

Immunisation Guidelines for Ireland

2008 EDITION



ROYAL COLLEGE OF
PHYSICIANS OF IRELAND

NATIONAL IMMUNISATION ADVISORY COMMITTEE

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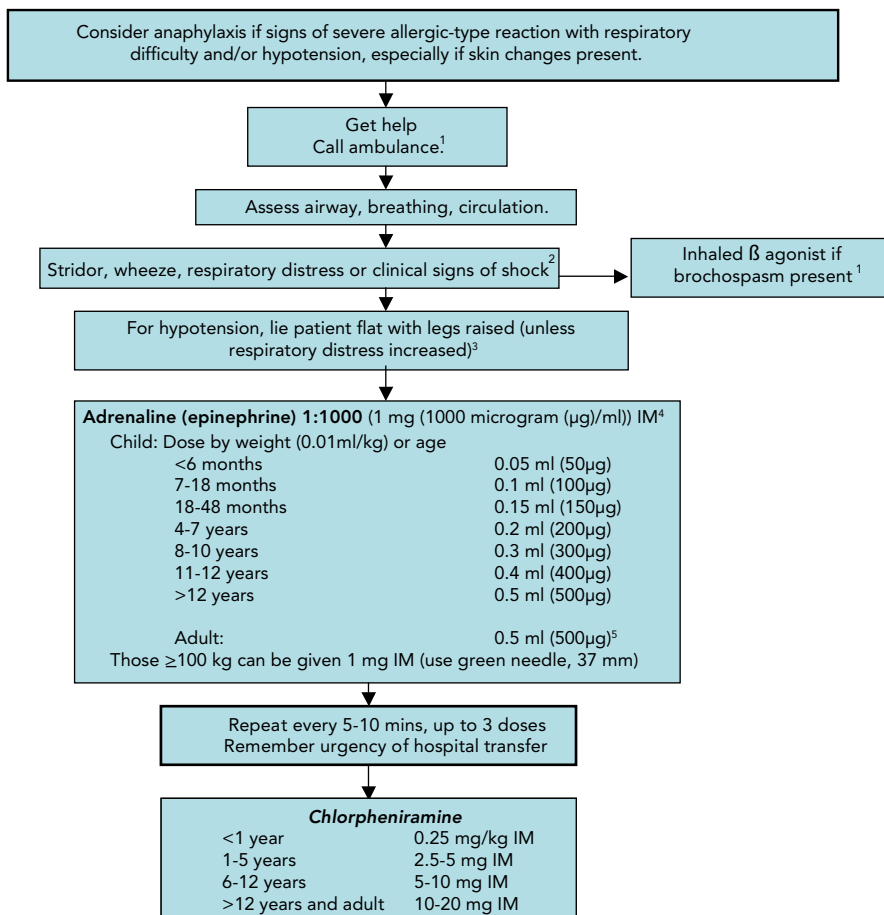


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Anaphylactic Reactions: Treatment in the Community



1. Ambulance will be equipped with oxygen, salbutamol and fluids.

2. If profound shock judged **immediately** life-threatening, give CPR if necessary.

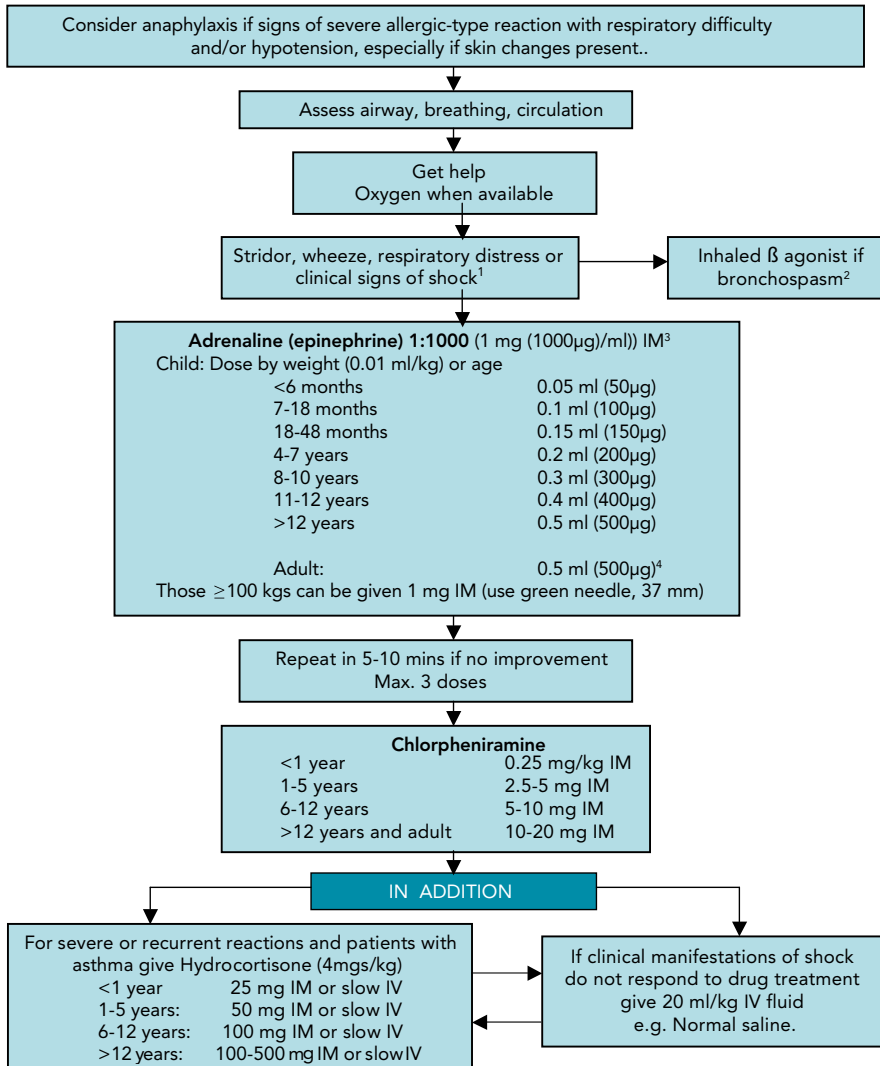
3. If respiratory distress present, elevate head, provided BP adequate to prevent loss of consciousness.

4. Adrenaline maximum effect 10 minutes after IM injection.

5. Half doses of adrenaline may be safer for patients on amitriptyline, imipramine or beta blocker.

Note: Microgram = μ g

Anaphylactic Reactions: Treatment Algorithm for First Medical Responders



1. If profound shock judged **immediately** life-threatening, give CPR/ALS if necessary. Consider slow IV adrenaline (epinephrine) 1:10,000 solution if severe hypotension. Dose 10 microgram/kg., max. 500 micrograms, over several minutes. This is **hazardous** and is recommended only for hospital setting. Note the different strength for IV use.
2. An inhaled β_2 -agonist such as salbutamol may be used if bronchospasm is severe and does not respond rapidly to other treatment.
3. Adrenaline maximum effect 10 minutes after IM injection.
4. Half doses of adrenaline may be safer for patients on amitriptyline, imipramine or beta blocker.

Preface & Anaphylaxis

Anaphylaxis

Anaphylaxis is a potentially life-threatening allergic reaction to foreign protein antigens such as food and bee stings. It is a very rare complication of immunisation (0.4-2 per million doses). Most episodes begin within 30 minutes of vaccination. Shorter intervals to onset generally indicate more severe reactions. However, due to the unpredictable nature of anaphylactic reactions, it is not possible to define a particular time period over which all individuals should be observed following immunisation. When possible, patients should remain in the vicinity of the place of vaccination for up to 15 minutes, as typically onset of anaphylaxis occurs within minutes.

Anaphylaxis must be distinguished from fainting (vasovagal episode), anxiety and breath-holding episodes, which are more common.

Table 1 shows features which may assist in differentiating fainting from anaphylaxis. Those experiencing an anxiety spell may appear fearful, pale and sweaty, and complain of light-headedness, dizziness and numbness or tingling of their hands or feet. Hyperventilation is usually present. During a breath-holding episode the child is suddenly silent but obviously agitated. Facial flushing or pallor can occur as breath-holding continues. Some episodes end with a resumption of crying, but others can be followed by a brief period of unconsciousness during which breathing resumes.

Swelling and an urticarial rash may appear at the injection site but are not always caused by an allergic reaction and may disappear without additional treatment. However, if any other symptoms occur, even if considered mild (sneezing, nasal congestion, coughing, etc.), Adrenaline should be given. There is little risk with the unnecessary use of Adrenaline, whereas delay in its administration in anaphylaxis may result in severe anaphylaxis and death. The features of severe disease include obstructive swelling of the upper airway, marked bronchospasm and hypotension.

Table 1 Vasovagal episode v. Anaphylaxis

		Vasovagal episode	Anaphylaxis
Onset		Immediate	Usually within 5 mins, but can occur within 1-2 hours
Symptoms/ signs	Skin	Generalised pallor; cold, clammy skin	Itch, generalised erythema, urticaria or angio-oedema (localised swelling of face, mouth, etc.)
	Respiratory	Normal or shallow, not laboured	Cough, wheeze, stridor, tachypnoea, recession, cyanosis
	Cardiovascular	Bradycardia but strong carotid pulse Hypotension corrected when lying down	Tachycardia, weak/absent pulse Sustained hypotension unless specific treatment
	Neurological	Light-headed Possible loss of consciousness Improves on lying down	Severe anxiety and distress Loss of consciousness

Preface & Anaphylaxis

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Acknowledgements

The National Immunisation Advisory Committee wishes to particularly acknowledge the Department of Health, United Kingdom in relation to extracts from its 2006 report entitled 'Immunisation against infectious disease (the Green Book)'.



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The National Immunisation Committee wish to especially acknowledge the contribution of the staff at the Health Protection Surveillance Centre for the provision of data and their technical expertise in the preparation of these guidelines. We also wish to gratefully acknowledge the financial support of the Health Protection Surveillance Centre, Health Service Executive in the production of this report.

Preface

This revised report on immunisation guidelines for Ireland has been prepared with the assistance of an active Committee from associated disciplines in Paediatrics, Infectious Diseases, General Practice, Public Health, Microbiology, Occupational Health, Travel Medicine and the Irish Medicines Board. The report itself continues to be simple and concise in design and of course does not claim to contain all information on any pharmacological material.

The report contains a considerable revision of chapters, reflecting updated epidemiological and vaccine information, and providing the current information and guidelines concerning immunisation. Since the last guidelines were issued in 2002 there has been an improvement in the uptake of childhood vaccines at 24 months, from 80% to 90% in 2006. There was a similar improvement for MMR vaccine uptake, from 70% to 85% over the same period. The health services have also undergone major reform and we have a new National Immunisation Office. There are exciting vaccine developments from the pharmaceutical industry and our guidelines will obviously change to reflect this.

As Chairman of the Committee I sincerely thank all those who spent so much time and put so much effort into this document. I also wish to thank those who participated in the concerted process, in particular the Chairpersons of each section, Dr Karina Butler, Dr Mary Cafferkey, Dr Jeff Connell, Dr Kevin Connolly, Dr Brenda Corcoran, Dr E. Gallagher and Dr Darina O'Flanagan. These Committees carried out their tasks with much enthusiasm and efficiency. It was indeed a pleasure to work with them. In particular, we must thank our Committee Medical Secretary, Dr Helena Murray, and past medical secretaries, Dr Denise McCarthy, Dr Patricia McDonald and Dr Emer Feely and also Ms Karen Doyle from the College. We would also like to thank Dr Paul Kavanagh and Ms Stephanie Mulcair who proof-read the document for their patience and time in delivering the final manuscript.

I would like to thank our many colleagues who made presentations to the committee, particularly Dr Michael Barry for his contributions to the economic evaluation of new vaccine programmes.

This document is not designed to be restricted to the medical profession alone and we hope it would be of interest to a broad section of our community involved in the medical, paramedical and tourist industry.

Finally, I would wish to thank the Department of Health and Children for their valuable input and the Health Protection Surveillance Centre, Health Service Executive for their financial support in producing this report.

Brian Keogh, MD
Past President, RCPI
Chairman, NIAC

Preface & Anaphylaxis

The 2008 Edition

Principal changes to this document

This publication continues to be A5 size but has changed to book format in the 2008 edition as this publication is larger. There is a folder in the back cover to hold additional information.

The year in which each of the principal childhood vaccines was introduced to Ireland is indicated at the start of the relevant chapter.

Changes to recommended immunisation schedule

Since the publication of the last version of these guidelines in 2002 there have been a number of changes to the recommended immunisation schedule:

- Hepatitis B vaccine is added to the routine childhood immunisation schedule (Hep B).
- Pneumococcal conjugate vaccine is added to the routine childhood immunisation schedule (PCV).
- Low-dose acellular pertussis vaccine is added to the current tetanus and low-dose diphtheria at 11-14 years (Tdap).
- A booster dose of *Haemophilus influenzae* type B (Hib) is to be given at 13 months, rather than at 12 months as at present.
- The Meningococcal C conjugate (MenC) vaccine is to be given at 4, 6 and 13 months of age.
- The indications for varicella vaccination have been updated for children and adults in the specified risk groups. All women of child-bearing age without a history of varicella infection should have their immunity checked. Women with negative serology should be vaccinated if no contraindications exist.
- NIAC recommends annual influenza vaccination for people aged 50 years or older. This may be implemented on a phased basis.

In addition, a catch-up schedule is set out for children aged 4 months to 10 years and for children aged 10 to 18 years.

Other chapters have been updated and expanded, particularly in relation to occupational risk from vaccine preventable disease. A new chapter on rabies was added because of occupational risk to this disease in Ireland.

New sections

This document has a new chapter on

- Rabies

Expanded sections

The following chapters have been expanded:

- Chapter 6, Hepatitis B, to reflect new recommendations for inclusion in primary immunisation schedule
- Chapter 12, Pneumococcal infection, to reflect new recommendations for inclusion in primary immunisation schedule
- Chapter 17, Varicella-Zoster, to include VZIG algorithms for neonates, pregnant women and immunosuppressed people who are exposed to chickenpox. Recommendations about active immunisation with varicella vaccine are given with an algorithm outlining the procedure for vaccinating health-care workers.

Amended sections

The following amendments have been made:

- Chapter 5, Hepatitis A, has been amended to reflect recently published information on the effectiveness of post-exposure prophylaxis with HAV vaccine compared to Human Normal Immunoglobulin (HNIG).
- Chapter 10, Mumps, has been amended to include more information on mumps illness and all the information on MMR vaccine as in Chapter 8, Measles.
- Chapter 11, Pertussis, has been amended in relation to changes to the guidance on contraindications and precautions for pertussis vaccine to reflect change in primary immunisation schedule.
- Chapter 14, Rubella, has been amended to include more information on congenital rubella syndrome and all the information on MMR vaccine as in Chapter 8, Measles.

Preface & Anaphylaxis

- Chapter 15, Tetanus, has been amended in relation to guidance for tetanus prophylaxis for clean and contaminated wounds.
- Chapter 16, Tuberculosis, has been amended to provide clearer guidance on indications for BCG vaccine other than newborn babies.

Future Developments

As we publish the 2008 edition of the Immunisation Guidelines for Ireland we are aware of developments for new vaccines on the horizon. This reflects the rapidly expanding environment in the immunisation field. Updates and new recommendations will be published on the RCPI, NIO, HPSC and the Department of Health and Children websites along with the electronic version of these guidelines.

An example of this is the planned introduction of the human papillomavirus vaccine (HPV). Once the details of the HPV vaccination programme are finalised a chapter on HPV vaccine will be made available online.

Updated July 2009

New chapter added

- Chapter 6a Human papillomavirus

Corrections and amendments

- Chapter 2, General Immunisation Procedures, corrections on pages 15 and 32 and clarifications on pages 18 and 25
- Chapter 5, Hepatitis A, clarification on page 54
- Chapter 6, Hepatitis B, correction on page 69 and amendment because of new information on page 67
- Chapter 7, Influenza, correction on page 78
- Chapter 8, Measles, correction on page 90
- Chapter 10, Mumps, correction on page 112 and removal of sections on pages 111 and 113
- Chapter 14, Rubella, correction on page 145 and removal of sections on pages 144 and 146.

The new chapter and a table listing the full details of corrections and amendments are now available on the RCPI, NIO, HPSC and Department of Health websites. Updated versions of the relevant individual chapters, with text changes in red, are also on these websites.

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01

General Information

This chapter provides information on the following:

- Vaccine uptake and surveillance of vaccine-preventable disease
- Reporting of adverse reactions and quality defects
 - Terms used for frequency of adverse events
- Procurement and distribution of vaccine within the cold chain
- Definitions
- Abbreviations
- Useful websites
- Bibliography

Vaccine uptake and surveillance of vaccine-preventable disease

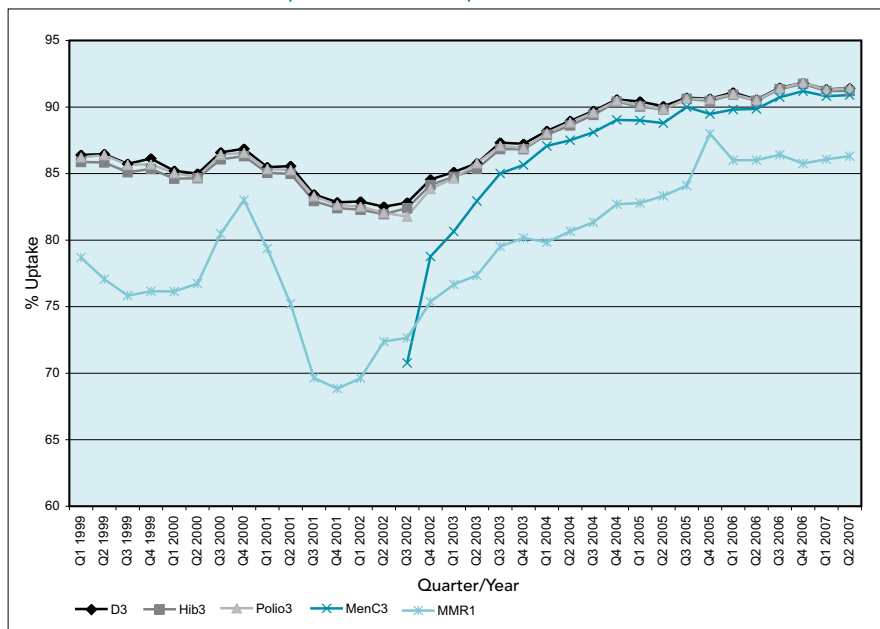
The Health Protection Surveillance Centre (HPSC), Middle Gardiner Street, Dublin 1 (www.hpsc.ie) is responsible for the surveillance of communicable diseases, examining the incidences of vaccine-preventable illness and examining trends in the uptake of vaccines (see figure 1.1).

The HPSC receives immunisation uptake data from each Health Service Executive (HSE) area and reports on uptake rates nationally, by HSE area and by Local Health Office area. These reports are published each quarter on its website www.ndsc.ie/hpsc/A-Z/VaccinePreventable/Vaccination/.

Irish legislation specifies the infectious diseases that medical practitioners are required to notify to a Medical Officer of Health as soon as they become aware of or suspect that a patient is suffering from or is the carrier of a notifiable infectious disease. There is a similar requirement for a clinical director of a diagnostic laboratory to notify a Medical Officer of Health as soon as an infectious disease is identified in that laboratory.

Chapter 1 General Information

Figure 1.1 Quarterly immunisation uptake rates (%) in Ireland at 24 months. Source: HPSC (1999-2007/Q2)



Note: T3 and P3 uptake rates similar to D3; therefore only D3 plotted

The HPSC collates and analyses these notifications weekly and also produces quarterly and annual reports.

The HPSC particularly monitors the notifications of vaccine-preventable diseases and seeks to determine if vaccine failure has occurred. A good example of how this works was the detection of an increase in the number of Hib cases in fully vaccinated children in 2005. This led to concerns that a 3-dose infant schedule was no longer sufficient to maintain long-term protection. A similar situation had emerged in the UK a number of years previously.

In response to this emerging trend in Ireland, and coupled with the scientific evidence that Hib vaccine efficacy is higher in those immunised at older than 12 months of age than in children vaccinated routinely as infants, the National Immunisation Advisory Committee (NIAC) recommended that a catch-up Hib dose be offered to children under 4 years of age, in order to further protect this age-group from Hib disease.

Reporting of adverse reactions and quality defects

All suspected adverse reactions should be reported to the Irish Medicines

Board (IMB), Kevin O'Malley House, Earlsfort Terrace, Dublin 2, using the Yellow Card System. This is a 'Freepost' system and cards are available from the Irish Medicines Board at the above address, or may be downloaded from their website, www.imb.ie. Reports should be as detailed as possible and include the batch number of the vaccine.

Terms used for frequency of adverse events

Description	Detectable range
Very common	>1/10
Common	>1/100 and <1/10
Uncommon	>1/1,000 and <1/100
Rare	>1/10,000 and <1/1,000
Very rare	<1/10,000

Quality defects are also monitored by the Irish Medicines Board (IMB), using a similar 'Freepost' Green Card System. Quality defects include missing labels/label texts, container defects, altered product appearance, particles in product etc. Full details of the defect and the batch number should be given on the Green Card. Cards are available from the Irish Medicines Board at the above address.

Procurement and distribution of vaccine within the cold chain

The National Immunisation Office (NIO) oversees the day-to-day implementation of the national immunisation programme by the Health Service Executive. The NIO is responsible for the procurement and distribution of vaccine within the cold chain. It also provides up-to-date information leaflets for parents and health-care professionals. It hosts a website www.immunisation.ie and is developing a national IT register for immunisations.

Cold chain management of vaccines

All vaccines are sensitive to heat, cold and light and must be kept at temperatures between 2-8°C. Leaving vaccines outside this temperature range can result in the loss of vaccine potency.

The 'Cold Chain' is the system of correct storage, transport and maintenance of vaccines to ensure that they are protected from inappropriate temperatures and light from the time of manufacture to administration.

Chapter 1 General Information

All routine vaccines are stored and delivered under temperature-controlled conditions by the HSE National Cold Chain Delivery Service to General Practitioner (GP) surgeries, hospitals and Local Health Offices.

Vaccine ordering and usage

- There should be a designated person in charge of the ordering, receipt and storage of vaccines.
- The designated person should order sufficient vaccines from the National Cold Chain Delivery Service on a monthly basis. In an emergency additional supplies can be delivered.
- When vaccines are delivered they should be checked against the order for any damage or discrepancy.
- Vaccines must be placed in the refrigerator immediately and not left at room temperature.
- Vaccines stored outside temperature-controlled conditions should not be used.

Vaccine storage

- Vaccine refrigerators are recommended for the storage of vaccines. Manufacturers' recommendations on storage should be observed.
- Vaccines should be stored in the pharmaceutical refrigerator which should not be overfilled, to allow air circulate around the packages. **They should not be stored on the shelves or storage compartments of the door of non-pharmaceutical refrigerators.**
- Vaccines must be stored in their original packaging, which should not touch the sides or back of the refrigerator.
- Door-opening should be kept to a minimum.
- **Vaccines with the shortest expiry date should be used first. Vaccine stocks should be rotated so that vaccines with shorter expiry dates are at the front of the refrigerator.**
- A maximum/minimum thermometer should be used in refrigerators where vaccines are stored, irrespective of whether the refrigerator incorporates a temperature indicator dial. The maximum and minimum temperatures reached should be monitored and recorded daily. Temperature record logs are best kept close to the refrigerator for ease of reference.
- If temperatures outside the permitted range are recorded, or if there is a breakdown in supply or equipment, the Chief Pharmacist of the National Immunisation Office or the Senior Medical Officer should be contacted for further advice.
- The vaccine refrigerator should be defrosted regularly as ice builds up, and cleaned with a 1:10 solution of sodium

hypochlorite. Vaccines should be stored in another refrigerator or cool box while doing this.

- Records should be kept of refrigerator maintenance and servicing.
- Care should be taken to ensure that the electricity supply to the vaccine storage refrigerator cannot accidentally be interrupted. This can be achieved by using a switchless socket or by placing cautionary notices on plugs and sockets.
- Food and drink must not be stored in refrigerators used for vaccines.

Disposal of vaccines

- Reconstituted vaccine must be used within the recommended period, varying from 1 to 4 hours, according to the manufacturer's instructions.
- Single-dose containers are preferable; once opened, multidose vials must not be kept after the end of the session.
- Unused vaccine, spent or partly spent vials should be disposed of safely by incineration.
- Contaminated waste and spillage should be dealt with by heat sterilisation, incineration or chemical disinfection as appropriate.
- **Expired vaccines must not be used and should be returned to the National Cold Chain Delivery Service company at the next delivery.**

Needles and syringes

- Needles and syringes must be securely stored and delivery and distribution recorded.
- Needles and syringes should be disposed of in sharps bins.
- Sharps bins must not be left unattended in schools.
- Sharps bins should be collected regularly and be disposed of safely.

Definitions

Adverse reaction is an event that is harmful and unintended and that occurs following administration of medicinal products (substances normally used in humans for the prophylaxis, diagnosis or treatment of disease or for the modification of physiological function).

Antitoxin is a solution of antibodies derived from the serum of animals immunised with specific antigens (e.g. diphtheria antitoxin) used to achieve passive immunity or for treatment.

Chapter 1 General Information

Basic reproductive number (R_0) is the average number of secondary infections resulting from each index case in a fully susceptible population. It is a measure of the transmissibility of an infection.

