

The Eastern Mediterranean Region has established a goal for measles elimination by 2010, and the European Regional Office is also planning elimination.

Measles remains a major cause of morbidity and mortality in the South-East Asian Region, where there are plans for strengthened control by the year 2003.

Vaccines

Two MMR vaccines are available in Australia. Monovalent vaccines are available for rubella, but no longer for measles or mumps. Vaccination with MMR results in sero-conversion to all 3 viruses in over 95% of recipients. Following a second dose of MMR vaccine, approximately 99% of subjects will be immune to measles. Since the MMR vaccine viruses are not transmissible, there is no risk of infection from vaccinees.

MMR vaccines

- MMR II - CSL/Merck, Sharp and Dohme. Live attenuated measles virus (Edmonston strain), mumps virus (Jeryl Lynn strain), and rubella virus (Wistar RA 27/3 strain), lyophilised + 25µg neomycin per 0.5 mL dose, and a small amount of porcine gelatin as stabiliser.
- Priorix - Smith Kline Beecham. Live attenuated measles virus (Schwarz strain), RIT 4385 strain of mumps virus (derived from the Jeryl Lynn strain) and the Wistar RA 27/3 rubella virus strain, lyophilised + lactose, neomycin sulphate, albumin and sorbitol and mannitol as stabilisers.

Transport, storage and handling

Measles-mumps-rubella (MMR) vaccine is a freeze-dried preparation containing live attenuated measles, mumps and rubella viruses. It must be stored in the dry state at 2ºC to 8ºC or colder and protected from light. The freeze-dried (lyophilised) form of the vaccine can be stored frozen, but the vaccine must not be frozen after it has been reconstituted with diluent.

Transport un-constituted vaccine (freeze-dried or lyophilised) in insulated container with approved time-temperature monitor which is capable of indicating exposures to temperatures greater than 10ºC over a 2 week period (eg. Monitor Mark ™ 3M, 10N/34AA). Observe national guidelines for packing vaccines in insulated containers. Maintain temperature at 2ºC to 8ºC or colder. Protect from light. If transported with ice, diluent must be transported separately. Diluent can be stored at room temperature (15-30ºC) but do not freeze. If time-temperature

monitor indicates vaccine has been exposed to temperature above 10ºC do not use. Store un-constituted vaccine in refrigerator at 2ºC to 8ºC or colder on arrival at storage site. Store vaccine separately to diluent and protect from light since exposure to light may inactivate vaccine. Check date on vial or container for shelf-life (check diluent and vaccine). Rotate stock so that short-dated stock is used first.

The lyophilised vaccine should be reconstituted with the diluent supplied by the manufacturer and should be used within 1 hour after reconstitution, provided it has been kept cool and protected from sunlight. Reconstituted measles vaccine is very unstable and quickly loses potency at room temperature after reconstitution. At 22-25ºC it loses 50% of potency in 1 hour; at temperatures over 37ºC it is completely inactivated after 1 hour. The reconstituted vaccine can be stored in the plastic syringe in a dark place between 2ºC to 8^0C without loss of potency and must be discarded if not used within 8 hours.

Dosage and administration

A single dose of 0.5 mL is given by intramuscular or deep subcutaneous injection.

Recommendations

Two doses of MMR are required. The doses should be given one month or more apart. MMR vaccine is recommended for all children at 12 months of age and at 4 years of age, unless there is a genuine contraindication. It is also recommended for pre-school and school age children who have not previously received it. A second dose of MMR vaccine is recommended for children over 5 years of age who have only had one dose of MMR vaccine. Adults born since 1970 should also have evidence of having received two doses of MMR.

MMR vaccine should be given to all susceptible persons (refer below) who are older than 12 months of age. There are no ill effects from vaccinating those with pre-existing immunity to one or more of the three diseases. The two available vaccines are interchangeable.

Transmissibility of MMR vaccine viruses

MMR vaccine viruses are not transmitted to contacts. It is, therefore, safe to vaccinate the healthy siblings of immunocompromised children and safe for immunocompromised children to go to school with children recently vaccinated with the MMR vaccine.

Infants and children at high risk of measles infection

Unvaccinated children in the following groups are at particular risk from severe measles infection:

- children with chronic conditions such as cystic fibrosis, congenital heart or kidney disease, failure to thrive, Down's syndrome;
- children from the age of 1 year upwards in child care centres, family day care, and playgroups;
- children living in institutions;
- Aboriginal and Torres Strait Island children.
- HIV-positive individuals, unless severely immunocompromised, may be given MMR vaccine in the absence of other contraindications (see Part 1.7, page 33).

Definition of a person who is susceptible to measles

A susceptible person (to measles) is someone who can not provide acceptable presumptive evidence of immunity to measles.

A person can be considered to have acceptable presumptive evidence of immunity to measles if they meet one of the following criteria:

- children aged 1-4 years who have documented evidence of having received one dose of a measles containing vaccine; or
- persons over 4 years of age and born after 1970 (unless serosurveillance data shows otherwise) who have documented evidence of receiving two doses of a measles-containing vaccine; or
- persons born before 1970 (unless serosurveillance data shows otherwise); or
- documented evidence of immunity; or
- documented evidence of confirmed measles.

Delayed MMR vaccination

MMR vaccine can be given to children of any age greater than 12 months, and no opportunity should be missed to ensure that this is done. If the primary vaccinations have not been completed at the time that MMR vaccine is due, they can be given at the same time, using separate syringes and different sites. Similarly, if children who attend for pre-school vaccination (diphtheria, tetanus and polio) have not received MMR vaccine, it should be given then. Two doses are required.

MMR vaccine should be given to all non-immune adults, provided there are no contraindications.

Adolescents and young adults who have received only one dose of the MMR vaccine should be given a second dose unless they have serologic evidence of immunity to all three components. This is especially important for health and child care workers.

Children with a history of convulsions

Children with a personal or close family history of convulsions should be given MMR vaccine, provided the parents understand that there may be a febrile response 5-12 days after vaccination. Advice for reducing fever with paracetamol and other measures should be given. Doctors should seek specialist paediatric advice rather than refuse to provide MMR vaccination.

Vaccination of contacts

As vaccine-induced measles antibody develops more rapidly than that following natural infection, MMR vaccine can be used to protect susceptible contacts. To be effective, the vaccine must be administered within 72 hours of exposure. If there is doubt about a person's immunity, vaccine should be given since there are no ill effects from vaccinating individuals who are already immune.

Immunoglobulin is available for contacts for whom vaccine is contraindicated (see below) and for infants aged 6-9 months and susceptible persons who did not receive a MMR vaccination within 72 hours of contact (Table 3.12.1). Immunoglobulin needs to be given within 7 days of contact to be effective.

Children aged between 12 months and 4 years who have received one dose of MMR can be offered their second dose of MMR early if they are considered at risk of coming in contact with measles. This may apply during an outbreak or if a child is going to travel to a country that has a high incidence of measles. If a child receives the second dose early they are considered to have completed their MMR vaccination schedule and therefore, they do not require another dose at 4 years of age.

It must be noted that antibody responses to the rubella and mumps components of MMR vaccine are too slow for effective use of vaccine as prophylaxis after exposure to these infections.

Vaccination during an outbreak

During a measles outbreak, MMR vaccine may be given (on the direction of public health authorities) to infants aged between 9 and 12 months, and even to those aged between 6 and 9 months. In these cases, another

dose should be given at 12 months of age or one month after the first dose, whichever is the later. This should be followed by the standard dose of MMR at the 4th birthday.

MMR and tuberculin

Measles virus inhibits the response to tuberculin, so tuberculin-positive individuals may become tuberculin-negative for up to a month after measles infection or MMR vaccine. Mantoux testing is unreliable for at least 1 month after the administration of MMR. Because the measles virus may cause exacerbation of tuberculosis, patients with tuberculosis should be under treatment when vaccinated.

Adverse events and precautions

Hypersensitivity reactions occur rarely, are usually mild and consist of a wheal and flare reaction or urticaria at the injection site. Such reactions have been attributable to trace amounts of neomycin or gelatin, or some other component of the vaccine. Anaphylaxis is extremely rare. Malaise, fever and/or a rash may occur after MMR vaccination, most commonly about a week after vaccination and lasting about 2-3 days. In a study of over 6,000 children aged 1-2 years, the symptoms reported were similar in nature, frequency, time of onset and duration to those commonly reported after measles vaccination. In the period from 6-11 days after vaccination, febrile convulsions occurred in 0.1% of children, the same rate reported in this period after measles vaccine. The rate of vaccine-induced encephalitis is about 1 in 1 million doses. Parotid swelling occurred in about 1% of children up to 4 years, usually in the 3rd week and occasionally later.

Culture positive mumps meningo-encephalitis occurs at a rate of approximately 1 case per million distributed doses of vaccine that contain the Urabe strain of mumps vaccine, but the rate is lower in vaccines that contain the Jeryl-Lynn strain. Vaccines containing the Urabe strain are not available in Australia. The encephalitis is invariably mild or asymptomatic and resolves spontaneously. When mumps virus is isolated from the cerebro-spinal fluid in such cases, laboratory tests can distinguish between wild and vaccine strains. The assistance of State virology laboratories should be sought in such cases.

Thrombocytopenia, which is usually self-limiting, is occasionally associated with the rubella component of MMR. Other adverse events caused by rubella vaccine are described in Part 3.23, page 210.

In 1998 Wakefield and colleagues from the Royal Free Hospital in the United Kingdom postulated that measles, mumps and rubella (MMR)

vaccination might be causally linked with inflammatory bowel disease and autism. There has been no scientific evidence to support this claim and there is now good evidence to refute it.

During the Australian Measles Control Campaign in 1998, 1.7 million doses of MMR vaccine were used. There was a very low incidence of adverse events during the Campaign with only 7 reports of children with anaphylaxis/anaphylactoid reactions each of whom recovered fully following administration of adrenaline.

Parents should be told about possible symptoms, and given advice for reducing fever, including the use of paracetamol in the period 5-12 days after vaccination. They should also be reassured that these post-vaccination syndromes are not infectious.

As with all suspected adverse events following vaccines, severe adverse events following MMR vaccine should be reported as set out in Part 1.6, page 22.

Contraindications

- Persons with untreated malignant disease or altered immunity; those receiving immunosuppressive or X-ray therapy or high-dose steroids (equivalent to 2 mg/kg/day prednisolone). Note: it can given to HIV positive children (see Part 1.6, page 33)
- Persons who have had an anaphylactic reaction to neomycin or gelatin.
- Children who have an acute febrile illness when they present. Defer MMR vaccination until after the illness has resolved.
- If MMR vaccine is given to adult women, pregnancy should be avoided for 2 months, as for rubella vaccine.
- MMR vaccine should not be given within 3 months of an injection of immunoglobulin or a whole-blood transfusion.
- MMR vaccination should be deferred for at least 1 month following vaccination with another live vaccine (including BCG and live virus vaccines). The exception to this rule is OPV.

Oral polio vaccination is not a contraindication to MMR. MMR can be given at any time before, after or with OPV.

Egg allergy, even anaphylactic egg allergy, is NOT a contraindication to vaccination with measles vaccine or MMR. At the Royal Children's Hospital, Melbourne, Aicken et al administered MMR vaccine to 400 children who had a history of egg allergy and a positive skin prick test. Only 4 children had minor reactions and none had any adverse event

that required treatment. Children with egg allergy can safely be given MMR vaccine provided this is done under close supervision, with adrenaline ready for injection.

If there is genuine concern over possible egg allergy, a paediatrician should be consulted with a view to vaccination under closely supervised conditions such as hospital day case admission. Skin testing with small doses of vaccine has been shown to be of no value in management of these cases.

Use of immunoglobulin for prevention of measles

Normal immunoglobulin (human) should be considered for contacts of patients with confirmed or suspected measles. If immunoglobulin is administered within 7 days of exposure, it can prevent or modify measles in non-immune persons. It should be given to:

- infants between six and nine months of age if contact was within the last seven days;
- all persons aged nine months and over where administration of MMR vaccine would be contraindicated or where the person is assessed to be at risk;
- persons exposed to measles who are immunocompromised; and
- infants under six months of age where the infant's mother is the person infected;
- susceptible persons who did not receive a MMR vaccination within 72 hours of contact

If an unvaccinated child over 9 months old has contact with measles, measles infection can be prevented by immediate vaccination (within 72 hours) with MMR vaccine. The reason for this is that the incubation period of the vaccine strain (4-6 days) is shorter than the incubation period of wild measles virus (10-14 days). However, in children with compromised immunity, for whom MMR vaccine is contraindicated, normal human immunoglobulin (NIGH) should be given as soon as possible (within 7 days) after exposure.

Testing for measles antibody does not assist with the decision to use immunoglobulin since neither previous vaccination nor demonstrated low level serum antibody guarantees immunity to measles in immunocompromised individuals. Testing for measles antibody may delay the appropriate use of immunoglobulin. However, testing may be of value in making a definitive diagnosis of measles.

Infants 6-9 months of age who have direct contact with a person with

measles are at risk of developing complications from the disease, and should be offered NIGH within 7 days of contact. MMR vaccine should then be given as close as possible to 12 months of age, after an interval of at least 3 months following the administration of immunoglobulin. NIGH is not usually given to babies under 6 months old, who are protected by passive maternal antibodies (see Table 3.12.1). However, if the mother of an infant under the age of 6 months has measles, then the infant should be given immunoglobulin. The dose of NIGH is 0.2 mL/kg IMI for normal children and 0.5 mL/kg IMI for immunocompromised persons (the maximum dose is 15 mL).

Non-immune pregnant women who are exposed to measles can be given NIGH in a dose of 0.2 mL/Kg.

Table 3.12.1 Management of significant measles exposure

Age	Action
<6 months	Nil*
6-9 months	NIGH 0.2 ml/kg IMI
>9 months	MMR vaccine within 72 hours of exposure or NIGH if 3-7 days after exposure#
Immunocompromised	NIGH 0.5 ml/kg IMI

* If the mother is the contact, then the infant should be given immunoglobulin.

Immunoglobulin is not required if the person has received one or more measles containing vaccines or is assessed to be not susceptible.

Use in pregnancy

MMR is not recommended in pregnancy.

Conflict with product information

The PI states that MMR should not be given to children who have received another live vaccine (including BCG and live virus vaccines) within 4 weeks, and that MMR vaccination should be deferred for at least 1 month after the time of the previous vaccination. However, ATAGI recommends that MMR can safely be given with, or at any time before or after, oral polio vaccines.

The PI does not recommend administration of MMR with DTP, but ATAGI recommends that this is safe and both are recommended at 4 years of age. They can be given concomitantly at different sites.

The PI states that reconstituted vaccine can be used for up to 8 hours. ATAGI recommends that it be discarded after 1 hour, unless stored cold

(2-8ºc) and protected from sunlight. The maximum time it can be used after opening in this circumstance is 6-8 hours.

The PI for MMR II states that allergy to eggs is a contraindication to MMR, but it is established that MMR can be given safely in this situation.

The PI for MMR II also states that children vaccinated at 12 months or older do not require revaccination – the routine schedule recommends revaccination at 4 years of age after a first dose at 12 months.

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3.13 MENINGOCOCCAL INFECTIONS

Bacteriology

Meningococcal infections are caused by a Gram-negative coccus, *Neisseria meningitidis* ('meningococcus'), which differs from other *Neisseria*, in that it has a polysaccharide capsule. Meningococci are divided into 13 antigenically distinct serogroups (the most common are A, B, C, W135, and Y) on the basis of surface polysaccharides, and can be further subtyped on the basis of surface proteins. There is no consistent relationship between serogroup or type and virulence.

Clinical features

Meningococcus is a common cause of bacterial meningitis in Australia. The case fatality rate from invasive meningococcal disease is about 10%. *N. meningitidis* is also an important cause of overwhelming sepsis in otherwise healthy young people. Asymptomatic respiratory tract carriage of the organism is present in up to 20% of the population, and the prevalence may be higher when groups of people occupy small areas of living space. Persons with inherited disorders of phagocytosis associated with properdin deficiency or absence of the terminal components of complement, as well as individuals with functional or anatomical asplenia, have an increased risk of meningococcal infection.

Epidemiology

The organism is spread by droplets. The risk of nasopharyngeal colonisation, which precedes systemic spread, is increased by exposure to cigarette smoke and by a recent upper respiratory tract infection. While most cases are sporadic, localised clusters may occur within the members of a household, in child care centres, in adolescents and young adults attending high schools, universities, colleges or night clubs, and in military units. This is probably because of the spread within the group of a virulent clone of the organism. There is an annual winter peak of cases.

As in many other industrialised countries, the incidence of meningococcal disease, and the frequency of clusters and outbreaks, has been rising in Australia over the last decade. While this has resulted in large-scale emergency vaccination programs in New Zealand, Canada, Britain and the United States, the outbreaks have to date been of smaller magnitude in Australia.

In Australia, notification rates increased from less than 1/100,000 in 1986 to 1.9 in 1991 and 2.7 (499 notifications) in 1997. In 1997, 64% of the

invasive isolates were reported to be serogroup B and a further 32% serogroup C, including a relatively high proportion of virulent clones previously identified during heightened disease activity in New Zealand, Europe and Canada.

Epidemics due to serogroups A are periodically reported in the "meningitis belt" of sub-Saharan Africa.

Vaccines

- Mencevax ACWY - SmithKline Beecham (lyophilised purified polysaccharides from *N. meningitidis* serogroups A, C, W135, and Y; 50µg of each antigen in 0.5 mL + phenol 0.25% as a preservative). Available as a 0.5 mL monodose vial with separate saline diluent and as 10-dose vials in packs of 50, with saline diluent for each vial.
- Menomune - CSL/Pasteur Merieux (lyophilised purified polysaccharides from *N. meningitidis* serogroups A, C, W135, and Y; 50µg of each antigen in 0.5 mL + thiomersal 0.01% as a preservative). Available as a 0.5 mL monodose vial with separate saline diluent.

Serogroup C vaccine was first used in the late 1960s to prevent severe outbreaks in the US armed forces. The current tetravalent polysaccharide vaccines induce antibodies in 10-14 days in 90% of recipients over the age of 2 years. Immunity decreases markedly during the first 3 years following a single dose of vaccine, particularly in infants and young children. However, clinical protection persists for at least 3 years in school children and adults. A new generation of protein-conjugated polysaccharide vaccines will eventually provide more lasting protection from infection due to groups A and C. The problem of raising protective antibodies to group B meningococci, the polysaccharide of which is too weakly immunogenic to induce antibody formation, may be solved by vaccines directed against outer membrane proteins.

Special situations

Children less than 2 years of age - there is little response to serogroup C below 18 months of age and little response to serogroup A below 3 months of age.

Infections due to serogroup B - the quadrivalent vaccine does not protect against infections due to serogroup B, so there is no benefit in using the vaccine in individuals exposed to this serotype.

Transport, storage and handling

Transport vaccine and diluent in an insulated container with approved freeze monitor, and time-temperature monitor. Freeze dried vaccine in un-constituted form should be stored in the refrigerator between 2 – 8ºC. It can also be stored in freezer in its un-constituted form. Diluent should not be frozen and can be stored at room temperature. Check expiry date on vial or container before storage. Rotate stock so that shortest date vaccines are used first. Reconstituted vaccine can be stored in the refrigerator 2ºC to 8ºC, but must be discarded if not used within 8 hours. Protect from light and do not freeze. Once reconstituted, inspect for any foreign particulate matter and/or colouration prior to administration. Discard if there is discolouration or particulate matter.

Dosage and administration

The dose is 0.5 mL and should be administered by deep subcutaneous injection.

Recommendations

Routine vaccination is not recommended. The risk of meningococcal disease in Australia is relatively low, and most disease is due to serogroup B or occurs in children too young to be adequately protected by the current vaccine. Vaccination is recommended for the following:

- Australians who intend 'travelling' (ie. hitchhiking, backpacking, living in shared rural accommodation) in areas of the world where epidemics of group A or C disease are frequent. A current list of those countries is available from International Health Advisory Clinics/Services;
- control of outbreaks caused by serogroup A, C, W135 or Y (see below);
- persons over the age of 2 years with inherited defects of properdin or complement, or functional or anatomical asplenia;
- pilgrims attending the annual Hajj (Saudi Arabian authorities require a valid certificate of vaccination).

Revaccination may be indicated for persons at high risk of infection (eg. persons living in endemic areas, and those with immunodeficiencies defined above), particularly for children first vaccinated before 4 years of age.

As antibody levels decline rapidly over 2 to 3 years, revaccination may be considered within 3 to 5 years.

Adverse events and precautions

Adverse events such as local erythema and tenderness are mild and infrequent. Fever occurs in approximately 2% of young children, but significant general adverse events are rare.

Contraindications

The only absolute contraindication to the vaccine is a severe adverse event following phenol (if a phenol containing meningococcal vaccine is used) or following previous injections with meningococcal polysaccharide. A severe acute febrile illness is a relative contraindication, and vaccination should be postponed.

Use in pregnancy

Studies of vaccination with meningococcal and other polysaccharide vaccines during pregnancy have not documented adverse events in either pregnant women or newborns.

Management of outbreaks

It is vital that all cases of meningococcal disease are notified, so that outbreaks can be identified. Health care workers should be guided by State or Territory health authorities in the management of outbreaks. An outbreak of meningococcal disease in an institutional or community setting is a public health emergency needing a rapid response from clinicians and public health practitioners.

Close contacts of a case who have become colonised with a virulent strain may develop invasive meningococcal disease; the risk is greatest in the 1st week after contact but may persist for many months. Those at the greatest risk include household members and contacts in day care centres, who have presumably been exposed to the carrier who infected the index case in the 7 days preceding onset of illness in the case. Persons exposed to oral secretions (eg. by kissing or by mouth to mouth resuscitation) are also at risk. All those at risk should receive chemoprophylaxis.

The decision to control an outbreak with a vaccination program will depend on identifying a well-defined population at risk, and estimating the magnitude of ongoing risk. The NHMRC guidelines on the control of outbreaks of meningococcal disease have defined criteria for conducting such vaccination programs.

Prophylaxis is not recommended for health care workers unless they have been engaged in mouth to mouth resuscitation of an infected person.

Antibiotics which reduce or eliminate nasopharyngeal carriage of *N. meningitidis* include rifampicin, ceftriaxone and ciprofloxacin.

- Rifampicin is given to children and adults in an oral dose of 10 mg/kg (maximum dose of 600 mg) twice daily for 2 days. The recommended dose for infants less than 1 month of age is 5 mg/kg twice daily for 2 days. Pharyngeal carriage will be eliminated in 75-90% of recipients unless the strain is rifampicin resistant.

  The side-effects of rifampicin should be explained. Those that should be mentioned are: orange-red discolouration of contact lenses, urine and tears; gastro-intestinal upset; dizziness; drowsiness; headache; interference with the contraceptive pill (necessitating other means of contraception); and interference with the metabolism of many drugs including warfarin, chloramphenicol, phenobarbitone and phenytoin. Rifampicin is teratogenic in animals, but although there is no evidence of teratogenicity in humans, it is not recommended for use in pregnant women.

- Ceftriaxone is administered as a single intramuscular dose of 250 mg for adults and 125 mg for children less than 12 years of age. Although it is considerably more expensive, ceftriaxone has a number of advantages over rifampicin: it is more likely to eradicate pharyngeal carriage; it eliminates problems with compliance; it does not interact with concurrently administered drugs; and it is potentially safer in pregnancy.

- Ciprofloxacin in a single oral dose of 500 mg is effective and safe, but it should not be given to children under the age of 12 years, or to pregnant women.

It is important to note that, even after adequate chemoprophylaxis, household contacts of patients with *N. meningitidis* remain at increased risk for several months.

Conflict with product information

The PI for rifampicin states that the dose of rifampicin for meningococcal prophylaxis is 600mg daily for 4 days. ATAGI recommends up to a maximum of 600mg twice daily for 2 days.