Immunisation denotes the process of artificially inducing or providing immunity. This may be either active or passive.

Active immunisation is the administration of a vaccine or toxoid in order to stimulate production of an immune response.

Passive immunisation is the administration of preformed antibodies (such as HNIG, specific antibody preparation and antitoxins) in order to provide temporary immunity.

Immunoglobulin

Human immunoglobulin is that fraction of blood plasma that contains antibodies, notably those against infectious agents. Preparations of immunoglobulin belong to two main categories:

- Human Normal Immunoglobulin (HNIG).
- Human Specific Immunoglobulin/Hyperimmune Globulin.

Toxoid is a modified bacterial toxin that has been rendered non-toxic but has the ability to stimulate the formation of antitoxin.

Vaccine is a suspension of live attenuated or inactivated micro-organisms or fractions thereof, administered to induce immunity and thereby prevent infectious disease.

Inactivated vaccine is a vaccine that contains killed bacteria or viruses. The response may be weaker than for a live vaccine and so repeated doses are often needed.

Live attenuated vaccine is a vaccine that contains a weakened strain of live bacteria or viruses that replicate in the body and induce a longer-lasting immunity than inactivated vaccines.

Vaccination is the term used to refer to the administration of any vaccine or toxoid.

Abbreviations

AIDS:	Acquired Immunodeficiency Syndrome
ALS:	Advanced Life Support
Anti-HBc:	Antibody to Hepatitis B Core Antigen
Anti-HBs:	Antibody to Hepatitis B Surface Antigen
Anti-HCV:	Hepatitis C antibody
BCG:	Bacille Calmette Guerin vaccine
CNS:	Central Nervous System
CPR:	Cardiopulmonary Resuscitation
DTaP:	Adsorbed Diphtheria, Tetanus and acellular Pertussis vaccine
HAV:	Hepatitis A Virus
HBV:	Hepatitis B Virus
HBIG:	Specific Hepatitis B Immunoglobulin/Hyper-immunoglobulin
HBeAg:	Hepatitis B e Antigen
HBsAg:	Hepatitis B Surface Antigen
HCW:	Health-Care Worker
HDCV:	Human Diploid Cell Rabies Vaccine
Hib:	<i>Haemophilus influenzae</i> type b
HIV:	Human Immunodeficiency Virus
HNIG:	Human Normal Immunoglobulin
HRIG:	Human Rabies Immunoglobulin
HPSC:	Health Protection Surveillance Centre
HPV:	Human Papilloma Virus
HSE:	Health Service Executive
IBTS:	Irish Blood Transfusion Service
IM:	Intramuscular
IPD:	Invasive Pneumococcal Disease
IPV:	Inactivated Polio Virus vaccine
IU:	International Units
MDR-TB:	Multi-Drug Resistant Tuberculosis
MenC	Meningococcal C
MMR:	Measles, Mumps and Rubella
NIAC:	National Immunisation Advisory Committee
NIO:	National Immunisation Office
NVRL:	National Virus Reference Laboratory
OPV:	Oral Polio Vaccine
PCV:	Pneumococcal Conjugate Vaccine
PPD:	Purified Protein Derivative
PPV:	Pneumococcal Polysaccharide Vaccine
RCPI:	Royal College of Physicians of Ireland
ROI:	Republic of Ireland
SC:	Subcutaneous

Chapter 1 General Information

SSPE:	Subacute Sclerosing Panencephalitis
Td:	Tetanus toxoid, low-dose diphtheria toxoid
Tdap:	Tetanus, low-dose diphtheria and low-dose acellular pertussis vaccine
TIG:	Tetanus Immunoglobulin
TST:	Tuberculin Skin Test
Tu:	Tuberculin
VZ:	Varicella-Zoster
VZIG:	Varicella-Zoster Immunoglobulin
VZV:	Varicella Zoster Virus
WHO:	World Health Organization
XDR-TB:	Extensively Drug-Resistant Tuberculosis

This document is available on the RCPI, NIO, HPSC and Department of Health and Children websites in pdf format. The electronic version of the document will be regularly updated as changes are introduced to our immunisation schedule.

Useful websites

For further information and debate on immunisation, the following websites may be useful.

American Academy of Pediatrics
www.aap.org/new/immpublic.htm

American Medical Association
www.ama-assn.org/medsci/immunize/vacautism.htm

Australian Skeptics Dr Steve Basser: Anti-immunisation scare: The inconvenient facts
skeptics.com.au/journal/anti-immune.htm

Centers for Disease Control and Prevention (USA)
www.cdc.gov

Department of Health and Children
www.dohc.ie/

Health Protection Surveillance Centre
www.hpsc.ie

Immunisation Action Coalition
immunize.org

National Alliance for Autism Research
www.naar.org/naar.asp

National Immunisation Office
www.immunisation.ie

National Institutes of Health
www.nih.gov

National Network for Immunization Information
www.immunizationinfo.org

Royal College of Physicians of Ireland
www.rcpi.ie

United Kingdom, Medical Research Council
www.mrc.ac.uk/OurResearch/ResearchFocus/index.htm

Chapter 1 General Information

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Ramsay M, McVernon J, Andrews N, Heath P, Slack M (2003). Estimating *Haemophilus influenzae* type b vaccine effectiveness in England and Wales by use of the screening method. *J Infect Dis*; 188: 481-5.

02

General Immunisation Procedures

This chapter provides information on the following:

- Immunisation schedules
 - Routine childhood immunisation schedule
 - Interrupted immunisation courses
 - Late primary immunisation
 - Catch-up schedule for children aged 4 months to 10 years
 - Catch-up schedule for children aged 10 to 18 years
 - Vaccination before minimum recommended interval
 - Vaccination after the expiry date
 - Immunisation of late entrants to Irish health-care system
- Conditions that are NOT contraindications to immunisation
- Contraindications and precautions to vaccines
- Immunisation of specific groups
 - Adults
 - Intramuscular vaccination in those with bleeding disorder or on anticoagulants
 - Live vaccines and pregnancy
 - Immunocompromised children
 - Congenital (primary) immune deficiencies
 - Severe immunodeficiency
 - Moderate or non-specific immunodeficiency
 - Asplenia and hyposplenism
 - Intensive chemotherapy and bone marrow transplant recipients
 - Solid organ transplantation
 - Standard cancer chemotherapy
 - Corticosteroid therapy
 - HIV Infection
 - Vaccination of preterm infants
- Immunoglobulin
 - Human Normal Immunoglobulin (HNIG)

- Specific immunoglobulins
- Live viral vaccines following immunoglobulin administration
- General guidelines for spacing the administration of killed and live antigens
- How to administer intramuscular (IM) injections
- How to administer subcutaneous (SC) injections
- How to administer intradermal injections
- How to hold a child during immunisation
- Bibliography

Adrenaline should be available at all times before giving vaccines.

Immunisation Schedules

Routine childhood immunisation schedule

Table 2.1 Routine childhood immunisation schedule

Age	Immunisations	Comment
Birth	BCG	1 injection
2 months	DTaP/Hib/IPV/Hep B + PCV	2 injections
4 months	DTaP/Hib/IPV/Hep B + MenC	2 injections
6 months	DTaP/Hib/IPV/Hep B + PCV + MenC	3 injections
12 months	MMR + PCV	2 injections
13 months	MenC + Hib	2 injections ¹
4 to 5 years	DTaP/IPV + MMR	2 injections
11 to 14 years	Tdap + BCG ²	1 injection

¹ If a combined MenC/Hib vaccine is available only one injection is required.

² Only for those who are known to be tuberculin negative and have no previous BCG (see Chapter 16).

BCG	Bacille Calmette Guerin vaccine
DTaP	Diphtheria, Tetanus and acellular Pertussis vaccine
Hib	<i>Haemophilus influenzae</i> b vaccine
IPV	Inactivated Polio Virus vaccine
Hep B	Hepatitis B vaccine
PCV	Pneumococcal Conjugate Vaccine
MenC	Meningococcal C vaccine
MMR	Measles, Mumps and Rubella vaccine
Tdap	Tetanus, low-dose diphtheria and low-dose acellular pertussis vaccine

Available evidence suggests that simultaneous administration of multiple

vaccines as in the Irish schedule is not only safe and effective, but can potentially increase uptake rates by up to 17%.

Interrupted immunisation courses

If an immunisation course is interrupted, it should be resumed as soon as possible. It is not necessary to repeat the course, *regardless of the time interval from the previous incomplete course*. With Hib and MenC vaccine, the course should be completed with the same brand of vaccine if possible. Some children for a variety of reasons may not have been immunised, or their immunisation history may be unknown or unreliable. Advice regarding vaccination of these children is provided in this chapter.

Late primary immunisation

Children who are not immunised or who are incompletely immunised and are older than the recommended age range should be immunised as soon as possible. Injections of vaccines that are not already combined by the manufacturer must be given in separate sites. It is currently recommended that PCV is not given at the same time as Hib/MenC booster. This is a precautionary measure until more data accumulates as to whether these two particular conjugate vaccines can be given at the same time without any interference between them. The number of Hib, PCV and MenC doses required depends on the child's age. Hib and DTaP are not recommended over 10 years of age and MenC is not recommended over 22 years of age.

Table 2.2 Catch-up schedule for children aged 4 months to 10 years

Vaccine	Minimum age for dose 1	Minimum interval between doses		
		Dose 1 to Dose 2	Dose 2 to Dose 3	Dose 3 to Dose 4
Diphtheria, Tetanus, Pertussis	8 weeks	4 weeks	4 weeks	6 months
Hib ⁽¹⁾	8 weeks	4 weeks if aged <12 months No further dose if 1 st dose given aged ≥12 months	4 weeks if aged <12 months No further dose if any dose given aged ≥12 months	
Hepatitis B	Birth	4 weeks	8 weeks (and 16 weeks after first dose)	
IPV	8 weeks	4 weeks	4 weeks	4 weeks
MMR	12 months	4 weeks ⁽²⁾		
MenC ⁽³⁾	8 weeks	As for Hib	8 weeks for those aged 12 months to 23 years who have not had a dose aged >12 months	
PCV(not recommended if >2years unless at-risk; see Ch. 12) ⁽⁴⁾	8 weeks	4 weeks No further dose if any dose given aged 12 to 23 months	8 weeks No further dose if any dose given aged 12 to 23 months ⁽⁵⁾	

1. Hib vaccine is not generally recommended for children aged ≥10 years.
2. MMR: The second dose of MMR is recommended routinely at age 4-5 years but may be administered earlier. However, if children aged less than 18 months are given the second dose less than 3 months after the first dose, they need a third dose to ensure full protection. This can be given at age 4-5 years.
3. A single dose of MenC is required for children over 12 months to 23 years.

4. PCV vaccine is not generally recommended for children aged ≥ 2 years, except for at-risk children aged 24-59 months. See Chapter 12 for detailed recommendations.
5. For schedule for children at risk see detailed recommendations in Chapter 12.

Note A: This schedule may be altered in certain circumstances, e.g. during a measles outbreak.

Note B: For catch-up schedule the intervals between doses may be less than those routinely recommended in order to complete the immunisation schedule rapidly.

Catch up schedule for children aged 10 to 18 years

Table 2.3 Catch-up schedule for children aged 10 to 18 years

Vaccine	Minimum interval between doses		
	Dose 1 to Dose 2	Dose 2 to Dose 3	Dose 3 to Dose 4
Tdap	4 weeks	6 months	<u>5 years</u> if third dose given at age <7 years and current age ≥ 10 years <u>10 years</u> if third dose given at age ≥ 7 years
IPV	4 weeks	4 weeks	5 years
Hepatitis B	4 weeks	8 weeks (and 16 weeks after first dose)	
MMR	4 weeks		
Men C	ONE dose only		

Vaccination before minimum recommended interval

If a vaccine is given before the minimum interval recommended in Table 2.3, it should not be considered as part of the primary series as there may be a sub-optimal immune response. If this happens, disregard the dose and give another dose at the recommended time, at least 1 month after the disregarded dose. However, inadvertently giving a dose less than 4 days before the minimum recommended interval is unlikely to have a significantly adverse effect on the immune response to that dose.

Vaccination after the expiry date

If a vaccine is given after the last day of expiry month there may be a reduced immune response and that dose should be disregarded. A further dose should be given 1 month later. There is an increased likelihood of a local reaction following the repeat dose with diphtheria-

and tetanus-containing vaccines, and parents/guardians should be informed of this.

Immunisation of late entrants to Irish health-care system

Immunisation records of children adopted from some low-income countries may not be accurate, and should be accepted with caution. Lack of protection against vaccine-preventable diseases may be due not only to erroneous records, but also to improper storage or handling of vaccines, or to immune defects such as those that can occur during severe malnutrition.

Decisions regarding whether to give or withhold vaccines are based on a number of factors, including the slight risk of over-vaccinating children. The following guidelines are based on the best available evidence:

1. *MMR*

Because adverse reactions to the MMR vaccine are rare, two doses should be given at 12 months and 4-5 years of age (or at least 4 weeks apart if aged over 4 years) unless there is a very reliable history of previous vaccination. Serological testing may be carried out if there are well-founded concerns about revaccination.

2. *Hib, MenC and Pneumococcal*

Because adverse reactions are rare and because it is very unlikely that these vaccines would have been given to such children, age-appropriate immunisation should be given (see Tables 2.2 and 2.3).

3. *Polio*

Adverse reactions to IPV are extremely rare. It is recommended that 4 doses of IPV be given, preferably before the age of 4-6 years, in keeping, as far as possible, with the current Irish schedule.

4. *DTaP*

More than 4-5 doses of each of the components may very occasionally result in severe local (Arthus) reactions if given without regard to appropriate intervals. If a major local or systemic reaction occurs after a dose, tetanus and diphtheria antibody levels may need to be checked. A high level indicates that subsequent doses are not necessary for at least 5 years. If a child at presentation is over 10 years of age acellular pertussis is given as appropriate (see Chapter 15).

5. Hep B

A 3-dose series may be given to children who are unvaccinated, as per the Irish recommendations (see Chapter 6).

If there is uncertainty regarding previous vaccine history, it is preferable to give the vaccines, as the risk of lasting adverse events from administering extra doses is very small.

Conditions that are NOT contraindications to immunisation

1. Family history of any adverse reactions following immunisation.
2. Minor infections without fever or systemic upset.
3. Family or personal history of convulsions. Antipyretic measures are advisable following immunisation of children under 5 years with a family history of febrile convulsions.
4. History of pertussis, measles, rubella or mumps infection in the absence of proof of immunity.
5. Prematurity or low birth weight (defer Hep B in those under 2kg unless there is a maternal history of HBV infection).
6. Stable neurological conditions e.g. cerebral palsy.
7. Recent contact with an infectious disease.
8. Asthma, eczema, hay fever, migraine or food allergy.
9. Therapy with antibiotics or low-dose oral or locally-acting steroids.
10. Child's mother is pregnant.
11. Child being breastfed.
12. History of jaundice.
13. Child over the age recommended in immunisation schedule.
14. Recent or imminent surgery or general anaesthesia.
15. Corticosteroid replacement therapy.

Contraindications and precautions to vaccines

- Minor illness with a temperature of less than 38°C is not a reason to defer immunisation.
- Sometimes these recommendations differ from those in licensed information on the Summary of Product Characteristics (SPC).
- The benefits and risks of giving specific vaccines should be carefully considered when the events listed as precautions exist.
- When there are doubts as to whether or not to give a vaccine contact a Paediatrician or Public Health Specialist.

Table 2.4 Contraindications and precautions for specific vaccines

Vaccine	Contraindications	Precautions
General for all vaccines	Confirmed anaphylactic reaction to the vaccine or to a constituent See introduction	Moderate or severe illness; defer until recovery, unless the benefits outweigh the risks Latex allergy (see note 2 below)
DTP/DTaP/Tdap (see note 1 below)	As above (see note 1 below)	Evolving neurological conditions; defer until stable
IPV	As above	Pregnancy; give if benefits outweigh risks
MMR	As above Pregnancy	<ul style="list-style-type: none"> – Recent administration of blood or blood product (defer for at least 3 months) – Immune deficiency or suppression (see note 3 below) – Thrombocytopenia within 6 weeks of a previous dose (see Chapter 8)

Notes

1. Encephalopathy, temp >40.5°C, seizures, prolonged crying or hypotonic-hyporesponsive episodes following a previous dose of a whole-cell pertussis-containing vaccine have **not** been shown to result in permanent damage, are far less likely to occur following acellular pertussis vaccines, and **are no longer regarded as either precautions or contraindications**.
2. Vaccines supplied in vials or syringes containing rubber should not be used in those who had an anaphylactic reaction to latex.
3. **May need to seek medical guidance from treating physician, regarding severity of immunosuppression (see page 20).**

Immunisation of specific groups

Adults

Adults should receive the following vaccines:

- (a) Women sero-negative for rubella: **MMR**
- (b) Women sero-negative for varicella: **varicella vaccine** (see Chapter 17)
- (c) Previously non-immunised individuals: **polio, tetanus, diphtheria and MenC (if under 23 years)** (see relevant chapters)
- (d) Individuals in specific high-risk groups: **hepatitis B, hepatitis A, MMR, Hib, MenC, influenza, pneumococcal, varicella and BCG vaccines** (see relevant chapters)
- (e) Those travelling abroad (see Chapter 19).
- (f) Those aged over 50 years: **influenza** (see Chapter 7).
- (g) Those aged over 65 years: **pneumococcal polysaccharide vaccine (PPV23)** (see Chapter 12).

Intramuscular vaccination in those with bleeding disorders or on anticoagulants

There is little published information regarding the administration of intramuscular vaccines to persons with bleeding disorders or receiving anticoagulant treatment.

If vaccines are given intramuscularly to such persons, it is prudent to use a 23-gauge needle, and to apply pressure to the vaccine site for 1-2 minutes after the injections.

Administration of vaccines by the subcutaneous route may be considered in those with severe bleeding disorders. However, immunogenicity of vaccines recommended for IM administration may not be as long-lasting if they are given subcutaneously. The patient or parent should be advised of this.

Live vaccines and pregnancy

Live vaccines should generally not be administered to pregnant women because of the theoretical possibility of harm to the foetus. However, where there is a significant risk of exposure, the need for immunisation should be balanced against the remote possibility of risk to the foetus.

Immunocompromised children

Over the last number of years there has been an increase in the number of immunocompromised children for a number of reasons such as better survival after cancer chemotherapy and in those with chronic disease such as cystic fibrosis. There is also an increase in the number of those with dysfunctional spleens (sickle cell disease, thalassaemia major) and with HIV.

For detailed guidance regarding vaccination of immunocompromised persons, consult the Royal College of Paediatrics and Child Health document 'Immunisation of the Immunocompromised Child (2002)', at www.rcpch.ac.uk/Health-Services/Immunisation

The decision whether or not to give a vaccine to such children must be made on an individual basis, and the risks and benefits carefully weighed. It is important to realise that the extent of immunocompromise can vary over time, as in those recovering from chemotherapy and those with HIV infection. The following, therefore, are to be regarded as guidelines.

Congenital (primary) immune deficiencies

Persons with B lymphocyte (humoral) defects or complement deficiencies are susceptible to infection with encapsulated bacteriae, especially *Strep. pneumoniae*, *Haemophilus influenzae* type b, *N. meningitidis*, and also to enteroviruses. Those with T-lymphocyte (cell-mediated immunity) defects are susceptible to most viruses and to a number of intracellular bacteria, fungi and parasites.

Severe immunodeficiency

This group includes severe combined immunodeficiency (SCID), X-linked agammaglobulinaemia, and some children with Di-George syndrome (the degree of immune compromise in Di-George syndrome is very variable, with many only having relatively minor impairment). They can be given non-live vaccines. Some can receive MMR, but they should not be given BCG.

Moderate or non-specific immunodeficiency This group includes IgA and IgG subclass deficiencies, chronic neutropaenia, chronic granulomatous disease, and complement deficiency diseases. These children should be given all routine vaccines, including MMR. They should also be given pneumococcal and influenza vaccines. Those with complement deficiencies should get meningococcal ACW₁₃₅Y vaccine.

In addition to vaccination as recommended in this section, persons with these conditions who intend travelling abroad should be vaccinated as recommended in Chapter 19.

Asplenia and hyposplenism

This may be congenital, post-surgical or functional (sickle cell disease, thalassaemia major, storage disorders, coeliac disease etc.) Such persons are at risk of infection caused by encapsulated bacteria (*Strep. pneumoniae*, *Hib*, *Meningococci*, etc.)

Children with these conditions can receive all routine childhood vaccines. In addition they should be given conjugated pneumococcal vaccine (PCV) up to the age of 5 years and polyvalent pneumococcal vaccine (PPV) over the age of 2 years (see Chapter 12). They should be re-immunised with this after a period of 5 years and should also be given long-term penicillin prophylaxis. They should also get annual influenza vaccine.

Adults with asplenia should receive PPV, Hib and MenC vaccines, and annual influenza vaccine.

Intensive chemotherapy and bone marrow transplant recipients

It is likely that all those who receive an allogenic or autologous marrow transplant lose some or all of their natural and vaccine-derived immunity against vaccine-preventable diseases. Therefore such persons should be fully revaccinated with all age-appropriate vaccines.

Inactivated vaccines should be deferred for at least 12 months after bone marrow transplant, and at least 6 months after immunosuppressive treatment has been stopped; even then immune response may be sub-optimal.

Those with graft versus host disease should not be vaccinated if they are receiving Intravenous Immunoglobulin (IVIG).

Live vaccines should be deferred for up to 2 years, and then given only if there is no graft versus host disease or ongoing immunosuppressive treatment.

Solid organ transplantation

Prior to surgery children should be up-to-date with routine primary and booster vaccination. Varicella vaccine should be given to non-immune

persons. Those having haemodialysis prior to renal transplant should be given hepatitis B vaccine if they are unvaccinated.

After transplant, the routine schedule should continue. Pneumococcal (PPV or PCV depending on age – see Chapter 12) and annual influenza vaccines should be given.

Standard cancer chemotherapy

The degree of immune compromise varies depending on the disease and the treatment. It is often not possible to give a definite recommendation regarding when to give vaccines after such treatment has been completed.

During treatment, non-live vaccines should be given according to the schedule, as long as the child is free from infection and major organ toxicity, and is likely to remain so for 3 weeks.

Six months after treatment, a booster of DTaP/IPV/Hib, MenC, and MMR should be given. (Give Tdap if child is over 10 years of age.)

Live vaccines generally should be withheld for at least 6 months. However, the interval may vary depending on the type and intensity of immunosuppressant treatment, radiation treatment, underlying disease etc. An adequate immune response to inactivated vaccines should occur between 3 and 12 months post-treatment.

Corticosteroid therapy

The minimum amount and the duration of administration of systemic corticosteroids sufficient to cause immune suppression are not well defined. The following are empiric guidelines for administration of **live** virus vaccines to previously healthy persons receiving steroid therapy for non-immunocompromising conditions:

1. Topical (skin or inhaled) or locally injected steroids do not usually cause immunosuppression, so live vaccines are not contraindicated.
2. Children receiving less than 2 mg/kg/day of prednisolone or its equivalent can be given live viral vaccines during treatment.
3. Children getting more than 2 mg/kg/day of prednisolone or its equivalent, or more than 20 mg per day *for under 2 weeks*, can be given live viral vaccines immediately after treatment is stopped.

4. Children getting over 2 mg/kg/day of prednisolone or its equivalent, or more than 20 mg/day, for *more than 2 weeks*, and those getting 1 mg/kg/day for over 1 month should not receive live viral vaccines for at least 3 months after treatment has been stopped.
For adults the equivalent dose of prednisolone is 40 mg or more per day for more than 2 weeks.
5. For those receiving combination immunosuppressant therapy, such as corticosteroids and methotrexate, live viral vaccines should be deferred for 6 months after stopping treatment.
6. Inactivated vaccines can be given when due, but immune response may be sub-optimal.

HIV infection

Active immunisation of HIV-positive persons

HIV-infected individuals, whether symptomatic or asymptomatic, should be immunised with all inactivated vaccines recommended in the primary vaccine schedule. Pneumococcal conjugate and polysaccharide vaccines should be given as recommended in Chapter 12. Yearly influenza vaccine beginning at 6 months of age is also recommended.

MMR vaccine should be given at 12-14 months of age to HIV-infected children unless they are severely immunocompromised. The second dose should be given 1-2 months later, in order to ensure seroconversion as early as possible.

Varicella vaccine should be considered for asymptomatic or mildly symptomatic children with CD4 counts above 25%.

Since the immune response of HIV-infected children to all vaccines may be inadequate, these children may be susceptible to vaccine-preventable diseases even if they have been vaccinated. Hence, chemoprophylaxis or immunoglobulin treatment should be considered in the event of exposure to these diseases.

Table 2.5 Vaccination of those who are HIV positive

Vaccine	Asymptomatic HIV infection	Symptomatic HIV infection
Diphtheria, tetanus, pertussis, polio	Yes	Yes
MMR	Yes	Yes
Haemophilus	Yes	Yes
Meningococcal	Yes	Yes
PPV, PCV	Yes	Yes
Influenza	Yes	Yes
Hepatitis A and B	Yes	Yes
Varicella	Yes	Yes if CD4 >25%
BCG ^{1, 2}	No	No
OPV ¹	No	No
Yellow fever ¹	No	No

¹There is insufficient evidence at present to recommend the use of OPV, yellow fever or BCG in symptomatic HIV-infected individuals.

²See Chapter 16 re HIV and BCG.

Passive immunisation of individuals with HIV infection

Measles

Vaccine efficacy may be reduced in HIV-positive individuals. Human Normal Immunoglobulin (HNIG) may be used for susceptible symptomatic and asymptomatic HIV-positive individuals after exposure to measles if the response to vaccination has not been documented or is inadequate.

Tetanus

In the management of wounds classified as tetanus prone, HIV-positive individuals should receive Tetanus Immune Globulin (TIG) if the response to vaccination has not been documented or is inadequate.

Varicella

- Asymptomatic HIV-positive individuals do **not** require Human Varicella-Zoster Immunoglobulin (VZIG) after contact with chickenpox since there is no evidence of increased risk of serious illness in these individuals.
- Symptomatic HIV-positive individuals should be given VZIG after contact with chickenpox unless they are known to have varicella-zoster antibodies.

Vaccination of preterm infants

Preterm infants are more vulnerable when exposed to infections, particularly pertussis – 30% of pertussis deaths in the USA occur in preterm infants. Therefore, routine vaccines should be started at 8 weeks post-natal age in preterm infants of any gestational age. If the infant is still in hospital, the first vaccines should be given under cardiorespiratory monitoring for 48 hours, as there may be an increase in bradycardia and/or apnoeic episodes in these infants. Such episodes do not recur after subsequent vaccinations, nor have they been reported in preterm infants who have been discharged from hospital.

When compared with infants born at term, there is less of a rise and a more rapid decline in antibody levels following vaccination of preterm infants. However, there may be less interference from maternal antibodies in this group of infants, as most antibody transfer occurs in the third trimester.

Hepatitis B vaccine may not give an adequate immune response in infants weighing less than 2kgs, until they are aged one month. However, if a mother is HBsAg positive, her infant should be given the HepB vaccine at birth and further doses (as 6-in-1 vaccine) at 2, 4 and 6 months of age.

BCG vaccine should be given to preterm infants prior to discharge from hospital.

The presence of an intraventricular haemorrhage is not a contraindication to vaccination.

There is a lack of information regarding the effects of antenatal steroids on the immune response of preterm infants. Such infants should be vaccinated according to the current schedule.

Immunoglobulin

Human Normal Immunoglobulin (HNIG) is prepared from the pooled blood of donors who are negative to hepatitis B surface antigen (HBsAg), hepatitis C antibody (anti-HCV) and antibody to human immunodeficiency virus (HIV).

Human Normal Immunoglobulin (HNIG) for intramuscular use

It usually contains antibodies to varicella, hepatitis A and other viruses currently prevalent in the population. HNIG is available in 2, 5 and 10 ml vials. It is given by deep intramuscular injection. It should be stored at

2-8°C and the expiry date on the package observed. Unused portions of an ampoule must be discarded. As recipients of intramuscular immunoglobulin can experience local pain and discomfort at the injection site, it should be administered deep into a large muscle mass, such as the gluteus maximus. Ordinarily, no more than 5 ml should be administered at any one site.

Intramuscular HNIG should not be administered to any patient with severe thrombocytopenia or with a coagulation disorder. Caution should be exercised with any patient who has a history of adverse experience following HNIG administration.

Indications for use of HNIG include post-exposure prophylaxis or modification of hepatitis A infection and post-exposure modification of measles infections (see Chapters 5 and 8).

HNIG may interfere with the immune response to live viral vaccines; these should not therefore be given from 3 weeks before to at least 3 months after an injection of HNIG. Yellow fever vaccine is an exception, as HNIG obtained from donors is unlikely to contain antibody to this virus; a similar situation applies to Oral Polio Virus vaccine when given as a booster dose.

The vaccine and HNIG should be given in different limbs. If indicated, vaccination should be repeated approximately 3 months later.

Specific immunoglobulins

At present specific immunoglobulins are available for administration following exposure to tetanus, hepatitis B, rabies* and varicella-zoster virus. They are prepared from the pooled plasma of blood donors who have high antibody titres to specific infections. Recommendations for their use are found in the relevant sections.

When medicinal products prepared from human blood or plasma are administered, infectious diseases due to the transmission of infective agents cannot be totally excluded. This applies also to pathogens of hitherto unknown origin and pathogens as yet unidentified.

To reduce the risk of transmission of infective agents, stringent controls are applied to the selection of blood donors and donations. In addition, virus removal and/or inactivation procedures are included in the production process.

* At present available from Cherry Orchard Hospital

The current procedures applied in the manufacture of medicinal products derived from human blood or plasma are effective against enveloped viruses such as HIV, hepatitis B and hepatitis C viruses, and non-enveloped viruses.

Live viral vaccines following immunoglobulin administration

Live viral vaccines, with the exception of yellow fever and BCG vaccine (see below and Chapter 16), should not be given for at least 3 months following injection of immunoglobulin because the immune response may be inhibited.

BCG vaccine

Administration of blood or plasma transfusions, hepatitis B vaccine, hepatitis B immunoglobulin and normal immunoglobulin are thought not to reduce the effectiveness of BCG vaccine. A baby who has received blood or plasma transfusions can be subsequently immunised with BCG, after the observation period for transfusion reactions has ended (24 hours).

General guidelines for spacing the administration of killed and live antigens

The following table shows the recommended minimum intervals between vaccine doses.

Table 2.6 Recommended minimum interval between vaccine doses

Antigen combination	Recommended minimal interval between doses
≥2 killed antigens	No minimum; may be administered simultaneously or at any interval between doses
Killed and live antigens	No minimum; may be administered simultaneously or at any interval between doses
≥2 live antigens	Four-week minimum interval if not administered simultaneously; however, oral polio vaccine (OPV) can be administered at any time before, with or after other live vaccines.

Specific contraindications to individual vaccines are given in the relevant sections and must be observed.

How to administer intramuscular (IM) injections

This route is used for the majority of vaccines. For individual vaccines see relevant chapters.

Needle insertion

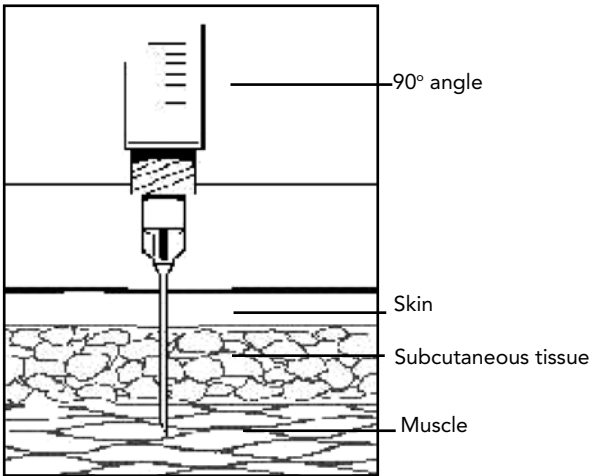
Giving an infant a carbohydrate-containing drink 1-2 minutes before injection reduces the pain of insertion.

- Insert needle at a 90° angle to the skin. The tissue around the injection site may be bunched up in young infants.
- Retain pressure on skin around injection site with thumb and index finger while needle is inserted.
- It is not necessary to aspirate before injecting, as there are no large blood vessels at the preferred injection sites.
- Multiple injections given in the same limb should be separated by at least 2.5 cm.

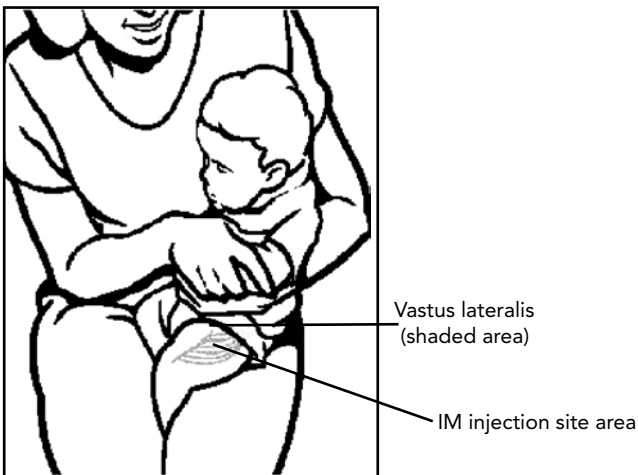
Table 2.7 Recommendations regarding preferred site and needle size for intramuscular injections

Patient's age	Site (see illustrations below)	Needle size
Birth to 12 months*	Vastus lateralis muscle in anterolateral aspect of mid- or upper thigh	25 mm needle 23-25 gauge
12 to 36 months	Vastus lateralis or deltoid muscle	25 mm needle 23-25 gauge
From 3 years upwards*	Densest portion of deltoid muscle – between acromion and muscle insertion	25 mm needle 23-25 gauge

*Note: Use a 16 mm length needle in infants under 2.5-3 kg. Use 38 mm length needle in women >90 kg, men >118 kg.

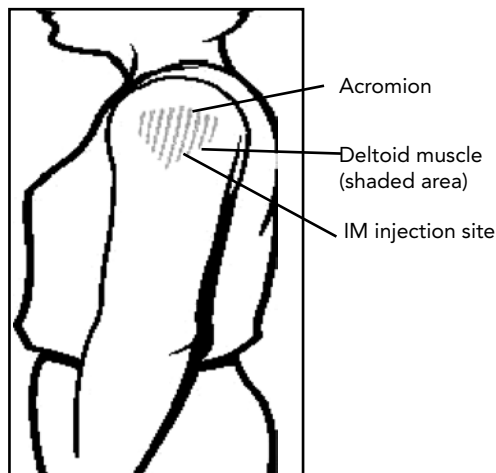


IM site for infants and toddlers (birth to 36 months of age)



Insert needle at 90° angle into anterolateral aspect of middle or upper thigh.

IM site for older toddlers, children and adults



Insert needle at 90° angle into densest portion of deltoid muscle
– between acromion and insertion.

How to administer subcutaneous (SC) injections

Use this route for varicella and yellow fever vaccines.

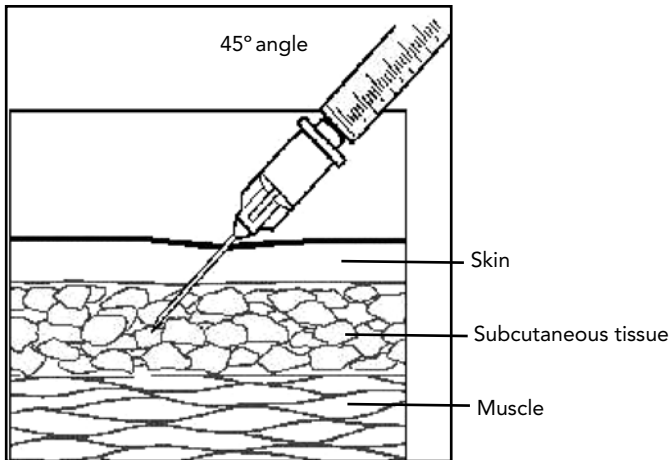
Table 2.8 Recommendations regarding preferred site and needle size for subcutaneous injections

Patient's age	Site (see illustrations below)	Needle size
Infants (birth to 12 months of age)	Fatty area of the Anterolateral thigh	16 mm needle 23-25 gauge
Toddlers (12 to 36 months of age)	Fatty area of the anterolateral thigh or triceps region	16 mm needle 23-25 gauge
Children and adults	Triceps region	16 mm needle 23-25 gauge

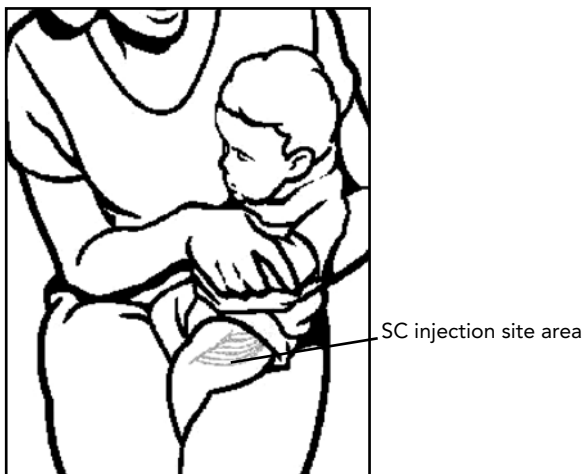
Needle insertion

Insert needle at 45° angle to the skin

- Pinch up on SC tissue to prevent injection into muscle.
- There is no need to aspirate prior to injection as there are no large blood vessels at the preferred injection sites.
- Multiple injections given in the same limb should be separated by at least 2.5cm.

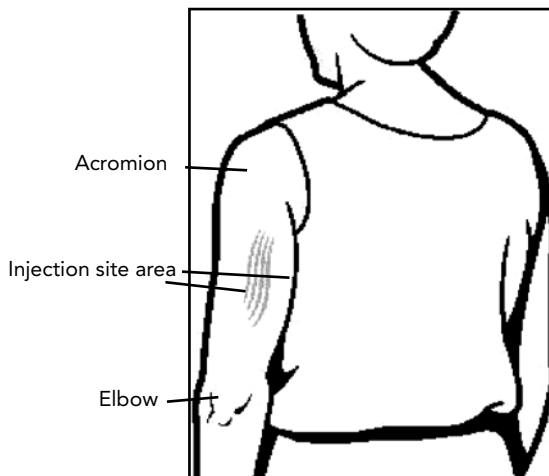


SC site for infants and toddlers (birth to 36 months of age)



Insert needle at 45° angle into fatty area of anterolateral thigh. Pinch up skin to prevent injection into muscle.

SC site for toddlers, children and adults



Insert needle at 45° angle into outer aspect of upper arm. Pinch up skin to prevent injection into muscle.

How to administer intradermal injections

Use for BCG and tuberculin PPD (Mantoux).

Site:

The BCG is given into the skin at one site over the distal insertion of the deltoid muscle (approx. one third down the upper arm); tuberculin is generally injected into the ventral surface of the forearm

Technique:

A 1 ml syringe with a 10-16 mm, 25-26G short-bevelled needle is used for BCG. A 1 ml tuberculin syringe can also be used for the Mantoux test. All air bubbles are removed. The skin is slightly stretched with thumb and index finger of one hand. The needle is inserted almost parallel to the surface, with the bevel upwards, to a length of approx. 5 mm and the dose is slowly injected.

A bleb 7-10 mm in diameter should result (3 mm if the dosage is 0.05 ml as for neonatal BCG). If little resistance is felt when injecting and a diffuse swelling occurs rather than a tense bleb, the needle is too deep. If this occurs:

- for BCG the needle should be withdrawn and the same needle reinserted intradermally at a site at least 5 cm away
- for Mantoux the test should be repeated at least 5 cm away from the first injection.

No further immunisation should be given in the arm used for BCG immunisation for at least 3 months because of the risk of regional lymphadenitis.

BCG intradermal injection



How to hold a child during immunisation

This method involves the parent/carer in embracing the child and controlling all four limbs. It avoids 'holding down' or overpowering the child, but it helps steady and control the limb of the injection site.

For infants and toddlers

Have parent hold the child on parent's lap.



1. One of the child's arms embraces the parent's back and is held under the parent's arm.
2. The other arm is controlled by the parent's arm and hand. For infants, the parent can control both arms with one hand.
3. Both legs are anchored with the child's feet held firmly between the parent's thighs, and controlled by the parent's other arm.

For older children

Hold the child on parent's lap or have the child stand in front of the seated parent.



1. Parent's arms embrace the child during the process.
2. Both legs are firmly between parent's legs.

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Department of Health UK (2006). Immunisation against infectious disease (the Green Book). 3rd ed. London: The Stationery Office.

03

Diphtheria

Introduced in 1930s (DT) and 1952/3 (DTP)

NOTIFIABLE

Introduction

Diphtheria is an acute infectious disease affecting the upper respiratory tract and occasionally the skin. It is caused by *Corynebacterium diphtheriae* or *C. ulcerans*. Effective protection against the disease is provided by active immunisation.

Since the introduction of vaccination against diphtheria, the disease and the organism have been virtually eliminated from Ireland. However, an immunisation rate of at least 85% must be maintained to protect the population against the possibility of a resurgence of the disease which could follow the introduction of cases or carriers of toxigenic strains from overseas.

Immunity decreases with age; approximately 65% of those over 30 years of age may be susceptible to diphtheria.

Approximately 5 secondary infections will result from each index case in a fully susceptible population.

Epidemiology

Humans are the only known reservoir of *Corynebacterium diphtheriae*. Transmission results primarily from close contact with a patient or carrier. Spread is by droplet infection, and on rare occasions through contact with articles soiled by contact with skin lesions of infected persons (fomites). The incubation period is usually 2-5 days, but occasionally can be longer. The disease is communicable for up to 4 weeks, but carriers may shed the organism for longer.

Chapter 3 Diphtheria

There is little likelihood of acquiring natural immunity from sub-clinical infection. However, while no cases have been recently reported in Ireland, they have occurred in the UK, the former USSR states, India, China, and Bangladesh among other countries.

Effects of diphtheria

The disease is characterised by an inflammatory exudate which forms a greyish membrane in the upper respiratory tract resulting in nasopharyngitis and/or obstructive laryngotracheitis. There may also be moderate enlargement of cervical lymph nodes and oedema of the soft tissue of the neck. These local manifestations are associated with a low-grade fever and the gradual onset of generalised manifestations over 1-2 days. Cutaneous manifestations are less common.

A toxin is produced by diphtheria bacilli which affects particularly myocardial, nervous and adrenal tissues and may result in life-threatening complications including myocarditis and neurological problems such as vocal cord paralysis and ascending paralysis similar to the Guillain-Barré syndrome.

Milder infection, particularly in vaccinated persons, may cause tonsillitis or pharyngitis with toxin production.

The case-fatality rate ranges from 3-29%, and is highest in the young and the elderly.

Diphtheria toxoid

Diphtheria immunisation protects by stimulating the production of antitoxin which provides immunity to the effects of the toxin. After a primary series of 3 properly spaced doses in adults and 4 doses in infants, efficacy is estimated at over 97%.

Toxoid should be stored at 2-8°C.

Indications

Immunisation of infants and children under 10 years

Primary immunisation

Diphtheria toxoid is recommended for infants from 2 months of age. The primary immunisation course consists of 3 doses given I.M. at 2, 4 and 6 months of age. If a course is interrupted it may be resumed without the need to start again (see Chapter 2).

Booster immunisation

A booster dose is recommended at 4-5 years of age. Booster doses should be given at least 3 years from the last dose of the primary course unless there is a documented history of 5 doses of tetanus toxoid having been given or the child is over 10 years of age. This is because all diphtheria vaccines are combined with tetanus toxoid. A further booster using low-dose diphtheria toxoid (Tdap) is recommended 10 years later.

If pertussis vaccine is refused by parents, the only available diphtheria and tetanus vaccines are Td and Td/IPV, which contain insufficient tetanus and diphtheria toxoid for primary immunisation. They are not intended for use as part of the primary vaccine schedule, may not give a sufficient immune response if so used, and are not licensed for such use.

Dose and route of administration

For primary immunisation of children under 10 years the dose is 0.5 ml given by intramuscular injection into the deltoid region or the anterolateral thigh.

Immunisation of persons aged 10 years and over (unimmunised or partially immunised)**Primary immunisation**

A special low-dose diphtheria toxoid such as Td must be used because of the possibility of a serious local reaction in an individual who is already immune. Three doses should be given, by intramuscular injection.

Booster Immunisation

Low-dose diphtheria toxoid must be used when the primary vaccination course has been delayed; the first booster may be given 1 year after the third dose, and the second booster 10 years after that. (If a person is at increased risk, the second booster may be given 5 years later.)

Contraindications

Anaphylactic reaction to a preceding dose or any of the constituents.

Precautions

Acute severe febrile illness, defer until recovery.

HIV positivity

HIV positive individuals may be immunised against diphtheria in the absence of any contraindications.

Adverse reactions

Local: Transient local reactions (pain, palpable lump, and erythema) may occur. They are more frequent with subsequent doses. Sequelae are very rare.

General: Malaise, transient fever and headache may occasionally occur. Dyspnoea, urticaria, angioedema, anaphylaxis and neurological reactions are very rare. Anaphylaxis is extremely rare (0.6-3 per million doses).

Contacts of a diphtheria case or carriers of a toxigenic strain

Table 3.1 Recommendations for vaccination of contacts of diphtheria cases and carriers

Immune status	Age-group	Action
Immune (3 or more previous doses)	Under 10 years	One injection of diphtheria toxoid as DT or DTaP/IPV
	10 years and over	One injection of low dose diphtheria toxoid such as Td or Tdap
Non-immune (<3 previous doses)	Under 10 years	Three injections of DTaP/IPV diphtheria toxoid, DT or DTaP at monthly intervals*
	10 years and over	Three injections of Td or Tdap at monthly intervals*

* See Catch-up section, Chapter 2, for number of doses. These children may also need Hib and MenC vaccines.

Non-immunised contacts of a case of diphtheria should, in addition, be given a prophylactic course of Erythromycin, 20-30 mg/kg, 12 hourly for 7 days, max 1g per dose.

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04

Haemophilus influenzae type B (Hib)

Introduced in 1992

NOTIFIABLE

Introduction

Infections due to *Haemophilus influenzae*, a gram-negative coccobacillus, are an important cause of morbidity and mortality, especially in young children. Humans are the only known reservoir. The Hib vaccine was introduced into the primary schedule in Ireland in 1992 and subsequently there has been a dramatic fall in the incidence of invasive Hib disease. A booster dose at 12 months was introduced in 2006. The vaccine is specific for diseases caused by *H. influenzae* type *b*, and does not protect against infections caused by other haemophilus strains.

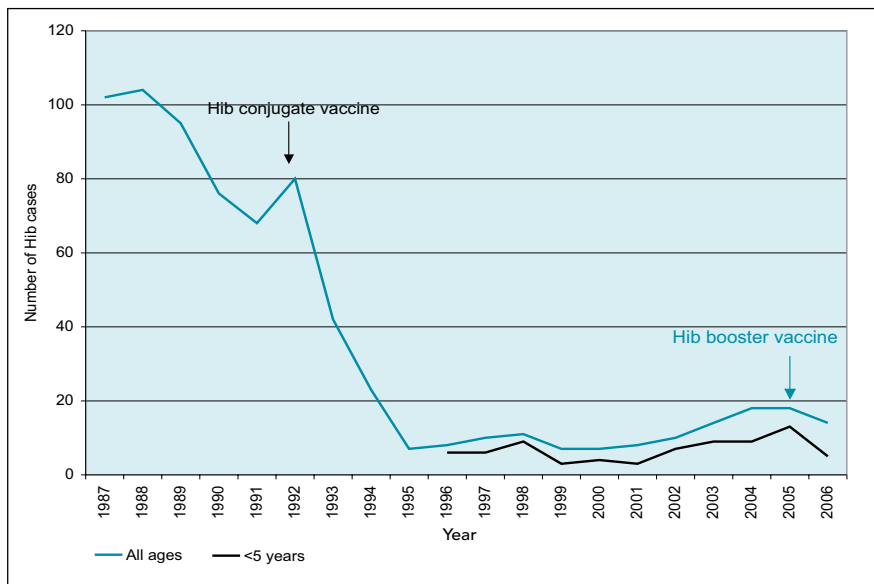
Epidemiology

The incidence of Hib disease fell significantly following introduction of the vaccine into the primary schedule in 1992. In 2002-2003 an increase of invasive Hib disease was noted in unvaccinated children aged under 5 years. However, in late 2004 and 2005 an increase of disease in fully vaccinated children was observed. A catch-up booster vaccination of all children aged 12-47 months, and the addition of routine Hib booster vaccine to those aged 12 months was therefore recommended.

Haemophilus
influenzae type B
(Hib)

Chapter 4 *Haemophilus influenzae* type B (Hib)

Figure 4.1 Number of invasive Hib cases by year, 1987-2006. Source: HPSC



Almost all invasive *H. influenzae* infections are caused by encapsulated strains, of which there are 6 serotypes (a-f). Type b (Hib) caused more than 80% of these infections in the pre-vaccine era. Non-encapsulated strains of haemophilus cause mucosal infection (e.g. otitis media) but rarely lead to serious invasive disease. Transmission is presumed to be by droplet spread.

The epidemiology has changed since the vaccine was introduced to the primary schedule. Prior to 1992, the highest incidence was in those under 1 year of age, with approximately 90% of all Hib disease occurring in those under 5 years of age. These infants are now protected if fully vaccinated. While there is evidence that carriage has been reduced, lessening the risk of exposure of unvaccinated persons, sporadic cases still occur in all age groups.

Effects of Hib disease

Invasive disease caused by *H. influenza* can affect many organs. The commonest effects are:

Meningitis The mortality rate is 2-5%, and neurological sequelae occur in 15-30% of survivors

Epiglottitis, with up to 10% mortality

Pneumonia, septic arthritis, cellulitis (usually involving the face or neck), *otitis media, osteomyelitis, and pericarditis*.

Hib vaccines

Hib vaccines consist of *Haemophilus influenzae* b capsular poly- or oligosaccharide conjugated with tetanus or diphtheria toxoid. Vaccines currently licensed are listed in Appendix 1. An updated list can be found on the IMB website (www.imb.ie).

All Hib vaccines are inactivated. They should be stored at 2-8°C. When the product brand given in the first and second courses is not known or not available, the 3-dose series can be completed with any Hib vaccine.

Dose and route of administration

The dose is 0.5 ml given by intramuscular injection. If BCG has been given within the previous 3 months, a different limb should be used.