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3.14 MUMPS

Virology

Mumps is a paramyxovirus with a single stranded RNA genome. It is rapidly inactivated by heat, formalin and ultraviolet light.

Clinical features

The incubation period is 12-25 days. It is characterised by bilateral, or occasionally unilateral, parotid swelling, but some infections are asymptomatic. About 15% of reported cases occur in adolescents and adults. Benign meningeal signs appear in up to 15% of cases, but permanent sequelae are rare. Nerve deafness is one of the most serious of the rare complications (1 in 500 hospitalised cases). Orchitis (usually unilateral) has been reported in up to 20% of clinical mumps cases in post-pubertal males, but subsequent sterility is rare. Symptomatic involvement of other glands and organs has been observed less frequently (pancreatitis, oophoritis, hepatitis, myocarditis, thyroiditis).

A few experimental, clinical and epidemiological studies indicate that permanent pancreatic damage may result from injury caused by direct viral invasion. However, further research is needed to determine whether mumps infection contributes to the overall incidence of diabetes mellitus. Patients are infectious from 6 days before parotid swelling to 9 days after.

Epidemiology

Mumps is reported world-wide, and is a human disease with transmission by the airborne route or direct contact. It is primarily a disease of children, with a peak incidence in the group aged 5-9 years. Eighty percent of adults in urban areas have serological evidence of immunity. A study of mumps in Alberta, Canada, confirmed the benign outcome in most cases, but indicated the potential of mumps vaccination for reducing hospital admissions for aseptic meningitis. Vaccination with the live attenuated vaccine has proved successful in the United States, with a 98% reduction in the number of reported cases between 1967 (when the vaccine was introduced) and 1985. In Australia, there have been 10 reported deaths from mumps between 1978 and 1997.

Vaccines

Monovalent mumps vaccine is no longer available in Australia. See information on MMR vaccine under "Measles".

Use of immunoglobulin for prevention of mumps

Immunoglobulin (NIGH) has not been shown to be of value in post-exposure prophylaxis for mumps.

Live mumps vaccine does not provide protection if given after an individual has been exposed to mumps. However, if the exposure did not result in infection, the vaccine would induce protection against subsequent infection.

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3.15 PERTUSSIS

Bacteriology

Pertussis is caused by *Bordetella pertussis*, a fastidious, Gram-negative, pleomorphic bacillus. There are other organisms (such as *Bordetella parapertusssis, Mycoplasma pneumoniae* and *Chlamydia pneumoniae*) which can cause a pertussis-like syndrome.

Clinical features

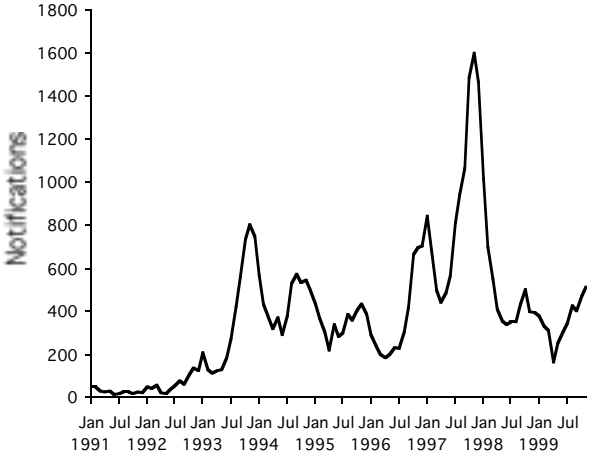
Pertussis (whooping cough) is an epidemic bacterial respiratory infection. *Bordetella pertussis* is highly infectious, spreading by respiratory droplets to 70-100% of household contacts. Most school-aged children with pertussis have the characteristic paroxysmal cough with inspiratory whoop. The cough may persist for up to 3 months and is often associated with vomiting. The illness often causes much family disruption and dysfunction. The overall mortality from pertussis is 0.3% but the mortality in babies under 6 months of age is higher (0.5%). Babies, particularly if preterm, may present with apnoea and little or no whoop or cough. Pertussis causes hypoxic encephalopathy, which can result in brain damage and death. The most common cause of death in pertussis infection is pertussis pneumonia, sometimes complicated by seizures and encephalopathy.

Epidemiology

Epidemics occur every 3 to 4 years. In unvaccinated populations, these outbreaks can be very large. In vaccinated populations, smaller outbreaks occur every 3-4 years, but with greatly reduced mortality and morbidity. During epidemics, most cases occur in school-aged children, who can in turn infect infant siblings, the group at highest risk. Maternal antibody does not give adequate protection against pertussis, so babies can be infected before they are old enough to be vaccinated. In recent years, many cases of pertussis have been recognised in adults and adolescents, and these individuals are thought to form a significant reservoir of infection.

Pertussis kills about 250,000 children worldwide each year. Many children are left with brain damage from pertussis infection. In 1993-1997 there was a large prolonged epidemic of pertussis in Australia, with more cases reported than for any time since the 1960s. Nine babies in Australia died from pertussis in 1996-97, and there have been 28 deaths from pertussis between 1978-1997.

Figure 3.15.1 Reported pertussis cases, Australia, 1992 to 1999



In this outbreak, nearly 50% of reported cases were in adults and in children over 9 years of age. This supports the need for booster doses in 4 year olds. If supported by evidence from studies currently in progress, boosters may be recommended in the future for adolescents and adults.

Special features

A. Management of outbreaks

Since a course of 3 or more injections is required to protect against pertussis, vaccination cannot be effectively used to control an outbreak. Active case finding and identification of contacts is important. Unvaccinated or incompletely vaccinated contacts up to their 8th birthday should be offered DTPa-containing vaccines (primarily to increase coverage with these vaccines). Infants as young as 4 weeks of age can commence vaccination. Passive immunisation with immunoglobulin is not effective in the prevention of pertussis.

B. Treatment

Children and adults with a clinical or laboratory diagnosis of pertussis should be treated with erythromycin (10 mg/kg/dose up to 250mg orally 6-hourly for 10 days) as this reduces infectivity and may reduce the duration of illness. Persons are considered not to be infectious after the 5th day of treatment. Household and other close contacts should be managed as described below ('Care of exposed persons').

C. Care of exposed persons

Vaccination

Close contacts under 8 year of age who are unvaccinated against pertussis or have received fewer than 4 doses of pertussis vaccine should have pertussis vaccination started or the series completed (with DTPa-hepB or DTPa).

Chemoprophylaxis

Oral erythromycin 10 mg/kg/dose up to 250mg orally 6–hourly for 10 days is recommended for all household contacts and other close contacts, such as in child care situations, irrespective of vaccination status. Cotrimoxazole or one of the newer macrolides (eg. roxithromycin) may be used as an alternative in children who do not tolerate erythromycin, although their efficacy has not yet been established. Chemoprophylaxis is not recommended routinely for health care staff caring for infected children.

D. Pertussis in pregnancy

Maternal antibodies do not protect newborn babies against pertussis. For this reason, pregnant women with pertussis around the time of delivery should be given oral erythromycin (250 mg 4 times daily for 10 days). Their newborn babies should be given erythromycin syrup (10 mg/kg/dose 4 times daily for 10 days).

Vaccine

The efficacy of pertussis vaccines around the world has been demonstrated in several populations, although only in a few instances by randomised controlled trials. When pertussis vaccination levels fell in the United Kingdom, Japan, and Sweden in the 1970s, a series of very large outbreaks of pertussis occurred. Following this, there was an effort to raise pertussis vaccination levels, and pertussis infection became rare. In the 1980s, pertussis vaccine was not used in West Germany, and 40% of children developed pertussis during massive outbreaks of infection. This contrasts sharply with the situation in East Germany, where there was universal infant pertussis vaccination and pertussis infection was rare. However, protective efficacy of both natural infection and pertussis vaccine wanes over time, and booster doses are required.

A. Acellular pertussis vaccines

Acellular pertussis containing vaccines were funded for use in both primary and booster vaccination schedules in Australia in February 1999, and as such are now recommended for the standard childhood

vaccination schedule. Acellular pertussis vaccine has similar efficacy to that of good quality whole cell vaccines, but is significantly less reactogenic. No monovalent pertussis vaccines are available in Australia. There are a number of acellular pertussis vaccines, which contain three or more purified components of Bordetella pertussis - pertussis toxin (PT), filamentous haemagglutinin (FHA), pertactin, and fimbrial antigens or agglutinogens. Acellular vaccines are up to 85% effective in preventing pertussis in field trials. They cause fewer local reactions than whole cell pertussis vaccine, and although hypotonic-hyporesponsive episodes can occur, they do so less frequently than with the whole cell vaccine.

Acellular vaccines are immunogenic in adults, but are not yet routinely recommended for adolescent or adult vaccination in any country except in France, where a booster is recommended at 13 years of age.

- Infanrix-hepB (diphtheria-tetanus-acellular pertussis adsorbed-hepatitis B) - SmithKline Beecham; (diphtheria toxoid 25 Lf, tetanus toxoid 10 Lf, pertussis toxoid 25µg, pertussis filamentous haemagglutinin 25µg, pertactin 8µg, hepatitis B surface antigen 10µg; adsorbed to aluminium hydroxide 0.5 mg, aluminium phosphate 0.2 mg, polysorbate 80 <100µg, polysorbate 20 < 5µg; preservative - phenoxyethanol 2.5µg; formaldehyde < 1µg; 0.5 mL dose)
- Infanrix (diphtheria-tetanus-acellular pertussis adsorbed) – SmithKline Beecham (diphtheria toxoid 25 Lf, tetanus toxoid 10 Lf, pertussis toxoid 25µg, pertussis filamentous haemagglutinin 25µg, pertactin 8µg; adsorbed on to aluminium hydroxide; phenoxyethanol as preservative; 0.5 mL dose).
- Tripacel (diphtheria-tetanus-acellular pertussis adsorbed) - CSL/Pasteur Merieux Connaught (diphtheria toxoid LFL equal or > 30 IU, tetanus toxoid LFL equal or > 40IU, pertussis toxoid 10µg, pertussis filamentous haemagglutinin 5µg, pertussis fimbriae 2+3 5µg, pertactin 3µg; 1.5µg aluminium phosphate as an adjuvant, and 3.4µg phenoxyethanol as a preservative; 0.5 mL dose).

B. Whole cell pertussis vaccines

There are a number of different whole cell pertussis vaccines that have been used around the world, and field studies of efficacy have generally shown them to be 85-95% protective against pertussis infection in children.

- Triple Antigen (diphtheria-tetanus-pertussis adsorbed) - CSL (diphtheria toxoid 30 IU, tetanus toxoid 60 IU, killed *B. pertussis*

<20,000 million per 0.5 mL, adsorbed on to aluminium phosphate; thiomersal 0.01% w/v; 0.5 mL dose).

Transport, storage and handling

Transport in an insulated container with approved freeze monitor, and time-temperature monitor. Observe the national guidelines for packing vaccines in insulated containers. Do not freeze or store vaccine in direct contact with ice packs. If vaccine has been exposed to temperature less than 0ºC, do not use. Vaccine which has been frozen may contain a flocculant precipitate which does not resuspend. Store in refrigerator at 2ºC to 8ºC. Check expiry date on vial or container before storage. Rotate stock so that shortest date vaccines are used first.

Dosage and administration

The dose is given by intramuscular injection. Pertussis vaccines should be given in a different limb from other concurrently administered vaccines. Accurate recording of the sites of injection of concurrently administered vaccines allows any local reactions to be attributed to the appropriate antigen or antigens.

Unless a combination vaccine containing DTPa and Hib is used, it is standard to give DTPa-containing vaccines on the right side and Hib on the left side.

Do not mix DTP-containing vaccines and other vaccines in the same syringe.

Recommendations

Acellular pertussis vaccine, as a component of the primary course of vaccination against diphtheria, tetanus and pertussis, is recommended for all infants from 2 months of age, unless there is a genuine contraindication. The same brand of vaccine should be used for each of the three doses at 2, 4 and 6 months. If it is not known which brand was used, vaccination should still be provided with the available brand.

The primary course consists of 3 doses with an interval 2 months between each dose. If the primary course is interrupted, it should be resumed but not repeated, allowing appropriate intervals between the remaining doses.

Booster doses with DTPa are recommended at 18 months and at the time of school entry (4 years). DTPa brands are interchangeable for booster doses. It is important that children receive both scheduled boosters to maintain their immunity. Pertussis vaccination is most needed before the

age of 2 years, but older children and adults are also at risk. An upper age limit of the 8th birthday is now recommended for DTPa vaccine. The reason for the upper age limit for DTPa is that DTPa contains a higher dose of diphtheria toxoid than Td, which should be used instead of DTP or DT after the 8th birthday. For details on the management of children who have missed doses in the standard childhood vaccination schedule, see Part 1.9, page 43.

Children with minor illness (not obviously unwell and a temperature below 38.5°C) may be vaccinated safely. Major illness or high fever might be confused with vaccine side effects and might increase discomfort to the child, and are therefore a sufficient reason to postpone vaccination for 2-3 days until the child is well. A return appointment for vaccination should be made at the time of deferral.

Adverse events and precautions

Acellular pertussis vaccines cause a much lower incidence of fever and local reactions than whole cell vaccines. The incidence of other adverse events with acellular vaccines has not been as extensively documented as it has with whole cell vaccines.

Pertussis vaccine does not cause infantile spasms, sudden infant death syndrome or epilepsy. Vaccine-induced fever may uncommonly lead to a febrile convulsion, though less commonly with DTPa than with DTPw. The risk is even lower in infants who complete their primary course by 6 months of age.

Sudden infant death syndrome (SIDS) is not associated with pertussis or DTP vaccination. Some studies suggest a decreased risk of SIDS in children who have been vaccinated.

It is important to note that the incidence of acute neurological complications after pertussis disease in unvaccinated individuals (more than 1% of cases) is considerably higher than after vaccination (estimates range from 0 to 10 per million vaccinations).

The systemic and local adverse event of whole cell pertussis vaccine can be significantly reduced by the routine use of paracetamol (15 mg/kg per dose) given 30 minutes before vaccination, and at 3-4 hourly intervals afterwards if required, up to a maximum of 6 doses per 24 hours. Paracetamol is not routinely recommended in children receiving acellular pertussis vaccine.

If a febrile convulsion occurs after a dose of DTP, such children are at increased risk of further febrile convulsions following further

vaccinations. However, these risks can be minimised by appropriate measures to prevent fever, so vaccination is still recommended.

As with all suspected adverse events to vaccines, severe adverse events following pertussis vaccine should be reported as set out in Part 1.6, page 22.

What to do if severe adverse events occur following DTP-containing vaccines

1. Encephalopathy within 7 days of vaccination.

   Definition: severe acute neurological illness + prolonged seizures ± unconsciousness ± focal signs, but not a simple febrile convulsion.

   ACTION: DT should be used for subsequent vaccinations instead of DTP. Although the pertussis component is the most likely cause of adverse events, further vaccination with diphtheria and tetanus vaccines should be undertaken under careful observation.

2. Immediate severe allergic reaction.

   Definition: generalised urticaria, bronchospasm, hypotension, collapse or anaphylactic reaction.

   ACTION: Do not vaccinate with same vaccine again. Use DT instead. Although the pertussis component is the most likely cause of adverse events, further vaccination with diphtheria and tetanus vaccines should be undertaken under careful observation.

3. Convulsion, with or without fever, or a temperature of 40.5°C or more.

   ACTION: Safe to complete course with DTPa-containing vaccine.

4. Persistent inconsolable screaming for 3 or more hours, or unusual high-pitched cry.

   ACTION: Safe to complete course with DTPa-containing vaccine.

5. Hypotonic-hyporesponsive episode (HHE).

   HHEs rarely follow vaccination with DTPw, and less commonly after DTPa and DT vaccines.

   Definition: An episode of pallor, limpness, and unresponsiveness 1-12 hours after vaccination, often preceded by irritability and fever. Shallow respiration and cyanosis may also occur. The whole episode lasts from a few minutes to 36 hours. Follow- up of children with HHE shows no longterm neurological or other sequelae.

ACTION: Safe to complete course with DTPa-containing vaccine.

6. Extensive circumferential limb swelling and redness.

   Definition: Commences within 48 hours of vaccination, sometimes followed later by a sterile abscess. Possibly due to inadvertent subcutaneous rather than intramuscular injection.

   ACTION: If the reaction is following DTPw, use DTPa subsequently. If following DTPa, ensure deep intramuscular injection. It is safe to use DTPa again.

Contraindications

Contraindications to pertussis vaccine have been overstated in the past.

Before administration of each dose of DTPa or DTPa-hepB, the child's parents or guardian should be questioned about possible adverse events following the previous dose.

Severe adverse events which CONTRAINDICATE further doses of DTP (DTPa, DTPa-hepB or DTPw) - (in these cases DT should be used for further vaccination. Although the pertussis component is the most likely cause of adverse events, further vaccination with diphtheria and tetanus vaccines should be undertaken under careful observation):

- encephalopathy within 7 days, defined as severe acute neurological illness with prolonged seizures and/or unconsciousness and/or focal signs (but not a simple febrile convulsion);
- immediate severe allergic or anaphylactic reaction to vaccination with DTP.

Previous pertussis infection

Children who have had culture-positive pertussis after the age of 3 months DO NOT need to receive pertussis vaccine. However, vaccination of previously infected children with pertussis vaccine is safe.

Pre-existing neurological disease and pertussis vaccination

It is advisable to defer pertussis vaccines for infants or children known to have active or progressive neurological disease, as neurological deterioration might erroneously be attributed to pertussis vaccine. Pertussis vaccination may be deferred in children who have had a convulsion in the previous 3 weeks. For infants with stable neurological disease (including controlled epilepsy), or a family history of idiopathic epilepsy or other familial neurological disorder, the risks from pertussis

vaccination are essentially the same as for other infants of the same age. Because the risk of pertussis infection is high, routine vaccination, including DTP, should still be commenced, subject to the normal precautions. If there is doubt in individual cases, consultation with a paediatrician or paediatric neurologist may be appropriate.

Other conditions

A personal or family history of allergy is not a contraindication to pertussis vaccination, nor are stable neurological conditions such as cerebral palsy or spina bifida.

If there is doubt about the risk of pertussis vaccination in any of the situations described above, advice should be sought from a paediatrician or a public health physician with extensive experience in vaccination.

Use in pregnancy

Pertussis vaccine is not yet recommended for use in anyone aged over 8 years.

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3.16 PLAGUE

Bacteriology

Plague is a zoonotic infection caused by the Gram positive bacillus, *Yersinia pestis*, which has been the cause of three great pandemics of human disease in the modern era. Plague is transmitted from an animal reservoir by fleas to humans. While most carnivores, except cats, are resistant to plague infection, animals such as domestic dogs, all rodents, and even owls may mechanically transmit fleas. Mammals that are partially resistant to plague infection may serve as a continuous reservoir of plague, and highly susceptible animal species may amplify both fleas and bacilli.

After a flea ingests a blood meal on a bacteraemic animal, bacilli multiply and eventually block the flea's foregut with a mass of fibrous material and bacteria. When an infected flea subsequently feeds it regurgitates clotted bacteraemic material into the victim's blood stream and so passes the infection on to the next mammal.

Clinical features

Naturally occurring plague in humans is characterized by the abrupt onset of high fever, painful local lymphadenopathy draining the exposure or flea bite site and bacteraemia. Septicaemia can sometimes follow. Patients with the bubonic form of plague may develop secondary pneumonic plague, which in turn can cause primary pneumonic plague following human to human spread via the respiratory route.

Epidemiology

Plague occurs in many parts of the world, including Asia, Africa, South America and the southwestern United States. Epidemic and epizootic activity has been recently recorded in Africa, Asia and South America.

Plague exists in one of two states in nature, enzootic and epizootic. In the enzootic state, fleas have no need to seek less desirable hosts to feed upon. However, during a epizootic situation, plague bacilli are introduced into other susceptible animals, including domestic rat populations and high mortality is often apparent. Under such circumstance man is an accidental host, usually being infected when living under unsanitary conditions close to large wild rodent populations. *Y pestis* has been a significant threat to military formations for thousand of years both as a naturally occurring biological threat and as a biological warfare agent.

Vaccine

- Plague Vaccine - CSL: heat killed agar-grown suspension of Y. pestis 3,000 million per mL + phenol 0.5% as preservative.

While plague vaccines have been used since the late 19th century, their efficacy has not been demonstrated in controlled trials. However, field experience indicates that vaccination with plague vaccine reduces the incidence and severity of disease.

Transport, storage and handling

Transport in an insulated container with approved freeze monitor, and time-temperature monitor. Do not freeze or store vaccine in direct contact with ice packs. If vaccine has been exposed to temperature less than 0ºC, do not use. Store in refrigerator at 2ºC to 8ºC.

Check expiry date on vial or container before storage. Rotate stock so that shortest date vaccines are used first. Protect from light.

Dosage and administration

The vaccine is given by subcutaneous injection. The initial course consists of 2 doses for adults and adolescents, and 3 doses for children under 12 years of age, at intervals of 1-4 weeks. Booster doses should be given every 6 months to persons living in areas where plague is prevalent. If booster doses are required in people who have previously had adverse events following this vaccine, 0.1 mL may be given intradermally, and precautions taken to manage anaphylactic reaction.

Table 3.16.1 Recommended dosage schedule for plague vaccine

Recommended dosage schedule for plague vaccine				
Age of vaccination	1st dose	2nd dose	3rd dose	Booster dose
6 months – 2 years	0.1 mL	0.1 mL	0.1 mL	0.1 mL
3 –6 years	0.2 mL	0.2 mL	0.2 mL	0.2 mL
7 - 11 years	0.3 mL	0.3 mL	0.3 mL	0.3 mL
Over 12 years	0.5 mL	0.5 mL	-	0.5 mL

Recommendations

Because human plague is rare in most parts of the world, there is no need to vaccinate persons other than those at particularly high risk of exposure. Vaccination is not generally indicated for travellers to countries reporting cases, particularly if their travel is limited to urban areas with

modern hotel accommodation. However, following natural disasters, and at times when regular sanitary practices are interrupted, in countries of South America, Asia, and Africa (including South Africa), plague can extend from its usually endemic areas into urban centres. In such circumstances tourist travel to those specific locations should be avoided.

Routine bacteriological precautions are sufficient to prevent accidental infection with plague in laboratory settings.

Vaccination is recommended for:

- all laboratory and field personnel who are working with Y. pestis organisms;
- persons engaged in field operations or who reside in plague enzootic areas where preventing exposure cannot be assured (veterinarians in rural areas; medical and other aid workers in some disaster areas);

Adverse events and precautions

Local and general adverse events following plague vaccines are usually mild and infrequent. They are more common after booster injections.

Contraindications

There are no absolute contraindications to plague vaccine.

Use in pregnancy

There is no evidence that plague vaccine causes fetal damage.

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3.17 PNEUMOCOCCAL INFECTIONS

Bacteriology

Streptococcus pneumoniae are lancet shaped Gram positive cocci. To date 90 capsular antigenic types have been recognised, each eliciting type specific immunity. Some of these types are commonly carried in the upper respiratory tract, and some are more frequently associated with invasive disease. The emergence of antibiotic-resistant strains of this organism has become an increasing challenge for the management of invasive pneumococcal disease. Recent reports in Australia indicate that up to 21% of strains are resistant to two or more classes of antibiotics.

Clinical features

The major clinical syndromes of invasive pneumococcal disease include pneumonia, meningitis, otitis media and bacteraemia. Pneumococcal pneumonia is the most common clinical presentation of invasive pneumococcal disease.

The risk of invasive disease is highest in patients who cannot mount an adequate immune response to pneumococcal capsular antigens, including those with anatomical or functional asplenia, immunoglobulin deficiency, acute nephrosis, multiple myeloma, AIDS, chronic renal failure, organ transplantation and lymphoid malignancies. Another group of patients, although generally immunocompetent, are also at increased risk of invasive pneumococcal disease; these include patients with chronic cardiovascular or pulmonary disease, diabetes mellitus, alcohol-related problems, cirrhosis and patients with CSF leak after cranial trauma or surgery.

Epidemiology

Based on data from the United States the annual incidence of pneumococcal bacteraemia is estimated to be 15-19/100,000 and pneumococcal meningitis 1-2/100,000. The case fatality rate for pneumococcal meningitis ranges from 10% to 30%. Pneumococcal meningitis is now the leading cause of meningitis in children under five years of age. In the less developed world and in some groups of Australian Aboriginal people, the incidence of invasive pneumococcal disease is as high as 200/100,000 per year with a mortality of 10%. In central Australia Aboriginal children are admitted to hospital 80 times more frequently than non-Aboriginal children for x-ray proven pneumonia. In Papua New Guinea, at least half the deaths from respiratory infection in young children are associated with S. pneumoniae.

In an intensive surveillance program in Western Australia the crude rate for invasive pneumococcal disease was reported at 8.3/100,000 person years with the highest incidence in children less than two years of age and in adults 65 years and over. In all age groups, Aboriginality was associated with higher rates of invasive disease, the crude rate for invasive pneumococcal disease being 76.2/100,000 person-years, compared with the non-Aboriginal population of 6.3/100,000 person-years. The case fatality was 10.3% with most deaths occurring in the over 65 year age group. The mortality rate for the Aboriginal population was 8/100,000 person-years. For cases over 15 years of age, 51% had at least one risk factor, the most significant being excessive alcohol consumption (26%) followed by chronic lung disease (14%), cardiac disease (9%), malignancy (9%), and diabetes (7.5%). This compares with 93% of cases having a known risk factor in a Queensland study. In WA, 18 serotypes were found responsible for causing disease in 92% of cases. All of these serotypes are included in the current 23-valent vaccine.

Vaccine

- Pneumovax 23 – CSL/Merck, Sharpe and Dohme (single dose vials containing 25µg of each of 23 pneumococcal polysaccharides in 0.5 mL of normal saline plus 0.25% phenol).

Controlled trials have demonstrated that pneumococcal vaccine reduces mortality from pneumonia in certain populations in developing countries with high attack rates. For at-risk individuals with much lower attack rates in developed countries, (eg. the elderly and those with chronic diseases) it has proved more difficult to establish the efficacy of the vaccine. However, it is generally accepted that the overall efficacy of the vaccine is 60% - 70% in these groups of individuals.

The current vaccine contains polysaccharides derived from the 23 most frequent or most virulent capsular types of S. pneumoniae in the USA. Similar serotypes are responsible for most of the pneumococcal infection in Australia.

At least 90% of healthy adults respond to the vaccine with a four-fold rise in type-specific antibody within two to three weeks. Response to vaccine is diminished in immunocompromised patients and is in poor in children less than two years of age.

Conjugated pneumococcal vaccines have recently been reported to provide very high efficacy and are likely to be available in the near future.

Transport, storage and handling

Transport in an insulated container with approved freeze monitor, and time-temperature monitor. Do not freeze or store vaccine in direct contact with ice packs. If vaccine has been exposed to temperature less than 0ºC, do not use. Store in refrigerator at 2ºC to 8ºC.

Check expiry date on vial or container before storage. Rotate stock so that shortest date vaccines are used first.

Pneumovax 23 is a clear, colourless solution. Inspect visually for particulate matter and discoluration prior to administration. Shake the syringe vigorously before withdrawing dose and inject vaccine as soon as possible. No dilution or reconstitution is necessary.

Dosage and administration

The vaccine should be given as a single dose of 0.5 ml, either deep subcutaneously or intramuscularly (preferably into the deltoid muscle or antero-lateral thigh).

Recommendations

Pneumococcal vaccine should be given to the following:

- all individuals aged 65 years and over;
- individuals with asplenia, either functional or anatomical, including sickle-cell disease in persons more than two years of age; Where possible, the vaccine should be given at least 14 days before splenectomy;
- immunocompromised patients at increased risk of pneumococcal disease (eg. patients with HIV infection before the development of AIDS, acute nephrosis, multiple myeloma, lymphoma, Hodgkin's disease and organ transplantation);
- Aboriginal and Torres Strait Islander people aged 50 years and over;
- immunocompetent persons at increased risk of complications from pneumococcal disease because of chronic illness (eg. chronic cardiac, renal or pulmonary disease, diabetes and alcohol-related problems);
- patients with CSF leaks.

Note that in groups with the highest risk of severe pneumococcal disease (those with acute nephrosis, splenectomised children, those with

sickle-cell disease), many authorities recommend continuous penicillin prophylaxis in addition to pneumococcal vaccine.

Pneumococcal vaccine is now funded by the Commonwealth for all Aboriginal and Torres Strait Island adults aged 50 years and over and for those aged 15 to 50 years who have any of the high risk underlying conditions. With the introduction of this funding policy, enhanced surveillance for pneumococcal disease is essential. Surveillance data should include the vaccination status of Aboriginal and Torres Strait Island adults with invasive pneumococcal disease and the serotypes of invasive isolates.

Revaccination

Revaccination is recommended every five years for those at-risk of invasive pneumococcal disease. However, revaccination within three years of the previous dose is not recommended.

It should be noted that the recommendations for use of the pneumococcal vaccine are somewhat similar to those for influenza vaccine, and that the two vaccines can be administered at the same visit. (NB. Revaccination with influenza vaccine is annual, whereas revaccination with pneumococcal vaccine is every five years).

Adverse events and precautions

About half the recipients will experience erythema or or mild pain at the site of injection. Severe adverse events such as anaphylactic reactions are rare. Low grade fever occurs occasionally, but fever above 39ºC is rare.

Contraindications

The only absolute contraindication is anaphylaxis after prior use of the vaccine.

Relative contraindications include the following:

- age less than two years - the immune response in infants and very young children is too poor to warrant the use of the vaccine;
- recent use of immunosuppressants or radiation of lymph nodes;

Revaccination with pneumococcal vaccine within three years may result in an increase in local reactions.

Use in Pregnancy

Safety of the use of the vaccine in pregnancy has not been evaluated, so deferral of vaccination is recommended unless the risk of pneumococcal

disease is very high. Recently reported trials show no protective effect in infants following vaccination of pregnant women. Serious side-effects were not noted in these women. Women who are candidates for pneumococcal vaccine ideally should be vaccinated before pregnancy.

Conflict with Product Information

The production information does not recommend revaccination of adults and specifically states that "revaccination of adults is contraindicated". However five-yearly revaccination is recommended by ATAGI.

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3.18 POLIOMYELITIS

Virology

Poliovirus is an enterovirus in the family picornaviridae. It has an RNA genome, and is a transient inhabitant of the gastrointestinal tract (GIT). There are three poliovirus serotypes, P1, P2 and P3. The virus enters through the mouth, multiplies in the pharynx and GIT and continues to be excreted in the stools for several weeks. The virus invades local

lymphoid tissue, enters the blood stream and may then infect and replicate in cells of the central nervous system.

Clinical features

Poliomyelitis is an acute illness following gastro-intestinal infection by 1 of the 3 types of poliovirus. Transmission is through faecal-oral spread. The infection may be clinically inapparent. If symptoms occur, they may include headache, gastro-intestinal disturbance, malaise and stiffness of the neck and back, with or without paralysis. Aseptic meningitis may also occur. Paralytic polio may be spinal (79%), bulbar (2%) or bulbospinal (19%). The case fatality rate in paralytic polio is 2-5% in children, 15-30% in adults and up to 75% in bulbar polio. The infection rate in households with susceptible young children can reach 100%. The proportion of inapparent to paralytic infections may be as high as 1,000 to 1 in children and 75 to 1 in adults, depending on the poliovirus type and social and environmental conditions.

The incubation period ranges from 3-21 days. Cases are most infectious from 7-10 days before and 7-10 days after the onset of symptoms. The vaccine virus may be shed in the faeces for 6 weeks or more.

Epidemiology

The incidence of poliomyelitis has been dramatically reduced worldwide, but cases still occur in developing countries, particularly in the Indian subcontinent, the Eastern Mediterranean and Africa. The World Health Organization aims to eradicate poliomyelitis by the year 2000 or soon after. In 1994, the continents of North and South America were certified to be free of polio. In countries where the disease incidence is low but transmission is still occurring, poliomyelitis cases are seen sporadically or as outbreaks amongst non-vaccinated individuals. 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 notified case of wild poliomyelitis in Australia occurred in 1978, but there have been two vaccine-associated cases notified in 1986 and 1995. The last case in the Western Pacific region was in 1997.

Vaccines

Oral poliomyelitis vaccine (OPV)

- Polio Sabin (Oral) - SmithKline Beecham (live attenuated poliovirus (Types 1, 2, and 3) + neomycin B sulphate 5µg per dose.

Inactivated poliomyelitis vaccine (IPV)

- IPOL (Inactivated poliomyelitis vaccine) - CSL/Pasteur Merieux (poliovirus types 1, 2 and 3 grown on monkey kidney VERO cells, inactivated with formaldehyde. Traces of formaldehyde are present in the vaccine and traces of neomycin, streptomycin and polymyxin B may also be present).

Inactivated poliomyelitis vaccine (IPV) contains polioviruses of all 3 types inactivated by formaldehyde. A course of 3 injections with an interval of 2 months between each dose produces long-lasting immunity (both mucosal and humoral) to all 3 poliovirus types. IPV produces considerably lower levels of intestinal immunity than OPV.

Live oral poliovirus vaccine (OPV) is routinely used for vaccination in Australia and is always given as 2 drops by mouth. It contains live attenuated strains of poliovirus types 1, 2 and 3, grown in cultures of monkey kidney cells or on human diploid cells. The attenuated viruses become established in the intestine and promote antibody formation both in the blood and the gut epithelium, providing local resistance to subsequent challenge with wild polioviruses. This reduces the frequency of symptomless excretion of wild poliovirus in the community.

OPV inhibits simultaneous infection by wild polioviruses and is thus of value in the control of epidemics. Vaccine strain poliovirus may persist in the faeces for up to 6 weeks after OPV. Whilst many recipients are protected after a single dose, a course of 3 doses should produce long-lasting immunity to all 3 poliovirus types.

Transport, storage, handling and administration

Oral poliomyelitis vaccine (OPV)

Transport in insulated containers. Maintain temperature at 2ºC to 8ºC or can be transported with ice. OPV should be transported with approved time-temperature monitor which is capable of indicating exposures to temperatures greater than 10ºC over a 2-week period. Observe national guidelines for packing vaccines in insulated containers.

If time-temperature monitor indicates that OPV has been exposed to temperature above 8ºC or more, do not use. Store OPV vaccine in freezer or it can be stored (unopened) in refrigerator at 2ºC to 8ºC. Keep lid on OPV container. Once OPV container is opened, OPV may lose potency due to exposure to air.

OPV contains phenol red as a pH indicator. The usual colour is pink Opened multi-dose vials of OPV can be used in subsequent sessions if

the following conditions are met:

- the expiry date has not passed
- it has been stored under appropriate cold-chain conditions (at 2ºC to 8ºC)
- opened vials of OPV which have been taken out of the health care centre for out reach vaccination activities are discarded at the end of the day.

OPV may also be stored at –20ºC. Frozen OPV should be rapidly thawed and mixed by rolling the vial between the fingers, with the colour remaining pink/orange/yellow. If this procedure is followed, a maximum of 10 freeze – thaw cycles are permissible provided that the cumulative duration of the thaw does not exceed 24 hours and provided the temperature does not exceed 8ºC during the period of thawing.

OPV is only for oral use; it must never be given by injection. Plastic spoons used for OPV, must be disposed of immediately following administration of vaccine and at its point of use.

Inactivated poliomyelitis vaccine (IPV)

Transport in insulated container at temperatures of 2ºC to 8ºC. Do not freeze or store vaccine in direct contact with ice packs. IPV should be transported with the approved time-temperature monitor which is capable of indicating exposures to temperatures greater than 10ºC over a 2 week period and an approved freeze monitor. Store IPV in refrigerator at 2ºC to 8ºC. IPV should be perfectly clear and pink or red in colour. Any vaccine showing particulate matter, turbidity or change of colour should be discarded. Check date on vial or container of IPV or OPV for shelf- life. Rotate stock so that short-dated stock is used first.

Dosage and administration

The dose of OPV is 2 drops given by the oral route. IPV is 0.5 ml given by deep subcutaneous injection using the correct technique and needle. The correct needle for subcutaneous injection is 25 gauge needle 16 mm in length. IPV can be administered on the same day as other vaccines but should be given in a different limb from other concurrently administered vaccines.

Interchangeability of OPV and IPV

IPV and OPV may be used interchangeably in the schedule, except where contraindications exist to OPV. Premature infants commenced on IPV may complete the course with OPV. Extra doses are not required.

Global eradication of polio

Because of the rapid progress in global polio eradication and diminished risk of wild virus associated disease, IPV is now preferred in the USA for all 4 polio vaccine doses. This change also came about because of concern about the 8-10 cases of vaccine-associated paralytic poliomyelitis (VAPP) out of a birth cohort of 2 million per year, or 4-5 cases per million children, reported each year in the USA. The advantage of using IPV was considered to be a potential cessation of VAPP. The disadvantages of IPV are the complexity of the schedule, the increased number of injections required at each vaccination visit for young infants, and the very much greater cost of the IPV than OPV in countries such as Australia, compared with the USA. The WHO strongly supports the use of OPV to achieve global eradication of poliomyelitis, especially in countries with continued or recent circulation of wild type poliovirus. This recommendation is endorsed by the US and European authorities including those who routinely use IPV. The polio vaccination schedule in Australia is under constant review and may change in future. There have only been 2 cases of VAPP in Australia in the past 13 years, from birth cohorts of about 260,000 children per year (0.5 cases per million children), which is 10 times lower than the US rate. When combination vaccines containing IPV are available, the feasibility and costs of changing the Australian schedule will be reviewed, bearing in mind that once polio is eradicated within a few years (possibly as early as 2007), polio vaccination will no longer be necessary.

Recommendations

Primary vaccination of infants and children

Oral poliomyelitis vaccine is recommended for infants from 2 months of age. The primary course consists of 3 separate doses of 2 drops of vaccine. An interval of 2 months between each dose is recommended so that it can be given at the same time as diphtheria/tetanus/pertussis and Hib vaccines. If the vaccine is regurgitated within 10 minutes of administration, the dose should be repeated.

IPV is also acceptable for primary vaccination of children.

Breast-feeding does not interfere with the antibody response to OPV and vaccination should not be delayed on this account. For preterm or hospitalised babies, OPV, which might spread the live vaccine virus to other babies in the hospital, should not be given until the time of discharge. Alternatively, IPV (inactivated polio vaccine) can be used.

Immunosuppressed individuals and their close contacts should be vaccinated with IPV because of the small risk of clinical illness caused by live poliovirus in these individuals.

Faecal excretion of vaccine virus from OPV can last for 6 weeks and may lead to infection of unvaccinated contacts. There is a slightly increased risk of vaccine-acquired poliomyelitis in non-immune adults (those with no history of previous poliomyelitis vaccination). Unvaccinated or incompletely vaccinated household contacts, including adults, should be offered OPV at the same time as the child who is to be vaccinated. This reduces the risk of vaccine associated poliomyelitis in contacts. Unvaccinated adult contacts should be counselled about the risk to them of VAPP both from receiving the vaccine themselves, or from being in contact with the vaccinated child. They should also be advised of the cost of IPV in deciding whether to be vaccinated with IPV or OPV.

The contacts of a recently vaccinated baby should be advised of the need for strict personal hygiene, particularly for washing their hands after changing the baby's nappies, and about safe disposal of nappies.

Vaccination of parents whose children are being vaccinated

Unvaccinated or incompletely vaccinated household contacts of children who are to be given OPV should be offered a basic course of OPV at the same time as the children. If the parents prefer to be given IPV then the child's OPV should be deferred until after their second dose of IPV, because the risk of infection from the child occurs before immunity develops in response to IPV in the contact.

There is no need to give booster doses to individuals who have been previously vaccinated according to the recommended schedule (see below).

If necessary, the recommended minimum interval between doses can be extended and the course completed without repeating any dose.

Booster vaccination

A booster dose of oral poliomyelitis vaccine (OPV) should be given before school entry, at the same time as the booster dose of DTP vaccine; a further dose of OPV should be given at 15-19 years of age or before leaving school.

Vaccination of adults

A course of 3 doses (each of 2 drops) of OPV at intervals of 1-2 months is recommended for the primary vaccination of adults. No adult should remain unvaccinated against poliomyelitis. IPV may also be used for adults according to the same schedule as OPV.

Individuals who have received a total of 4 doses of trivalent polio vaccine, irrespective of the type of vaccine (either OPV, IPV or both) should be protected.

Booster doses for adults are not necessary unless they are at special risk, such as:

- travellers to areas or countries where poliomyelitis is epidemic or endemic;
- health care workers in possible contact with poliomyelitis cases.

For those exposed to a continuing risk of infection, a single booster dose (2 drops) is desirable every 10 years.

Vaccination of immunocompromised individuals and their household contacts

In individuals for whom a live vaccine is contraindicated, ie. individuals with immunosuppression from disease or chemotherapy, IPV should be used for poliomyelitis vaccination. It should also be used for siblings and other household contacts of immunosuppressed individuals. A primary course of 3 doses of 0.5 mL, at intervals of 1 or 2 months, should be given by deep subcutaneous or intramuscular injection. Individuals who are immunocompromised should receive a fourth dose 12 months after the third. Booster doses should be given as for OPV. HIV-positive individuals and their household contacts should receive IPV.

Adverse events and precautions

Cases of vaccine-associated paralytic poliomyelitis (VAPP) have been reported in recipients of OPV and their contacts. It has been estimated that 1 case of vaccine associated paralytic poliomyelitis occurs for every 2.5 million doses of OPV distributed. The risk is greater for the first dose than for subsequent doses and is slightly greater for adults than children. This very small risk of poliomyelitis induced by OPV cannot be ignored, but is insufficient to warrant a change in vaccination policy because of the enormous benefits of vaccination. The incidence of VAPP can be reduced by inquiring about the vaccination status of relatives at the time of vaccination. Unvaccinated relatives should be vaccinated

with OPV at the same time as the baby. The need for strict personal hygiene for contacts of recent vaccinees must be stressed.

A small proportion of recipients have mild symptoms after vaccination (eg. headache, loose stools, muscular aches).

Although an Institute of Medicine Committee noted an increased risk of Guillain-Barré syndrome following OPV administration in two studies in Finland, reanalysis of these data and subsequent study in the United States indicate that the risk is not increased.

As with all vaccines, severe adverse events following poliomyelitis vaccine should be reported as set out in Part 1.6, page 22.

Up until the early 1960s, some doses of polio vaccine contained simian virus 40 (SV40). Since then, polio vaccines have not contained SV40. SV40 has no relationship to human immunodeficiency virus (HIV) or simian immunodeficiency virus (SIV). There is no evidence that SV40 causes human health problems, although it has been found in some rare human tumours. Extensive follow- up of populations who received SV40-containing polio vaccine has shown no increase in cancer or other disorders.

Contraindications

OPV is contraindicated in the following circumstances:

- acute or febrile illness (temperature greater than 38.5ºC) - vaccination should be postponed;
- vomiting or diarrhoea - vaccination should be postponed;
- individuals or household contacts receiving high-dose oral or injectable corticosteroids or immunosuppressive therapy, including whole-body irradiation;
- malignant conditions (in the individual or household contacts) that involve the reticulo-endothelial system (such as lymphoma, leukaemia, and Hodgkin's disease) and where the normal immunological mechanism may be impaired as, for example, in hypogammaglobulinaemia;
- HIV infection in the individual or in their household contacts;
- although adverse events in the fetus have not been reported, oral polio vaccine should not be given to pregnant women during the first 4 months of pregnancy unless there are compelling reasons, such as travel to an endemic poliomyelitis area.

OPV may be given at the same time as inactivated vaccines and with other live virus vaccines. It may also be given shortly before after or with MMR vaccine. When BCG is given to infants, there is no need to delay vaccination with OPV, because the OPV viruses induce local immunity and serum antibodies by replicating in the intestine.

Both OPV and IPV may contain trace amounts of antibiotics (both contain neomycin; IPV may also contain polymyxin and trace amounts of streptomycin) but these do not contraindicate their use except in cases of documented extreme hypersensitivity.

Recent administration of immunoglobulin or blood transfusion is not a contraindication to oral poliomyelitis vaccine administration, although vaccine efficacy may be diminished. OPV or IPV may be given either before or after immunoglobulin.

OPV should not be used for the siblings and other household contacts of immunosuppressed children or adults; such contacts should be given IPV.

Use in pregnancy

Although there is no evidence that attenuated polio viruses have an adverse effect on the fetus, in accordance with general principles, the vaccine should not be given to pregnant women unless they are at a definite risk from poliomyelitis.

Conflict with product information

The product information for IPV suggests that the 4th dose be given 12 months after the 3rd dose for both adults and children, followed by a 5th dose for children at age 4 years. ATAGI recommends the 4th dose for children at age 4 years and no 4th dose for adults unless they are at special risk.

The PI suggests that any sensitivity to vaccine components is a contraindication, whereas ATAGI recommends that only extreme hypersensitivity is a contraindication.

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3.19 Q FEVER

Bacteriology

Q fever is caused by a small obligate intracellular bacterium, *Coxiella burnetii*. The organism is highly resistant to heat, drying and sunlight, and may be disseminated in dust or on fomites such as wool, hides, clothing, straw and packing materials.

Clinical features

Acute primary Q fever has an incubation period of 15 to 25 days and commonly presents with rapid onset of high fever, rigors, profuse sweats, extreme fatigue, muscle and joint pain, severe headache and photophobia. As the attack progresses there is usually evidence of hepatitis, sometimes with frank jaundice; in addition a proportion of patients may have pneumonia. The systemic symptoms are provoked by the acute phase cytokine cascade induced by the interaction of coxiella with the developing cellular immune response and are not specific for Q fever (eg. found in *M pneumoniae* and Legionella infection); laboratory confirmation is therefore essential. The acute illness lasts 1 to 3 weeks or so and may be accompanied by substantial weight loss in the more severe cases.

There has been evidence that *C. burnetii* may persist in the body after the primary infection and may recrudesce as subacute endocarditis, bone and joint infection, chronic hepatitis or as placental infection at parturition in women infected earlier in pregnancy or even before

conception. Recent studies have also identified a prolonged post Q fever fatigue syndrome with general symptoms which are essentially a down-sized version of those of the primary infection but without fever or a clear-cut organ system involvement.

Epidemiology

From 400 to 600 human Q fever infections are notified in Australia each year. Non-immune new employees or visitors to animal-related industries are at highest risk. The infection may be transmitted to humans through the handling of infected animals (eg. transporting animals, slaughtering of animals, washing of carcasses), or by handling infected uterine or placental tissue. A variety of animals, both domestic and wild, may be infected, but remain well. These include kangaroos, dogs, cats, cattle, sheep, wallabies, and goats. Of these animals, cattle, sheep and goats are often the most significant source for human infection. The organism is mainly transmitted by the respiratory route by droplet infection through aerosols, or inhalation of 'dry' organisms in infected dust. *C. burnetii* can be found in milk, excreta and the placentae of infected farm animals, particularly goats, sheep and cows.

Vaccine

- Q-Vax - CSL (purified killed suspension of *Coxiella burnetii* 25µg per 0.5 ml).

Q fever vaccine consists of a purified killed suspension of *C. burnetii*. It is prepared from Phase I Henzerling strain of C. burnetii grown in the yolk sacs of embryonated eggs. The organisms are extracted, inactivated with formalin, and freed from excess egg proteins by fractionation and ultracentrifugation. Thiomersal 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 antigen. In subjects weakly seropositive before vaccination, the response is mainly IgG antibody to Phase I and Phase II antigens. Although the seroconversion rate may be low (50% to 80%), long term cell-mediated immunity develops and the vaccine has been shown in field trials to be protective.