The primary course consists of three doses at 2, 4 and 6 months of age, as DTaP/IPV/Hib/Hep B. A booster dose of Hib vaccine is given at 13 months of age. Children aged 12-47 months require only 1 dose. Booster immunisation is not normally required over 4 years of age. Unvaccinated children up to 10 years of age should be vaccinated. Such children may also need age-appropriate vaccination with DTaP, IPV, MenC, and MMR (see Chapter 2).

Indications

1. All infants at 2, 4 and 6 months of age, with a booster at 13 months of age.
2. Those less than 2 years of age who developed invasive Hib disease should be given Hib vaccine after one month. Immunocompetent children over 2 years of age who develop invasive Hib disease do not need to be immunised because the disease will most likely have induced a protective immune response
3. Persons at increased risk of invasive Hib disease, e.g. asplenia, hyposplenism, complement deficiency, etc *irrespective of age*, should be vaccinated. Those aged over 1 year should be given 2 doses of Hib vaccine (Hib/MenC if available) administered 2 months apart.
4. Children and adults who have completed a primary series and are undergoing elective splenectomy may benefit from an additional dose of Hib vaccine, preferably at least 2 weeks prior to the operation. Those who have developed hyposplenism should also get 2 doses.
5. Children aged 1-10 years who have never received Hib vaccine should be given 1 dose.

Contraindications

Anaphylactic reaction to a preceding dose or any of the constituents.

Precautions

Acute severe febrile illness, defer until recovery.

Hib vaccine may be given to immunocompromised patients, but adequate antibody levels may not be reached.

Adverse reactions

Local: These include local redness, warmth or swelling at the injection site. Mild local reactions occur in about 20% of children.

General: Systemic reactions are uncommon, and include fever, irritability, headache, vomiting, diarrhoea, and rashes. Seizures have rarely been reported.

Immunisation and chemoprophylaxis of cases and contacts of invasive Hib disease

1. Household contacts (except pregnant women):
Household contacts are regarded as those who share living or sleeping accommodation with the case.
 - (a) Non-immunised contacts aged under 10 years should be given Hib vaccine.
 - (b) Chemoprophylaxis is indicated for all household contacts irrespective of age or immunisation history in the following situations:
 - (i) if there are any children under 4 years of age who are unvaccinated or incompletely vaccinated
 - (ii) if there are any unvaccinated children under 10 years of age
 - (iii) if there are any persons at increased risk of invasive Hib disease (asplenia, hyposplenism, etc.) irrespective of their age or immunisation status.
2. Play-group, creche or primary school contacts aged less than 10 years:
Non-immunised room contacts under the age of 10 years should be offered Hib vaccine. When two or more cases occur within 2 months, chemoprophylaxis should be offered to all room contacts, both adults and children.

3. Index case:
The index case, if younger than 2 years of age, may have low levels of anticapsular antibodies and could get a second episode of disease. Therefore immunisation should be given according to the current recommended schedule irrespective of vaccine history, starting 1 month after onset of disease or as soon as possible thereafter.

The index case should also be given chemoprophylaxis prior to discharge if not treated with cefotaxime or ceftriaxone. These drugs eradicate Hib from the nasopharynx. Immunised children who develop invasive Hib disease have an increased incidence of IgG2 deficiency and should be considered for immunological evaluation.

Notes:

1. Rifampicin dose for prophylaxis:
(a) Infants under 1 year of age – 10 mg/kg once daily for 4 days
(b) Children and adults – 20 mg/kg once daily for 4 days, max. 600 mg/day
2. Chemoprophylaxis is not recommended for pregnant women who are contacts of cases because rifampicin is not licensed for this indication.

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05

Hepatitis A

NOTIFIABLE

Introduction

Hepatitis A is an acute, usually mild and self-limiting disease of the liver caused by the hepatitis A virus (HAV). The disease varies in clinical severity from a mild illness lasting 1-2 weeks to a severely disabling disease lasting several months. Most patients make a complete recovery. HAV hepatitis does not progress to chronic liver disease and there is no chronic carrier state. On rare occasions the disease may be very severe, with fulminant hepatitis, liver coma and death.

Severity of illness increases with age. Case fatality can reach 2% for adults over 50 years of age. Persons with pre-existing chronic liver disease have an elevated risk of death from fulminant hepatitis A. Infection confers life-long immunity.

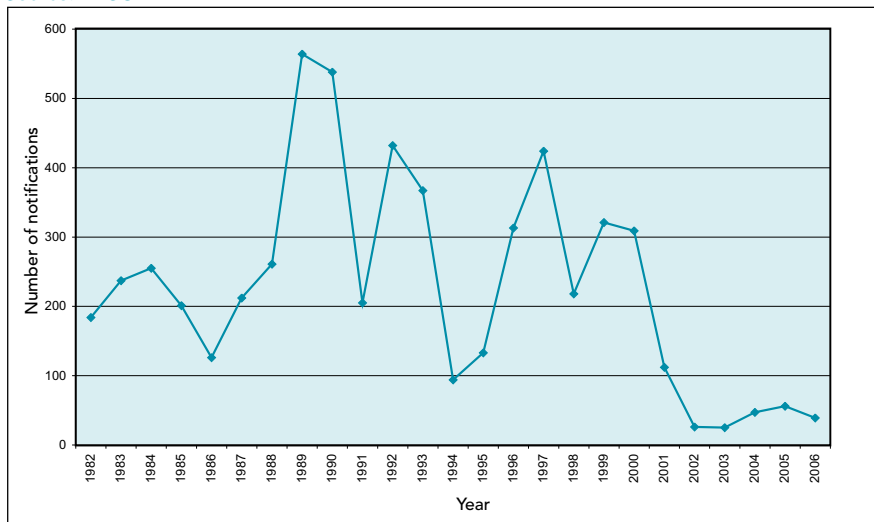
Epidemiology

Hepatitis A infection is common worldwide. The incidence of hepatitis A has been decreasing in developed countries over the past 50 years because of improved hygiene and sanitary conditions. In these countries, disease transmission is most frequent among household and sexual contacts of acute cases. It occurs sporadically in day-care centres with small children. It also occurs among travellers to endemic countries. Outbreaks have been reported frequently in injecting drug users and in men who have sex with men. In the developing world where standards of sanitation are poor, HAV infection is common and occurs in early life.

The incidence of hepatitis A in Ireland has fallen substantially since 2002, with fewer than 60 cases notified per year (Figure 5.1). The age-standardised incidence rate in 2005 was 1.4 per 100,000 population. It is likely that most people under the age of 50 in Ireland are now susceptible to HAV.

Figure 5.1 Number of hepatitis A notifications in Ireland, 1982-2006.

Source: HPSC



Transmission

Person-to-person transmission

HAV infection is spread primarily by the faecal-oral route from person to person.

The risk of faecal-oral transmission is increased where there is close person-to-person contact, e.g. among infants, young children and those with learning disability, especially in day-care and residential homes. The risk is also increased where there is overcrowding and where poor hygiene standards prevail. Because most children have asymptomatic or unrecognised infections, they play an important role in HAV transmission and serve as a source of infection for others.

Sexual transmission: HAV may be transmitted by sexual oral-anal contact or by oropharyngeal secretions. There is an association with multiple anonymous sexual contacts.

HAV is transmitted by the faecal-oral route.

Infected persons are most likely to transmit HAV 1-2 weeks before the onset of illness.

Less common modes of transmission*Food and water contamination*

Contamination of water supplies with infected faeces occurs where sewage disposal is inadequate. Food washed in contaminated water or prepared by an infected person with poor standards of hygiene may cause viral transmission and infection. Shellfish harvested from contaminated sea water may also cause HAV outbreaks.

Percutaneous-intravenous transmission

A viraemia occurs briefly during HAV infection. Outbreaks of hepatitis A have rarely been linked to blood and blood product administration. The observed increased incidence of infection among intravenous drug users is probably due to poor standards of hygiene, although contamination of drugs, and needle-sharing, may contribute.

Effects of hepatitis A

The incubation period for HAV is approximately 28-30 days, with a range of 15-50 days. After 10-12 days the virus is present in the blood and is excreted into the faeces via the biliary tract. The virus is present in the blood but the viral load is much higher in the faeces. In children under 6 years of age, most (70%) infections are asymptomatic. The frequency and severity of symptoms increase with age, with jaundice occurring in 70% of infected adults.

The illness usually lasts up to 2 months, although 10-15% have prolonged or relapsing signs and symptoms for up to 6 months. There is no chronic carrier state and chronic liver damage is rare. Fulminant hepatitis can occur but is rare.

Prevention

Good hygiene, particularly hand washing, is the cornerstone of prevention and should be promoted in settings and communities with higher rates or risk of infection. A selective vaccination policy is of benefit for certain groups with greater likelihood of infection.

Hepatitis A vaccine

HAV vaccines have been shown to be safe, immunogenic and efficacious. The vaccines are not licensed for use in children under 1 year of age and are not recommended by the manufacturers for use in pregnancy. The risk associated with vaccination should be weighed against the risk for hepatitis A in pregnant women who might be at high risk for exposure

to HAV. HAV vaccines are available as either monovalent vaccines, or combined with either typhoid or hepatitis B vaccines.

Monovalent vaccines

HAV vaccine is a formaldehyde inactivated vaccine prepared from hepatitis A virus grown in human diploid cells (MRC5) and adsorbed onto an aluminium hydroxide adjuvant. The vaccine should be stored at 2-8°C and should be protected from light.

The primary course of HAV vaccine is a single dose followed by a booster at 6-12 months. Approximately 95% of subjects acquire protective levels of HAV antibodies within 4 weeks of one dose, and over 99% after the second dose. It is expected that immunity for at least 20 years is conferred by the full course.

Combined hepatitis A and hepatitis B (HBV) vaccine

A combined vaccine containing purified inactivated HAV virus and purified recombinant HBsAg may be used when protection against both HAV and HBV is required.

Combined HAV and typhoid vaccine

A combined vaccine containing purified inactivated HAV and purified Vi polysaccharide typhoid vaccine may be used where protection against HAV and typhoid fever is required.

Route of administration

Hepatitis A vaccine should be given intramuscularly in the deltoid region. For patients with severe bleeding tendencies (e.g. persons with haemophilia), subcutaneous injection may be considered. Hepatitis A vaccine should not be administered intravenously.

Indications

Pre-exposure prophylaxis

Active immunisation with hepatitis A vaccine is recommended for:

- Travellers, including children 1 year and over, to endemic areas (Africa, Asia, Central and South America, Eastern Europe, the Middle East). Vaccination should be carried out 2 or more weeks before departure. However, if the time before departure is short, the vaccine is still considered likely to prevent or at least modify the infection (see Chapter 19). HNIG could be used (if available) for travellers who are immunocompromised and should be given at a separate site

- Susceptible persons with chronic liver disease
- Non-immune patients with chronic hepatitis B or hepatitis C infection
- Solid organ transplant recipients who have not been immunised previously – should be immunised prior to transplantation
- Persons with haemophilia and other recipients of plasma-derived clotting factors
- Injecting drug users
- Men who have sex with men
- Clients of learning disability services whose capacity to maintain good standards of hygiene is limited, and their carers
- Laboratory workers who may be exposed to HAV in the course of their work
- Sewage workers exposed to raw untreated sewage
- Susceptible staff who work with non-human primates that are susceptible to hepatitis A infection.

For those with recent close contact with infected individuals, see *Post-exposure prophylaxis, below*.

Where indicated, HAV vaccination can be combined with HBV vaccination.

For those aged over 50 years or with a history of jaundice, haemophilia or residence in a high-risk area, prevaccination testing for immunity to hepatitis A may be considered in order to reduce costs. Post-vaccination testing for anti-HAV is not indicated.

Contraindications

Anaphylactic reaction to a preceding dose or any of the constituents. Individuals who have had a confirmed anaphylactic hypersensitivity to egg products should not be given the hepatitis A vaccine Epaxal, as a component of that vaccine is prepared on hens' eggs.

Precautions

Acute severe febrile illness, defer until recovery. Safety data in pregnant women are not available, but the risk is considered to be low or non-existent because the vaccines contain inactivated purified viral proteins.

Adverse reactions

Side effects are infrequent and mild.

Post-exposure prophylaxis

Either passive immunisation (with HNIG, if available) or active immunisation (with HAV vaccine), or a combination of the two, may be used in the management of contacts of cases and for outbreak control, depending on the circumstances as outlined below. Vaccine and HNIG may be given at the same time, but in different sites, when both rapid and prolonged protection is required.

When HNIG is given within 2 weeks of exposure, its effectiveness in preventing hepatitis A is greater than 85%. In general the use of HNIG more than 2 weeks after the last exposure is not indicated. If HNIG is given after 2 weeks from last exposure it may modify disease severity rather than prevent infection.

Decisions to use vaccine or HNIG should take into account patient characteristics associated with more severe manifestations of hepatitis A, including older age and chronic liver disease. HAV vaccine is not licensed for use in children under 1 year of age. Results of a recent randomised, double-blind, noninferiority clinical trial comparing the efficacy of hepatitis A vaccine and HNIG after exposure to HAV have suggested that the performance of vaccine when administered up to 14 days after exposure approaches that of HNIG in healthy children over 2 years of age and in adults aged under 40 years.

However, information about the relative efficacy of vaccine compared with HNIG post exposure is limited. For persons aged 40 years and over and those with underlying medical conditions, HNIG is still preferred because of the absence of information regarding vaccine performance and the more severe manifestations of hepatitis A in these groups.

It is becoming increasingly difficult to access supplies of HNIG and therefore the use of HAV vaccine for healthy contacts aged 1 year to 39 years may be a viable alternative. For those aged 40 and over and those with underlying medical conditions, HAV vaccine can also be used if HNIG cannot be obtained.

A single dose of monovalent vaccine will provide more rapid protection than the combined preparations where more than one dose is required.

If a contact is at ongoing risk of HAV infection because of their lifestyle or for any other reason, they should be offered vaccine irrespective of whether they are offered HNIG.

Serological testing of the contacts is usually not recommended as it may delay administration of prophylaxis.

Immunoprophylaxis should be given to previously unvaccinated household and close contacts of cases as soon as possible after exposure to HAV.

- *Child-care centre staff, children, and their household contacts.* If one or more hepatitis A cases are associated with a centre, immunoprophylaxis (as above) should be offered to the children and the adult carer(s) in contact with the index case. If the centre admits children in nappies, immunoprophylaxis should be offered to all children and staff in the centre. Where HAV infection is confirmed in 2 or more households of children attending such a centre, immunoprophylaxis should similarly be offered to all children and staff. When an outbreak occurs (i.e. hepatitis cases in 3 or more families) immunoprophylaxis should also be considered for members of households that have children in nappies. As hepatitis A vaccine does not have product authorisation for children of less than 1 year, HNIG is recommended for this group.
- *Schools, hospitals, prisons and work settings.* Immunoprophylaxis is not normally indicated when a single case occurs in a school, office or other work-setting. Immunoprophylaxis as above should be offered to persons who have close contact with index patients if an epidemiological investigation indicates HAV transmission has occurred.
- *Food or waterborne outbreaks.* If a food handler is diagnosed with hepatitis A, immunoprophylaxis should be offered to other food handlers at the same location, if the risk of transmission is high. Administration of immunoprophylaxis to patrons should only be considered if, during the time the food handler was likely to be infectious, the food handler had both directly handled uncooked foods or foods after cooking and had diarrhoea or bad hygiene practices.
- *Close personal contact.* Immunoprophylaxis should be offered to previously unvaccinated household or sexual contacts of, and those who have shared illicit drugs with, persons with serologically confirmed recent HAV infection.

HNIG can interfere with the response to live virus vaccines, (see Chapter 2 for more information on HNIG).

06

Hepatitis B

NOTIFIABLE

Introduction

Hepatitis B virus (HBV) is an important cause of serious liver disease including acute and chronic hepatitis, cirrhosis and primary hepatocellular carcinoma. People with chronic HBV infection can transmit the infection for many years. A safe and effective vaccine is available for the prevention of HBV infection.

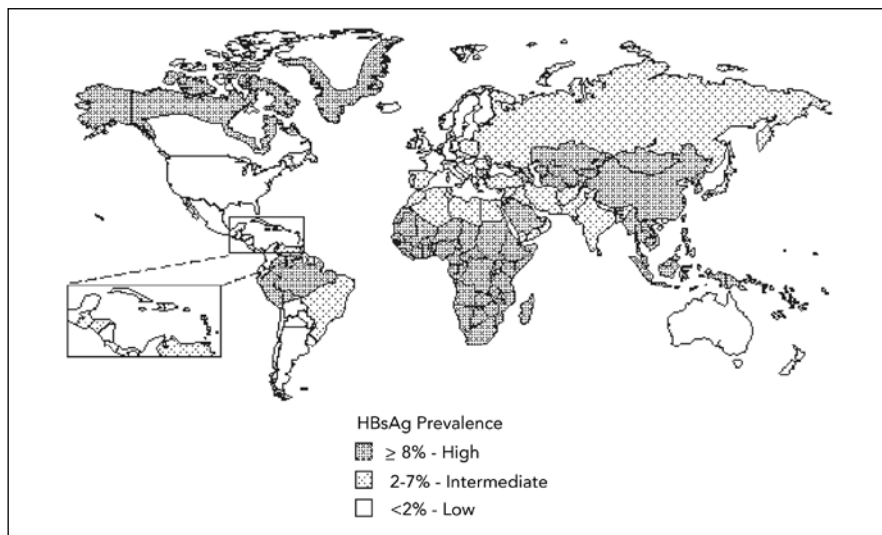
Epidemiology

The World Health Organization (WHO) estimates that over 350 million people worldwide are chronically infected with HBV (Figure 6.1). The WHO has categorised countries based upon the prevalence of hepatitis B surface antigen (HBsAg) into:

- High endemicity ($\geq 8\%$): sub-saharan Africa, most of Asia and the Pacific Islands
- Intermediate endemicity (2-7%): Southern parts of Eastern and Central Europe, Middle East and Indian sub-continent, Central and South America
- Low endemicity ($< 2\%$): Most of Western Europe and North America, Australia.

In Ireland the prevalence of serological markers of hepatitis B infection is low. A national study in the general population in 1999 estimated the prevalence of past exposure to hepatitis B (anti-core antibody, anti-HBc) to be 0.51%. Between 2003 and 2006, a prevalence of HBsAg of 0.01% was detected in new blood donors tested by the Irish Blood Transfusion Service donor screening programme. One in 2,000 to 1 in 6,000 pregnant Irish-born women are HBsAg positive, depending on the population surveyed.

Figure 6.1 Geographic distribution of hepatitis B prevalence. Source: WHO

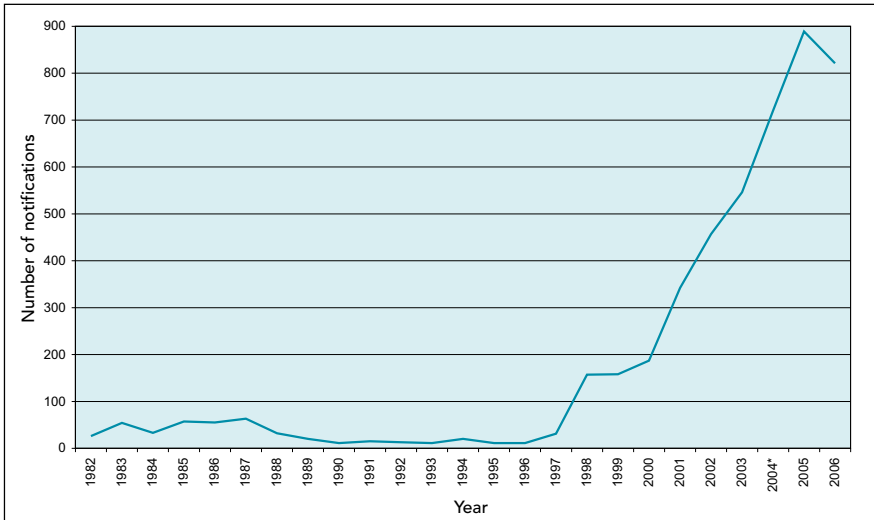


A higher HBV prevalence is seen in some population groups in Ireland. The prevalence of anti-HBc in Irish prisoners in 1998 was 8.7% overall and in injecting drug-using prisoners was 18.5%. Homeless people also have evidence of increased exposure to hepatitis B, with a prevalence of anti-HBc of 9% in a study performed in Dublin in 1999-2000.

Figure 6.2 shows the number of statutory notifications of hepatitis B infection in Ireland, 1982-2006. The increase in notifications since 1998 may be largely attributed to changes in immigration patterns and the introduction of active screening in high-risk populations. Most of these notifications are cases of chronic infection. For HBV notifications received by the Health Protection Surveillance Centre in 2006, 90% of the chronic HBV cases, where country of birth was known, were born in a country of either high or intermediate prevalence.

Figure 6.2 Number of notifications of hepatitis B, 1982-2006.

Source: HPSC

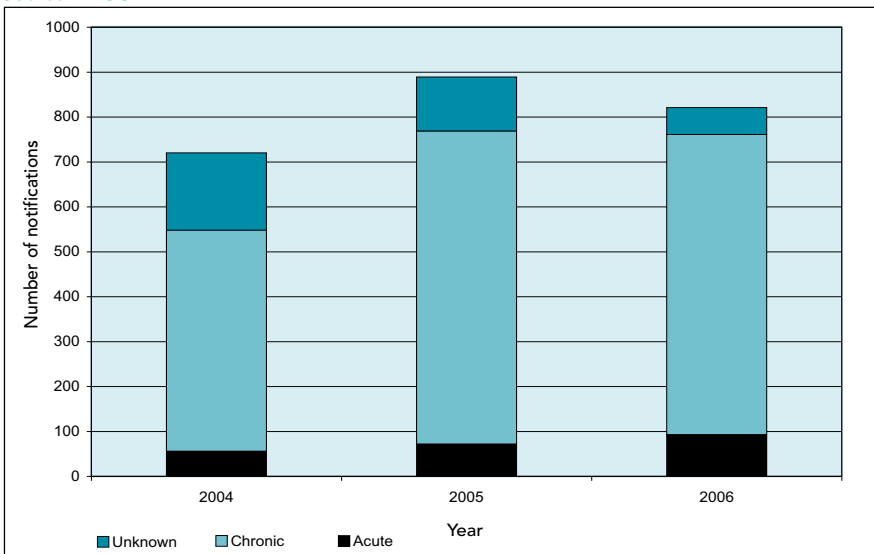


*Case definitions introduced and laboratories required to notify cases of notifiable infectious diseases from January 2004.

Changes to the Infectious Diseases Regulations in January 2004, with the introduction of case definitions, the differentiation between acute and chronic cases, and mandatory laboratory notification, have had a positive impact on the quality of information available on HBV in Ireland and may also have resulted in increased numbers of notifications (see Figure 6.3).

Figure 6.3 Number of hepatitis B notifications by status, 2004-2006.

Source: HPSC



Transmission

The virus is transmitted by infected blood or body fluids. Transmission mainly occurs by:

- Sexual intercourse, including vaginal and anal
- Blood-to-blood contact (e.g. sharing of personal care items such as toothbrushes, razors or by other equipment used by injecting drug users (IDUs), needlestick injuries, ear-piercing, tattooing)
- Perinatal transmission from infected mother to child
- Transmission has rarely followed bites from infected individuals

Transmission by transfusion of contaminated blood or blood products is now rare because of routine screening of blood donors and viral inactivation of certain blood products.

HBV has been found in virtually all body secretions and excretions. However, only blood (and serum-derived fluids), saliva, semen and vaginal fluids have been shown to be infectious. People with chronic HBV infection are the primary reservoirs of infection.

Patterns of transmission vary according to the prevalence in a particular country. In areas of high prevalence, infection is predominantly acquired by perinatal transmission in infants, or by horizontal transmission among children younger than 5 years. In low-endemicity countries, most infections are acquired in adulthood where sexual transmission or sharing blood-contaminated needles by IDUs account for most new infections. In areas of intermediate endemicity, the pattern of perinatal, childhood and adult infection is mixed and nosocomial infection may be important.

In household settings, non-sexual transmission may occur. However, the precise mechanisms of transmission are unknown but may possibly be due to contact of non-intact skin or mucous membranes with blood-containing secretions or saliva. Transmission from sharing towels, razors or toothbrushes also may occur. HBV can survive in the environment for 1 week or longer.

The risk of an infant acquiring HBV perinatally from an infected mother is 70-90% where the mother is HBsAg and hepatitis B e antigen (HBeAg) positive; the risk is 5-20% where the mother is HBsAg positive but HBeAg negative.

Effects of Hepatitis B infection

The incubation period ranges from 40 to 160 days, with an average of 60-90 days. HBV infection has different clinical manifestations depending on the patient's age at infection. In general, the frequency of clinical disease increases with age, whereas the percentage of chronic infections decreases.

Many acute infections with HBV are sub-clinical or may present with a 'flu-like illness. In patients with clinical illness, the onset is usually insidious, with tiredness, anorexia, vague abdominal discomfort, nausea and vomiting, and sometimes arthralgias and rash. Jaundice occurs in approximately 10% of young children and in 30-50% of adults. Acute HBV may occasionally lead to fulminating fatal hepatic necrosis.

Chronic infection, defined as the presence of HBsAg in the serum for at least 6 months, occurs in more than 90% of those infected perinatally, but this decreases to 20-50% in children infected between 1 and 5 years of age. Between 2 and 10% of infected immunocompetent adults become chronically infected and the risk is probably greater for those whose immunity is impaired. **Those in whom HBeAg is detectable (indicating active viral replication) are most infectious.** However, recent evidence indicates that those infected with mutant HBV may have high levels of HBV DNA in the absence of HBeAg and are therefore also highly infectious. Approximately 20-25% of individuals with chronic HBV infection develop progressive liver disease leading to cirrhosis and are at increased risk of developing hepatocellular carcinoma. Globally, HBV causes 60-80% of the world's primary liver cancers.

Hepatitis B vaccine

HBV vaccine contains recombinant HBsAg, derived from yeast cells, adsorbed onto aluminium hydroxide adjuvant. The vaccine is effective at preventing infection in individuals who produce specific antibodies to HBsAg (anti-HBs). However, around 10-15% of adults fail to respond or have a poor response to 3 doses of vaccine. Poor response is associated with age over 40 years, male gender, obesity and smoking. Lower seroconversion rates have also been reported in alcoholics, particularly those with advanced liver disease. Patients who are immunosuppressed or have chronic renal failure may respond less well and may require larger or more frequent doses of vaccine (see below).

HBV vaccine is used for pre-exposure and post-exposure protection and provides long-term protection. Pre-exposure immunisation with HBV

vaccine is the most effective means of preventing HBV transmission. Non-responders at risk of HBV exposure need to report promptly any inoculation injury, as passive prophylaxis with specific immunoglobulin may be required in these cases. Post-exposure, HBV vaccine is highly effective at preventing infection, provided that the vaccine is administered preferably within 48 hours but up to 7 days post-exposure.

Vaccine efficacy studies have shown that 90-100% of vaccinated persons who develop anti-HBs concentrations greater than or equal to 10 mIU/ml after a primary series are protected from HBV infection.

Indications

In 1992 the WHO recommended that HBV vaccine be incorporated into all national programmes by 1997.

In 2007 the National Immunisation Advisory Committee (NIAC) recommended that universal infant HBV vaccination should be introduced in Ireland. This is to run in parallel with the pre-existing targeted immunisation programme for those individuals who are at increased risk of HBV because of their occupation, lifestyle or other factors (e.g. close contact with a case or carrier).

Ideally, immunisation should be carried out **before** the risk of exposure to HBV (pre-exposure prophylaxis) but it may also follow exposure (post-exposure prophylaxis).

Pre-exposure prophylaxis

Universal immunisation

All infants should be offered HBV vaccine as part of the routine childhood immunisation schedule at 2, 4 and 6 months (see schedule Chapter 2).

Targeted immunisation programme

The following groups are at increased risk of HBV infection and should receive HBV vaccine if non-immune:

1. *Persons with occupational risk of exposure to blood or blood-contaminated environments*
 - Doctors, nurses, dentists, midwives, laboratory staff, mortuary technicians, ambulance personnel, cleaning staff, porters, medical, nursing and dental students, other health-care professionals

- Staff and carers in centres for those with learning disability (including day-care facilities, special schools and other centres)
- Security and emergency services personnel
- Prison staff in regular contact with prisoners

2. *Family and household contacts*

- The spouses, sexual partners, family and household contacts of acute cases and individuals with chronic infection. Where testing for markers of current or past infection is clinically indicated, this should be done at the same time as the administration of the first dose. **Vaccination should not be delayed while waiting for results of the tests.** Further doses may not be required in those with clear evidence of past exposure
- Families adopting children from countries with a high or intermediate prevalence of hepatitis B. These children should be tested for evidence of current or past hepatitis B infection and the household contacts offered immunisation if required, preferably before the adoption. If the status of the child is unknown these families should be recommended vaccination
- All short-term foster carers who receive emergency placements, and their families, should be offered HBV vaccination. Permanent foster carers, and their families, who accept a child known to be at high risk of HBV should also be offered immunisation
- Babies born to mothers with acute or chronic HBV infection (see also *Post-exposure prophylaxis below*)

3. *Injecting drug users and their contacts*

- All IDUs
- Sexual partners of IDUs (whether they inject or not)
- Children of IDUs
- Non-injecting drug-users living with current injectors
- Those who are at risk of progressing to injecting drug use (e.g. on other illicit substances)

4. *Individuals at high risk due to medical conditions*

- People with haemophilia and those receiving regular transfusions of blood or blood products, and carers responsible for the administration of such products
- Clients in centres for those with learning disability (including day-care facilities, special schools and other centres)
- Patients with chronic renal failure. Early immunisation of patients with evolving chronic renal failure is advised, before they require dialysis or transplantation. The immune response to HBV may be reduced in patients with chronic renal failure compared to

- immunocompetent individuals and a more rapid decline in anti-HBs has been observed
- Patients with chronic liver disease including those with persistent hepatitis C infection. Such patients should be vaccinated against HBV as concurrent HBV infection may increase the risk of liver disease
5. *Members of other high-risk groups*
- Individuals who change sexual partner frequently, men who have sex with men (MSM), male and female commercial sex workers, attendees at clinics for sexually transmitted infections (STIs) and those diagnosed with an STI
 - Inmates of custodial institutions
 - Tattoo and body piercing artists/practitioners
 - Immigrants from areas with a high or intermediate prevalence of HBV
 - Travellers to areas with a high or intermediate prevalence of HBV
 - Homeless people
 - Children born to parents from high or intermediate endemicity countries

Post-vaccination serological testing

Routine post-vaccination testing for anti-HBs is recommended 2 months after completing the course of vaccination for persons who are at continuing risk of HBV exposure, e.g. health-care workers, patients on renal dialysis, sexual partners of HBsAg positive persons. This does not apply to children receiving routine childhood immunisation with hepatitis B vaccine.

Following primary vaccination, it is preferable to achieve anti-HBs levels above 100 mIU/ml although levels above 10 mIU/ml are generally accepted as protecting against infection. Anti-HBs titre often declines post-vaccination but a rapid anamnestic response develops after exposure to the virus.

Table 6.1 Actions required following post-vaccination testing (except for patients with renal failure)

Anti-HBs level	Action required
0 or <10 mIU/ml	Non responder. It is advisable to test for anti-HBc*. If anti-HBc negative, repeat full course of hepatitis B vaccine (a different brand of vaccine is advised). Recheck anti-HBs at 2 months post completion. If anti-HBs remains <10 mIU/ml, person is susceptible to HBV.
10-99 mIU/ml	Low response. If low level anti-HBs confirmed by 2 different assays, administer booster dose of vaccine but there is no need to retest for anti-HBs.
100 mIU/ml or greater	Good response. No need for further vaccination or anti-HBs investigations.

*For those who are performing exposure-prone procedures, HBsAg testing should also be carried out.

Table 6.2: Actions required following post-vaccination testing for patients with renal failure* (If there is no evidence of HBV infection)

Anti-HBs level	Action required
0 or <10 mIU/ml	<p>Non responder. Repeat full course of hepatitis B vaccine (a different brand of vaccine is advised). Recheck anti-HBs 2-months post completion. If anti-HBs remains <10 mIU/ml, person is susceptible to HBV.</p> <p>– Test for HBsAg every month</p>
10-99 mIU/ml	<p>Low response. Give booster dose of vaccine. Check anti-HBs 2 months later using 2 different assays. Adequate response if both ≥ 10 mIU/ml. Re-check anti-HBs annually and if anti-HBs decreases to <10 mIU/ml give booster dose but no need to check the anti-HBs level until next annual check is due.</p> <p>– Test for HBsAg every 3 months</p>
100 mIU/ml or greater	<p>Good response. Re-check anti-HBs annually and if anti-HBs decreases to <10 mIU/ml give booster dose but no need to check the anti-HBs level until next annual check is due.</p>

* REF: The Prevention of Transmission of Blood-Borne Diseases in the Health Care Setting 2005

Booster doses

To date there are no conclusive data to support the need for booster doses of HBV vaccine in immunocompetent individuals who have responded to a primary course. Studies have shown that those who show a protective response after vaccination are protected for at least 15 years and it is likely that protection is life-long.

For haemodialysis patients and other immunocompromised people at continued risk of infection, the need for booster doses should be assessed by annual anti-HBs testing, and a booster dose should be given if the anti-HBs level is <10 mIU/ml.

Dose

Currently licensed vaccines contain different concentrations of antigen per ml. The appropriate manufacturer's dosage should be adhered to. **Higher doses of vaccine (40 mcg) should be used for adult patients with chronic renal failure, and considered for other immunosuppressed adults.**

Schedules

(a) *Infant HBV vaccination*

HBV vaccine should be administered at 2, 4 and 6 months of age as part of the routine childhood immunisation schedule.

(b) *Vaccination of those other than infants*

The basic schedule consists of three doses of vaccine at 0, 1 month and 6 months.

Alternative accelerated schedules (e.g. 0, 1 and 2 months; 0, 7 and 21 days) exist (see manufacturer's guidelines) if more rapid protection is required for those at immediate risk or for those where compliance with the duration of the basic schedule is difficult to achieve. These should be followed by a dose of vaccine at 12 months to complete the course.

Route of administration

The vaccine is given intramuscularly in the deltoid region. In the case of infants, the vaccine may be given in the anterolateral thigh. The gluteal region should not be used as the vaccine efficacy may be reduced. Exceptionally, the vaccine may be administered by deep subcutaneous injection in patients at risk of haemorrhage.

Hepatitis B vaccine should not be given in the gluteal region.

Vaccine interchangeability

Different HBV vaccine products can be used to complete a primary immunisation course or, where indicated, as a booster dose in individuals who have previously received another HBV vaccine. **One of the licensed higher dose vaccine products (used for adult patients with chronic renal failure, and considered for other immunosuppressed adults) is NOT interchangeable.**

Contraindications

Anaphylactic reaction to a preceding dose of a HBV-containing vaccine or any of the constituents.

Precautions

Acute severe febrile illness, defer until recovery. The response may be impaired in those who are immunocompromised, and a further dose of vaccine may be necessary.

Pregnancy and breastfeeding

No adverse effect on the developing foetus has been observed when pregnant women have been immunised against HBV. Because HBV infection may result in severe disease in the mother and chronic infection in the newborn infant, pregnancy is not a contraindication to immunisation. If an antenatal patient is HBsAg negative but at risk of HBV infection, she should be immunised during pregnancy. Breastfeeding is not a contraindication to immunisation.

Adverse reactions

Local: Hepatitis B vaccine is generally well tolerated. The commonest reactions are soreness and redness at the injection site.

General: Fever, rash, malaise and influenza-like symptoms are less commonly reported after vaccination.

Post-exposure prophylaxis

Specific hepatitis B immunoglobulin (HBIG) is available for passive protection and is normally used in combination with HBV vaccine to confer passive/active immunity after exposure. At present only one HBIG preparation is authorised in Ireland and this is an intravenous preparation. HBIG provides short-term protection (3-6 months).

Post-exposure prophylaxis is recommended for the following groups

1. Babies born to mothers who are HBV infected (HBsAg positive)

Perinatal transmission of HBV infection can be prevented in approximately 95% of infants born to HBsAg positive mothers by early active and passive immunoprophylaxis of the infant. Routine screening of all antenatal patients for HBsAg is essential for identifying women whose infants will require post-exposure immunoprophylaxis beginning at birth. All babies born to these mothers should receive a complete course of vaccine at 0, 2, 4 and 6 months and also HBIG within 24 hours of birth. The doses at 2, 4 and 6 months may be given as the routine 6 in 1. Following the administration of HBIG and the first dose of vaccine, arrangements should be made to follow up the child for serological assessment and subsequent doses of vaccine.

Pre-term babies: It is important that premature infants receive the full paediatric dose of HBV vaccine, and HBIG.

Hepatitis B vaccine should be administered concurrently with HBIG in the anterolateral thigh (in a different site from the HBIG).

Infants born to mothers who are HBV infected should be tested 2 months after completing HBV immunisation to determine HBV status and post-vaccination response.

2. Household exposures

HBIG and hepatitis B vaccine are recommended for unimmunised infants under 12 months of age if the mother or primary care giver has acute HBV infection. Prophylaxis with HBIG is not indicated for other unimmunised household members of persons with acute HBV infection unless they have identifiable blood exposure to the index patient, such as by sharing of toothbrushes or razors. Such exposures should be managed as in sexual exposures. All household contacts of acute and chronic cases should be screened and offered hepatitis B vaccine if susceptible.

Vaccination should not be delayed while waiting for results of the tests.

3. Sexual exposure

Exposure to acute cases: Sexual partners of individuals suffering from acute hepatitis B and who are seen within one week of last contact should be offered both HBIG and vaccine.

Exposure to chronic cases: Sexual contacts of newly identified chronic cases should be offered vaccine. HBIG may be added if unprotected sexual contact occurred in the past week (a risk assessment may be needed depending on whether the contact is a long-term sexual partner or recent partner).

4. HCW or others accidentally exposed to blood or body fluids

Individuals who sustain such injuries should wash the affected area well with soap and warm water and seek medical advice. The response required in terms of vaccination and/or HBIG will depend on a detailed risk analysis of the source, the vaccination/anti-HBs status of the person exposed, and the type of exposure. The appropriate prophylaxis should be commenced immediately according to Table 6.3.

A significant exposure is one from which HBV transmission may result:

- Percutaneous exposure to blood or body fluids, e.g. needlestick or other contaminated sharp object injury, a bite that causes

- bleeding or other visible skin puncture
- Mucocutaneous exposure to blood or body fluids, e.g. contamination of non-intact skin, conjunctiva or mucous membrane
- Sexual exposure (unprotected sexual intercourse, oral sex)
- Community needlestick injury (discarded needles and syringes in public places)

Dose and route of administration of HBIG

HBIG should be administered according to the manufacturer's guidelines and should ideally be given within 48 hours of exposure but not later than a week after exposure.

Injuries from discarded needles in the community

Injuries from discarded needles and syringes in public places create considerable anxiety regarding the possible transmission of blood-borne pathogens. While these injuries pose less of a risk than that resulting from a needlestick injury in health-care settings, the perception of risk often results in the necessity for evaluation, testing and counselling of the injured person.

Management of such injuries includes acute wound care and consideration of the need for prophylactic management. Hepatitis B virus is the most stable of the major blood-borne viral pathogens and can survive in the environment for 1 week or longer. It is advisable to administer a full course of HBV vaccine to those susceptible to HBV infection. HBIG is not usually required unless the needle comes from a known hepatitis B positive source and a risk assessment identifies a significant risk of HBV transmission. The likelihood of transmission of other blood-borne viruses such as hepatitis C or HIV is very remote.

Recommendation: archive a baseline serum specimen from the injured person, initiate hepatitis B vaccination and test samples collected at 3 and 6 months for HBsAg and anti-HBc, and at 2 months post-completion of course of vaccination, for anti-HBs.

Interpretation of Hepatitis B results is set out in Table 6.4, provided for reference.

Table 6.3 Hepatitis B vaccine prophylaxis for reported exposure incidents

Significant exposure						Non-significant exposure	
Vaccination status of person exposed	HBsAg-negative source	Unknown source ⁽¹⁾	HBsAg-positive source	Continued risk	No further risk		
≤1 Dose HBV vaccine pre-exposure	Initiate/ finish course of HBV vaccine	Accelerated course of HBV vaccine ⁽²⁾	Accelerated course of HBV vaccine ⁽²⁾ HBIG x1 ⁽³⁾	Initiate course of HBV vaccine	Initiate course of HBV vaccine		
≥2 doses HBV vaccine pre-exposure	Finish course of HB vaccine	One dose of HBV vaccine	One dose of HBV vaccine followed by second dose one month later	Finish course of HBV vaccine	Finish course of HBV vaccine		
Known responder to HBV vaccine (anti-HBs ≥10 mIU/ml)	Consider booster dose of HBV vaccine	Consider booster dose of HBV vaccine	Booster dose of HBV vaccine	Consider booster dose of HBV vaccine	No HBV prophylaxis Reassure		
Known non responder to HBV vaccine (anti-HBs <10mIU/ml 2-4 months post vaccination)	Give second course of vaccine if not previously received	HBIG x 1 dose ^(1,4) and initiate reimmunisation or HBIG x 2 doses	HBIG x 1 dose ⁽⁴⁾ and initiate reimmunisation or HBIG x 2 doses	Give second course of vaccine if not previously received	Give second course of vaccine if not previously received		

⁽¹⁾ If the patient source is not known, individual assessment of each case should be made.

⁽²⁾ An accelerated course of vaccine consists of doses spaced at 0, 1 and 2 months. A booster dose is given at 12 months to those at continuing risk of exposure to HBV.

⁽³⁾ HBIG should be given preferably within 48 hours and not later than a week after exposure.

⁽⁴⁾ The option of giving 1 dose of HBIG and reinitiating the vaccine course is preferred for nonresponders who have not completed a second 3-dose course. For people who previously completed a second vaccine course but failed to respond, 2 doses of HBIG are preferred, 1 dose as soon as possible after exposure and the second 1 month later.

Table 6.4 Interpretation of hepatitis B results

HBsAg	HBsAg	Anti-HBe	IgM	Anti-HBc	Total anti-HBc	Anti-HBs	Interpretation
Neg	Neg	Neg	Neg		Neg	Neg	Susceptible to HBV
POS	POS	Neg	Neg		Neg	Neg	Acute HBV infection
POS	POS	Neg	POS		POS/Neg	Neg	Acute HBV infection
Neg	Neg	Neg	POS		POS*	Neg	Recent HBV infection (HBsAg window)
POS	POS	Neg	WEAK POS/ Neg		POS	Neg	Chronic HBV infection**
POS	Neg	Neg	WEAK POS/ Neg		POS	Neg	HBsAg neg chronic HBV infection***
Neg	Neg	POS/ Neg	Neg		POS*	POS/Neg	Resolved HBV infection
Neg	Neg	Neg	Neg		Neg	POS	Response to HBV vaccine

Notes

*Anti-HBc detected in 2 assays

**Follow-up sample required to confirm chronic HBV infection

***Follow-up sample required and also HBV DNA viral investigations may be required

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07

Influenza

NOTIFIABLE

Introduction

Influenza is an acute illness of the upper and/or lower respiratory tracts. It is usually self-limited, with recovery in 2-7 days, but it can be severe. It affects all age groups and is characterised by the abrupt onset of fever, headache, myalgia, cough, sore throat and malaise.

Epidemiology

Influenza is highly infectious, spreading rapidly especially in institutions. It is a segmented, single-stranded RNA virus of the family orthomyxoviridae. There are three types of influenza virus: A, B and C. The first two types are responsible for most clinical illnesses. Influenza A viruses can infect a wide range of animal and avian species. Two surface antigens make these viruses antigenically labile. These are haemagglutinin antigen (H: 15 different types) and neuraminidase (N: 9 different types), although only H1, H2, H3, N1 and N2 have been implicated in widespread human infection.

Influenza A undergoes two kinds of antigenic mutation due to changes in these surface antigens. Minor changes, due to point mutations in the haemagglutinin antigen, termed 'antigenic drift' are seen progressively from season to season, and this is the reason why the vaccine composition changes each year. Major changes, termed 'antigenic shift', occur periodically and can result in the introduction of virtually novel viruses, with a different haemagglutinin, into a population, facilitating pandemic spread with the potential for severe morbidity and high mortality. Mutations only rarely occur in influenza B.

Antigenic variation results in the circulation of viruses to which a given population may have little immunity, accounting for the high attack rates commonly seen in influenza outbreaks.

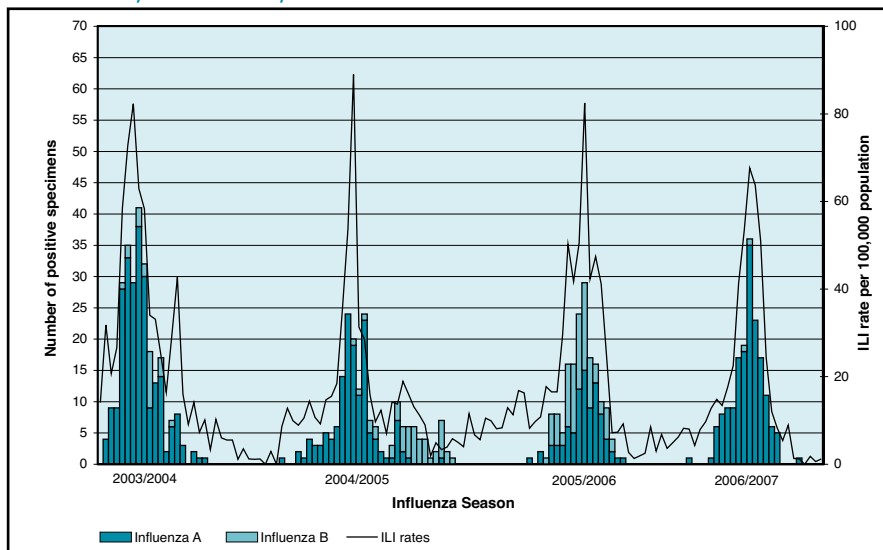
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Influenza outbreaks occur virtually every year (Fig 7.1), although the extent and severity of the outbreaks vary widely. Localised outbreaks occur at variable intervals, usually once every 1-3 years. In some outbreaks, influenza B viruses circulate simultaneously with influenza A viruses. Although pandemics provide the most dramatic evidence of the impact of influenza overall, outbreaks that occur between pandemics account for greater mortality and morbidity, although over a longer period of time. Since 1977 influenza A (H1N1), influenza A (H3N2) and influenza B viruses have been in circulation.

There is increasing concern regarding the emergence and distribution of the highly pathogenic avian influenza (H5N1) and the potential for the emergence of a new pandemic strain. Human infections have occurred but predominantly only in those in close contact with infected poultry. Efficient person-to-person transmission, a pre-requisite for a pandemic strain, has not yet been documented.

Influenza A epidemics begin abruptly, reach a peak over a 2-3 week period, generally last for 2-3 months and often subside as rapidly as they began. Epidemics begin almost exclusively during the winter months. A major determinant of the extent and severity of an outbreak is the level of immunity in the population, although all the factors that result in epidemics are not fully understood.

Figure 7.1 Influenza-like illness (ILI) rate per 100,000 population and the number of positive influenza specimens detected by the NVRL during the 2003/2004, 2004/2005, 2005/2006 & 2006/2007 seasons. Source: HPSC



Effects of Influenza

Influenza outbreaks result in significant morbidity in the general population. In those with chronic underlying disease, especially the elderly, complications are common and hospitalisation rates high. Eighty to 90% of reported deaths from influenza occur in the elderly, mainly from bacterial pneumonia, but also from the underlying disease.

Primary influenza A pneumonia is uncommon and is characterised by the abrupt onset of a rapidly progressive diffuse pneumonia with pulmonary haemorrhage which is often fatal. The frequency of overt pulmonary involvement in influenza A infection is age dependent: 4% in those 10-39 years, 36% in those aged 60-69 years and to 73% in those 70 years of age or older.

Severe influenza can be complicated also by encephalitis or meningoencephalitis.

Transmission

Influenza is spread from person to person by direct contact, by droplet infection or by contact with materials recently contaminated by nasopharyngeal secretions. Airborne spread can also occur. It is highly contagious, especially in close contact environments such as homes for the elderly. Virus can be detected in respiratory secretions from just before the onset of clinical illness to 4-5 days after symptom onset. Shedding can be more prolonged in young children and in the immunocompromised.

Influenza vaccine

A vaccine, recommended by WHO, is prepared each year, using virus strains similar to those considered most likely to circulate in the forthcoming season. Current vaccines are trivalent, containing antigens from two type A and one type B virus strains.

The virus is egg-grown, inactivated with formalin, and 'split-virus' or subvirion; preparations are made using solvents or detergents. 'Surface antigen' vaccines containing highly purified preparations of viral neuraminidase and haemagglutinin antigens are also available. Whole-virus, split-virus (subvirion), and surface-antigen vaccines are of equivalent efficacy but the latter two are less likely to induce febrile reactions in children. All are supplied in a prefilled syringe.

Currently available inactivated influenza vaccines provide 70-90% protection against influenza in persons under 65 years of age. Protective

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efficacy against infection is lower in the elderly. However, morbidity and mortality in the elderly are significantly reduced. Protection lasts about 1 year. Annual vaccination with the most recent strains is recommended. The vaccines should be stored at 2-8°C and protected from light. They should be allowed to reach room temperature and shaken well before they are given.

The World Health Organization monitors the strains of influenza circulating every year.

The Department of Health and Children and the HSE advise on the appropriate vaccine for annual use each year, based on WHO recommendations.

Remember annual immunisation is necessary. Ideally, give in September/October each year but can be given throughout the year. (Antibodies may take up to 10-14 days to reach protective levels so give early.)

Children under 9 years of age require two doses of vaccine, separated by 4-6 weeks, if receiving the vaccine for the first time.