In the original field trials no cases of Q fever were observed in vaccinees although cases continued to occur in unvaccinated workers in the same environment.

During the last 5 or so years with much larger numbers vaccinated, a

few instances (8-10 by 1999) of laboratory proven Q fever have been observed in vaccinated subjects. It is important that these apparent vaccine failures are fully investigated and they should be reported to the manufacturer.

Transport, storage and handling

Transport in an insulated container with approved freeze monitor, and time-temperature monitor. Do not freeze or store vaccine in direct contact with ice packs. If vaccine has been exposed to temperature less than 0ºC, do not use. Store in refrigerator at 2ºC to 8ºC. Check expiry date on vial or container before storage. Rotate stock so that shortest date vaccines are used first. Protect from light.

Dosage and administration

A single dose of 0.5 mL of Q-Vax is given by subcutaneous injection after ascertaining that serology and skin testing have been performed and that both the tests are negative. Immunity produced by the vaccine appears to be long lasting (in excess of 5 years). Until further information becomes available, revaccination or booster doses of the vaccine are not recommended because of the risk of accentuated local adverse events.

Recommendations

Q fever vaccine is recommended for those at risk of infection with *C. burnetii*. Abattoir workers, veterinarians, stockyard workers, shearers, animal transporters and many others exposed to cattle, sheep or goats or their products should be considered for vaccination. Note also that Q fever has occurred among persons culling and processing kangaroos, and that laboratory personnel handling veterinary specimens, or visiting abattoirs, are at risk.

Pre-vaccination testing

> Prior to vaccination, persons must have serum antibody estimations and skin tests to exclude those likely to have hypersensitivity reactions to the vaccine resulting from previous exposure to the organism.

Antibody studies were originally done by complement fixation tests at serum dilutions of 1 in 2.5, 5 and 10 against Phase II antigen of *C. burnetii*. Although this is generally satisfactory, many testing laboratories now utilise EIA (Elisa) or IFA to detect IgG antibody to *C. burnetti* as an

indicator of past exposure. Subjects CF positive at 1 in 2.5, IFA positive at 10 or more, or with a definite positive absorbence value in the EIA should not be vaccinated.

Skin tests are performed by diluting 0.1 mL of vaccine in 30 mL of sodium chloride (injection grade). Diluted vaccine for skin testing should be freshly prepared, stored at 2ºC to 8ºC and used within 6 hours. 0.1 mL of the diluted vaccine is injected intradermally into the volar surface of the forearm using methylated spirits as a skin cleansing agent (commercial isopropyl alcohol skin wipes are not satisfactory for this purpose). A positive reaction is indicated by induration at the site of injection after 7 days. Individuals giving such a reaction must not be vaccinated.

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.

Adverse events and precautions

Vaccination of subjects already immune to *C. burnetii*, as a result of prior infection, or of subjects rendered hyperimmune by repeated vaccination, may result in severe local or general adverse events. Local abscess formation may occur in some cases.

Non-immune subjects commonly show local tenderness and erythema at the vaccination site. Local induration or oedema is rare. General symptoms are infrequent but may include mild influenza-like symptoms, rarely fever, chills and minor sweating. Vaccine-associated chronic fatigue syndrome may occur rarely.

No information is available on interactions between Q fever vaccine and other drugs.

Contraindications

- Persons with a history of an illness suggestive of or proven to be Q fever; persons shown to be immune by serological investigation or sensitivity to the organism by skin test; persons who have been previously vaccinated against Q-fever.
- Persons with anaphylaxis induced by egg proteins.

There is no information available on the efficacy and safety of Q fever vaccine in immunodeficient or immunosuppressed individuals.

Use in pregnancy

Q fever vaccine contains inactivated products and inactivated bacterial vaccines are not considered to be harmful in pregnancy. However, safety of use in pregnancy has not been established. Vaccination during pregnancy carries a risk of chance association of vaccination with complications of pregnancy not caused by vaccination. No information is available on use of Q fever vaccine during lactation.

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3.20 RABIES

See "Australian Bat Lyssavirus" (see page 77)

3.21 RESPIRATORY SYNCYTIAL VIRUS

Virology

Respiratory Syncytial Virus (RSV) is a single stranded RNA virus of the family paramyxovirus, genus pneumovirus. There are two subtypes, A and B.

Clinical features

RSV has an incubation of 4-6 days, and causes a wide spectrum of

respiratory illnesses. In infants, 25-40% of infections lead to pneumonia, bronchiolitis or tracheobronchitis. In adults, RSV usually causes coryzal symptoms.

Epidemiology

RSV is the major respiratory pathogen of young children and the major cause of lower respiratory infections in infants. The peak incidence is between 1 and 6 months of age. It occurs worldwide, with annual epidemics in winter. RSV is transmitted by close contact with contaminated fingers or fomites, but may also be spread by coarse aerosols produced by coughing or sneezing. Attack rates in day care centres can approach 100%. Babies with chronic cardiorespiratory disease, babies born prematurely, immunocompromised hosts and the elderly are at risk of severe RSV infection.

Vaccine

RSV immunoglobulin

Several clinical studies of immunoglobulin against RSV have been conducted overseas using hyperimmune polyclonal RSV immunoglobulin (RSVIG) derived from blood donations. It has been shown to reduce the incidence and severity of RSV infections when given prophylactically in some babies and infants at high risk of severe infection. Benefit has been shown for babies and infants with bronchopulmonary dysplasia (BPD) and for those with prematurity without BPD.

Monthly infusions are needed throughout the RSV season. Cost-benefit analyses suggest that the costs of prophylactic RSVIG outweigh the benefits, even for high-risk infants. RSVIG has caused severe cyanotic episodes and poor outcome after surgery in children with congenital heart disease and is contra-indicated in such children. RSVIG is not registered in Australia. The product reduces hospitalisation in high-risk infants who were born preterm or have bronchopulmonary dysplasia. About 20 infants need to be treated each winter to prevent one hospitalisation due to RSV infection.

A humanised mouse monoclonal antibody to RSV produced by cultured cells – Palivizumab (Synagis: Abbott Australia) – is now registered in Australia for prevention of serious lower respiratory tract disease caused by respiratory syncytial virus (RSV) in children at high risk of RSV disease. Its use has not been studied in children with congenital heart disease, and it should not be used for such children. This product

is given by intramuscular injection each month during periods of anticipated risk of RSV. The product was found to reduce hospitalisation by about 5% for both preterm and BPD babies. It has not been shown to prevent ICU admission. No cost-benefit analysis has been published to date but the costs are likely to be comparable to those of RSVIG.

- Palivizumab (Synagis) is supplied in single use vials of powder, to be reconstituted with Sterile Water for Injection; 50mg in 4mL vial; 100mg in 10mL.

Transport, storage and handling

Palivizumab should be transported as set out in section 1.12 (page 54), and stored at 2 to 8º C. Do not freeze. Store in the original container. Do not use beyond the expiration date.

Dosage and administration

The recommended dose of Palivizumab is 15 mg/kg of bodyweight, given once a month during anticipated periods of respiratory syncytial virus (RSV) risk in the community. Where possible, the first dose should be administered prior to commencement of the RSV season and subsequent doses should be administered monthly throughout the RSV season.

Palivizumab is administered in a dose of 15 mg/kg once a month intramuscularly, preferably in the anterolateral aspect of the thigh. The gluteal muscle should not be used routinely as an injection site because of the risk of damage to the sciatic nerve. The injection should be given using standard aseptic technique.

Contraindications

Palivizumab is contraindicated in children with a history of a severe prior reaction to Palivizumab or any of its ingredients, or other humanised monoclonal antibodies. It is also contraindicated in children with congenital heart disease.

Conflict with product information

ATAGI recommends that Palivizumab is contraindicated in children with congenital heart disease; this is not a listed contraindication in the PI.

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3.22 RHESUS DISEASE OF THE NEWBORN

Rh(D) immunoglobulin

Rh(D) antibody can prevent the development of Rh antibodies in an Rh-negative mother who gives birth to an Rh-positive baby.

Administration of high titre Rh(D) immunoglobulin to an Rh(D)-negative mother within 72 hours of delivery of an Rh(D)-positive infant results in the removal of D-positive fetal cells from the mother's circulation, and thus prevents the development of her own Rh(D) antibodies.

The dose of Rh(D) IG is 625 IU given by intramuscular injection. It should be administered as soon as possible after the blood group of the infant has been determined, and not later than 72 hours after delivery. If rubella vaccine or MMR is required, it can be given along with anti-D immunoglobulin, at the same time in different sites, with separate syringes. Anti-D immunoglobulin does not interfere with the antibody response to rubella or MMR vaccine.

In Australia, Rh(D)IG is supplied only by the Australian Red Cross Blood Service. The State Director of the Service must be contacted and the case must meet strict criteria.

- Rh(D) immunoglobulin - CSL (16% solution of gamma globulin fraction of pooled human plasma from donors immunised to Rh antigen 'D'
  125µg /mL (625 IU/mL) 1 mL ampoules).

Contraindications

Rh(D) immunoglobulin should not be given to women who already have Rh antibodies in their blood, and it should never be administered to the baby.

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3.23 RUBELLA

Virology

Rubella is an enveloped togavirus with an RNA genome. It is related to group A arboviruses, but does not cross-react with other members of the togavirus group. It is relatively unstable, and is inactivated by extremes of heat and pH, amantadine and UV light.

Clinical features

Rubella is generally a mild infectious disease. It causes a transient erythematous rash, lymphadenopathy involving 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 diagnostic of rubella. A history of rubella should therefore not be accepted without serological evidence of previous infection. The incubation period is 14-21 days, and the period of infectivity is from 1 week before until 4 days after the onset of the rash. Infection is spread by respiratory droplets.

Epidemiology

Rubella occurs world-wide and is spread from person-to-person by airborne transmission. In temperate climates, the incidence is highest in late winter and early spring. Rubella incidence has fallen rapidly since vaccine licensure, and there has been in shift in the age distribution of cases, with comparatively more cases seen in older age groups. Rubella is more common in males than females, as selective vaccination for females preceded universal childhood vaccination. In 1992 and 1993, rubella epidemics were reported in those States where rubella was notifiable. Notifications rose from a crude rate of 3.7 per 100,000 in 1991 (620 notifications) to 22.6 per 100,000 in 1992 (3,810 notifications). Over

3,000 cases were reported again in 1993, 1994, and 1995. In 1997 this fell to 1,446 cases, with an overall notification rate of 7.8/100,000. The highest incidence in males aged 15-19 years (45.5/100,000). There have been 2 deaths from rubella notified in Australia between 1978 and 1997.

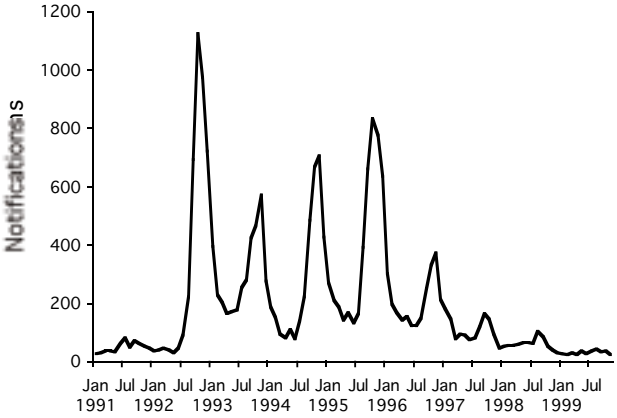
The rubella virus was isolated in cell culture in 1962. Vaccines are prepared from strains of attenuated virus and have been approved for use in Australia since 1970. Mass vaccination of schoolgirls commenced in 1971. Non-pregnant, seronegative adult women were also vaccinated. These programs were successful and there was a significant reduction in the incidence of congenital rubella from 1977. There has also been a significant increase in the percentage of pregnant women immune to rubella (in New South Wales from 82% in 1971 to 96% in 1983).

Many teenaged and young adult males are non-immune to rubella because they did not receive MMR vaccine. The MMR vaccination program for all adolescents replaced the rubella program for girls in 1993/94. A recent serosurvey by the National Centre for Immunisation Research & Surveillance of Vaccine Preventable Diseases 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. For this reason, males in these age groups should receive MMR vaccine both for their own protection and to prevent transmission of the infection in the community.

Rubella in pregnancy

Maternal rubella infection in the first 8-10 weeks of pregnancy (counted from the first day of the last menstrual period) results in fetal damage in up to 90% of affected pregnancies, and multiple defects are common. This group of fetal abnormalities is called the congenital rubella syndrome (CRS). The risk of damage declines to about 10-20% by 16 weeks gestation. After this stage of pregnancy, fetal damage is rare but has been reported up to 20 weeks. Fetal defects include mental handicap, cataract, deafness, cardiac abnormalities, retardation of intra-uterine growth, and inflammatory lesions of brain, liver, lungs and bone-marrow. Any combination of these defects may occur, but defects which commonly occur alone are perceptive deafness and pigmentary retinopathy, following infection after the first 8 weeks of pregnancy. Some infected infants may appear normal at birth, but defects, especially sensorineural deafness, may be detected later.

Figure 3.23.1 Reported rubella cases, Australia, 1992 to 1999



Rubella reinfection in pregnancy

Rubella reinfection can occur in individuals with both natural and vaccine induced antibody. Occasional cases of congenital rubella syndrome after reinfection in pregnancy have been reported. However, fetal damage is very rare in cases of infection in women in whom antibody has previously been detected.

Confirmation of rubella infection in pregnant women

Because the rash is not diagnostic, and also because infection can occur with no clinical symptoms, acute rubella can only be confirmed by laboratory tests.

Investigation of pregnant women exposed to rubella

All pregnant women with suspected rubella or exposure to rubella must be investigated serologically, irrespective of a history of prior vaccination, clinical rubella or a previous positive rubella antibody result.

As soon as possible after the exposure to rubella, a blood sample should be taken and sent to the laboratory with 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 (see below) or a low level of antibodies and remains asymptomatic, a 2nd blood specimen should be collected 28 days after the exposure and

tested in parallel with the first. If the woman develops symptoms, the specimen should be collected and tested as soon as possible. A 3rd blood specimen may be required in some circumstances.

As some patients may have more than 1 exposure to a person with a rubella-like illness, or because exposure may occur over a prolonged period, it is important to ascertain the dates of the first and last exposures.

Serologic testing for rubella

A number of commercial assays for testing rubella serology are available. These vary according to the method used in determining 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. Antibody levels below the cut-off are likely not to be protective, particularly if the antibodies have been generated by vaccination rather than natural infection. Expert consultation and referral of sera to a reference laboratory are recommended if there is a difficulty interpreting results.

Vaccines

Two MMR vaccines are available in Australia. For information about MMR vaccines, see "measles". Monovalent vaccines for rubella are also available. A single dose of rubella vaccine produces an antibody response in over 95% of vaccinees, but antibody levels are lower than after natural infection. Vaccine-induced antibody has been shown to persist for at least 16 years in the absence of endemic disease. Protection against clinical rubella appears to be longterm in those who seroconvert.

Susceptible pregnant women will continue to be at risk of rubella infection in pregnancy until the transmission of rubella virus is interrupted by a sufficiently high uptake of MMR vaccine in children and adults of both sexes.

The vaccine virus is not transmitted from vaccinees to susceptible contacts. There is therefore no risk to pregnant women from contact with recently vaccinated individuals.

Monovalent rubella vaccines

- Ervevax - SmithKline Beecham (live attenuated rubella virus (Wistar RA 27/3 strain), lyophilised + neomycin 25µg. Single dose vial + diluent, 0.5ml).

- Meruvax II - CSL/Merck, Sharp and Dohme (live attenuated rubella virus (Wistar RA 27/3 strain), lyophilised + neomycin 25mg. Single dose vial + diluent, 0.5ml).

Transport, storage and handling

Rubella vaccine is a freeze-dried preparation. It must be stored in the dried state at 2ºC to 8ºC (or colder) and reconstituted with the separate diluent fluid supplied by the manufacturer. Transport un-constituted vaccine (freeze-dried or lyophilised) in insulated container with approved time-temperature monitor which is capable of indicating exposures to temperatures greater than 10ºC over a 2 week period. Observe national guidelines for packing vaccines in insulated containers. Maintain temperature at between 2ºC to 8ºC or colder. Protect from light. If transported with ice diluent must be transported separately. Diluent can be stored at room temperature (15 to 30ºC) but do not freeze. If time-temperature monitor indicates vaccine has been exposed to temperature above 10ºC do not use. Store un-constituted vaccine in refrigerator at between 2ºC to 8ºC or colder on arrival at storage site. Store vaccine separately to diluent and protect from light since exposure to light may inactivate vaccine. Check date on vial or container for shelf- life (check diluent and vaccine). Rotate stock so that short-dated stock is used first.

Dosage and administration

For both children and adults, the dose of MMR and monovalent vaccines is 0.5 mL given by deep subcutaneous or intramuscular injection.

Recommendations

The principal aim of rubella vaccination is to prevent congenital rubella syndrome by stopping the circulation of rubella virus in the community.

All infants should be vaccinated with MMR vaccine at the age of 12 months (see Part 1, page 38). All girls and boys should receive a second dose of MMR vaccine at the age of 4 years. A history of rubella does not contraindicate vaccination. Individuals who are already immune to rubella will experience few, if any, side effects of vaccination. Non-pregnant seronegative women of child-bearing age should be given single antigen rubella vaccine or MMR and advised not to become pregnant for 2 months after vaccination. Pregnant women found to be seronegative should be vaccinated immediately after delivery.

Female immigrants, especially those from Asia, who have entered Australia after the age of school vaccination are particularly likely to require vaccination.

Women should be tested for seroconversion 2 months after vaccination and revaccinated if necessary.

Rubella vaccine may be given to HIV-positive individuals in the absence of contraindications.

Teenaged and young adult males are especially likely to be non-immune to rubella (see "Epidemiology") and should be vaccinated with two doses of MMR at least one month apart if they have no record of receiving the vaccine.

Women who have negative or very low antibody levels after vaccination should be revaccinated. If their antibody levels remain low after a 2nd vaccination, it is unlikely that further vaccinations will improve this.

Rubella vaccination in pregnancy

Vaccination should be avoided in early pregnancy. Doctors should ascertain the date of the last menstrual period before vaccinating. However, despite active surveillance in the USA, UK and Germany, no case of vaccine-induced congenital rubella syndrome has been reported among more than 400 women inadvertently vaccinated with rubella vaccine during pregnancy, whose pregnancies continued. Based on this evidence, the vaccine cannot be considered to be teratogenic, and termination of pregnancy following vaccination is not indicated

Rubella vaccination postpartum

Women found to be seronegative on antenatal screening should be vaccinated after delivery and before discharge from the maternity unit. If anti-D immunoglobulin is required, the two may be given at the same time in different sites with separate syringes or at anytime in relationship to each other. Anti-D immunoglobulin does not interfere with the antibody response to vaccine, but whole-blood transfusion does inhibit the response in up to 50% of vaccinees. In such cases, a test for antibody should be performed 8 weeks later, with revaccination if necessary. All women found on antenatal screening to be susceptible to rubella should be vaccinated after delivery and screened before the next pregnancy. Either monovalent rubella vaccine or MMR can be used for this purpose.

Testing women of child-bearing age for rubella immunity

Every effort must be made to identify and vaccinate seronegative women and to test them for seroconversion 2 months after vaccination. All women should be informed in writing of the result of their antibody test.

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. Very occasionally, errors may result in patients who are seronegative being reported as seropositive. Where possible, specimens from pregnant women should be stored until the completion of the pregnancy.

Serological testing of non-pregnant women should be performed whenever possible before vaccination, but need not be undertaken where this might interfere with the acceptance or delivery of vaccine.

Testing health care and child care staff

All health care and child care staff, both male and female, including medical, nursing, and other health professional students, should be screened, and those without vaccination records, or who are seronegative, should be vaccinated both for their own protection and to avoid the risk of transmitting rubella to pregnant patients. Where necessary, those vaccinated can be tested for seroconversion 2 months after vaccination and revaccinated if seronegative.

Adverse events and precautions

Mild adverse events such as fever, sore throat, lymphadenopathy, rash, arthralgia and arthritis may occur following vaccination. Symptoms usually begin 1-3 weeks after vaccination and are usually transient; joint symptoms are more common in adults than in children. Thrombocytopenia, usually self-limiting, has occasionally been reported after rubella vaccine. Very rarely, neurological symptoms have been reported, but a causal relationship has not been established.

Contraindications

Rubella vaccine should not be given to a woman known to be pregnant, and pregnancy should be avoided for 2 months after vaccination. If the patient is suffering from a significant febrile illness, vaccination should be postponed until recovery is complete.

The vaccine should not be administered to patients receiving high-dose corticosteroid (see Part1.7, page 26) or immunosuppressive treatment, including general radiation. It should not be given to those suffering from malignant conditions of the reticulo-endothelial system (such as lymphoma, leukaemia, Hodgkin's disease), or in cases where the normal immunological mechanism may be impaired, as in hypogammaglobulinaemia.

Rubella vaccine should not be given within 3 months of an injection of immunoglobulin, other antibody-containing blood product, or whole-blood transfusion. It may be administered simultaneously with anti-D immunoglobulin, but at a separate site.

Rubella vaccines contain traces of neomycin. Previous anaphylactic reaction to neomycin contraindicates rubella vaccination.

Use of normal immunoglobulin (human) in the prevention of rubella

Post-exposure prophylaxis with immunoglobulin does not prevent infection in non-immune contacts and is therefore of little value for protection of pregnant women exposed to rubella. It may, however, prolong the incubation period, which may marginally reduce the risk to the fetus. It may also reduce the likelihood of clinical symptoms in the mother. Immunoglobulin should only be used if termination for confirmed rubella would be unacceptable. In such cases, it should be given soon after exposure. Serological follow-up of recipients is essential, and should continue for up to 8 weeks.

There is some evidence to suggest that in outbreak situations pre-exposure immunoglobulin 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.

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3.24 SMALLPOX AND VACCINIA

The last case of endemic smallpox occurred in Somalia in 1977. The World Health Organization officially announced the eradication of smallpox in December 1979. There is now no indication for vaccination of individuals with the possible exception of research staff working with viable or potentially viable vaccinia or related pox virus strains, and medical and nursing staff caring for patients given gene therapy using a vaccinia virus as the vector. Such staff should be informed of the benefits and risks of vaccination.

Vaccinia vaccine ('smallpox vaccine') is no longer made or registered in Australia. The vaccine is manufactured in the USA because of concern about bioterrorism. Information about sources of an unregistered vaccinia vaccine for use in research and hospital staff may be obtained from the Experimental Drugs Section, Drug Safety and Evaluation Branch, Therapeutic Goods Administration - telephone (02) 6232 8111.

References

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3.25 TETANUS

Bacteriology

Tetanus is caused by *Clostridium tetani*, a motile, non-capsulated, Gram-positive rod which 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).

Clinical features

Tetanus is an acute, often fatal, disease caused by the toxin produced by *Clostridium 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 4-21 days (range 1 day to several months). The median time of onset after injury is 7 days; 15 percent of cases occur within 3 days and 10 percent after 14 days. Generalized tetanus, the most common form of the disease, is characterized by increased muscle tone

and generalized spasms. Early symptoms and signs include increased tone in the masseter muscles (trismus, or lockjaw), dysphagia, stiffness or pain in the neck, shoulder, and back muscles. Some patients develop paroxysmal, violent, painful, generalized muscle spasms. A constant threat during generalized spasms is reduced ventilation or apnea or laryngospasm. The patient may be febrile, although many have no fever; mentation 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 ulcer, and rhabdomyolysis. Death results from respiratory failure, hypertension, hypotension or cardiac arrhythmia.