Indications

Vaccination is recommended for:

1. Those older than 6 months of age who are at increased risk of influenza-related complications including the following groups:
 - a) Persons aged 50 years or older
 - b) Those with chronic illness requiring regular medical follow-up (e.g. chronic respiratory disease, including cystic fibrosis, moderate or severe asthma, chronic heart disease, bronchopulmonary dysplasia, diabetes mellitus, haemoglobinopathies, chronic renal failure, etc.)
 - c) Immunosuppression due to disease or treatment, including asplenia or splenic dysfunction
 - d) Children on long-term aspirin therapy (because of the risk of Reyes Syndrome)
 - e) Children with any condition (e.g. cognitive dysfunction, spinal cord injury, seizure disorder, or other neuromuscular disorder) that can compromise respiratory function
 - f) Residents of nursing homes, old people's homes, and other long-stay facilities where rapid spread is likely to follow introduction of infection

2. Those likely to transmit influenza to a person at high risk for influenza complications (including household contacts and out-of-home care givers)
3. Health-care workers, both for their own protection – as these are a group likely to come in contact with influenza during outbreaks – and for the protection of their patients (see Chapter 18)
4. Poultry workers, veterinary inspectors, agricultural workers, park rangers and those with likely contact with water fowl (as this puts them at risk of co-infection with avian influenza)
5. Pregnant women in the risk groups 1b and 1c listed above should be vaccinated before the influenza season, regardless of the stage of pregnancy. Studies indicate that pregnancy may increase the risk of complications from influenza because of the alterations in heart rate, lung capacity, and immunological function. It is estimated that immunisation could prevent 1-2 hospitalisations per 1,000 pregnant women. Because influenza virus vaccine is not a live vaccine it is considered very safe in pregnancy.

Dose and route of administration

As dose recommendations for children can vary between products please consult the individual data sheets.

Table 7.2 Dose and route of administration of influenza vaccine

Age group	Dose
Adults and children ≥ 13 years	A single injection of 0.5 ml IM or by deep subcutaneous injection
Children aged 3-12 years	0.5 ml IM, or by deep subcutaneous injection For children ≤ 9 years of age, the dose should be repeated 4-6 weeks later if receiving influenza vaccine for the first time
Children 6 months to 3 years	0.25 ml IM, repeated 4-6 weeks later if receiving influenza vaccine for the first time

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- The deltoid muscle is the recommended site for adults and older children.
- The anterolateral thigh may be used for infants and young children.
- Antibody levels take from 10-14 days to rise.
- The ideal time for immunisation is before the influenza season, i.e. from September to October. Note: if travelling to the southern hemisphere check Chapter 19.

Influenza vaccine may be given at the same time, but at a different site, as pneumococcal vaccine.

Anyone, including pregnant women, may choose to have the 'flu vaccine.

Contraindications

Anaphylactic reaction to a preceding dose or any of the constituents. The vaccine should not be given to persons with known anaphylactic hypersensitivity to eggs.

Precautions

Acute severe febrile illness, defer until recovery.

Adverse reactions

Local: Soreness and redness around the vaccination site occurs in up to one-third of people.

General: Injectable influenza vaccines contain inactivated virus and cannot cause influenza.

- Fever, malaise and myalgia commencing 6-12 hours after immunisation and lasting for about 48 hours, occur rarely.
- Immediate reactions such as urticaria, angio-oedema, bronchospasm, and anaphylaxis occur very rarely. Such reactions are most likely due to hypersensitivity to the egg protein.
- Guillian Barré syndrome has on rare occasions been temporally associated with influenza vaccination.

Antiviral agents

If considering using antivirals check the HPSC website to discover whether influenza is circulating and only use antivirals if this is confirmed. Antivirals such as neuraminidase inhibitors can be used for treatment and prophylactic purposes during influenza epidemics. People who may be considered for prophylaxis include:

- Unimmunised patients in the 'at risk' groups, including health-care workers, for 2 weeks while the vaccine takes effect

- At-risk patients, who had an anaphylactic reaction to egg, for the duration of an outbreak
- Control of influenza outbreaks in a closed setting such as institutions with high-risk individuals
- Protection of immunocompromised children who may not respond to vaccine.

Antiviral agents are not a substitute for immunisation for the control and prevention of influenza.

Influenza surveillance

The Health Protection Surveillance Centre in partnership with the Irish College of General Practitioners (ICGP) and the National Virus Reference Laboratory (NVRL) have established a network of 52 computerised sentinel practices who report on a weekly basis the number of patients seen with influenza-like illness. Virological confirmation by the NVRL is required to identify that influenza is the causative virus, with classification of type and sub-type.

A weekly influenza report, including clinical and virological data, is compiled throughout the influenza season, from October to May. Since the 2005/2006 season there has been reporting during the inter-season period, of clinical data on a weekly basis, virological data on a fortnightly basis, and monthly surveillance reports are produced. Reports of worldwide influenza activity are also provided as part of the overall monitoring of influenza activity.

Chapter 7 Influenza

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08

Measles

Introduced in 1985 / MMR introduced in 1988

NOTIFIABLE

Introduction

Measles is an acute viral illness caused by a morbillivirus of the paramyxovirus family. There is only one antigenic type, with a number of genotypes. Humans are the only known host. Both infection and appropriate immunisation confer long-lasting immunity.

One case of measles can infect 15-20 unvaccinated people. A vaccine uptake rate of at least 90-95% with 2 doses is required to halt endemic transmission of the virus and thus eliminate measles.

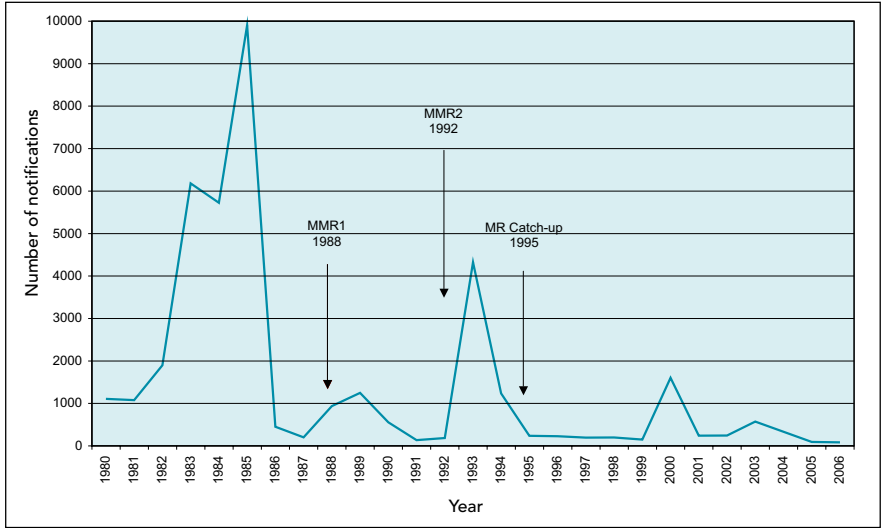
Measles remains a leading cause of vaccine-preventable death worldwide. In 2004 an estimated 450,000 people died from measles, mostly in low-income countries. Eighty percent of those dying were aged under 5 years. In Europe in 2004, 29,000 cases were reported. The WHO has set a target date of 2010 for the elimination of measles and rubella in Europe.

Epidemiology

The incidence of measles in Ireland declined dramatically after the introduction of monocomponent measles vaccine in 1985, from 10,000 cases in that year to 201 cases in 1987. In 1988 a combined measles, mumps and rubella vaccine (MMR) was introduced for children aged 12-15 months. In 1992 a second dose of MMR was recommended to be given at 10-14 years of age. In 1995 a measles and rubella (MR) catch-up campaign was carried out. In 1999 the age for the second dose of MMR was reduced to 4-5 years.

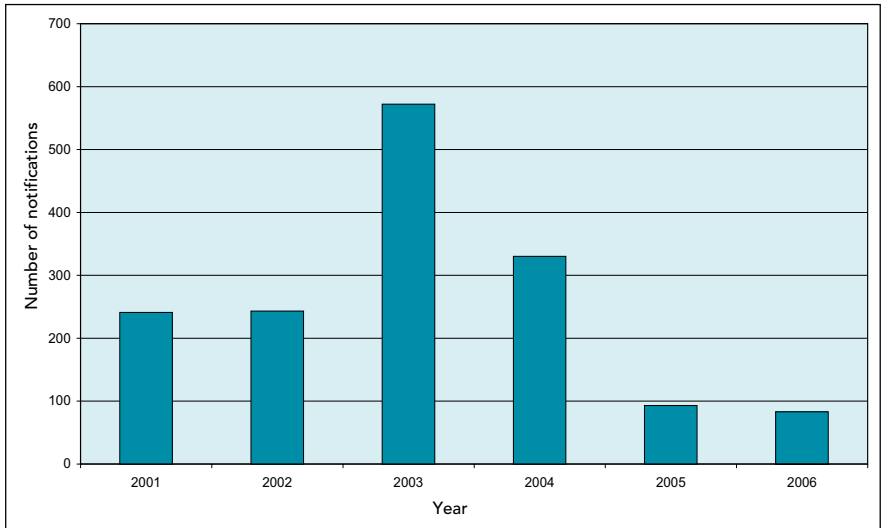
An outbreak of measles in 1993 affected more than 4,000 people, and in 2000 over 1,600 cases of measles were reported, with 3 associated deaths (Figure 8.1).

Figure 8.1 Number of measles notifications in Ireland, 1980-2006.
Source: HPSC



From 2001-2006 there were 1,562 cases of measles notified in Ireland. Incomplete vaccine coverage together with a pool of susceptible unvaccinated older children resulted in rapid spread of the infection during these outbreaks (Figure 8.2).

Figure 8.2 Number of measles notifications in Ireland, 2001-2006.
Source: HPSC



Transmission of measles is by droplet infection. The virus can remain viable on infected surfaces for up to 2 hours.

The incubation period is 10 days (range 7-18 days) with a further 2-4 days before the rash appears. Patients are infectious from 4-5 days before to 4 days after the onset of rash.

Effects of measles

The prodromal phase is characterised by fever, malaise, rhinitis, conjunctivitis and cough. The erythematous and maculopapular rash first appears behind the ears and spreads to the face, trunk and limbs over 3-4 days. The rash may become confluent in places. It begins to fade after 3-4 days, leaving a temporary brownish discolouration. Koplik's spots, which are small red spots with blueish-white centres, may appear on the mucous membranes of the mouth from 2 days before to 2 days after the rash appears.

Approximately 30% of measles cases have one or more complications, which are more common in children under 5 years of age and in adults over 20 years of age. The complications include pneumonia (1-6%), otitis media (7-9%), diarrhoea (8%), convulsions (0.5%) and encephalitis (0.1%). Transient immunodeficiency can occur, with decreased numbers of T cells and leucopenia, which can last for weeks.

There are three types of measles encephalitis:

1. Acute demyelinating encephalomyelitis occurs about one week after the onset of the rash in approx 1/1,000 cases, has a mortality of about 15% and results in residual neurological sequelae in 20-40% of survivors.
2. Measles inclusion body encephalitis, a delayed type of encephalitis, occurs in immunocompromised patients. It can occur without a preceding measles-like illness, and is characterised by acute neurological compromise, loss of consciousness, seizures and progressive neurological damage.
3. Sub-acute sclerosing panencephalitis (SSPE), a degenerative CNS disease progressing to death. If measles infection occurs in children under 2 years of age the rate of SSPE is 1 in 8,000 infections. If infection occurs in children under 1 year of age, the risk of SSPE is 16 times greater than with infection occurring over 5 years of age.

Death occurred in 1 in 500 notified cases in Ireland in the outbreak

of 2000. The case fatality rate is highest in children under 1 year of age, lowest in those aged 1-9 and rises again in teenagers and adults. Pneumonia accounts for 56-86% of measles-associated deaths.

Complications and mortality rates are high in the immunocompromised, the malnourished and in those with vitamin A deficiency. Severe complications may occur in up to 80% of these patients, with case-fatality rates of 70% in patients with cancer. Measles is the most important cause of blindness in children with borderline vitamin A levels, by precipitating xerophthalmia.

Modified measles occurs primarily in those who receive immunoglobulin as post-exposure prophylaxis or in infants with residual maternal antibodies. It is characterised by a prolonged incubation period, mild prodrome and a sparse, discrete rash of short duration. A similar illness has been reported in previously vaccinated persons.

Measles vaccine

Measles vaccine is only available as MMR (Measles, Mumps and Rubella vaccine). The vaccine contains attenuated measles, mumps and rubella viruses which are cultured separately and mixed before lyophilisation.

The lyophilised powder is reconstituted using the diluent supplied and shaken well to completely dissolve the pellet. The reconstituted vaccine is yellow in colour and should only be used if clear and free from particulate matter.

An up-to-date list of licensed vaccines is contained in Appendix 1, or can be accessed on the IMB website, www.imb.ie.

MMR does not contain thiomersal or any other preservatives. It must be kept refrigerated at 2-8°C, and protected from light. It should be used within 1 hour of reconstitution. Failure to adhere to these recommendations can result in loss of vaccine potency and diminished effectiveness.

Over 90% of individuals develop immunity to measles and rubella after 1 dose of vaccine. Two doses give protection in over 98% of people (see point 1, Indications). Between 61% and 91% are protected against mumps after 1 dose; and 98% are protected after 2 doses. Serological and epidemiological evidence indicates that vaccine-induced immunity is possibly lifelong.

Low rates of seroconversion occur in those under 12 months of age, because of maternal antibodies.

Deferral of MMR following blood or immunoglobulin transfusion

Blood and blood products may contain significant levels of virus-specific antibody, which could prevent vaccine virus replication. Where possible, MMR should be deferred for at least 3 months after receipt of low-dose immunoglobulin, 6 months after red-cell transfusion, and 11 months after high-dose immunoglobulin (as for Kawasaki Disease). If the MMR vaccine is administered within these timeframes, a further dose should be given outside these times.

Laboratory investigation to determine vaccine response is not routinely recommended.

Persons who are tuberculin-positive may have a negative tuberculin test for 3 months after measles infection or MMR vaccine.

Scientific evidence shows no association between the MMR vaccine and autism or inflammatory bowel disease.

Dose and route of administration

The dose is 0.5 ml by deep intramuscular injection. The deltoid is the recommended site of administration. The anterolateral thigh may also be used.

Alcohol swabs are best avoided as alcohol can inactivate the MMR vaccine. If alcohol is used to clean the skin it must be allowed to evaporate completely before the injection is given.

When other injectable vaccines are being given concurrently with MMR, different sites should be used.

MMR may be given at the same time as DTaP, IPV, MenC, Hib and Hep B in situations where the latter are overdue.

Indications

1. All children at 12-15 months of age, with a second dose at 4-5 years of age. For older children who have not received 2 doses, MMR vaccine should be given as soon as possible, and a second

dose one month later. Allowing 3 months between doses is likely to maximise the response rate in children aged under 18 months. Where protection against measles is urgently required the second dose can be given 1 month after the first. If children aged under 18 months are given the second dose less than 3 months after the first dose, they need a third dose to ensure full protection. This can be given at 4-5 years.

MMR vaccine can be given to those who have a history of measles, mumps or rubella infection.

2. Measles outbreaks

Outbreaks of measles should be controlled by immunising all susceptible individuals within 72 hours of contact, as vaccine-induced immunity develops more rapidly than natural antibody.

- If these persons have had no previous measles vaccine, a second dose is given one month later.
 - During an outbreak, particularly if there are high attack rates in younger infants, MMR vaccine may be given to children as young as 6 months of age. However, maternal antibodies may compromise the response to the vaccine. Therefore children vaccinated before their first birthday should have a repeat vaccination at 12-15 months of age, at least 1 month after the first vaccine, with a further dose at 4-5 years of age.
 - Some persons may require HNIG (see below).
3. Children with chronic conditions such as cystic fibrosis, congenital heart or kidney disease, failure to thrive or Down syndrome are at particular risk of measles infection and should be immunised with MMR vaccine.
 4. Children coming from low-income countries have probably received measles vaccine but not rubella or mumps vaccine. Therefore, unless there is a reliable history of vaccine administration, these children should be regarded as unimmunised, and given 2 doses of MMR one month apart.
 5. Individuals born before 1978 are likely to have had measles infection. MMR vaccine should be offered to such individuals on request if they are considered at high risk of exposure.
 6. Health-Care Workers (HCWs) in the following situations (see Chapter 18). Protection is important both for themselves and in the context of their ability to transmit measles to vulnerable groups.
 - Those who do not have evidence either of measles infection or of having received 2 doses of MMR vaccine should be given 2 doses of MMR, separated by at least 1 month.

- If an outbreak occurs in an institution or an area served by an institution, HCWs should be given 1 dose of MMR.

When measles outbreaks occur, susceptible persons should be given MMR within 72 hours of contact with a case.

Antibody response to the mumps and rubella components of the MMR vaccine **does not** develop quickly enough to provide effective prophylaxis after exposure to suspected mumps or rubella. Human normal immunoglobulin is not recommended for the post-exposure protection of pregnant women exposed to rubella. Human normal immunoglobulin is not routinely used as post-exposure protection from mumps.

Contraindications

1. Anaphylaxis following a previous dose of MMR or one of its constituents (e.g. Neomycin, Gelatin)
2. Significantly immunocompromised persons, such as those with untreated malignant disease and immunodeficiency states other than HIV infection, and those receiving immunosuppressive therapy, high-dose x-ray therapy and current high-dose systemic corticosteroids (see Chapter 2)
3. Pregnancy. Furthermore, pregnancy should be avoided for 1 month after MMR

There is no evidence to recommend or support the use of single vaccines against measles, mumps or rubella in place of the combination MMR vaccine.

The following are **NOT** contraindications to MMR vaccine

1. Allergy to egg, even anaphylaxis following egg. If there is a genuine concern regarding serious allergy, a paediatrician may be consulted and the vaccine given in hospital although this is not medically necessary. Currently-used measles and mumps vaccines do not contain significant amounts of egg cross-reacting proteins and recent data suggest that anaphylactic reactions to MMR are not associated with hypersensitivity to egg antigens but to other vaccine components (Gelatin or Neomycin)
2. Breast-feeding

3. HIV-positive patients who are not severely immunocompromised
4. Personal or family history of convulsions. Advice regarding the possibility and treatment of pyrexia should be given
5. Immunodeficiency in a family member or household contact
6. Uncertainty as to whether a person has had 2 previous MMR vaccines
7. If women have received anti-RhD immunoglobulin it is not necessary to defer rubella vaccination as the response to the vaccine is not affected

Precautions

1. Acute severe febrile illness, defer until recovery
2. Injection with another live vaccine within the previous 4 weeks
3. Recent administration of blood or blood products (see above)
4. Patients who developed thrombocytopenia within 6 weeks of their first dose of MMR should undergo serological testing to decide whether a second dose is necessary. The second dose is recommended if the patient is not fully immune to the 3 component viruses.

Adverse reactions

Soreness and erythema may occur at the injection site (3-8%). Fever (6%), rash (7%), headache, vomiting and salivary gland swelling may occur. A febrile convulsion occurs in 1 in 1,000 children.

'Mini-measles' may occur 6-10 days after immunisation and consists of mild pyrexia and an erythematous rash. 'Mini-mumps' with salivary gland swelling may rarely occur during the third week after immunisation. Very rarely, anaphylaxis, erythema multiforme, thrombocytopenia, and nerve deafness have been reported.

The rubella component may occasionally produce a rash, mild arthralgia, and lymph-node swelling 2-4 weeks post-vaccination, particularly in post-pubertal females (up to 25% of recipients). The incidence is lower than after natural disease.

There is no evidence of congenital rubella syndrome or increase in other teratogenic effects in women inadvertently given rubella vaccine before or during early pregnancy, but pregnancy remains a contraindication.

Adverse reactions are considerably less common (under 1%) after a second dose of MMR.

Protection of contacts with immunoglobulin

The following children and adults who come into contact with measles should be considered for treatment with human normal immunoglobulin (HNIG) as soon as possible after exposure (at least within 5 days):

1. Those with compromised immunity (see Chapter 2)
2. Infants age 5-12 months (those aged under 5 months will usually have maternal antibodies)
3. Infants of mothers who develop measles, as such infants will not have maternally derived antibodies
4. Non-immune pregnant women. As most such women are immune to measles, measles IgG should be checked. HNIG can be offered to non-immune subjects. They should also be offered MMR vaccine after delivery, at least 3 months after receiving HNIG.

Although administration should not wait for laboratory confirmation of measles in the index case, a complete risk assessment should be undertaken prior to administration of the HNIG.

If HNIG is not available, in certain high-risk situations IVIG can be given, as it usually contains similar measles antibody levels to HNIG.

Those contacts on maintenance IVIG do not need either HNIG or IVIG if they have been given IVIG within 3 weeks prior to exposure.

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Meningococcal Infection

Group C vaccine introduced 2000

NOTIFIABLE

Introduction

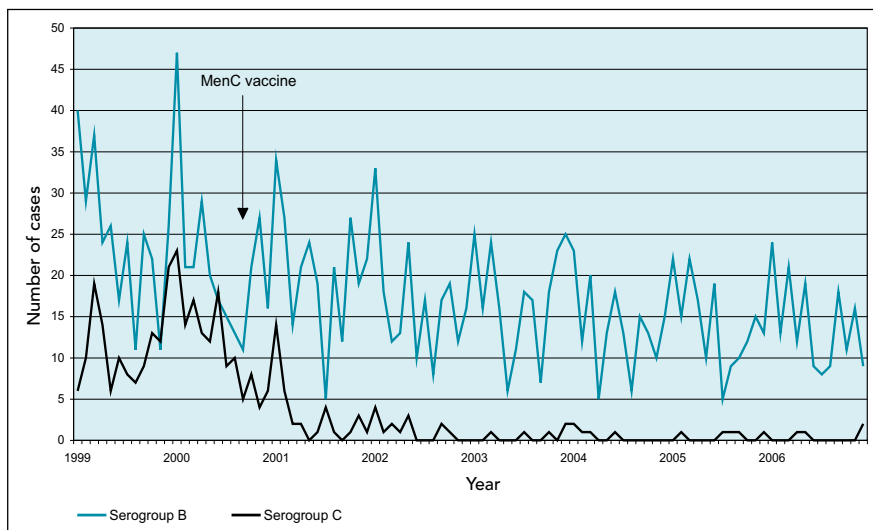
Meningococcal infection is the spectrum of disease caused by *Neisseria meningitidis* and includes meningitis, septicaemia and, less commonly, other invasive infections such as septic arthritis or endophthalmitis. The meningococci are gram-negative diplococci and are divided into at least 13 antigenically distinct serogroups; most disease-associated strains belong to serogroups A, B, C, Y or W₁₃₅. In Ireland serogroup B and C strains accounted for over 99% of all invasive disease prior to the introduction of the serogroup C conjugate vaccine in 2000.

The significance of the meningococcus as a pathogen lies in the potential severity of the illness, the absence of effective vaccines against all individual meningococcal serogroups, the unique ability of the organism to cause outbreaks or epidemics, and the intense public anxiety that follows a case or outbreak. In Ireland the majority of cases of meningococcal infection are sporadic.

Epidemiology

N. meningitidis is a human-only pathogen and is carried in the nasopharynx. Overall approximately 10% of the population are asymptomatic carriers. Carriage is uncommon in infancy and early childhood with peak carriage rates (up to 25%) occurring in the 15-19 year age group. Transmission occurs from person-to-person by aerosol, respiratory droplets or direct mucosal contact with respiratory secretions of a person carrying the organism. Naturally acquired serum bactericidal antibodies to *N. meningitidis* result from carriage, the duration of immunity induced is unknown.

Figure 9.1 Notifications of serogroup B and serogroup C meningococcal infection in Ireland, 1999-2006. Source: HPSC



A small minority of individuals who pick up *N. meningitidis* develop invasive infection after an incubation period which is typically 2-3 days. The reasons why invasive infection develops in some individuals but not in others are unclear. Factors that have been identified as increasing the risk of invasive infection include active or passive smoking, a preceding severe respiratory tract infection particularly influenza A, and living in closed or semi-closed communities such as military barracks or halls of residence. Individuals with late complement component (C5-C9), C3 or properdin deficiencies, or those with functional or anatomic asplenia, have an increased risk of invasive and/or recurrent meningococcal disease.

Invasive meningococcal disease occurs in all countries worldwide. The infection is endemic in Northern Europe, with a background incidence of 2-3 culture confirmed cases per 100,000. In Ireland the infection shows a seasonal variation, the majority of cases occurring in winter and early spring. Periodic upsurges in meningococcal activity resulting in hyperendemic disease occur, associated with increased circulation of distinct subtypes and/or a hypervirulent strain or strains.

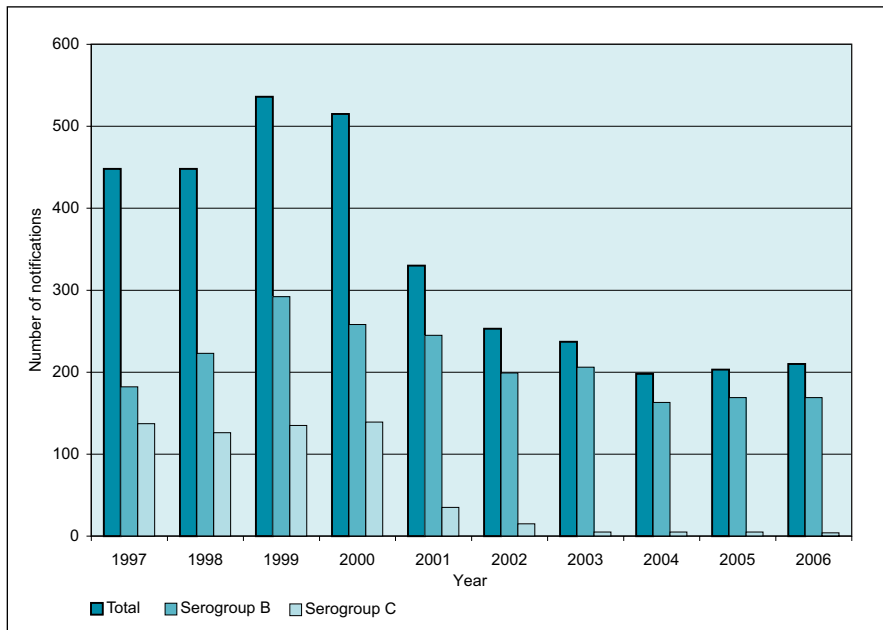
There have been many large epidemics of meningococcal disease following introduction and spread of hypervirulent strains. Epidemic disease is characterised by an increased case-attack rate and altered age distribution, with increased numbers of cases seen in adolescents

and adults. Examples include serogroup A epidemics in England and Wales that coincided with each of the two world wars, and large epidemics involving serogroup A or serogroup W₁₃₅ strains have occurred in association with the annual pilgrimage (Hajj) to Mecca, Kingdom of Saudia Arabia, with importation into other countries by returning pilgrims.