Tetanus has been reported very rarely in patients who appear to have been adequately immunised and to have received booster doses of vaccine. Clinicians should consider this diagnosis when there are appropriate symptoms and signs irrespective of the person's immunisation record.

Neonatal tetanus usually occurs as the generalized form and is usually fatal if left untreated. It develops in children born to inadequately immunized mothers, frequently after unsterile treatment of the umbilical cord stump. Its onset generally comes during the first 2 weeks of life. Poor feeding, rigidity, and spasms are typical features of neonatal tetanus.

Epidemiology

In Australia, tetanus is rare, occurring in older adults who have never been vaccinated or who have neglected to maintain adequate immunity through vaccination. An average of 8.5 cases of tetanus per year are notified in Australia, but there are a mean of 29 hospitalisations, suggesting undernotification. There have been 52 deaths from tetanus between 1976 and 1995; 80% of the cases are in persons over 55 years of age, and 60% of the cases are in women. A serosurvey in Sydney in 1993 confirmed a significant decline in immunity with increasing age in subjects more than 50 years old. Only 52% of this group of adults were immune, and women were less likely to be immune than men. The case fatality rate in Australia is about 10%. Neonatal tetanus is a frequent cause of death in parts of Asia, Africa and South America, killing about 800,000 babies a year.

Effective protection against tetanus is provided by active immunisation. 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. For this reason, routine boosters every 10 years are no longer recommended for fully vaccinated adults (see "Recommendations" below): this is similar to the current recommendations in the UK.

Special features

Tetanus-prone wounds

Types of wounds likely to favour the growth of tetanus organisms include compound fractures, deep penetrating wounds, wounds containing foreign bodies (especially wood splinters), wounds complicated by pyogenic infections, wounds with extensive tissue damage (eg. 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). Re-implantation 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 re-implantation.

General measures for treatment of tetanus-prone wounds

Table 3.25.1 Guide to tetanus prophylaxis in wound management

History of tetanus vaccination	Time since last dose	Type of Wound	DTP, DT, Td or Tetanus toxoid as appropriate	Tetanus immuno-globulin*
≥ 3 doses	< 5 years	All wounds	NO	NO
≥ 3 doses	5-10 years	Clean minor wounds	NO	NO
≥ 3 doses	5-10 years	All other wounds	YES	NO
≥ 3 doses	>10 years	All wounds	YES	NO
< 3 doses, or uncertain	-	Clean minor wounds	YES	NO
< 3 doses, or uncertain	-	All other wounds	YES	YES

*The recommended dose for TIG is 250 IU, to be given as soon as practicable after the injury, unless >24 hours has elapsed, in which case 500 IU should be given.

Use a combination vaccine in preference to tetanus toxoid alone in order to boost community protection against diphtheria. Use DTPa (or DT if

DTP is contraindicated) for children who have not reached their 8th birthday and Td for adults and for children after their 8th birthday. DTPa is recommended in children up to 8 years of age as it reduces the risk of pertussis in the vaccinated child and it lowers the risk of spread to other children, particularly those who are younger and more vulnerable. In children aged over 8 years and in adults, use Td vaccine.

Whatever the immune status of an individual with a tetanus-prone wound, local disinfection and, where appropriate, surgical treatment of tetanus-prone wounds must never be omitted. The use of antibiotics (such as penicillin or metronidazole) for preventing infection is a matter for clinical judgement.

The recommended use of booster tetanus vaccines, and the use of human tetanus immunoglobulin is set out in Table 3.25.1. These should be administered as soon as possible after the injury.

Other people at special risk

Adults who were born in foreign countries without adequate vaccination programs may never have received primary vaccination against tetanus. Older adults may have inadequate antitoxin levels.

Travellers to countries where health services are difficult to access should be adequately protected against tetanus prior to departure. They should receive a booster vaccination if more than 10 years have elapsed since the last dose.

Vaccines

Diphtheria-tetanus-acellular pertussis and hepatitis B vaccine (DTPa-hepB)

- Infanrix-hepB (diphtheria-tetanus-acellular pertussis adsorbed-hepatitis B) - SmithKline Beecham (diphtheria toxoid 25 Lf, tetanus toxoid 10 Lf, pertussis toxoid 25µg, pertussis filamentous haemagglutinin 25µg, pertactin 8µg, hepatitis B surface antigen 10µg; adsorbed to aluminium hydroxide 0.5 mg, aluminium phosphate 0.2 mg, polysorbate 80 <100µg, polysorbate 20 < 5µg; preservative - phenoxyethanol 2.5µg; formaldehyde < 1µg; 0.5 mL dose)

Acellular pertussis-containing vaccines

- Infanrix (diphtheria-tetanus-acellular pertussis adsorbed) - SmithKline Beecham (diphtheria toxoid >25 Lf, tetanus toxoid 10 Lf, pertussis toxoid 25µg, pertussis filamentous haemagglutinin 25µg,

pertactin 8µg; adsorbed on to aluminium hydroxide; phenoxyethanol as preservative; 0.5 mL dose).

- Tripacel (diphtheria-tetanus-acellular pertussis adsorbed) - CSL/Pasteur Merieux Connaught (diphtheria toxoid LFL equal or > 30 IU, tetanus toxoid LFL equal or > 40IU, pertussis toxoid 10µg, pertussis filamentous haemagglutinin 5µg, pertussis fimbriae 2+3 5µg, pertactin 3µg; 1.5µg aluminium phosphate as an adjuvant, and 3.4µg phenoxyethanol as a preservative; 0.5 mL dose).

Whole cell pertussis-containing vaccines

- Triple Antigen (diphtheria-tetanus-pertussis adsorbed) - CSL (diphtheria toxoid 30 IU, tetanus toxoid 60 IU, killed *B. pertussis* <20,000 million per 0.5 mL, adsorbed on to aluminium phosphate; thiomersal 0.01% w/v; 0.5 mL dose).

Adsorbed diphtheria tetanus vaccine - DT (paediatric formulation) and Td (adult formulation)

- Diphtheria tetanus vaccine (CDT) - CSL (diphtheria toxoid 30 Lf and tetanus toxoid 6 Lf per 0.5 mL adsorbed on to aluminium phosphate; thiomersal 0.01% w/v).
- Diphtheria tetanus vaccine (ADT) - CSL (diphtheria toxoid 2 Lf and tetanus toxoid 6 Lf per 0.5 mL adsorbed on to aluminium phosphate; thiomersal 0.01% w/v).

Tetanus toxoid vaccine (only to be used if diphtheria toxoid is contraindicated)

- Tet-tox tetanus vaccine, adsorbed - CSL (tetanus toxoid 6 Lf per 0.5 mL adsorbed on to aluminium phosphate).

Tetanus vaccination protects by stimulating the production of antitoxin, which protects against the toxin produced by the organism. The immunogen is prepared by treating a cell-free preparation of toxin with formaldehyde and thereby converting it into the innocuous tetanus toxoid. Tetanus toxoid is usually adsorbed on to an adjuvant, either aluminium phosphate or aluminium hydroxide, to increase its immunogenicity. Antigens from *Bordetella pertussis* also act as an effective adjuvant.

Tetanus vaccine is available as DTPa-hepB, DTPa-Hib, DTPa, DTPw, DT, Td and tetanus toxoid. Because the proportion of the population with immunity to diphtheria is poor and is at a level at which outbreaks might occur, a vaccine with a combination of tetanus and diphtheria toxoid should always be used in preference to tetanus toxoid alone. Tetanus toxoid should only be used alone if diphtheria toxoid is contraindicated.

Transport, storage and handling

Transport in an insulated container with approved freeze monitor, and time-temperature monitor. Observe the national guidelines for packing vaccines in insulated containers. Do not freeze or store vaccine in direct contact with ice packs. If vaccine has been exposed to temperature less than 0ºC, do not use. Store in refrigerator at 2ºC to 8ºC and protect from light. Check expiry date on vial or container before storage. Rotate stock so that shortest date vaccines are used first.

The ampoule should be shaken vigorously immediately prior to use and the vaccine injected as soon as possible.

Dosage and administration

The dose is 0.5 mL given by deep intramuscular injection into the anterolateral aspect of the thigh or the deltoid region of the arm. Tetanus vaccines should be given in a different limb from other concurrently administered vaccines. Accurate recording of the sites of injection of concurrently administered vaccines allows any local reactions to be attributed to the appropriate vaccine. Unless a combination vaccine containing DTPa and Hib is used, DTP-containing vaccines (or DT if DTP is contraindicated) should routinely be injected on the right side and Hib on the left side. Do not mix DTP-containing vaccines or DT vaccine with any other vaccine in the same syringe.

Recommendations

Primary vaccination

Tetanus vaccination is part of the standard childhood vaccination schedule (see Part 1.8, page 38). Primary vaccination for children or adults is achieved with 3 doses of a tetanus toxoid-containing vaccine at 2 monthly intervals (minimal interval 1 month). Children should be given boosters at 18 months and 4 years. Prior to the 8th birthday, a DTPa-containing vaccine should be given. After the 8th birthday Td should be given (see 'catch-up' schedule, Part 1.9, page 45). The change to Td (low dose diphtheria toxoid) after the 8th birthday is related to the reduced tolerance of older children and adults to diphtheria toxoid. For details on the management of children who have missed doses in the standard childhood vaccination schedule, see Table 1.9.1.

Booster doses for adolescents and adults

Young adults who have received 5 doses in their first 5 years of life should have a further dose at the age of 15-19 years. Those who have received a primary course of 3 doses as adults should receive 2 booster doses at 10 yearly intervals. Immunity following complete vaccination is long lasting. Maintenance of immunity with routine booster doses at 10 yearly intervals is no longer recommended. A booster dose is recommended at the age of 50 (unless a booster has been documented within 10 years). Older adults who have not received a dose at age 50 should receive a booster vaccination if more than 10 years have elapsed since the last dose.

The dose can be given either as tetanus toxoid vaccine or as Td. The latter is preferred.

In the event of a tetanus-prone injury (see Table 3.25.1), a booster dose of tetanus vaccine (Td or tetanus toxoid) should be given if 5 or more years have elapsed since the previous dose.

Adverse events and precautions

Mild discomfort or pain at the injection site persisting for up to a few days is common. Uncommon general adverse events following tetanus toxoid include headache, lethargy, malaise, myalgia and fever. Acute anaphylactic reactions, urticaria and peripheral neuropathy rarely occur (brachial neuritis occurs in 0.001% of cases). Too frequent administration of tetanus vaccine may provoke hypersensitivity reactions.

As with all suspected adverse events to vaccines, severe adverse events following tetanus vaccine should be reported as set out in Part 1.6, page 22.

Contraindications

The need for further tetanus vaccine or Td should be carefully assessed if an individual has previously had a severe adverse event associated with a tetanus vaccine. If an individual has a tetanus-prone wound and has previously had a severe adverse event following tetanus vaccine, alternative measures, including the use of human tetanus immunoglobulin, can be considered (see below).

Tetanus immunoglobulin

Tetanus immunoglobulin (TIG) should be used for passive protection of individuals who have sustained a tetanus-prone wound, where the person has not received 3 or more doses of a tetanus toxoid-containing vaccine or where there is doubt about their tetanus vaccination status.

The recommended dose for TIG is 250 IU IMI, to be given as soon as practicable after the injury. If more than 24 hours have elapsed, 500 IU should be given. 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.

For wounds not categorised as tetanus-prone, such as clean cuts that have been treated appropriately, TIG is unnecessary.

- Tetanus Immunoglobulin (TIG) - CSL (16% solution of immunoglobulin from selected human plasma with high concentration of antibodies to tetanus toxin 250 IU).

Tetanus immunoglobulin (human, for intravenous use)

This product is used in the management of clinical tetanus. The recommended dose is 4000 IU 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.

Tetanus immunoglobulin (human, for intravenous use) - CSL (6% solution of immunoglobulin fraction of selected human plasma with high concentration of antibodies for tetanus toxin 4000 IU).

Use in pregnancy

Tetanus vaccine is safe in pregnancy and lactation.

Conflict with product information

The PI recommends routine 10 yearly tetanus boosters, whereas ATAGI no longer routinely recommends this.

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3.26 TUBERCULOSIS

Bacteriology

Tuberculosis (TB) is caused by *Mycobacterium tuberculosis* complex (*M.TB complex*), a slow growing, aerobic, acid-fast bacillus. M.TB complex consists of *Mycobacterium tuberculosis*, *M. bovis* and *M. africanum*. *M. tuberculosis* is the commonest cause of TB in Australia. *M. bovis* and *M. africanum* as a cause of disease in Australia are rare.

Clinical features

Lung disease is the most common form, accounting for 60-70% of TB notified in Australia. Cough, fever, sweats, weight loss and haemoptysis are common symptoms of pulmonary TB. TB lymphadenitis is the most common extra-pulmonary manifestation, but the disease can occur in any part of the body, including the meninges, bone and kidneys. Disseminated disease (miliary TB) and meningeal TB are the most serious forms, particularly in children.

Most individuals infected with M. tuberculosis remain asymptomatic, but a small proportion develop clinical illness, sometimes many years after the original infection. Infants, the elderly and patients rendered immunodeficient by drugs or disease or as a result of socio-environmental circumstances (eg. malnutrition, alcoholism etc) are more prone to rapidly progressive or generalised infection.

Epidemiology

About 1,000 cases of TB are notified to Australian health authorities each year. The annual notification rate for TB over the last decade has been stable at 5-6 cases per 100,000 population and multi-drug resistance remains rare, occurring in less than 2% of notified cases. Tuberculosis in animals (M. bovis) has been virtually eradicated by screening and culling programs. In Australia, most TB (70-80%) occurs in migrants, particularly from Asia, Southern and Eastern European countries and the Pacific Islands. Rates of TB are also high in Aboriginal and Torres Strait Islander people in some parts of Australia. Immunocompromised patients are at high risk of developing active TB if they are infected with

M. tuberculosis. Screening programs in Australia now concentrate on those at high risk, including contacts of notified patients.

Vaccine

- BCG vaccine - CSL/Connaught (multidose vial containing 1.5 mg freeze dried lyophilised vaccine containing live attenuated M. bovis + 1.5 mL buffered saline diluent in a separate ampoule. The reconstituted vaccine provides 10 adult or 20 infant doses of the vaccine).

BCG (Bacille Calmette-Guèrin) vaccine is a suspension of live attenuated *M. bovis*. Worldwide, there are many BCG vaccines available but they are all derived from the strain propagated by the Institut Pasteur and first tested in humans in 1921. BCG vaccination does not always prevent TB in adults. The wide variation in protective efficacy in adults, demonstrated in controlled trials (ranging from 0-80%) has been attributed to differences in vaccine strains, prevalence of (protective) local environmental mycobacteria and host factors such as age at vaccination and nutritional status. None of these hypotheses can adequately explain the variation in efficacy. However, it should be noted that BCG is highly effective in children, offering high levels of protection against meningeal and miliary TB. A recent meta-analysis found that the overall protective efficacy of BCG for preventing serious forms of TB in children is over 80%. This finding encourages the continued use of the vaccine in high-risk infants.

Transport, storage and handling

Un-constituted (freeze-dried or lyophilised) BCG vaccine: if transporting under normal (non-frozen) conditions, transport in an insulated container with approved freeze monitor, and time-temperature monitor.

BCG can be stored in refrigerator at 2 ºC to 8ºC or stored un-constituted (freeze-dried) in a freezer at -20ºC. Storage at -20ºC to - 30ºC does not appear to affect the viability of freeze-dried BCG vaccines. Diluent should be stored at 2ºC to 8ºC and not frozen. Check expiry date on vial or container before storage. Rotate stock so that shortest date vaccines are used first. Protect from light (sunlight or fluorescent).

BCG vaccine must be reconstituted using the diluent supplied. Reconstituted BCG vaccine is very unstable and should be used during one working session of 5 – 6 hours. Reconstituted BCG vaccine must not be frozen and any unused vaccine discarded at the end of one 5 to 6 hour session regardless of how many doses remain in the vial or ampoule.

Dosage and administration

BCG vaccine is administered as a single dose by intradermal injection. BCG vaccine should only be given by medical or nursing staff who have been trained and are fully conversant with the following recommended procedure.

- A tuberculin test should be performed prior to BCG vaccination in all individuals, except in infants under 6 months of age. Only subjects in whom a test dose of 10 units produces less than 5 mm of induration should receive BCG.
- The dose of BCG is 0.1 mL for children and adults; 0.05 mL for infants under 12 months of age.
- A short (10 mm) 26-27 gauge needle with a short bevel should be used. The risk of spillage can be minimised by using an insulin syringe to which the needle is already attached.
- Protective eye-wear should be used to protect against the risk of eye splash from the intradermal injection. If an eye splash occurs, the eye should be washed with saline or water immediately.
- The site of injection is very important if the risk of keloid formation is to be minimised. The skin over the region of the insertion of the deltoid muscle into the humerus is recommended. This is just above the mid-point of the arm. For consistency aimed at assisting those who may subsequently want to find evidence of prior BCG vaccination, it is recommended that the internationally agreed convention of using the left upper arm for BCG vaccination be adopted wherever possible.
- The skin should be swabbed with alcohol and allowed to dry. Stretch the skin between a finger and thumb and insert the bevel into the dermis, bevel uppermost, to a distance of about 2 mm. The bevel should be visible through the transparent epidermis.
- The BCG injection should raise a blanched bleb of about 7 mm in diameter with the features of peau d'orange. This indicates that the injection was truly intradermal. Considerable resistance will be felt as the injection is given. If this resistance is not felt, the needle may be in the subcutaneous tissues. If that is the case, withdraw the needle and insert at a new intradermal site.
- The subject should be advised of expected adverse events following the injection.

The size of the tuberculin reaction induced by BCG ranges from 0-15

mm, but it should be noted that clinical trials have not shown a consistent relationship between the size of tuberculin reactions and the protection provided by the vaccines. For this reason, Mantoux testing of BCG vaccinees to test for a response is not routinely recommended. Because of waning hypersensitivity, most adults who were vaccinated with BCG in early childhood will have a negative tuberculin test.

Response to BCG vaccination

A small red papule forms and eventually ulcerates, usually within 2-3 weeks of vaccination. The ulcer heals with minimal scarring in several weeks. There may be swelling and tenderness in local lymph nodes. Subjects who are given BCG despite previous tuberculous infection will experience an accelerated response characterised by induration within 24-48 hours, pustule formation in 5-7 days and healing within 10-15 days.

Recommendations

Given the low incidence of TB in Australia and the variable efficacy in adults, BCG is not used in the general population.

BCG is recommended for the following:

- Aboriginal and Torres Strait Island neonates living in regions of high incidence;
- neonates born to patients with leprosy or TB; In the case of neonates born to patients with TB, give BCG after completion of isoniazid prophylaxis, as isoniazid will inactivate BCG;
- neonates or children who live in households with migrants or visitors from countries of high incidence;
- children under the age of 5 years who will be travelling to live in countries of high TB prevalence for longer than 3 months; (the WHO defines "high-risk "countries as those with an annual incidence of TB in excess of 100 per 100,000 population);
- children and adolescents aged less than 16 years who continue to be exposed to an individual with active TB; and where the child or adolescent cannot be placed on isoniazid therapy or has completed isoniazid therapy. Children and adolescents who are currently on isoniazid therapy should not be given BCG.

In addition to the above categories, there are other groups of individuals who are at increased risk of TB, but for whom the value of BCG vaccine is less certain:

- In the case of tuberculin negative health care workers, the decision to commence a program of BCG vaccination is often a matter for staff health authorities who should follow the guidelines as set down by their State TB Control Unit. These authorities should arrange for periodic surveillance of tuberculin reactivity, or should initiate special surveys after accidental exposure in keeping with the policy of their State.
- Travellers over the age of 5 years who will spend prolonged periods in countries of high TB prevalence.

Adverse events and precautions

Abscesses, lymphadenopathy, gross local reactions and disseminated infections occur rarely. Anaphylactoid reactions have also been reported. Gross local or generalised infection can be treated with antituberculous drugs. Keloid formation can occur, but the risk is minimised if the injection is not given higher than the level of the insertion of the deltoid muscle into the humerus.

BCG can cause disseminated infection in immunocompromised individuals, and is therefore contraindicated in this group.

Contraindications

The use of BCG vaccine is contraindicated in the following:

- individuals with tuberculin reactions greater than 5 mm;
- patients with HIV infection and those who are immunocompromised by use of corticosteroids, immunosuppressive drugs, radiation therapy, or malignancies involving bone marrow or lymphoid systems (because of the risk of disseminated BCG infection in these individuals);
- individuals with a high risk of HIV infection where HIV antibody status is unknown;
- individuals with significant fever;
- individuals with generalised skin diseases;
- pregnant women - BCG has never been shown to cause fetal damage, but use of live vaccines in pregnancy is not recommended;
- individuals who have previously had TB.

The tuberculin skin test

Hypersensitivity to tuberculin Purified Protein Derivative (PPD) follows natural infection with M.tuberculosis, or with other mycobacteria that

induce cross-reactivity or BCG vaccination. The skin test is used (a) to detect latent infection in contacts of patients with TB and other potentially infected individuals, (b) as an aid to the diagnosis of TB, and (c) as a prelude to vaccination with BCG.

Most tuberculin testing in Australia is performed using the Mantoux technique. The PPD preparation for this test is supplied by CSL in multidose vials containing either 100 or 1,000 units/mL. For routine testing, 0.1 mL of PPD at a strength of 100 units/mL (ie. a dose of 10 units) is injected intradermally into the skin of the upper third of the flexor surface of the forearm, producing a peau d'orange bleb 7-10 mm in diameter. The reaction is examined 48-72 hours later, and the diameter of the palpably indurated skin is measured and recorded. Two stage skin testing is recommended.

Erythema without induration should be disregarded. Strongly positive reactions may be accompanied by skin necrosis, lymphangitis and regional adenitis. Patients with a history of such reactions should either not be tested or given a dose of 1 unit.

The reaction to PPD may be suppressed by viral infections, live viral vaccines (including MMR), recent surgery, sarcoidosis, immunosuppressant drugs and immunosuppressing illnesses such as Hodgkin's disease, lymphoma and HIV infection. The reaction also wanes with increasing age, so that most adults vaccinated with BCG in childhood have negative tuberculin reactions.

The use of the Heaf gun, a multiple puncture apparatus primed with highly concentrated PPD, is not recommended.

Conflict with product information

The PI states that BCG should not be frozen. ATAGI advises that BCG can be stored un-constituted (freeze-dried) in a freezer at -20ºC.

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3.27 TYPHOID

Bacteriology

Typhoid fever is caused by the Gram-negative bacillus *Salmonella typhi*. *S. typhi* is an exclusively human pathogen.

Clinical features

A generalised infection of non-specific onset characterised by involvement of lymphoid tissue, fever, bradycardia, splenomegaly, 'rose spots' and abdominal symptoms of pain, constipation or diarrhoea. Complications such as intestinal haemorrhage or perforation can develop in untreated patients or when treatment is delayed. Untreated the infection has a mortality rate of 10-20% due to bowel perforation, haemorrhage, toxaemia and effects on remote organs. 2-5% of patients may become permanent carriers even in spite of treatment. The likelihood of becoming a chronic carrier increases with age, especially in females.

Epidemiology

Typhoid is spread mainly by the faecal-oral route, usually through contaminated food or drink. For travellers, the common sources are water or ice, raw vegetables, salads and shellfish. There are approximately 50-70 cases of typhoid reported in Australia each year, and most follow travel to countries in Asia, Africa, Oceania, Central and South America and some parts of Southern Europe. A high level of

typhoid endemicity exists in Indonesia and Papua New Guinea. Whilst most cases follow travel overseas, occasional cases result from consumption of food prepared by long term excretors of S. typhi living in Australia. Longterm carriage is an occasional feature of typhoid and hence any individual who is an excretor should be barred from being involved in the food industry.

Vaccines

- Typh-vax oral – CSL Live attenuated typhoid vaccine containing *S. typhi* strain Ty21A Berna, not less than 2 x 10^9 viable organisms; enteric coated capsules.
- Typherix-SmithKline Beecham purified Vi capsular polysaccharide 25mg plus 0.5% phenol as preservative; 0.5 mL injection.
- Typhim Vi – CSL/Pasteur Merieux 0.5mL solution containing 25mg of purified Vi capsular polysaccharide plus 0.5% phenol as preservative; 0.5mL injection.

The live attenuated vaccine is prepared from a non-pathogenic strain of *S. typhi*, which lacks the enzyme UDP-galactose-4-epimerase and Vi capsular polysaccharide. It undergoes only a few cycles of division in the gut and is eliminated within 3 days of ingestion. The immune response includes secretory IgA. The vaccine is licensed for use in individuals 6 years of age and above.

The Vi polysaccharide vaccine elicits an antibody response in more than 90% of recipients and provides 50-77% protection for at least two years.

The live attenuated oral vaccine and the Vi antigen injectable vaccine cause few adverse events. The advantage of using the injectable Vi vaccine is that clients may not comply with storage and dosage instructions for the oral vaccine.

Transport, storage and handling

Oral typhoid vaccine (Typh-vax) should be stored at 2ºC to 8ºC and protected from light and moisture. Injectable Vi vaccines should be stored at 2ºC to 8ºC. Do not freeze, and protect from light. Transport in an insulated container with approved freeze monitor, and time-temperature monitor. Check expiry date on container before storage. Rotate stock so that shortest date vaccines are used first. Discard any unused Vi vaccine within 4 hours of opening or at the end of the session.

Dosage and administration

i) Oral Live Attenuated Vaccine

The vaccination schedule consists of one capsule of vaccine on days 1, 3, and 5, to be taken 1 hour before food. A fourth capsule taken on day 7 will elicit an even greater and longer lasting immune response, and is recommended by some travel advisers. The use of a fourth dose requires partial use of a second pack and therefore may involve the subject in considerable extra expense. However, for any individual going to live for a long time in an endemic area the four-dose regime may be preferred, as boosters will then be needed only at five yearly intervals.

Booster doses of oral live attenuated vaccine are required at three yearly intervals when the primary vaccination has been with three doses. If the primary vaccination is with four doses, boosters are required at five yearly intervals.

The capsule must be swallowed whole and must NOT be chewed since the organism is destroyed by gastric acid. The vaccine should NOT be given concurrently with antibiotics, sulphonamides or the antimalarial proguanil. The vaccine may be administered at the same time as either OPV or Yellow Fever vaccine. If it is not administered at the same time as OPV, the administration of OPV should be delayed for two weeks after the last dose of typhoid vaccine. This is because the oral typhoid vaccine engenders a strong mucosal interferon response, which may reduce the efficacy of OPV. If oral cholera vaccine is to be administered, there should be an interval of at least eight hours between administration of oral cholera and oral typhoid vaccines.

ii) Vi Polysaccharide Vaccine

It is given as a single intramuscular dose of 0.5mL. Booster doses of Vi polysaccharide vaccine should be given at two yearly intervals. Both Typherix and Typhim Vi can be used from the age of 2 years.

Recommendations

Typhoid vaccination is only recommended for travellers to countries where hygiene is poor or drinking water is unsafe, and where the traveller is likely to be placed at risk, that is in endemic countries. Laboratory workers may be considered for vaccination, based on an assessment of risk. Typhoid vaccination is recommended for those persons with intimate exposure to a documented typhoid fever carrier, such as occurs with continued household contact.

Adverse events and precautions

Oral Live Attenuated Vaccine

These are infrequent and generally mild. The following have been reported in trials: constipation, abdominal cramps, diarrhoea, nausea, vomiting, anorexia and fever.

Vi Polysaccharide Vaccine

Side effects are normally mild and transient. Erythema, swelling and pain commonly occur at the site of injection. Systemic adverse events are infrequent and include fever, headache, malaise and nausea.

Contraindications

Oral Live Attenuated Vaccine - this vaccine should not be given to the following individuals:

- those with an intercurrent febrile illness or acute gastrointestinal infection;
- those who have had severe adverse events following the oral vaccine on previous exposure;
- those who are immunocompromised, including those known to be infected with HIV;
- in children less than 6 years of age because studies of efficacy and safety have not been carried out in this group;
- those who are taking sulphonamides, other antibiotics or the antimalarial proguanil.

Polysaccharide Vaccine- this vaccine should not be given to the following individuals:

- any individual suffering or convalescing from an acute febrile illness;
- those who have had a severe systemic or allergic reaction following a prior dose;
- children under 2 years of age.

Use in Pregnancy

There is no evidence of risk to the fetus from vaccination with the Vi inactivated vaccine. Studies in animals are inadequate but available data shows no evidence of an increased occurrence of fetal damage with oral live attenuated vaccine. Its use in pregnancy however, should be based on an assessment of the real risk of disease.

Conflict with Product Information

Product information for Typh-vax (oral) and Typhim Vi (injectable) vaccines do not give recommendations for booster doses. The Typherix PI recommends a booster dose every 3 years but acknowledges that the data are limited.

The PI does not recommend a 4th capsule of Typh-vax (oral). ATAGI recommends that a 4th capsule can be used.

The PI does not recommend Typhim Vi vaccine for children <5 years of age, but ATAGI recommends it for children 2 years and over.

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3.28 VARICELLA-ZOSTER

Virology

Varicella (chickenpox) is a highly contagious infection caused by the varicella-zoster virus, a member of the herpes virus family. It is a DNA virus with a lipid envelope surrounding a nucleocapsid with icosohedral symmetry.

Clinical features

Chickenpox is usually a mild disease of short duration in healthy children. It is more severe in adults and can cause serious and even fatal illness in immunosuppressed subjects of any age. The mortality rate in immunocompromised individuals is 7-10% compared with 0.1-0.4% in healthy children. The average incubation period is 14-15 days, followed by the appearance of a rash. Acute varicella may be complicated by cerebellitis, aseptic meningitis, transverse myelitis, thrombocytopenia, and pneumonia. In rare cases, it involves the viscera and joints. Aspirin or other salicylates should not be given to patients with varicella because of the association with Reye's syndrome.

Herpes zoster is a localised vesicular rash resulting from the reactivation of latent varicella-zoster virus in a period of waning immunity. Herpes zoster is often a serious illness in older adults and immunocompromised individuals, and some may develop disseminated zoster with visceral, CNS, and pulmonary involvement.

Severe neonatal varicella infection can result from perinatal maternal varicella. Congenital varicella syndrome has been reported after varicella infections in the first half of pregnancy and may result in congenital malformations, skin scarring, and other anomalies. Recent data from Europe indicate a higher risk when maternal infection occurred between 13 and 20 weeks of gestation compared with those infections between 0 and 12 weeks (2% vs. 0.4%). Infants with intrauterine exposure also have a risk (0.8-1.7%) of developing Herpes zoster in infancy with the greater risk following exposure between 25 and 36 weeks. The onset of chickenpox in pregnant women from 5 days before delivery to 2 days after delivery is estimated to result in severe varicella in 17-30% of their newborn infants.

Epidemiology

By the age of 12 years, about 75% of children will have had varicella. About 5% of cases are sub-clinical. There are 240,000 cases, 1,200 hospitalisations and 4.2 deaths each year from varicella in Australia.

Zoster is uncommon before the age of 12 years (1% of cases), and most cases (81%) occur over the age of 40 years. Vaccination results in a lower rate of zoster (2.6/100,000) compared to natural infection (68/100,000).

Vaccine

Live attenuated varicella-zoster vaccine (OKA strain) is presented in a freeze-dried (lyophilised) form. A single dose is sufficient for infants and children but immunosuppressed individuals, healthy adolescents (13 years and older) and adults require 2 doses, 1-2 months apart. Seroconversion occurs in 90-100% of those vaccinated and about 70% are protected when exposed to infection within the household. Breakthrough infection after exposure occurs at a rate of 1-2% a year in those vaccinated; these infections are usually mild. The duration of immunity from vaccination is not yet known and booster doses may be required. Two products will be available in Australia in 2000. The storage requirements are different for the two vaccines (see under "Transport, storage and handling").

- Varilrix – SmithKline Beecham (lyophilised preparation of live attenuated Oka strain of varicella-zoster virus). Prepared by propagation of virus in MRC5 human diploid cells. Reconstitution with diluent makes 0.5 mL dose, containing not less than $10^{3.3}$ plaque forming units. The vaccine also contains amino acids, human albumin, lactose, neomycin sulphate and polyalcohols. Varilrix does not contain a preservative.
- Varivax - CSL/Merck Sharpe Dohme (lyophilised preparation of live attenuated Oka/Merck strain of varicella-zoster virus). Prepared by propagation of virus in WI38 human diploid cells and further passage of virus in MRC5 human diploid cells. Reconstitution with diluent makes 0.5 mL dose, containing not less than 1350 plaque forming units. Each 0.5ml dose contains: approximately 25mg sucrose, 12.5mg hydrolyzed gelatin, 3.2mg sodium chloride, 0.5mg monosodium L-glutamate, 0.45mg sodium phosphate dibasic, 0.08mg potassium phosphate monobasic, 0.08mg potassium chloride; residual components of MRC-5 cells including DNA and protein; and trace quantities of sodium phosphate monobasic, EDTA, neomycin, and fetal bovine serum. This product contains no preservative.

Transport, storage and handling

Varicella vaccine is less stable than other live virus vaccines, and the storage temperature requirements are critical. The vaccine must be stored according to the manufacturer's instructions. In terms of storage,

commercially available varicella-zoster vaccines are of 2 types - those which must be kept frozen at -15ºC (Varivax - CSL/Merck Sharp Dohme), and those which can be stored at 2 ºC to 8ºC (Varilrix - SmithKline Beecham). It is important to recognise that the storage requirements for the two available vaccines are different. Varivax must be stored at -15ºC or below in a freezer which has a separate sealed freezer door, and that reliably maintains temperatures below -15 ºC; Varivax must be administered immediately after reconstitution, and should be discarded if not used within 30 minutes.

Varilrix, on the other hand, can be stored between 2 ºC to 8ºC for 24 months from the date of manufacture. The lyophilised vaccine is not affected by freezing, however the diluent should not be frozen and can be stored in the refrigerator or at ambient temperatures.

Dosage and administration

Varilrix and Varivax should be administered as a single 0.5ml dose by subcutaneous injection only. The upper arm (deltoid region) is the preferred site of injection. Under no circumstances should varicella vaccine be administered intravenously. They should not be administered intradermally or intramuscularly. The vaccine can be given at the same time as MMR or other vaccines using separate syringes and injection sites. If varicella vaccine is not given simultaneously with other parenterally administered live vaccines, they should be given at least one month apart.

Recommendations

The NHMRC has approved the use of varicella vaccine for children from 12 months of age. However, the vaccine has not been included in the standard childhood vaccination schedule, as this would require three injections (MMR, Hib or Hib(PRP-OMP)-hepB, V) at 12 months of age. Varicella vaccine may be included in the schedule in the future, particularly once a combined MMR-V vaccine is registered. Meanwhile, parents who express an interest in varicella vaccine should be encouraged to have their child vaccinated, as long as compliance with the schedule vaccines can be ensured. Although vaccination at the age of 12 months provides earlier protection, a convenient alternative is to offer the vaccine at 18 months of age, when only one other injection (DTPa) is given in the standard schedule.

Varicella vaccine is recommended for use in non-immune adolescents (13 years and older) and adults; these subjects require 2 doses, 1-2 months apart. The vaccine is especially indicated for non-immune

people in high-risk occupations (such as health-care workers, teachers and workers in child day-care centres); for non-immune women prior to pregnancy; for non-immune parents of young children and for non-immune household contacts, both adults and children, of immunosuppressed persons.

A past history of varicella is highly correlated with serologic evidence of immunity. Children who have a reliable history of varicella are considered immune and those who do not have such a history or who have an uncertain history are considered susceptible. Serologic testing of children 12 years of age and younger before vaccination is not warranted. Persons aged 13 years or older who have a reliable history of varicella should be considered immune. Many adults and adolescents who do not have a history of varicella are also immune (61% in a study of 300 adults aged 17-49 years in Sydney). Therefore serologic testing before vaccination is likely to be cost-effective for both adults and adolescents with a negative history of varicella-zoster. If it is more convenient, adolescents and adults can be vaccinated without testing (provided there are no contraindications), as the vaccine is well tolerated in seropositive persons.

Varicella vaccine has been used to prevent infection following exposure, in some small studies. This was successful if the vaccine was given within three days of exposure. However, the vaccine available in Australia has not been approved for use in post-exposure prophylaxis or outbreak control.

A number of matters pertaining to varicella vaccine use were still under consideration by ATAGI at the time of publication of this edition of the Handbook. These include: use of vaccine in outbreak control, guidelines for serologic testing and vaccination of healthcare workers, and vaccine use in children being treated with immunosuppressive agents. NHMRC will publish recommendations regarding these issues as soon as they are finalised and following the usual consultation process.

Adverse events

Adverse events are uncommon in healthy individuals. They include local reactions (20%), fever (1-6%), and a mild papular-vesicular rash which may be generalised (1-6%) or at the injection site (1-3%). After the second dose in adolescents and adults, local reactions are also observed in about 20% of vaccinees, but other reactions are rare. In immunosuppressed individuals, local reactions are no more common, but general adverse events occur much more frequently (about 12% of

cases; as high as 40% in leukaemia patients on maintenance therapy). Clinical varicella occurs in about 1% of immunosuppressed individuals after vaccination. In leukaemia patients, about 40% of those vaccinated develop a rash after the 1st dose, and in 4% the varicella is severe enough to warrant the use of acyclovir.

Transmissibility of vaccine virus

In the USA, where 15 million doses of varicella vaccine have been distributed, there have been only three reports of transmission of the vaccine-type virus from a healthy vaccinee to a healthy contact, and all contact cases have been mild. The risk of spread to contacts from immunosuppressed subjects is greater.

Contraindications

The vaccine should not be given during pregnancy and vaccinees should not become pregnant for one month after vaccination. Women who have been inadvertently vaccinated during pregnancy are being followed up in the USA, and to date there has been no congenital infection in about 150 completed pregnancies. In the USA, an immune pregnant household contact is not a contraindication for vaccination of another healthy child or adult in the same household. Recommendations cannot yet be made about the advisability of vaccinating non-immune post-partum women due to lack of data about communicability in this situation.

The vaccine is also contraindicated in subjects with HIV infection or other immunodeficiencies, and those taking high dose corticosteroids (equal to or greater than 2 mg/kg of prednisolone per day).

It is also contraindicated in those who have had an anaphylactic reaction to neomycin.

There are no data on the use of the vaccine before or after human immunoglobulin, which may inhibit a response to the vaccine virus. In the USA it is suggested that varicella vaccine not be given for 5 months following human immunoglobulin administered by intramuscular injection or blood transfusion, and 9 months following immunoglobulin administered intravenously. It is also suggested that immunoglobulin should not be given for at least 3 weeks after vaccination.

Conflict with Product Information

Varilrix™ vaccine is approved for use in healthy children from nine months of age, however the ATAGI recommends that this vaccine be used in healthy children who are twelve months of age or older.

The PI for Varilrix ™ states that in subjects who have received immune globulin or a blood transfusion, immunisation should be delayed for at least three months because of vaccine failure due to passively acquired varicella antibodies. Note that this is in conflict with the US recommendation of five months quoted above under "Contraindictions".

Use of immunoglobulins for prevention of varicella

High-titre varicella-zoster immunoglobulin (ZIG) is available from the Red Cross Blood Transfusion Service on a restricted basis for the prevention of varicella in high-risk subjects. ZIG must be given early in the incubation period (within 96 hours of exposure).

Normal immunoglobulin (human) can be used for the prevention of varicella if ZIG is unavailable.

ZOSTER IMMUNOGLOBULIN

Zoster immunoglobulin (human) - CSL (16% solution of gamma globulin fraction of human plasma from donors with high titre of varicella-zoster antibodies vials containing 200 IU V-Z antibody for intramuscular injection).

Recommendations

ZIG should be given to individuals in the following categories if they are significantly exposed to varicella or zoster:

- patients suffering from diseases associated with cellular immune deficiency (eg. Hodgkin's disease);
- those receiving immunosuppressive therapy;
- pregnant women who are susceptible to varicella infection (they should be tested for varicella-zoster antibodies);
- neonates whose mothers are susceptible to varicella infection (ie. who show no antibodies on testing);
- premature infants born at less than 28 weeks gestation (or less than 1,000 g), regardless of maternal history of varicella.

'Significant exposure' is defined as a household contact, play contact of longer than 1 hour, classroom contact, or other close prolonged exposure.

ZIG must be given to neonates whose mother develops chickenpox 7 or fewer days before delivery or 7 or fewer days after delivery, as the

neonatal mortality without ZIG was 30% in this setting. ZIG must be given as early as possible in the incubation period - within 96 hours of exposure if possible. ZIG is highly efficacious, but is often in short supply.

The following dose schedule is recommended for ZIG administration.

Table 3.28.1: Zoster immunoglobulin dose based on weight

Weight of patient (kg)	Dose	No. of vials
0-10	125	1
10-20	250	2
20-30	375	2
30-40	500	3
over 40	600	3

The dose may be repeated if a 2nd exposure occurs more than 3 weeks after the 1st dose. Normal immunoglobulin (human) can be used for the prevention of varicella if ZIG is unavailable (see part 3.9, page 136).

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3.29 YELLOW FEVER

Virology

Yellow fever is caused by an arbovirus, classified as a flavivirus. It is transmitted by the bite of a mosquito.

Clinical features

Yellow fever is an acute viral haemorrhagic fever. The incubation period is 2-5 days. It ranges from a clinically indeterminate condition to an illness of sudden onset with fever, vomiting and prostration that may progress to haemorrhagic symptoms and jaundice. The case fatality is about 5% in indigenous populations in endemic areas, whereas in non-indigenous individuals, or during epidemics, it may be as high as 50%.

Epidemiology

Yellow fever infection is currently restricted to parts of South America and Africa. Urban yellow fever is transmitted from person to person by the *Aedes aegypti* mosquito. In areas where *A. aegypti* has been eliminated or suppressed, urban yellow fever has disappeared. Jungle yellow fever is a zoonosis transmitted among non-human hosts (mainly monkeys) by a variety of forest mosquitoes, which may also bite and infect humans. Such infected humans may, if subsequently bitten by *A. aegypti* mosquitoes, become the source of outbreaks of the urban form of the disease.

Periodic outbreaks of urban yellow fever have occurred in some South American countries in recent years, and continue at frequent intervals in

West and East Africa, both in towns and rural villages. Hundreds of cases of jungle yellow fever occur each year in South America, and epidemics involving tens of thousands of cases occur frequently in different parts of Africa. It is believed that jungle yellow fever is greatly under-reported, and it may be active but unrecognised in forested areas of countries within the yellow fever endemic zone.

It should be noted that the WHO list of countries with yellow fever risk may not include countries with recent spread, particularly in West Africa. It may therefore be wise to vaccinate travellers going to countries adjacent to those with known yellow fever risk.

Preventive measures against urban yellow fever include eradication of *A. aegypti* mosquitoes, protection from mosquito bites, and vaccination. Jungle yellow fever can only be prevented in humans by vaccination.

Vaccine

- Yellow fever vaccine – Stamaril CSL/Pasteur Merieux : live attenuated yellow fever virus (17D strain) freeze-dried vaccine; each 0.5 mL dose contains not less than 1,000 mouse LD_{50} units. The vaccine is propagated in chick embryos. It is supplied as a single dose ampoule.

Yellow fever vaccine is a live freeze-dried preparation of the 17D attenuated strain of yellow fever virus. The 17D vaccine has proven extremely safe and effective.

Transport, storage and handling

The currently available vaccine has different storage requirements to the previous vaccine. The current vaccine must be protected from light and stored at 2ºC to 8ºC. It must not be frozen. After it has been reconstituted with the accompanying 0.4% sodium chloride solution as described in the product leaflet, it must be used within 1 hour.

Dosage and administration

A single deep subcutaneous or IM injection of 0.5 mL of reconstituted vaccine is used for persons of all ages.

Recommendations

- Persons 6 months of age or older travelling or living in yellow fever infected areas should be vaccinated.
- Vaccination is also recommended for travel outside the urban areas of countries in the yellow fever endemic areas.
- Infants under 6 months but over 4 months of age, and pregnant

women should be considered for vaccination if travelling to high-risk areas when travel cannot be postponed and a high level of prevention against mosquito exposure is not feasible. The vaccine must not be given if 4 months or younger.

- Laboratory personnel who might be exposed to virulent yellow fever virus should also be vaccinated.

Adverse events

Adverse events following 17D yellow fever vaccine are generally mild. 2-5% of vaccinees have mild headaches, myalgia, low grade fevers or other minor symptoms 5-10 days after vaccination. Adverse events so severe as to curtail regular activities occur in less than 0.2% of cases.

Immediate hypersensitivity reactions characterised by rash, urticaria, and/or asthma, are extremely uncommon (incidence less than 1 in 1,000,000) and occur principally in persons with histories of egg allergy. More than 34 million doses of vaccines have been distributed, but only 21 cases of encephalitis temporally associated with yellow fever vaccination have been reported worldwide since the early 1950's; in one fatal case, 17D virus was isolated from the brain.

Contraindications

If international travel regulations are the only reason to vaccinate a patient in whom any of the following contraindications apply, efforts should be made to obtain a waiver. A physician's letter clearly stating the contraindication(s) to vaccination is acceptable to some governments. Ideally, the letter should be written on letterhead stationery and bear the stamp used by the health authority and official vaccination centres to validate the International Certificates of Vaccination. Under these conditions, it is also useful for the traveller to obtain specific and authoritative advice from the country or countries he or she plans to visit, and their relevant embassies or consulates should be contacted. Subsequent waiver of requirements should be documented by appropriate letters.

Infants

Infants under 6 months of age are theoretically more susceptible to serious adverse events (encephalitis) than older children. However, as with pregnant women, vaccination may be considered if the risk of infection with yellow fever is high.

Pregnancy

Although specific information is not available concerning adverse effects

of yellow fever vaccine on the developing fetus, it is prudent on theoretical grounds to avoid vaccinating pregnant women, and to postpone travel to areas where yellow fever is present until after delivery. Pregnant women who must travel to areas where the risk of yellow fever is high should be vaccinated. It is believed that under these circumstances, the small theoretical risk for mother and fetus from vaccination is far outweighed by the risk of yellow fever infection.

Altered immune status.

Infection with yellow fever vaccine virus poses a theoretical risk to patients with leukaemia, lymphoma, symptomatic HIV infection, or generalised malignancy, and also to those whose immune responses are suppressed by corticosteroids, alkylating drugs, antimetabolites or radiation. Short-term (less than 2 weeks) corticosteroid therapy or intra-articular, bursal, or tendon injections with corticosteroids should not be immunosuppressive and constitute no increased hazard to recipients of yellow fever vaccine.

Hypersensitivity.

Live yellow fever vaccine is produced in chick embryos and should not be given to persons with anaphylaxis to eggs. Test doses are absolutely contraindicated for people with anaphylactic egg allergy. Generally, persons who are able to eat eggs or egg products may receive the vaccine.

Administration of other vaccines on the same day

The serological response to yellow fever vaccine is not inhibited by administration of certain other vaccines concurrently or at intervals of a few days to 1 month. However, if live virus vaccines (eg. measles) are not given concurrently with yellow fever vaccine, 4 weeks should elapse between sequential vaccinations. Similarly, cholera and yellow fever vaccines should be administered at a minimum interval of 4 weeks; if time constraints preclude this, they should be given simultaneously at separate sites. There are no data on possible interference between yellow fever and vaccines such as typhoid, typhus, hepatitis B, plague, rabies, or Japanese encephalitis.