However, in the last 100 years, the highest burden of disease has been in the so-called 'meningitis belt' of sub-Saharan Africa, due mainly to serogroup A or less commonly, serogroup W₁₃₅ with attack rates of up to 1/1,000 and reported mortality rates of up to 40%. Epidemic disease with distinct serogroup B strains has also occurred, including a large epidemic in Norway in the 1970s and in New Zealand in the last 10 years.

Invasive meningococcal disease may occur at any age but is most common in endemic countries, in infancy and early childhood, with a second smaller peak of incidence in adolescents and young adults. In Ireland, the overall case-fatality rate is less than 5%. Serogroup C infection is typically associated with higher morbidity and mortality rates in adolescents and young adults than in other age groups. Overall, the mortality rates are higher in individuals with septicaemia than in those

Figure 9.2 Number of invasive meningococcal disease notifications in Ireland, 1997-2006. Source: HPSC



with meningitis alone. Survivors may have permanent morbidity including skin scarring, digit and/or limb amputation, seizures, hearing loss, and brain damage.

Impact of *N. meningitidis* serogroup C conjugate vaccine in Ireland

Since the introduction of the *N. meningitidis* serogroup C conjugate (MenC) vaccine into the Irish schedule in 2000, the incidence of serogroup C disease has shown a 96% reduction, from 132 culture and/or PCR confirmed cases in 1999 to 3 culture and/or PCR confirmed cases in 2006 (Figure 9.1 and Figure 9.2). In the same period the number of culture and/or PCR confirmed cases of serogroup B disease fell from 285 in 1999 to 161 in 2006.

Effects of meningococcal disease

The onset of disease may be fulminant, with abrupt onset of fever, prostration, shock, a rapidly progressing purpuric rash and death; or it may be insidious, with a mild upper respiratory prodrome of 2 or 3 days. In an infant or young child the common early symptoms (reluctance to feed, trivial fever and irritability) are non-specific. Clinical recognition of meningococcal disease in the initial phase of the illness is problematic. The patient's skin may appear blotchy or pale. A typical non-blanching petechial or purpuric rash may be present with meningococcal septicaemia; however, the rash may be very scanty and may initially be erythematous.

One review of the course of illness in children prior to admission to hospital found that most had only non-specific symptoms in the first 4-6 hours, with the classic features of haemorrhagic rash, meningism and impaired consciousness developing later (median onset 13-22 hours). In contrast, early symptoms of sepsis (leg pains, cold hands and feet, abnormal skin colour) were present in 72% at a median time of 8 hours. The signs and symptoms of meningococcal meningitis are indistinguishable from the signs and symptoms of bacterial meningitis caused by other pathogens, with the exception of the rash, which may be present in some 40% of patients.

Management of suspected cases, contacts, carriers and outbreaks

A Initial management of suspected cases

Primary care

In view of the often rapid progression and high mortality rate of meningococcal disease, early treatment of suspected cases with penicillin

may be life-saving. It is recommended that GPs carry supplies of this drug in an emergency bag.

Recommended dosage of Benzylpenicillin

Adults and children >10 years	1,200 mg
Children 1-9 years	600 mg
Children <1 year	300 mg

This should be given intravenously when possible. It can be given by the intramuscular route in shocked patients but is not as effective.

Penicillin should not be given if there is a history of penicillin anaphylaxis (which is extremely rare) and patients should go to hospital as quickly as possible.

Hospital care

Each acute hospital should have readily available guidelines in place for the management of suspected invasive meningococcal disease.

Advice should be sought from the local Department of Public Health for management of suspected outbreaks. The most up-to-date information on management of contacts is available from Departments of Public Health.

B Chemoprophylaxis

Close contacts are at increased risk of developing infection. This risk is highest in the first 7 days following onset of symptoms in the index case, and falls during the following weeks. Chemoprophylaxis should be given as soon as possible after identification of the index case, but can be given up to 1 month later if a contact is not immediately identified or traced. The aims of chemoprophylaxis are to eliminate carriage from recently colonised susceptible individuals in the period before invasive disease may develop, and to reduce spread of the organism.

The following persons should be given prophylaxis:

- 1 The index case, as soon as the patient can tolerate oral medication, unless treatment was with cefotaxime or ceftriaxone
- 2 Those who in 7 days prior to the onset of illness of the index case
 - shared living or sleeping accommodation with the patient; including child-minders and baby-sitters
 - had mouth kissing contact with the patient

- were in the same nursery/crèche as the patient, where the nature of nursery/crèche contact is similar to that for household contacts. This includes adult carers.
- 3 HCWs (including those present at autopsy) who did not wear a (surgical) mask and whose mouth or nose was directly exposed to infectious airborne droplets or secretions within one metre of a probable or confirmed case of meningococcal disease, who has not received at least 24 hours appropriate antibiotic treatment. *HCWs should wear surgical masks when in close contact with an infectious case for the first 24 hours after the initiation of effective antimicrobial treatment.*
- 4 Chemoprophylaxis is not necessary for classmates of an index case unless a number of cases occur during the same term:
 - If two or more cases of infection with the same strain occur in one class all class members and staff should receive prophylaxis
 - If the cases occur in different classes, management is more difficult but should be guided by such considerations as
 - o the interval between the cases
 - o the size of the contact group
 - o the carriage rate in the school
 - o whether the cases are due to a vaccine-preventable strain
 - o the degree of public concern, particularly if a death has occurred
 - o the incidence of the disease in the wider community.*In such situations management should be discussed with a relevant Specialist.*
- 5 Special consideration is needed when an index case has attended a house party in the preceding 7 days, especially if pre-school children were present. If chemoprophylaxis is appropriate it should be given to all attendees, both adults and children.
- 6 Special consideration should be given to situations in which there is greater than usual interaction between members of the extended family and an index case, particularly where overcrowding or adverse environmental living conditions exist.
- 7 Ideally chemoprophylaxis should be given to all contacts as soon as possible after notification of the index case. However, it can be given up to a month after identification of an index case, as carriage may persist for a long period.

It is not recommended that prophylaxis be given routinely to passengers on public transport, e.g. bus, train, where an index case has been identified.

Prophylactic antibiotics**Rifampicin**

This is the drug of choice, and should be given promptly and preferably within 24 hours of diagnosis of the index case.

All close contacts should be advised that infection can occur even if prophylaxis is given. This is because the antibiotic may not be effective if the contact is incubating disease, or because the contact may become recolonised and then develop the disease. Contacts should be advised to seek medical advice should symptoms develop.

Dose of Rifampicin

Children 0-12 months	5 mg/kg 12 hourly for 2 days
Children 1-12 years	10 mg/kg 12 hourly for 2 days
Children over 12 years & adults	600 mg 12 hourly for 2 days

Side-effects

Rifampicin recipients should be informed about the following possible side-effects:

- interference with contraceptive pill
- interference with anticoagulants
- red coloration of urine, sweat and tears
- permanent discolouration of soft contact lenses

Precautions and contraindications to Rifampicin

Anaphylaxis to a previous dose, severe liver disease and pregnancy.

Alternative prophylaxis

- Ceftriaxone as a single intramuscular dose (250 mg in adults, 125 mg in children under 12 years).
- Although not licensed for this purpose a single dose of ciprofloxacin (500 mg orally for adults) has been shown to be effective.

Pregnancy

While no drug can be regarded as absolutely safe in pregnancy, harmful effects on the foetus have not been documented in relation to use of ceftriaxone.

C Meningococcal vaccine

Contacts of a case of infection with a vaccine-preventable strain should be immunised with the appropriate vaccine (see below). The aim of immunisation is to prevent late secondary cases.

(a) Meningococcal serogroup C conjugate vaccine (MenC)

The serogroup specific polysaccharide antigen is attached to a carrier protein. The conjugated vaccines induce a T-cell dependent memory response from 2 months of age.

Dose and route of administration

The dose at all ages is 0.5 ml, given by intramuscular injection in the anterolateral thigh or the deltoid region.

In patients with thrombocytopenia or bleeding disorders, MenC vaccine may be given subcutaneously (see Chapter 2).

Indications

Primary schedule

Infants under 12 months require 2 doses, generally at 4 and 6 months, with a booster in the second year of life. Those over 12 months need only 1 dose. The need for a later booster, e.g. in adolescence, has not yet been defined.

Contacts of cases

Close contacts of cases of meningococcal infection have an increased risk of developing the disease in subsequent weeks. If results of typing indicate a serogroup C strain, MenC vaccine should be given to all previously unimmunised close contacts (of all ages), in addition to chemoprophylaxis. Close contacts who are only partially immunised should complete the course of vaccine. Children who have not received a dose of MenC vaccine over 1 year of age, should be offered a booster.

Index Cases

If the index case has been previously vaccinated, a booster dose of MenC vaccine is recommended although recurrent serogroup C disease is rare.

MenC vaccine should also be offered to any unimmunised index cases (whatever the serogroup) under the age of 23 years. This policy ensures that persons in this age group are given equivalent protection to their age-matched immunised peers.

Local outbreaks

Immunisation has been shown to be effective in controlling outbreaks in institutions (e.g. schools) and communities, reducing the incidence of infection.

Meningococcal serogroup C vaccine has no role in the management of outbreaks of non-serogroup C infection.

Children and adults with asplenia or splenic dysfunction

Children and adults with asplenia or splenic dysfunction are believed to be at increased risk of invasive meningococcal disease. However, these individuals may have a sub-optimal response to meningococcal vaccines.

- These children, if under 1 year of age, should be immunised in accordance with the routine schedule.
- Children over 1 year of age, and adults, should be immunised with 2 doses of MenC vaccine (Hib/MenC if available), administered 2 months apart.
- Those who have been fully immunised as part of the routine infant immunisation programme and who subsequently have a splenectomy or develop splenic dysfunction, should be given an additional dose of MenC vaccine (usually as Hib/MenC).
- If travelling to a country where there is an increased incidence of serogroup A, W₁₃₅ or Y meningococcal disease, such individuals should be immunised with the quadrivalent (ACW₁₃₅Y) polysaccharide vaccine (see below). Note: When the quadrivalent conjugated polysaccharide ACW₁₃₅Y vaccine becomes available, this should be administered instead of the polysaccharide vaccine.

Contraindications

Anaphylactic reaction to a preceding dose or any of the constituents, including meningococcal serogroup C polysaccharide, or the carrier protein (either diphtheria toxoid or the CRM197 carrier protein is the carrier protein contained in the currently available MenC vaccines, and in Hib vaccine).

Precautions

Acute severe febrile illness, defer until recovery.

Pregnancy: There is no evidence of risk from immunising pregnant women or those who are breast-feeding, with inactivated viral or bacterial vaccines or with toxoids. Hence, MenC vaccine may be given when there is a high risk of the individual developing the disease.

Adverse reactions

Local: Injection site reactions may occur, are generally mild and last for approximately 24-48 hours.

General: Generalised reactions are rare.

(b) Plain polysaccharide (PS) meningococcal vaccine

Quadrivalent A,C,W₁₃₅,Y meningococcal PS vaccine is effective against serogroup A C W₁₃₅ and Y meningococci. Immunity develops in more than 90% of recipients within 5-7 days of a single injection. However, young children respond less well than adults, with little response to the Group C polysaccharide before 24 months. Infants respond to serogroup A, polysaccharide from 2 months of age. However, the protection induced is short-lived.

Dose and route of administration

Primary immunisation

Those aged 2 months to 2 years of age. The primary course consists of 2 doses each of 0.5 ml, with an inter-dose interval of 3 months.

Children over 2 years and adults

A single dose of 0.5 ml is given by intramuscular injection.

Booster dose of vaccine

For those at continued risk, a reinforcing dose should be given every five years. Children who were immunised under the age of 5 years should receive an initial booster after 2-3 years if at ongoing risk.

Indications

Travel

ACW₁₃₅Y polysaccharide vaccine is indicated for immunisation of long-stay and high-risk travellers to areas where epidemics or hyperendemic disease with serogroup A, C or W₁₃₅ infection occur.

High-risk travellers are those who live or work with local people, and those who live or travel 'rough'. At present this recommendation includes travel to sub-Saharan Africa and the Kingdom of Saudi Arabia (for the latter, ACW₁₃₅Y vaccination is now a visa entry requirement).

From time to time, meningococcal disease outbreaks occur in various parts of the world. Where such outbreaks are due to vaccine-preventable strains, vaccination may be recommended for some groups of travellers to the affected areas. The advice of an appropriate Specialist should be sought.

Note: Visa entry requirements should be checked in good time prior to travel to individual countries.

Individuals with deficiencies in the complement pathway or properdin deficiency

Congenital complement deficiencies are rare. However, there is a strong association with susceptibility to meningococcal disease and deficiencies in the early complement components (C1, C4, C2 but especially C3) and the late lytic components (C5 – C9) of the complement pathway. C2 deficiency is the most common familial complement deficiency detected in Ireland.

- Individuals with C3 defects are at risk of severe infection with encapsulated bacteria including *N. meningitidis*.
- Meningococcal disease in individuals with deficiencies of late complement components (C5-C8) is almost always caused by serogroup W₁₃₅ and Y (serogroups B and C are less common).
- Recurrent meningococcal disease is typical in persons with C5-C8 deficiencies.

Individuals who have had recurrent meningococcal infection should be tested for complement deficiency; investigations should ideally be performed some weeks following infection.

Properdin deficiency is a very rare X-linked defect. Screening for properdin deficiency should be considered when there is a family history of meningococcal disease occurring in accordance with an X-linked pattern (many males affected).

Those individuals who are identified as having deficiencies of any complement component, or properdin deficiencies, should be immunised with the available meningococcal vaccines.

- These children, if under 1 year of age, should be immunised against *N. meningitidis* serogroup C in accordance with the routine schedule.
- Children over 1 year of age, and adults, should be immunised with 2 doses of MenC vaccine, administered 2 months apart.
- Those who have been fully immunised as part of the routine infant immunisation programme and who are subsequently found to have complement or properdin deficiency should be given an additional dose of MenC vaccine
- The quadrivalent polysaccharide ACW₁₃₅Y vaccine may be administered to those individuals in these groups who are over 2 years of age, and should be administered no less than 2 months after the final dose of MenC vaccine.

Contacts of cases

For confirmed serogroup A infection, immunisation with quadrivalent (A,C,W₁₃₅,Y) polysaccharide vaccine should be offered to all close contacts over 2 months of age. For confirmed infections with serogroups W₁₃₅ or Y, all close contacts over 2 years of age should be offered quadrivalent (A,C,W₁₃₅,Y) polysaccharide vaccine.

Contraindications

Anaphylactic reaction to a preceding dose or any of the constituents.

Precautions

- 1 Severe reaction to a previous dose
- 2 Acute severe febrile illness, defer until recovery.

Adverse reactions

Local: Injection site reactions occur in approximately 10% of recipients and last for approximately 24-48 hours.

General: Generalised reactions are rare although pyrexia occurs more frequently in young children than in adults.

Pregnancy and breast-feeding. Meningococcal vaccines may be given to pregnant women when clinically indicated. There is no evidence that it is harmful to vaccinate pregnant women, or those who are breast-feeding, with inactivated viral or bacterial vaccines or with toxoids.

Serogroup B vaccines

The serogroup B capsule is weakly immunogenic and also contains antigens that may cross-react with human neurological tissue. Hence it has not thus far been possible to develop serogroup B vaccines based on the capsule. In response to an epidemic of infection with a single serogroup B strain, a strain specific outer membrane vesicle (OMV) vaccine was developed in Norway. This vaccine did not go into general use because the epidemic came to an end as the vaccine became available.

The OMV technology was subsequently exploited to develop additional specific serogroup B vaccines, which have been successfully utilised to combat epidemic serogroup B disease in Cuba and New Zealand. Each of these 'designer' vaccines targets antigens that are specific to an individual strain and will not induce cross-protection against other serogroup B strains. In recent years throughout northern Europe,

including Ireland, many different serogroup B strains have been associated with disease. The Norwegian and Cuban strains are not found in Ireland and the New Zealand serogroup B vaccine would only give limited protection.

There is no available vaccine effective against the different serogroup B organisms circulating in Northern Europe, including Ireland.

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10

Mumps

Introduced in 1988 as part of MMR

NOTIFIABLE

Introduction

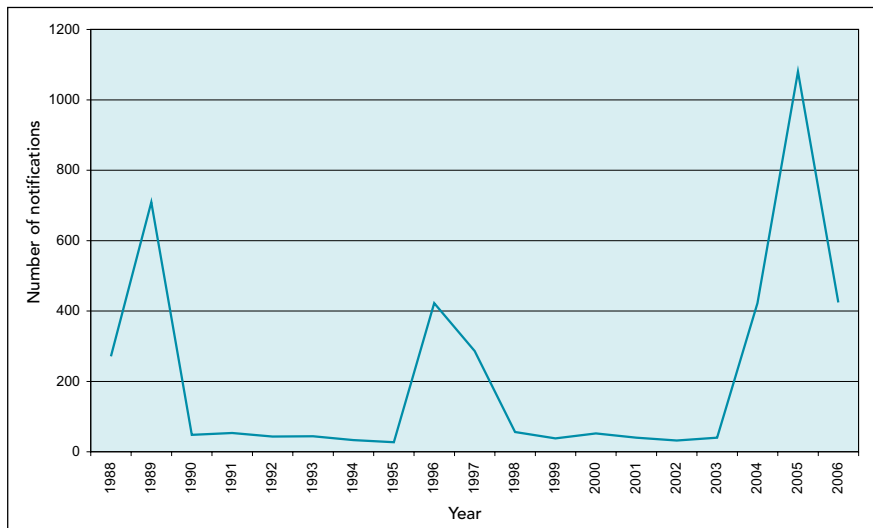
Mumps is an acute viral illness caused by a paramyxovirus. Humans are the only known host. It is characterised by swelling of one or more of the salivary glands, usually the parotid. The virus can be isolated from 2-7 days before to 9 days after onset of symptoms. Approximately 10 secondary infections will result from each index case in a fully susceptible population.

Epidemiology

Transmission is by airborne or droplet spread. The incubation period is approximately 17 days (range 14-25 days). Cases are infectious from about 6 days before to 10 days after onset of symptoms, although maximum infectivity is from 2 days before to 5 days after onset of symptoms. High-risk groups are those in a close-contact environment such as pre-school, school and third-level colleges, health-care workers, and international travellers. Recently in Ireland the highest incidence has been in 18-24 year olds.

A national mumps outbreak commenced in November 2004 (Figure 10.1). The outbreak predominantly affected those born before 1988, particularly those born between 1983 and 1986. MMR was first introduced in 1988.

Figure 10.1 Annual number of mumps notifications in Ireland, 1988-2006.
Source: HPSC



Effects of mumps

Up to 40% of mumps infections may be asymptomatic and up to 50% will have non-specific or primarily respiratory symptoms.

Prodromal symptoms are non-specific and include myalgia, low-grade fever, anorexia, and headache. Salivary gland inflammation, particularly of the parotid gland (unilateral or bilateral), is the most common manifestation and occurs in 50-70% of affected individuals.

Mumps virus affects the CNS in up to 50% of cases, but less than 10% are symptomatic. Typically, symptoms are mild, with meningism (headache, photophobia and neck stiffness) being the commonest. Other CNS manifestations include encephalitis, ataxia, transverse myelitis, and sensorineural deafness. Meningoencephalitis occurs more frequently in adults than children and in boys more than girls. It resolves without sequelae in 3-10 days. Parotitis may be absent in up to 50% of these cases.

Other complications include pancreatitis (4%), orchitis (approximately 25% of post-pubertal men, rarely causing sterility), oophritis and mastitis in post-pubertal females, and nephritis. Rarer complications include arthralgia, arthritis and cardiac abnormalities. Death is rare.

Mumps vaccine

Mumps vaccine is only available as MMR (Measles, Mumps and Rubella vaccine). The vaccine contains attenuated measles, mumps and rubella which are cultured separately and mixed before lyophilisation.

The lyophilised powder is reconstituted using the diluent supplied and shaken well to completely dissolve the pellet. The reconstituted vaccine is yellow in colour and should only be used if clear and free from particulate matter.

An up-to-date list of licensed vaccines is contained in Appendix 1, or can be accessed on the IMB website, www.imb.ie.

MMR does not contain thiomersal or any other preservatives. It must be kept refrigerated at 2-8°C, and protected from light. It should be used within 1 hour of reconstitution. Failure to adhere to these recommendations can result in loss of vaccine potency and diminished effectiveness.

Over 90% of individuals develop immunity to measles and rubella after 1 dose of vaccine. Two doses give protection in over 98% of people (see point 1, Indications). Between 61% and 91% are protected against mumps after 1 dose; and 98% are protected after 2 doses. Serological and epidemiological evidence indicates that vaccine-induced immunity is possibly lifelong.

Low rates of seroconversion occur in those under 12 months of age, because of maternal antibodies.

Deferral of MMR following blood or immunoglobulin transfusion

Blood and blood products may contain significant levels of virus-specific antibody, which could prevent vaccine virus replication. Where possible, MMR should be deferred for at least 3 months after receipt of low-dose immunoglobulin, 6 months after red-cell transfusion, and 11 months after high-dose immunoglobulin (as for Kawasaki Disease). If the MMR vaccine is administered within these timeframes, a further dose should be given outside these times.

Laboratory investigation to determine vaccine response is not routinely recommended.

Persons who are tuberculin-positive may have a negative tuberculin test for 3 months after measles infection or MMR vaccine.

Scientific evidence shows no association between the MMR vaccine and autism or inflammatory bowel disease.

Dose and route of administration

The dose is 0.5 ml by deep intramuscular injection. The deltoid is the recommended site of administration. The anterolateral thigh may also be used.

Alcohol swabs are best avoided as alcohol can inactivate the MMR vaccine. If alcohol is used to clean the skin it must be allowed to evaporate completely before the injection is given.

When other injectable vaccines are being given concurrently with MMR, different sites should be used.

MMR may be given at the same time as DTaP, IPV, MenC, Hib and Hep B in situations where the latter are overdue.

Indications

1. All children at 12-15 months of age, with a second dose at 4-5 years of age. For older children who have not received 2 doses, MMR vaccine should be given as soon as possible, and a second dose one month later. Allowing 3 months between doses is likely to maximise the response rate in children aged under 18 months. Where protection against measles is urgently required the second dose can be given 1 month after the first. If children aged under 18 months are given the second dose less than 3 months after the first dose, they need a third dose to ensure full protection. This can be given at 4-5 years.
MMR vaccine can be given to those who have a history of measles, mumps or rubella infection.
2. Measles outbreaks
Outbreaks of measles should be controlled by immunising all susceptible individuals within 72 hours of contact, as vaccine-induced immunity develops more rapidly than natural antibody.
 - If these persons have had no previous measles vaccine, a second dose is given one month later.
 - During an outbreak, particularly if there are high attack rates in younger infants, MMR vaccine may be given to

children as young as 6 months of age. However, maternal antibodies may compromise the response to the vaccine. Therefore children vaccinated before their first birthday should have a repeat vaccination at 12-15 months of age, at least 1 month after the first vaccine, with a further dose at 4-5 years of age.

- Some persons may require HNIG (see below).
3. Children with chronic conditions such as cystic fibrosis, congenital heart or kidney disease, failure to thrive or Down syndrome are at particular risk of measles infection and should be immunised with MMR vaccine.
 4. Children coming from low-income countries have probably received measles vaccine but not rubella or mumps vaccine. Therefore, unless there is a reliable history of vaccine administration, these children should be regarded as unimmunised, and given 2 doses of MMR one month apart.
 5. Individuals born before 1978 are likely to have had measles infection. MMR vaccine should be offered to such individuals on request if they are considered at high risk of exposure.
 6. Health-Care Workers (HCWs) in the following situations (see Chapter 18). Protection is important both for themselves and in the context of their ability to transmit measles to vulnerable groups.
 - Those who do not have evidence either of measles infection or of having received 2 doses of MMR vaccine should be given 2 doses of MMR, separated by at least 1 month.
 - If an outbreak occurs in an institution or an area served by an institution, HCWs should be given 1 dose of MMR.

Antibody response to the mumps and rubella components of the MMR vaccine **does not** develop quickly enough to provide effective prophylaxis after exposure to suspected mumps or rubella. Human normal immunoglobulin is not recommended for the post-exposure protection of pregnant women exposed to rubella. Human normal immunoglobulin is not routinely used as post-exposure protection from mumps.