A prospective study of persons given yellow fever vaccine and 5 mL of commercially available immunoglobulin revealed no alteration of the immunological response to yellow fever vaccine when compared with controls.

Vaccination for international travel

For purposes of international travel, yellow fever vaccines produced by different manufacturers worldwide must be approved by the World Health Organization and administered at an approved yellow fever vaccination centre. Vaccinees should have an International Certificate of Vaccination filled in, signed, and validated with the stamp of the centre where the vaccine is given.

The requirement for vaccination for international travel depends on the countries to be visited and the route taken. These requirements may change from time to time, so all travellers should seek current information from State or Territory health authorities (see Appendix 1). Travellers requiring yellow fever vaccination should be advised to contact the nearest official vaccination centre. Other countries may have differing requirements, and travellers should check with the appropriate consulates. Individuals who fail to comply with requirements for yellow fever vaccination may be quarantined.

All persons over 1 year of age who, within 6 days of arrival in Australia, have been in or passed through an infected area as listed by the World Health Organization must be in possession of a current valid International Certificate of Vaccination against yellow fever.

The validity of a yellow fever vaccination certificate extends for 10 years, commencing 10 days after the date of vaccination, or, in the case of revaccination before expiry of the previous certificate, from the date of that revaccination.

Conflict with product information

ATAGI recommends the vaccine for persons at risk aged 6 months or over, but states that it can be considered in infants under 6 months, if the risk of exposure is high. The product information states that it should not be used under 6 months and, in addition, that the vaccine should be used with caution between 6 and 12 months.

The PI recommends a test dose of yellow fever vaccine if there is a history of egg allergy. ATAGI states that test doses are contraindicated in people with a history of anaphylactic egg allergy.

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APPENDIX 1

CONTACT DETAILS FOR VACCINATION ISSUES WITHIN THE COMMONWEALTH GOVERNMENT HEALTH AUTHORITY

Commonwealth 02 6289 1555

Australian Childhood Immunisation Register: contact the Health Insurance Commission on 1 800 653 809.

This phone number can also be used by vaccination providers to obtain information on the vaccination history of individual children.

National Centre for Immunisation Research and Surveillance (02) 9845 0520

CONTACT DETAILS FOR IMMUNISATION IN STATE AND TERRITORY GOVERNMENT HEALTH AUTHORITIES

Australian Capital Territory Immunisation Inquiry Line	(02) 6205 2300
ACT Immunisation Unit	(02) 6205 0860
New South Wales - Contact the local Public Health Units	(look under "Health" in the White pages.)
Northern Territory	(08) 8922 8044
Queensland	(07) 32341500
South Australia Immunisation Coordination Unit	(08) 8226 7177
SA (24-hour) Parent Help-line (Child and Youth Health)	1300 364 100
Tasmania	(03) 6233 3762 or 1800 671 738
Victoria	(03) 9637 4144
Western Australia	(08) 9321 1312

APPENDIX 2

STANDARDS FOR CHILDHOOD VACCINATION

The following is a summary of the standards for childhood vaccination which were developed by the National Immunisation Committee in consultation with the National Immunisation Education sub-committee which consists of representatives from professional organisations. They are intended as a guide rather than a legalistic imposition on providers, and can provide the basis for quality assurance at all levels in the health system. As such they have been endorsed by the Australian Medical Association, the Royal Australian College of General Practitioners and the Australian College of Paediatrics and have been welcomed by a variety of other professional bodies.

Standard 1	Vaccination services are readily available.
Standard 2	There are no barriers or prerequisites to vaccination services.
Standard 3	NHMRC recommended childhood vaccines are offered free, without cost to parent or guardian.
Standard 4	Vaccination providers utilise all clinical encounters to assess vaccination status and, when indicated, vaccinate children.
Standard 5	Providers educate parents and guardians about vaccination.
Standard 6	Providers question parents or guardians about contraindications and, before vaccinating a child, inform them in specific terms about the benefits and risks of the vaccines their child is about to receive.
Standard 7	Providers withhold vaccination only for true contraindications.
Standard 8	Providers offer and administer, where possible, all vaccines for which a child is due at the one visit.
Standard 9	Providers use accurate and complete recording procedures.
Standard 10	Providers report adverse events following immunisation promptly, accurately and completely as set out in section 1.6.
Standard 11	Providers adhere to appropriate procedures for vaccine cold- chain management.

Standard 12 Vaccination providers maintain current and easily retrievable vaccination guidelines at all locations where the vaccines are administered.

Standard 13 Vaccines are administered by properly trained individuals who receive ongoing education and training on current vaccination recommendations.

APPENDIX 3: THE GOLDEN RULES OF IMMUNISATION & THE 'COLD - CHAIN'

GOLDEN RULES OF IMMUNISATION

Can be copied or made into a poster for vaccine service providers.

General issues related to the Schedule

1. Follow the Australian Standard Vaccination Schedule (ASVS) guidelines and the recommendations of the NHMRC at all times. All infants are now offered 1st hepatitis B vaccine at birth.
2. Administer all the recommended vaccines on the Schedule at the recommended time. Reducing the intervals between doses should only be done during a 'catch-up' schedule.
3. Check and record the immunisation status of all children and adults regularly, and offer opportunistic immunisation if needed.
4. Do not defer, postpone or advise against immunisation unless a true contraindication exists.

Prior to vaccination

5. Ensure there are adequate trained staff, emergency equipment and drugs to deal with rare post-vaccination complications. It is important that the correct strength of adrenaline is kept close at hand in case of anaphylaxis.
6. Discuss the risks and benefits of immunisation and ensure that valid consent is obtained prior to immunisation.
7. Use the pre-vaccination questionnaire to help assess the child or adult's health status prior to vaccination.

Administration of vaccines

8. Administer all due vaccines on the same day, but give them in separate sites (ie. use different limbs) using separate syringes.
9. Check the expiry date of all vaccines prior to drawing up, and record the batch number in the patient's records and the child's Personal Health Record.
10. Draw up vaccines using sterile technique.

11. Never mix separate vaccines in the same syringe and never mix vaccine with other drugs.

12. Do not give test doses or half doses of vaccine.

13. Give all injections in children less than 12 months old, in the antero-lateral thigh, NOT the buttock.

14. Give all injections to children 12 months or older in the deltoid.

15. Give vaccines intramuscularly with the exception of OPV (polio vaccine) which is given orally. Note that MMR, influenza and pneumococcal vaccines can be administered either by intramuscular or deep sub-cutaneous injection. JE and varicella vaccines are administered sub-cutaneously.

16. Opened vials of Oral Polio Vaccine can be re-used until they are empty, provided that when not in use, the vial is capped, stored between 2 to 8 degrees C and the expiry date has not passed.

Documentation and notification

17. Record all vaccinations:

    - on the Australian Childhood Immunisation Register (if under 7 years of age);
    - in the child's Personal Health Record folder (kept by parent or carer). Adults should also be given a "take-home" record of vaccination; and
    - in the child's clinical record file in your clinic or surgery.

18. Record and notify all significant adverse events following immunisation (see Part 1.6, page 22 of this Handbook for details).

After Vaccination

19. All parents/guardians should be given pre and post immunisation advice as per the NHMRC guidelines.

20. Keep all vaccinated patients under observation (in the waiting area near the clinic/surgery) for at least 15 minutes after vaccination.

Keeping vaccines potent (the 'Cold- Chain')

'Cold- Chain' Management'

21. Store, transport and maintain vaccines at a temperature of between 2 to 8 degrees C.

22. Have a maximum/minimum thermometer in the vaccine refrigerator. The temperature needs to be read and recorded daily and kept at between 2 to 8 degrees C. Do not allow vaccines or diluent to freeze (with the exception of oral polio vaccine).

23. Ensure there is one person responsible for the 'cold- chain' in your clinic/surgery and that other staff are aware of how to monitor and maintain the 'cold- chain'.

Vaccine Refrigeration and Storage

24. Ensure a separate vaccine refrigerator (preferably a 'frost free' type) exists solely for the storage of vaccines. Do not store food or other items in this refrigerator.

25. Store vaccine on the middle and upper shelves only and keep them away from the evaporation plate.

26. Fill lower drawers and door spaces with plastic bottles filled with salt water (label the salt water bottles).

27. Make sure your fridge is defrosted regularly and ice is not allowed to build (not necessary for frost-free types).

28. Store vaccine in an insulated container with an ice brick while defrosting the fridge. Keep vaccine away from direct contact with the ice brick.

29. Return all unused vaccine to the refrigerator immediately.

Vaccine delivery and transport

30. Unpack and check the 'cold- chain' monitors (heat and freeze) if they are used in your state or territory. Store vaccines promptly.

31. Transport vaccine in an insulated container with an ice brick and monitor temperatures during transport.

32. During transport, ensure the vaccines do not directly contact the ice bricks. Wrap them up.

Vaccine damage

33. In Australia freezing is the main cause of vaccine damage in both tropical and temperate areas.

FREEZING INACTIVATES MOST VACCINES.

DO NOT FREEZE: DTPa containing vaccines, Comvax, Pedvax Hib,

HibTiter, Hepatitis B vaccine, Influenza or Pneumococcal vaccines; Td, CDT, TT, Hepatitis A, any reconstituted vaccines and diluents.

34. DO NOT EXPOSE TO LIGHT: reconstituted MMR, BCG or Sabin (OPV)

35. Always contact your State/Territory Vaccine Distribution Centre before you discard any vaccine.

Remember - an un-immunised child is an 'at risk' child.

Acknowledgements: *This document is based on the Golden Rules developed by the North East Valley Division of General Practice in Victoria.*

APPENDIX 4

THE FUTURE - LIKELY DEVELOPMENTS IN VACCINE AVAILABILITY IN AUSTRALIA

Vaccines likely to be available in the short to medium term include:

Combination vaccines

The following combination vaccines are in advanced stages of clinical trial evaluation:

DTPa-Hib-hepB
DTPa-hepB-IPV given in the same syringe as Hib
MMR-varicella

Pneumococcal conjugate vaccines

A 7-valent conjugate pneumococcal vaccine may be licensed in the US in 2000. This vaccine is given as a 2, 4, and 6-month primary course with a booster in the second year of life. A number of other conjugate vaccines are in clinical trials including 9-valent and 11-valent vaccines.

Meningococcal conjugate vaccines

A Meningococcus C conjugate vaccine has been licensed and introduced into the British infant schedule. This vaccine will be given in the same infant schedule as is used for current UK vaccines (primary course at 2, 3 and 4 months). Work is progressing on combining conjugate meningococcal vaccine with conjugate pneumococcal vaccine, possibly in combination with other vaccines.

Influenza

A nasal spray cold-adapted heat-attenuated live influenza vaccine has been shown to have high efficacy and low reactogenicity in children and adults and this vaccine could be licensed in the US within a year. Dose frequency will be the same as for the injected killed vaccine in current use, namely annual vaccination for all, and 2 doses 1 month apart for the first year of vaccination in children under the age of 9 years.

APPENDIX 5

QUESTIONS OFTEN ASKED ABOUT VACCINATION BY PARENTS AND PROVIDERS

1. THE AUSTRALIAN STANDARD VACCINATION SCHEDULE

1.1 Can more than one vaccine be given at the same time?

The vaccines recommended for routine use in infants and children (DTPa, DTPa-hepB, Hib(PRP-OMP)-hepB, poliomyelitis, MMR, and Hib) can safely be administered at a single visit, as long as they are given in separate syringes in different parts of the body.

Other injectable inactivated vaccines, such as typhoid, cholera, meningococcal and pneumococcal vaccines, can be given on the same day but in separate syringes. Oral polio vaccine should not be given until 2 weeks after oral typhoid vaccine unless administered at the same time.

1.2 Do you have to start the schedule again if you miss vaccine dose(s)?

There is no need to repeat the already given doses and there is no need to give extra doses. The vaccine schedule can safely and effectively be continued as if there had been no delay. The usual intervals between the vaccine doses are maintained or can be reduced if needed. The immune system does not forget. To get full protection, a person needs to have all the recommended vaccine doses, preferably on time.

1.3 What vaccinations do you give to a child with no vaccination records?

The general recommendation is that the health care provider should consider a child or person with no records of vaccination as 'not vaccinated'. The reason for such a recommendation is because it has been repeatedly shown world-wide that a person's memory of their history of vaccination is very poor. Research has shown that only 50% of people can accurately remember the type of vaccine given, dates given and numbers of doses given, when the person's verbal vaccination history is checked against their record of vaccination. There is only a very low risk of causing illness from re-vaccination and this risk is usually related to severe local reactions from diphtheria and tetanus-

containing vaccines. If there is no satisfactory verbal or written record of vaccination, the child (or adult) should be given vaccinations as if they were never previously vaccinated. It is important that adults and parents of children maintain accurate records of vaccination throughout life. In some states and territories, a vaccination record is required before a child is enrolled into school or child care centres. In some countries, vaccination is mandatory and a person cannot enter those countries without a record of vaccination.

1.4 Can doses be split? Are test doses a good idea?

No. The use of split doses, half doses, or test doses in standard schedule vaccines is strongly discouraged. There are no data which support this practice. Such methods do not provide adequate protection. Test doses are generally just as likely to produce an adverse event as the full dose. Remember that serious adverse events occur very rarely. If a child has had a history of split, half or test doses, they should be considered not fully vaccinated and the complete vaccination schedule should be commenced for the relevant vaccine.

1.5 When should premature infants be vaccinated?

Babies born prematurely should receive their first dose of hepatitis B vaccine at birth or at 2 months (see part 1.7, page 26). They should receive their doses of DTPa-hepB, Hib and OPV (or IPV) two months after birth as normal, unless they are very unwell. For example, if they are still receiving parenteral nutrition or ventilator support, having frequent apnoea or bradycardia episodes, or have sepsis the start of vaccination should be postponed. It is particularly important that premature infants not miss their 18-month booster injections. It is advisable that very low birth weight infants have their antibody response to hepatitis B vaccine checked after primary vaccination since poor responses in such infants sometimes require an extra dose of vaccine.

1.6 Can the time between doses of DTPa or DTPa-hepB vaccine be reduced to one month?

In Australia, three doses of DTPa or DTP–hep B are recommended to be administered at 2-monthly intervals starting at two months of age. This is called the primary vaccine schedule and is followed by boosters of DTPa administered at 18 months and 4 years. The time between the first three doses of DTPa-containing vaccines can be reduced to one month if a child is overdue (eg. in a 'catch-up' program). This is not harmful although it is always better to stay with the recommended time intervals. In the United Kingdom, the normal primary schedule of DTPw is given at 2, 3 and 4 months of age.

1.7 Can newborn babies be given DTPa (eg. Infanrix or Tripacel) containing vaccines?

No. Newborn babies may develop a form of 'tolerance' to the vaccine, and the response to subsequent doses may be unsatisfactory. Infants younger than six weeks of age should not be vaccinated with these vaccines or with Hib for this reason. Hepatitis B vaccines can be given at birth.

1.8 Is chickenpox vaccine available in Australia?

Yes, varicella (chickenpox) vaccine is available in Australia, but is not part of the routine schedule.

2. CONTRAINDICATIONS (WHEN VACCINES SHOULD BE WITHHELD)

2.1 GENERAL QUESTIONS

2.1.1 Should children with coughs or colds have vaccination delayed?

Infants with minor coughs and colds without fever, or those receiving antibiotics in the recovery phase of an acute illness, can be vaccinated safely and effectively. Vaccination should only be postponed if a child is acutely unwell (eg. acute severe gastroenteritis or respiratory disease) or has a high fever (temperature above 38.5 º C). In such cases, vaccination should be arranged for when the child is well again (a week or two later).

2.1.2 How long after a severe illness (with high fever), should vaccination be delayed?

Vaccines can be given as soon as the infant is clinically well and the temperature has been normal for a couple of days. Vaccination should be delayed if a child or person has a fever greater than 38.5 º C. There is no need to delay giving vaccines unless the infant remains unwell, in which case consultation with a general practitioner should precede any decision about giving the vaccine.

2.1.3 Should children be given a particular vaccine if they have already had that disease?

It is safe to vaccinate against the vaccine preventable disease even if the child or person appears to have had the disease. Vaccination of an individual who is already immune to measles boosts immunity and carries no risk. In addition, diagnosis of measles and rubella without laboratory confirmation is very unreliable, so children who appear to

have had these diseases should certainly be vaccinated with MMR vaccine. If a child older than 3 months has had laboratory confirmed pertussis (whooping cough), vaccination is not required, but it will not hurt to give DTP. Of particular importance is the fact that children under 2 years of age do not get adequate natural immunity following Haemophilus influenzae type b infection and these children should be vaccinated whether or not they have had proven Hib disease.

2.1.4 Should children be vaccinated while the child's mother is pregnant?

There is no problem with giving routine vaccinations to a child whose mother is pregnant. In fact, MMR vaccine given to the child of a pregnant mother will reduce the risk of her being infected by her offspring if she is not immune. MMR vaccine viruses are not infectious.

2.1.5 Should chronically ill children be vaccinated?

In general, children with chronic diseases should be vaccinated as a matter of priority because they are often more at risk from complications from the diseases. Care is needed however, in situations where the child's illness, or its treatment, may result in impaired immunity.

2.1.6 Do breast-fed babies get normal vaccinations?

Breast-fed children should be vaccinated according to the standard schedule. Breast milk contains small amounts of antibodies, but this does not interfere with the immunisation process. Breast-fed babies need vaccines because the milk does not provide specific protection against diseases like whooping cough, measles or Hib disease.

2.1.7 If a person/ child has a severe adverse event after immunisation should they complete the normal schedule of vaccines?

Mild local reactions are not a reason to avoid giving further doses of vaccine. However if the adverse event is severe, it may be appropriate to omit further doses of the vaccine. If there has been a very severe adverse event following Triple Antigen (DTPw) or DTPa (Infanrix or Tripacel) eg. severe allergic shock-like reaction, it may be necessary to use a vaccine without pertussis vaccine (eg. DT). The doctor should report very severe adverse events to ADRAC or to State or Territory Government Health Authorities.

Most children can continue their normal vaccination schedule after a severe adverse event, subject to a review by a paediatrician specialising in vaccination before the decision is made. In some States and Territories, special vaccination clinics have been set up within hospitals to vaccinate

children who have had severe adverse events. At the time of publication, these clinics are available in Sydney (New Children's Hospital), Melbourne (Royal Children's Hospital), SA (contact 08 82267177 for information) and ACT (contact 02 6205 2300 for information).

2.1.8 Are steroids a contraindication to vaccination?

Live vaccines like MMR, OPV, or BCG, should not be given to children receiving high dose (more than 2mg/kg/day prednisolone for more than one week) oral or parenteral (injected) corticosteroid therapy, or extensive topical (skin) steroid therapy for more than two weeks. Inactivated vaccines (eg. DTPa-hepB) may be less effective in this group but are not contraindicated. Therapy with inhaled steroids is not a contraindication to vaccination.

2.1.9 Should vaccines be given to children who have problems with their immune systems?

Children with immunodeficiency or those on immunosuppressive therapy should not be given live vaccines (eg. OPV, MMR or BCG). These children and their household contacts should be given inactivated polio vaccine (IPV). Contacts can be given MMR without risk of transmission. Live vaccines can be given to children with leukaemia and other malignancies who are on chemotherapy 6 months after they have completed chemotherapy. Such measures would normally be carried out under the supervision of the child's oncologist.

Children with HIV infection should have all routine vaccinations according to the standard schedule. Oral polio vaccine (OPV) should not be given. Inactivated polio vaccine (IPV) should be given instead. Although it is a live vaccine, MMR only rarely causes adverse events, and only in immunosuppressed subjects, whereas natural measles infection can be life threatening in these children. MMR should be given to children with HIV, unless severely immunosuppressed (see Part 3.12, page 157). Children with HIV infection should also be given pneumococcal vaccine (at two years of age). Other killed vaccines (influenza and hepatitis A) should be considered although the level of protection may not be as good. They should not be given BCG.

2.2 EPILEPSY

2.2.1 Should children with epilepsy be vaccinated?

Yes. Stable neurological disease (such as epilepsy) is not a reason to avoid giving vaccines like pertussis (whooping cough). Pertussis vaccine is included in DTPa-hepB, DTPa-Hib, DTPa and DTPw-containing

vaccines. Children who are prone to have fits should have paracetamol before and for 48 hours after vaccination to reduce the chance of a fever after vaccination bringing on a convulsion. It should be remembered that the fever following measles vaccine occurs 5-12 days after vaccination (in less than 20% of vaccinees). A family history of fits or epilepsy is not a reason to avoid vaccination.

2.3 NEUROLOGICAL DISORDERS

2.3.1 Should children with neurological disease receive the normal vaccination schedule?

Children with neurological disease are often at increased risk of catching a disease such as whooping cough and measles if they attend centres where there are a number of other children. Such children are also often at increased risk of complications from diseases like measles and whooping cough, as they can be more prone to respiratory infections and chest problems. It is therefore very important for children with neurological diseases to be protected by vaccination. The only exception to this is children who have an undiagnosed neurological condition who are still being observed and undergoing medical tests. In this situation, vaccinations are often postponed until the situation is clearer, to avoid confusion about whether a new symptom or problem is due to the underlying illness or to vaccination.

Children who are prone to have fits should have paracetamol before and for 48 hours after vaccination to reduce the chance of a fever after vaccination bringing on a convulsion.

2.4 ALLERGIES & ASTHMA

2.4.1 Should children with allergies be vaccinated? What precautions are required for atopic or egg sensitive children?

Asthma, eczema, hay fever and allergies are not contraindications to any vaccine. An important exception is genuine severe egg allergy which is a severe anaphylactic reaction to egg (eg. generalised hives, swelling of the mouth or throat, difficulty breathing, wheeze, low blood pressure, and shock). If a person has a history of severe egg allergy, influenza, yellow fever and Q fever vaccines are usually not used. MMR can be given to such children under close observation as anaphylactic reactions to MMR are exceedingly rare even in children with proven severe egg allergy. Simply disliking eggs or having diarrhoea or stomach pains after eating eggs are not reasons to avoid MMR and these children require no special precautions. These children can also have all other routine vaccines without special precautions.

2.4.2 Does vaccination cause asthma?

No. There is no evidence that vaccination causes or worsens asthma. It is especially important that children with asthma be vaccinated like other children, as catching a disease like whooping cough can make an asthma attack worse. Influenza vaccine is not routinely recommended for asthmatics, but is recommended for severe asthmatics, such as those requiring hospitalisation

2.5 PERTUSSIS

2.5.1 When should pertussis-containing vaccines be omitted?

Absolute contraindications Pertussis-containing vaccines (DTPa, DTPw, DTPa-hepB) should not be given under the following circumstances:

- evolving neurological illness (illness of brain not yet diagnosed) – postpone until stable.
- encephalopathy after a previous dose (inflammation of the brain) – no further doses.
- anaphylaxis after a previous dose (severe allergic shock and collapse) – no further doses.

The following are not contraindications to DTP-containing vaccines, although it may be preferred to give them under hospital supervision:

- convulsions (fits) within 72 hours of vaccination
- severe, persistent inconsolable screaming or crying for 3 hours or more
- collapse, child floppy and unresponsive (hypotonic/ hyporesponsive episode)
- fever higher than 40.5ºC within 48 hours of vaccination
- local reaction (involving swelling of half a limb)

2.6 MEASLES

2.6.1 What are the contraindications to MMR vaccine?

- impaired immune competence (immune system suppressed);
- taking oral prednisone (more than 2 mg/kg/day for over one week);
- prolonged extensive skin corticosteroid therapy (more than 2 weeks) (note that use of inhaled steroids is NOT a contraindication);
- recent immunoglobulin (within 3 months): administer MMR three months after immunoglobulin;

- leukaemia or other cancers;
- anaphylaxis to a vaccine component (eg. neomycin). (NB. Anaphylactic sensitivity to egg is not a contraindication to MMR);
- HIV infection, but only if severely immunocompromised.

3. COMPLICATIONS, ADVERSE EVENT OR REACTIONS FROM VACCINES

3.1 Is there a link between vaccination and cot death (SIDS)?

Despite extensive studies, there is no evidence that vaccination causes cot deaths (cot death is also known as Sudden Infant Death Syndrome or SIDS). Deaths do occasionally occur shortly after vaccination but the relationship is simply a chance association, since SIDS tends to happen in babies of 2-6 months of age, whether they are vaccinated or not. In an American study which compared 400 babies with cot deaths with the same number of well babies of the same age, the babies who died from SIDS were less likely to have been vaccinated in the previous 24 hours than those who did not suffer cot death. In other words, babies who were vaccinated were less likely to die from SIDS. South Australian data show no association between cot death and vaccination.

3.2 Does whooping cough (pertussis) vaccine cause permanent brain damage?

No, it does not. Whooping cough disease is still common in Australia and it can affect the brain. It is vital that children are vaccinated against this disease in order to prevent severe illness, brain damage and/or death.

3.3 Do vaccines cause cancer, inflammatory bowel disease (IBD) chronic fatigue syndrome, multiple sclerosis (MS), allergies, or autoimmune disease?

Despite extensive studies and after millions of vaccinations over many decades, there is no evidence to suggest that vaccination causes these diseases. In fact, hepatitis B vaccination may significantly reduce the risk of liver cancer. Vaccination levels have increased over the past 20 years in most countries but there has been no evidence of an increase of these diseases during this time.

4. EFFECTIVENESS OF VACCINES

4.1 Do some children get the disease despite being vaccinated?

Yes it is possible, since no vaccine is 100% effective. 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 levels provided by vaccines differ. For example if 100 children are vaccinated with MMR, 5-10 of the fully vaccinated children might still catch measles, mumps or rubella (although the disease will often be less severe in vaccinated children). If 100 children are vaccinated with a full schedule of pertussis-containing vaccines, 20 of the children might still get whooping cough but once again the 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 (lung infection) or encephalitis (inflammation of the brain).

5. VACCINES AND IMMUNE SYSTEM

5.1 Isn't natural immunity better than immunity from vaccine?

While vaccine-induced immunity may diminish with time, 'natural' immunity, acquired by catching the disease is usually lifelong. The problem is that the wild or 'natural' disease has a high risk of serious illness and occasionally, death. Children or adults can be re-vaccinated (with some vaccines but not all vaccines) if their immunity from the vaccines falls to a low level. It is important to remember that vaccines are many times safer than the diseases they prevent.

5.2 Can too many vaccines overload or suppress the natural immune system?

No. There is no evidence that this occurs in standard vaccination programs. All children and adults confront enormous numbers of antigens (substances that provoke a reaction from the immune system) each day, and the immune system responds to each of the antigens in various ways to protect the body. Vaccine antigens have an advantage

over their corresponding wild antigens in that the immune response (such as making antibodies) to the wild antigens occurs only after the disease. With vaccine antigens, however, the 'illness', if it does occur, is usually insignificant. Vaccines provide protection (immunity) to diseases in the same way as the 'natural' immunity that occurs when a person 'catches' the disease. However while the risks associated with the diseases are high, the risks associated with the vaccine are low although they can occur from time to time.

5.3 How can you help a child's immune system function properly so that it can fight off infections?

Eating, sleeping and exercising adequately will help keep the child's immune system functioning well but are not in themselves enough to stop vaccine-preventable diseases like measles or whooping cough. Vaccination has an important role to play in protecting children from these specific diseases.

6. GENERAL QUESTIONS

6.1 Haven't diseases like measles, polio, whooping cough and diphtheria already disappeared from most parts of Australia? Why do we need to keep vaccinating children against these diseases?

These diseases are much less common now, but the bacteria and viruses that cause them are still present. The potential problem is kept in check by routine vaccination programs. In countries where vaccination rates have declined, the vaccine preventable diseases have 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 big outbreak of polio among a group of Dutch people who belonged to a religious group that object 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 with OPV (oral polio vaccine), which protected the rest of the Dutch community from the outbreak. 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 still occur. Vaccination has eradicated smallpox from the world, which means that smallpox vaccinations no longer necessary. In the same way polio be eradicated from the world in the next few years.

6.2 Does homeopathic 'immunisation' work?

No. Homeopathic 'immunisation' has not been proven to give protection against infectious diseases; only conventional immunisation produces a measurable immune response. The Council of the Faculty of Homeopathy, London, issued a statement in 1993, which reads: "The Faculty of the 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." The Executive Director of the Australian Natural Therapies Association has stated that no properly qualified natural therapist would recommend homeopathic 'immunisation' as an alternative to conventional immunisation.

6.3 Can doctors be sued after giving a vaccine?

If a doctor or nurse fully informs the parents or person to be vaccinated of the likely side effects of vaccination and the parents agree after understanding the possible consequences of vaccination, it would seem highly unlikely that a successful litigation could be carried out, even if complications arose. To ensure a person has enough information to make an informed choice, both the risks from being vaccinated and the risk from not being vaccinated should be discussed.

6.4 Can doctors be sued for *not* giving a vaccine?

This question would relate predominantly to the omission of whooping cough (pertussis), Hib or MMR vaccines. If the doctor in good faith feels that the vaccine has the potential to cause problems in the particular child and therefore advises against giving it and the child develops the disease with complications, it would be difficult to see how successful litigation could be carried out in the circumstances. If however the doctor's advice is not based on current recommended scientific guidelines and the child develops the disease and suffers complications, there may well be grounds for the doctor to be successfully sued.

There is no report of any successful legal actions having occurred in Australia at the time of publication.

7. PERTUSSIS (WHOOPING COUGH) VACCINE

7.1 What is acellular pertussis vaccine?

A number of vaccine manufacturers have produced acellular vaccines that protect against pertussis (whooping cough). Acellular pertussis is

part of DTPa or DTPa-hepB vaccines. These vaccines have replaced whole-cell pertussis vaccine (eg. DTPw) in the Standard Vaccination Schedule from 1999. The new acellular pertussis containing vaccines do not contain the whole organism but various combinations of purified antigens. Children who are given the new acellular vaccines have less frequent local and systemic adverse events but have about the same level of protection as is provided by the older DTPw (Triple Antigen) vaccine. The rate of encephalopathy (brain inflammation) after the acellular vaccines is not yet established but is likely to be very low or non-existent.

7.2 Should adults receive pertussis vaccine (whooping cough)?

The current acellular pertussis vaccines (DTPa or DTPa-hepB) are not approved for use in adults (or children older than 8 years) because of the increased risk of adverse events. However, adults can develop pertussis and spread it to children and other adults. With the development and increasing availability of new acellular pertussis vaccines, pertussis vaccination at the same time as tetanus and diphtheria boosters, may be introduced for adults some time in the future.

8. ORAL POLIO VACCINE (OPV)

8.1 What if a baby vomits the oral polio vaccine just after it has been given?

It is quite safe to repeat the dose of OPV for up to 10 minutes after it was given.

8.2 Should a child with acute diarrhoea or vomiting receive oral polio vaccine (OPV or Sabin)?

No. Oral polio vaccine should be delayed until the child has recovered.

8.3 Can oral polio vaccine (OPV or Sabin) cause poliomyelitis in people having the vaccine?

Cases of vaccine associated poliomyelitis have been reported in people who receive live oral polio (OPV) vaccine and sometimes in their close contacts. It is estimated that one case occurs for every 2-3 million doses of vaccine distributed. In Australia, there have been 2 reported cases in the past 20 years. Adults are also at risk. This is why it is important that parents or carers of children who are being vaccinated, if they are incompletely vaccinated or uncertain of their vaccination status, are themselves vaccinated with OPV at the same time as the child.

8.4 If a parent, grandparent or carer has not had a complete course of polio vaccine (OPV or IPV) as a child, should he/she be vaccinated against polio too?

He/she should receive OPV (Sabin) vaccine as a 'catch-up' schedule". This should be considered with every unvaccinated or incompletely vaccinated parent or carer of a child who is receiving OPV. This is because there is a very small risk of an unvaccinated parent (or contact) developing polio from the child's faeces for up to 6 weeks after receiving OPV. Transmission is from unwashed hands, so that hand washing is very important.

9. HEPATITIS B VACCINE

9.1 Should children attending childcare centres receive hepatitis B vaccination?

At present there is no evidence of significant spread of hepatitis B among children in schools or child care centres within Australia: the question of spread in child care centres and pre-schools has not been adequately examined. However, the vaccine is very safe, and although the risk of transmission is low, it is at least possible that it could occur in a childcare setting.

From 1 May 2000, a 4-dose course of hepatitis B vaccination will be recommended for all newborn infants, starting just after birth. Once the baby leaves hospital the follow-up doses should be administered according to the standard vaccination schedule.

9.2 Who should have the hepatitis B vaccine?

From 1 May 2000 it has been recommended that all infants born in Australia commence a 4-dose course of hepatitis B vaccine starting at birth. Since 1997 it has been recommended that all adolescents (10-13 years) complete a 3-dose course of hepatitis B vaccine.

It is also especially important that the following groups receive hepatitis B vaccine:

- infants born to carrier mothers (these infants should also receive hepatitis B immunoglobulin at birth)
- infants and young children in ethnic groups with a hepatitis B carrier rate of over 2% (this includes individuals from most countries in Asia, Africa, Oceania, Central and South America, Eastern Europe, and the Mediterranean region)

- long term household or sexual contracts of carriers
- persons whose lifestyle puts them at risk of acquiring hepatitis B
- health care workers at risk of needlestick injury or mucosal exposure to body fluids

10. HEPATITIS A

10.1 Who should be vaccinated with hepatitis A vaccine?

Hepatitis A is transmitted from person to person by contaminated faeces (faecal-oral transmission). Hepatitis A vaccine is recommended for those at high risk of exposure. These people include: -

- travellers going to endemic areas;
- people who are exposed through their occupation, including those working in child care centres; centres for the intellectual disabled; people working in Aboriginal communities; health care workers in high risk areas and sewage workers;
- men who have sex with men;
- people with chronic liver disease including hepatitis C;
- people who regularly receive blood products (eg. haemophiliacs).

11. INFLUENZA AND PNEUMOCOCCAL VACCINES

11.1 Who should receive influenza and pneumococcal vaccines?

Influenza (flu) vaccine is recommended for people 65 years or older, indigenous people aged 50 years or older, any individual receiving immunosuppressive therapy, and for children greater than 6 months of age with chronic heart or lung disease, renal or metabolic disorders. However, one of the vaccines, Fluvirin, is not registered for use in children younger than 4 years of age. It should also be considered for residents of nursing homes and other chronic care facilities. Staff caring for patients in these groups should also consider vaccination in an attempt to protect their patients.

Pneumococcal vaccine is not used in children aged less than 2 years. It is recommended for Aboriginal people aged 50 or older, or people with high-risk conditions, any asplenic patients, those with

immunosuppressive disorders at increased risk of pneumococcal infection, other individuals at increased risk of severe pneumococcal infection (eg person with chronic cardiac, renal or lung disease, diabetes, alcoholism, elderly persons) and patients with CSF leaks. No booster effect is obtained with these vaccines, but since immunity wanes with time, it is recommended that revaccination occurs every 5 years.

12. INJECTIONS

12.1 What is the correct site for vaccination of children? Is it the thigh or the buttock? What about the arm?

The top, outer part of the thigh is the preferred site for injections for infants under the age of 12 months. The deltoid region of the upper arm is the preferred site for vaccination of children 12 months of age and older because it is associated with fewer local reactions and has sufficient muscle bulk to facilitate the injection. The buttocks should never be used because of the risk of sciatic nerve damage.

12.2 How many injections can be given into the same leg?

Only one injection should be given in the leg (or the arm) at any time. However if 'catch-up' is required, two injections may given into the leg on the same day, but the injections should be given in the leg at least 2.5cm (1 inch) apart.

13. WHERE CAN I GET MORE INFORMATION ABOUT VACCINATION?

More information about vaccination can be found in the following publications published by the Commonwealth Department of Health and Family Services:

- 'Understanding Childhood Immunisation'
- 'Immunisation Myths: Responding to Arguments Against Immunisation'

Also check with your local State or Territory public health unit or your doctor, local council, maternal child health nurse, or public health vaccination clinic for more information. See Immunisation Contacts information on the inside cover of this Handbook.

APPENDIX 6

GLOSSARY OF TECHNICAL TERMS TO ASSIST PARENTS

Adverse event following immunisation - an unwanted reaction following 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.

ADT - trade name for diphtheria-tetanus vaccine made by CSL for use in adults (Td).

Anaphylaxis - a sudden and severe allergic reaction, which results in a serious fall in blood pressure and may cause unconsciousness and death if not treated immediately.

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.

BCG - a vaccine that protects against tuberculosis; the letters stand for the Bacillus of Calmette and Guerin, the two inventors of tuberculosis vaccine.

Carrier - a person who has an infection which may still be active and if so may spread to others; the carrier state may last for years; examples of infections that can result in the carrier state are hepatitis B and typhoid.

CDT - trade name for diphtheria-tetanus vaccine made by CSL for use in children (DT).

Contraindication - a reason why a vaccine or drug should not be given.

Corticosteroid - a drug used to reduce inflammation and other immune responses.

DT - diphtheria-tetanus vaccine for use in children.

DTP - a vaccine that protects against diphtheria, tetanus and pertussis (whooping cough). The recently released **DTPa** contains an acellular pertussis vaccine, made of refined pertussis extracts instead of whole cells and causes fewer adverse reactions such as fever and pain and swelling at the injection site than the older whole-cell vaccine, **DTPw**.

Encephalitis - an 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 because they spread at a low but constant rate; tuberculosis and malaria are endemic in many developing countries.

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.

Febrile - related to a fever, as in febrile illness and febrile convulsions.

HAV - Abbreviation for hepatitis A virus, the cause of infectious hepatitis, a common food-borne infection in travellers in developing countries.

HbOC - a type of Hib vaccine.

HBsAg - hepatitis B surface antigen; a marker in the blood that indicates that the person is a carrier of active hepatitis B virus infection.

HBV - Abbreviation for hepatitis B virus, a virus that is spread via blood-to-blood contact through sharing injection equipment and by sexual intercourse.

Hepatitis - an inflammation of the liver; can be caused by virus infections.

Hib - *Haemophilus influenzae* type b - a bacterium that causes meningitis and other serious infections in young children.

HIV - human immunodeficiency virus, or the AIDS virus; people with HIV infection have weakened immunity and need special programs of vaccination to protect them against other infections.

Hypotonic-hyporesponsive episode (HHE) - a rare reaction which may follow some hours after DTP vaccination; the child becomes pale, limp, and unresponsive; the condition may last from a few minutes to hours but causes no longterm serious problems.

Immunisation - the process of inducing immunity to an infectious agent by administering a vaccine.

Immunity - an ability of the body to fight off certain infections; immunity can result from natural ('wild') infections or from vaccination.

Immunoglobulin - a protein extract from blood, sometimes called 'antibody', which 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; this time 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 injection - an injection into the surface layers of the skin; this is used for the administration of BCG, the tuberculosis vaccine.

Intramuscular 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.

IPV - inactivated polio vaccine; an injectable vaccine formerly known as Salk vaccine.

JE - Japanese encephalitis; a viral encephalitis.

Jaundice - yellow skin colour that may result from severe hepatitis.

MMR - measles-mumps-rubella vaccine.

OPV - oral polio vaccine; also known as Sabin vaccine.

Paracetamol - a medicine that helps reduce fever which is given to minimise reactions to vaccination; it works in the same way as aspirin, but aspirin should never be given to children.

Pertussis - whooping cough, an illness caused by a bacterium, *Bordetella pertussis*.

Polyvalent vaccine - a combination vaccine which protects against more than one disease; examples are DTP and MMR.

PRP-OMP - a type of Hib vaccine.

PRP-T - a type of Hib vaccine.

Rubella – a viral illness, formerly known as German measles.

Sabin vaccine - oral polio vaccine (OPV).

Subcutaneous injection - an injection into the tissue between the skin and the underlying muscle.

Td - diphtheria-tetanus vaccine for use in adults.

Triple Antigen - a brand name for DTP vaccine.

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 infection.

Varicella - chicken pox, an infection caused by the varicella-zoster virus.

Virus - a tiny living organism, smaller than a bacterium, that can cause infections; measles, rubella, mumps, polio, influenza and hepatitis B are caused by viruses.

Zoster - an abbreviation for herpes zoster infection (also known as shingles), a painful rash and illness caused by the varicella-zoster virus.

APPENDIX 7: DEFINITIONS OF ADVERSE EVENTS

LIST OF DEFINITIONS FOR MONITORING ADVERSE EVENTS FOLLOWING IMMUNISATION.

Notify any events that the reporter considers serious and may be related to the vaccine or vaccines.

Abscess

Occurrence of a fluctuant or draining fluid-filled lesion at the site of injection with or without fever.

(a) Bacterial: Purulent collection.

(b) Sterile abscess: No evidence of bacterial infection.

Acute Flaccid Paralysis [Diagnosis must be made by a physician]

Acute onset of flaccid paralysis of one or more limbs following any vaccine.

Allergic reaction

Characterised by one or more of the following:

(a) skin manifestations (eg. hives, eczema, pruritus);

(b) wheezing or shortness of breath due to bronchospasm; and/or

(c) facial or generalised oedema.

(NB. See also "Anaphylactoid reaction" and "Anaphylaxis").

Anaphylactoid Reaction (acute hypersensitivity reaction)

Exaggerated allergic reaction, occurring within 2 hours of vaccination, characterised by one or more of the following:

(a) wheezing and shortness of breath due to bronchospasm;

(b) laryngospasm/laryngeal oedema; and/or

(c) one or more skin manifestations, eg. hives, facial oedema, generalised oedema.

Anaphylaxis

Circulatory failure (eg. alteration of the level of consciousness, low arterial blood pressure, weakness or absence of peripheral pulses, cold extremities secondary to reduced peripheral circulation, flushed face and increased perspiration) with or without bronchospasm and /or laryngospasm/laryngeal oedema, occurring within minutes of vaccination.

Arthralgia

Joint pain without redness or swelling.

Arthritis

Joint pain together with redness and/or swelling

Brachial neuritis

Pain in arm causing weakness of limb on side of vaccination. Usually described in adults following diphtheria-tetanus vaccines.

Death

Any death of a vaccine recipient temporally linked to vaccination, where no other clear cause of death can be established.

Disseminated BCG

Disseminated infection occurring after BCG vaccination and confirmed by isolation of *Mycobacterium bovis* BCG strain.

Encephalopathy [Diagnosis must be made by a physician]

Encephalopathy is an acute onset of major neurological illness temporally linked with vaccination and characterised by any two or more of the following three conditions:

(a) seizures;

(b) severe alteration in level of consciousness or mental status (behaviour and /or personality) lasting for one day or more; and/or

(c) focal neurological signs which persist for one day or more.

Encephalitis [Diagnosis must be made by a physician]

Encephalitis is characterised by the above mentioned symptoms and signs of cerebral inflammation and, in many cases, CSF pleocytosis and/or virus isolation.

Fever

Only very high fever should be reported, eg. over 40.5º

Guillain–Barré Syndrome (GBS) [Diagnosis must be made by a physician]

Acute onset of rapidly progressive, ascending, symmetrical flaccid paralysis, without fever at onset of paralysis and with sensory loss. Cases are diagnosed by cerebrospinal fluid (CSF) investigation showing dissociation between cellular count and protein content.

Hypotensive –Hyporesponsive Episode (Shock Collapse)

Episode of pallor, decreased level or loss of responsiveness, and floppiness occurring 1 to 48 hours following vaccination. The episode is transient and self-limiting.

Local Reaction (Severe)

Redness and/or swelling centred at the site of injection and one or more of the following:

(a) swelling beyond the nearest joint;

(b) pain, redness and swelling of more than 3 days duration, and/or

(c) requires hospitalisation.

Lymphadenitis (Includes Suppurative Lymphadenitis)

Occurrence of either:

(a) at least one lymph node, 1.5cm in diameter or larger; or

(b) a draining sinus over a lymph node.

(c) May be caused by BCG on the same side as vaccination (mostly axillary); or by the rubella component of MMR (usually occipital or post-auricular).

Meningitis – [Diagnosis must be made by a physician]

Acute onset of major illness with fever and often neck stiffness/positive meningeal signs (Kernig, Brudzinski). Symptoms may be subtle to similar to those of encephalitis. CSF pleocytosis is usual.

Orchitis

Swelling with pain and/or tenderness of testes.

Osteitis

Inflammation of the bone due to BCG vaccination.

Osteomyelitis

Proven bacterial infection of bone.

Parotitis

Swelling and/or tenderness of parotid gland or glands.

Rash

Severe or unusual rash.

Screaming (persistent)

Inconsolable, continuous crying lasting at least 3 hours, accompanied by high-pitched screaming.

Seizure

A seizure lasting from several minutes to more than 15 minutes and not accompanied by focal neurological signs or symptoms.

(a) febrile seizures: with fever >37.5ºC

(b) afebrile seizures: without fever.

Sepsis

Acute onset of severe, generalised illness due to bacterial infection and confirmed by positive blood culture.

Subacute Sclerosing Panencephalitis

[Diagnosis must be made by a physician.]

Degenerative CNS condition with laboratory confirmation of abnormal serum and CSF measles antibodies.

Thrombocytopenia

Platelet count < 50 x 10^9/L

Toxic-Shock Syndrome [Diagnosis must be made by a physician]

Abrupt onset of fever, vomiting, watery diarrhoea and shock within a few hours of vaccination.

Vaccine associated paralytic poliomyelitis

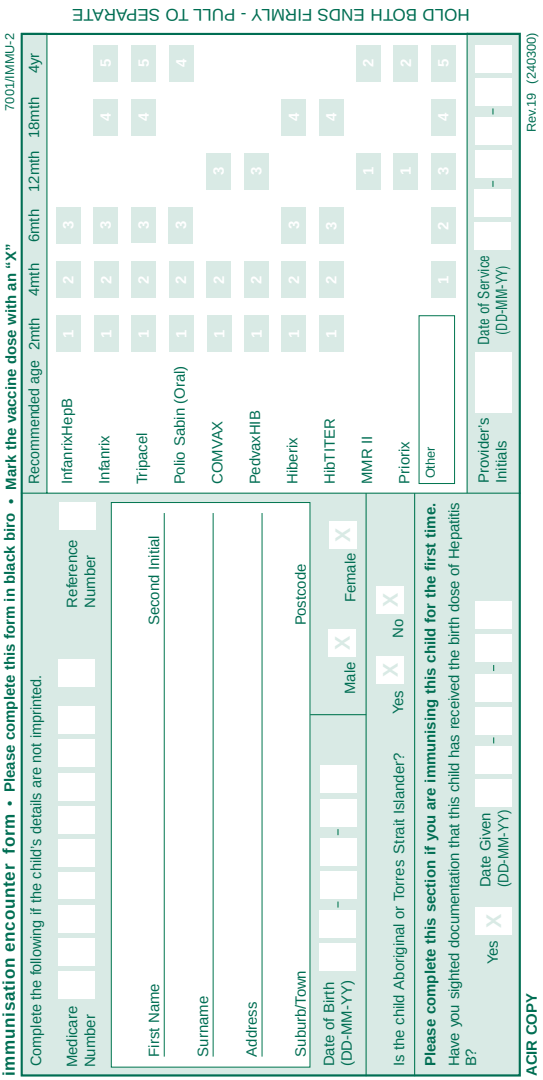
See "acute flaccid paralysis".

Other severe or unusual events

Any unusual event that does not fit into any of the categories listed above, but is of medical or epidemiologic interest should be reported with a detailed description of the clinical features.

Report by telephone to State or Territory Health Department or notify by the blue card to ADRAC (see part 1.6, page 22).

APPENDIX 8: ACIR ENCOUNTER FORM



This form may be updated regularly, according to changes in vaccination schedule.

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