Contraindications

1. Anaphylaxis following a previous dose of MMR or one of its constituents (e.g. Neomycin, Gelatin)
2. Significantly immunocompromised persons, such as those with untreated malignant disease and immunodeficiency states other than HIV infection, and those receiving immunosuppressive

- therapy, high-dose x-ray therapy and current high-dose systemic corticosteroids (see Chapter 2)
3. Pregnancy. Furthermore, pregnancy should be avoided for 1 month after MMR

There is no evidence to recommend or support the use of single vaccines against measles, mumps or rubella in place of the combination MMR vaccine.

The following are NOT contraindications to MMR vaccine

1. Allergy to egg, even anaphylaxis following egg. If there is a genuine concern regarding serious allergy, a paediatrician may be consulted and the vaccine given in hospital although this is not medically necessary. Currently-used measles and mumps vaccines do not contain significant amounts of egg cross-reacting proteins and recent data suggest that anaphylactic reactions to MMR are not associated with hypersensitivity to egg antigens but to other vaccine components (Gelatin or Neomycin)
2. Breast-feeding
3. HIV-positive patients who are not severely immunocompromised
4. Personal or family history of convulsions. Advice regarding the possibility and treatment of pyrexia should be given
5. Immunodeficiency in a family member or household contact
6. Uncertainty as to whether a person has had 2 previous MMR vaccines
7. If women have received anti-RhD immunoglobulin it is not necessary to defer rubella vaccination as the response to the vaccine is not affected

Precautions

1. Acute severe febrile illness, defer until recovery
2. Injection with another live vaccine within the previous 4 weeks
3. Recent administration of blood or blood products (see above)
4. Patients who developed thrombocytopenia within 6 weeks of their first dose of MMR should undergo serological testing to decide whether a second dose is necessary. The second dose is recommended if the patient is not fully immune to the 3 component viruses.

Adverse reactions

Soreness and erythema may occur at the injection site (3-8%). Fever (6%), rash (7%), headache, vomiting and salivary gland swelling may occur. A febrile convulsion occurs in 1 in 1,000 children.

'Mini-measles' may occur 6-10 days after immunisation and consists of mild pyrexia and an erythematous rash. 'Mini-mumps' with salivary gland swelling may rarely occur during the third week after immunisation. Very rarely, anaphylaxis, erythema multiforme, thrombocytopenia, and nerve deafness have been reported.

The rubella component may occasionally produce a rash, mild arthralgia, and lymph-node swelling 2-4 weeks post-vaccination, particularly in post-pubertal females (up to 25% of recipients). The incidence is lower than after natural disease.

There is no evidence of congenital rubella syndrome or increase in other teratogenic effects in women inadvertently given rubella vaccine before or during early pregnancy, but pregnancy remains a contraindication.

Adverse reactions are considerably less common (under 1%) after a second dose of MMR.

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11

Pertussis

Introduced in 1952/3 (DTP) DTaP introduced 1996

NOTIFIABLE

Introduction

Pertussis (whooping cough) is a highly infectious bacterial disease caused by *Bordetella pertussis*, a fastidious gram-negative coccobacillus. Following infection or immunisation immunity wanes over 1-2 decades. Subsequent infection tends to be milder, may not be diagnosed, but is infectious. Approximately 16 secondary infections will result from each index case in a fully susceptible population.

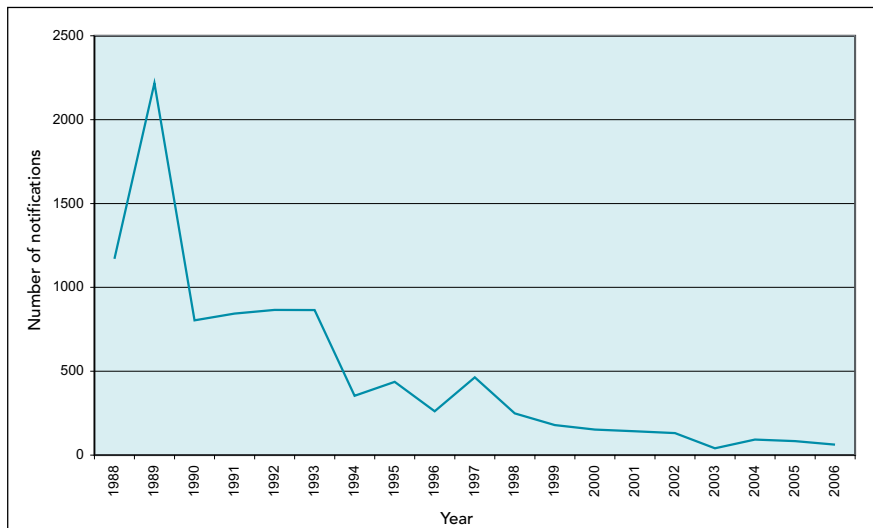
Epidemiology

Pertussis occurs endemically with periodic outbreaks. Worldwide, over 45 million cases occur annually, with more than 250,000 deaths. Epidemiological data on pertussis in the Republic of Ireland have been gathered annually since 1941. There has been a steady decline in mortality which commenced before the introduction of the vaccine, but the rate of decline accelerated following its introduction.

Prior to the introduction of vaccination most cases occurred in young children. Now the highest incidence, morbidity and mortality are in infants. More cases have recently been occurring in adolescents and adults. This change in the epidemiology of pertussis is due to the waning immunity that occurs after both disease and vaccination, and to a reduction in natural boosting. Thirty per cent of adults with a cough lasting longer than 2 weeks may have pertussis. Most infants and young children who contract pertussis are infected by a family member.

Figure 11.1 Number of pertussis notifications in Ireland, 1988-2006.

Source: HPSC



The large increase in notifications of pertussis that occurred in the 1980s followed a scare in the late 1970s regarding a possible association of the vaccine and encephalopathy, which led to low-vaccine uptake (see Figure 11.1).

Humans are the only known hosts of *B. pertussis*. Transmission occurs by close contact via droplet infection from the respiratory tract of symptomatic individuals. The incubation period is 7-10 days (range 4-21). As many as 90% of non-immune household contacts acquire the infection. Communicability is greatest in the catarrhal stage before the onset of paroxysms of coughing, but may last for up to 3 weeks. Macrolide antibiotics decrease infectivity and may limit secondary spread if given early in the course of the infection in those aged over 6 months. They have no effect on the course of the illness if given after the cough is established.

Effects of pertussis

Pertussis is primarily a toxin-mediated disease. Bacteria attach to the respiratory cilia and produce toxins which paralyse the cilia. This, and inflammation, interfere with the clearing of secretions. Many factors determine disease severity, including age of the patient and time since vaccination or previous infection.

The initial catarrhal stage has an insidious onset and is the most infectious period. Cough is limited, the main symptom being rhinorrhoea. An

irritating cough gradually becomes paroxysmal, with a characteristic inspiratory whoop and/or vomiting in about 50% of cases. This paroxysmal stage usually occurs within 1-2 weeks, and often lasts for 2-3 months. In young infants, the typical 'whoop' may never develop and coughing spasms may be followed by periods of apnoea and cyanosis.

Pertussis may be complicated by bronchopneumonia (in 22% of infants) and by cerebral hypoxia with resulting risk of seizures (3% of infants, more in those less than 6 months), and encephalopathy. These complications and deaths occur most commonly in infants under 6 months of age. The highest mortality rate is in preterm infants. The case-fatality rate ranges from 0.04-4%.

Among adolescents and adults the only symptom may be a prolonged cough. This lasts for at least 3 weeks in over 80%, and for up to 90 days in over 25% of cases.

Diagnosis on clinical grounds can be difficult. The organism can be grown on selective media, with incubation for 10-14 days. This requires rapid and careful transport of a nasopharyngeal aspirate or swab in an appropriate medium. Cultures cannot be considered negative until after 10 days. Cultures are less likely to be positive if the person has been immunised, if antibiotics have been taken, or if cough has been present for more than 2 weeks.

PCR, ELISA within 1 week of symptom onset and 4-6 weeks later, and direct fluorescent antibody testing can aid diagnosis.

Treatment

If treatment is begun within 3 weeks of onset of symptoms it can limit transmission, and may reduce the duration of the disease if started in the catarrhal stage. Prophylaxis is recommended for vulnerable household contacts. These may be defined as those who live in the same house or stayed overnight in the same room as the index case, and are under 5 years of age and unimmunised or partially immunised, or have congenital heart disease or severe asthma, or are immunocompromised

Suggested antibiotic prophylactic regimes:

1. Erythromycin, 20-25 mg/kg BD (max 2g per dose) for 7 days is effective in preventing culture positive pertussis in 67% of household contacts, but may have limited clinical impact
2. Clarithromycin, 10 mg/kg BD (max 500 mg/dose) for 7 days
3. Azithromycin, 10 mg/kg once daily (max 500 mg per dose) for 5 days.

Erythromycin has been associated with pyloric stenosis in those aged under 1 month, but the risks of pertussis are far greater than the risks from erythromycin in this age group. There are no large-scale trials of either Clarithromycin or Azithromycin in this situation.

Pertussis vaccine

This is no longer available as a single vaccine. Pertussis vaccines contain purified acellular pertussis antigens, which cause significantly less local and systemic reactions than whole-cell vaccines. Antigens differ between vaccines but usually include inactive pertussis toxin, filamentous haemagglutinin and pertactin.

The vaccine should be stored between 2-8°C. If the vaccine has been frozen, it should not be used.

A full course of vaccine confers protection in over 80% of recipients. Immunity wanes with age, and is low or absent 10-12 years after primary immunisation. High vaccine uptake rates, including booster doses, are therefore very important in order to reduce the incidence of pertussis. In those not fully protected the disease is usually less severe.

Dose and route of administration

The dose is 0.5 ml, given by intramuscular injection into the anterolateral thigh or deltoid.

Indications

The primary course consists of 3 doses given at 2, 4 and 6 months, with a booster at 4-5 years. A further booster, using Tdap which contains low-dose acellular pertussis vaccine, is recommended at 11-14 years. If the primary course is interrupted it should be resumed but not repeated, allowing appropriate intervals between the remaining doses.

If pertussis vaccine is refused by parents, the only available diphtheria and tetanus vaccines are Td and Td/IPV. They are not intended for use as part of the primary schedule, may not give a sufficient immune response if so used, and are not licensed for such use.

Pertussis vaccination should be considered for children aged less than 10 years who are exposed to pertussis, if they have received less than 4 doses of the vaccine. Children may be given dose four at as early as 12 months of age, preferably 6 months after dose three (for catch-up doses, see Chapter 2).

Contraindications

Anaphylaxis to a previous pertussis-containing vaccine or to one of its constituents.

Precautions

Acute severe febrile illness; defer until recovery.

Note; The following are no longer regarded either as contraindications or precautions. They have not been shown to cause permanent harm and are significantly less common after acellular than after whole-cell vaccines

- 1 Temperature of more than 40.5°C within 48 hours of a previous dose of a pertussis-containing vaccine
- 2 Hypotonic-hyporesponsive episode within 48 hours of a previous dose of a pertussis-containing vaccine
- 3 Seizures within 72 hours of a previous dose of a pertussis-containing vaccine
- 4 Persistent, inconsolable crying lasting more than 3 hrs within 48 hours of a previous dose of a pertussis-containing vaccine

Adverse reactions

Local: Minor side-effects (e.g. local redness, swelling) occur in about 15-20% of recipients. Very rarely a major local reaction involving swelling and erythema of most of the diameter of a limb can occur. This resolves without sequelae, and is not a contraindication to further vaccination.

General: Fever and irritability can occur. However, temperature over 40°C is rare. Serious side-effects such as prolonged, inconsolable crying or hypotonic-hyporesponsive episodes are very rare and have not been shown to cause long-term problems. Administration of paracetamol or ibuprofen at the time of immunisation may reduce the incidence of local and febrile reactions.

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12

Pneumococcal Infection

NOTIFIABLE

Introduction

Streptococcus pneumoniae (pneumococcus) is an important cause of serious infection, especially in young children, older adults and immunocompromised individuals. Invasive pneumococcal disease (IPD) is defined as the isolation of *S. pneumoniae* from a normally sterile site (e.g. blood, cerebrospinal fluid, or less commonly, joint, pleural, or pericardial fluid). Non-invasive manifestations of the disease include otitis media, sinusitis and bronchitis. IPD is a disease mainly of young children and older adults. Individuals with severe chronic conditions or immunodeficiencies are also at increased risk of this disease.

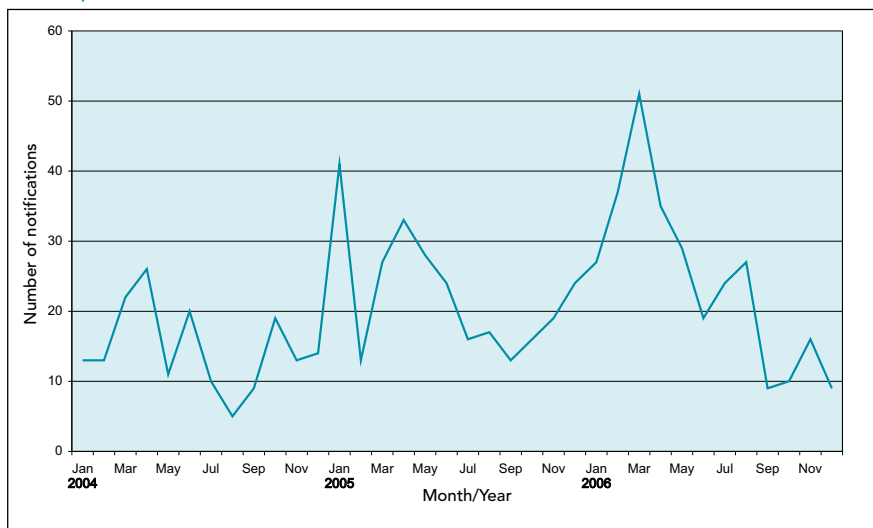
Although more than 90 polysaccharide capsular types, or serotypes of pneumococci are known, most infections are caused by a limited number of serotypes. In high-income countries the serotypes most commonly implicated are 1, 4, 6B, 7F, 9V, 14, 18C, 19F and 23F. The fact that relatively few serotypes cause most invasive disease has allowed for the development of effective vaccines.

Epidemiology

Pneumococcal infection is a leading cause of death worldwide. Mortality is highest in patients who develop sepsis or meningitis. Pneumococcal meningitis case fatality rates of 7-16% were reported in Ireland over the years 2000-2006. Transmission is from person to person by droplet infection. The incubation period varies by type of infection, and can be as short as 1-3 days. Infection can occur at any time throughout the year but rates peak during the winter months (Figure 12.1).

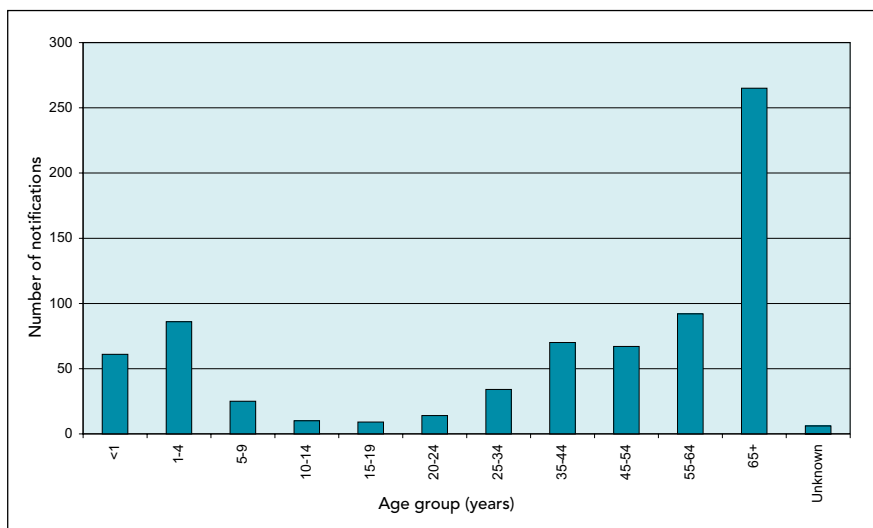
Chapter 12 Pneumococcal Infection

Figure 12.1 Invasive pneumococcal disease (IPD) notifications in Ireland by month, 2004-2006. Source: HPSC



During 2004-2006 a total of 739 cases of IPD were reported, 56% male and 44% female. Most cases were reported among the elderly (≥ 65 years of age) (36%) and in young children in the 0-4 year age group (20%) (Figure 12.2).

Figure 12.2 Age distribution of invasive pneumococcal disease notifications, 2004-2006. Source: HPSC



Effects of pneumococcal infection

Pneumococcal infection is the most common cause of bacteraemia, sepsis, meningitis, pneumonia, sinusitis, and acute bacterial otitis media in children. It can also cause periorbital cellulitis, endocarditis, pericarditis, peritonitis, and soft tissue, bone and joint infection. Individuals who are more susceptible to pneumococcal infection include those with hyposplenism or asplenia (including those with sickle cell and coeliac disease), those immunocompromised by disease or its treatment (e.g. leukaemia), or with other chronic illnesses.

Pneumococcal vaccines

There are two different types of pneumococcal vaccine:

1. Polysaccharide Pneumococcal Vaccine (PPV23). This incorporates 23 of the most common capsular types which together account for up to 90% of serious pneumococcal infections. It should be kept refrigerated at 2-8°C. It is only suitable for use in those ≥ 2 years of age. An adequate antibody response does not develop in those under 2 years of age.
2. A conjugate 7 valent vaccine (PCV7) containing polysaccharide antigens from the 7 most common serotypes conjugated to a protein (CRM 197) has enhanced immunogenicity compared with the polysaccharide vaccine. It is immunogenic even in infancy. It is active against approximately 70% of isolates causing invasive disease, and against a significant number of penicillin-resistant strains.

There is a lower response to PCV7 in preterm infants, but the response is probably adequate to confer protection.

PCV7 can be given as early as 6 weeks of age. The number of doses required for optimum immunogenicity depends on the age at which immunisation is initiated.

The introduction of PCV7 into the routine childhood immunisation schedule in the US in early 2000 has resulted in dramatic declines in the rates of invasive pneumococcal disease (IPD). In 2001 the rate of IPD in children under 2 years of age was 69% lower than 1998 and 1999. An additional unanticipated benefit following introduction of childhood vaccination has been the simultaneous reduction in the incidence of IPD in the adult population. This has been attributed to a decrease in transmission of pneumococci from children to adults. Conjugate vaccines reduce the rates of nasopharyngeal colonisation by vaccine serotypes,

thus decreasing the potential for transmission from children to adults. This rapid induction of 'herd immunity' is an additional benefit of childhood immunisation with PCV7.

Based on a recent study of IPD in children in the Greater Dublin Area, it is anticipated that the introduction of routine pneumococcal vaccination in infancy using a conjugate 7 valent vaccine (PCV7) could protect against 81% of all IPD and against 82% and 90% of meningitis and sepsis respectively.

Indications

Recommendations for pneumococcal vaccination:

1. All infants should be offered pneumococcal vaccination as part of the routine childhood immunisation schedule (see Chapter 2).
2. Those aged 65 years and older should be offered vaccination.
3. Individuals with the following conditions are at increased risk of pneumococcal infection, and should be vaccinated. (For vaccination schedule for individuals at risk of IPD see Table 12.2 below):
 - a. Asplenia or splenic dysfunction including surgical splenectomy, sickle cell disease and coeliac syndrome
 - b. Chronic renal disease or nephrotic syndrome
 - c. Chronic heart, lung, or liver disease, including cirrhosis
 - d. Diabetes mellitus
 - e. Complement deficiency (particularly early component deficiencies C1, C2, C3, C4)
 - f. Immunosuppressive conditions (e.g. some B- and T-cell disorders, HIV infection, leukaemia, lymphoma, Hodgkin's disease) and those receiving immunosuppressive therapies
[Individuals with primary immunodeficiency may have a suboptimal response to vaccine. Immunisation may be omitted in children with certain primary immune deficiencies involving significant B cell compromise and who are receiving regular IVIG replacement therapy. Immunisation is unlikely to be immunogenic in these children.]
 - g. CSF leaks either congenital or complicating skull fracture or neurosurgery
 - h. Intracranial shunt
 - i. Candidate for, or recipient of, a cochlear implant
 - j. Children under 5 years of age with a history of invasive pneumococcal disease, irrespective of vaccine history.

Pneumococcal vaccination should ideally be completed at least 2 weeks prior to elective splenectomy or cochlear implant.

Dose and route of administration

1. Pneumococcal Conjugate Vaccine (PCV7). A dose of 0.5 ml should be given by intramuscular injection in the deltoid area or the antero-lateral aspect of the thigh.
2. Polysaccharide Pneumococcal Vaccine (PPV23). A single dose of 0.5 ml should be given intramuscularly in the deltoid area or the antero-lateral aspect of the thigh.

Pneumococcal vaccination schedule

1. *For normal newborns and healthy children less than 2 years of age:*

Up to 3 doses of conjugate vaccine are recommended. The number of doses required depends on the age at time of initiation, (see Table 12.1 and also Primary immunisation schedule, Chapter 2).

Table 12.1 Routine childhood immunisation with Pneumococcal Conjugate Vaccine (PCV7)

Age at first vaccination	Number of doses and intervals between doses
<12 months (3 doses in total)	Doses 1 and 2 two months apart Dose 3 given at >12 months of age, at least 2 months after dose 2
12-23 months (1 dose in total)	One single dose

2. *For individuals at higher risk of pneumococcal infection* (see a-j above)

Immunisation with conjugate vaccine (PCV7) followed by immunisation with the polysaccharide vaccine (PPV23) is recommended for children to afford a greater breath of protection. For adults a single dose of PPV23 is generally sufficient, see Table 12.2.

Table 12.2 Pneumococcal immunisation for individuals at increased risk of IPD

Age at first vaccination	Pneumococcal vaccine type Number of doses and intervals between doses	
	7 valent conjugate vaccine (PCV7)	23 valent polysaccharide vaccine (PPV23)
<12 months (Minimum age for initiation 6 weeks) (4 doses in total (3PCV7 + 1PPV))	Doses 1 & 2 given 2 months apart Dose 3 given at >12 months of age, at least 2 months after dose 2	Single dose given ≥24 months of age at least 2 months after Dose 3 PCV7
12-23 months (2-3 doses in total (1 or 2 PCV7 + 1PPV))	1 or 2* doses at least 2 months apart	Single dose given ≥24 months of age at least 2 months after previous dose of PCV7
24 months to 5 years (2 or 3 doses in total (1 or 2 PCV7 + 1PPV))	1 or 2* doses with minimum interval of 2 months	Single dose as least 2 months after previous dose of PCV7
At risk children aged over 5 years and at risk adults	PCV is not recommended	Single dose of PPV23

* 2 doses of PCV7 required where it is anticipated that response may be blunted, e.g. children with asplenia/hyposplenia, IgA-, IgG subclass-, and specific antibody deficiencies, whereas for children with complement deficiency or chronic granulomatous disease a single dose of PCV7 followed by PPV23 is adequate.

3. For adults aged 65 and older

A single dose of Pneumococcal Polysaccharide Vaccine (PPV23).

Reinforcing doses of PPV23

Booster doses are not routinely recommended

- Once children and adults have completed the appropriate vaccination schedule, additional booster doses are not currently recommended, unless these individuals have antibody levels likely to decline more rapidly, e.g. those with no spleen, with splenic

dysfunction, immunosuppression including HIV infection, nephrotic syndrome or chronic renal disease. In these circumstances re-immunisation with 23-valent polysaccharide vaccine should be given 5 years after the first dose.

- Adults 65 years or older should receive a second dose of PPV23 if they received vaccine more than 5 years before and were less than 65 years of age at the time of the first dose.
- The need and benefit for repeated booster doses among high-risk individuals is unclear and is not routinely indicated.

Contraindications

Anaphylactic reaction to a preceding dose or any of the constituents.

Precautions

1. Revaccination within 5 years of a previous dose of Polysaccharide Pneumococcal Vaccine. However, if the vaccine has been given during chemotherapy or radiotherapy, revaccination 3 months after treatment is recommended.
2. Acute severe febrile illness, defer until recovery.
3. Pregnancy. As a general principle, unnecessary interventions in pregnancy should be avoided. Pneumococcal vaccination can however be given in pregnancy if there is an urgent need for protection.

Adverse reactions

Local: Localised tenderness and erythema at the injection site may occur. Intradermal administration may cause a severe local reaction. No increase in localised reactions with repeated doses of PCV7 has been reported. Reimmunisation with the PPV23 has produced severe local reactions especially if less than 5 years have elapsed since the first injection.

General: Occasional low-grade fever lasting less than 24 hours.

Management of cases, contacts and outbreaks

Cases of invasive pneumococcal disease (IPD)

Any case of invasive pneumococcal infection or lobar pneumonia believed to be due to *S. pneumoniae* should prompt a review of patients' medical history to establish whether they are in a recognised risk group and whether they have been vaccinated. Patients with risk factors who have not previously been vaccinated should be given vaccination on discharge from hospital.

Children under 5 years of age

All children under 5 years of age who have had IPD, e.g. pneumococcal meningitis or pneumococcal bacteraemia or lobar pneumonia attributed to pneumococcus, should be given a dose of PCV7 irrespective of previous vaccination history. Children under 13 months who are unvaccinated or partially vaccinated should complete the immunisation schedule.

Vaccine failure

These children should be evaluated for risk factors predisposing them to pneumococcal infection. If they are found to fall into one of the risk groups, they should continue vaccination as for other at-risk children (see section on recommendations for the use of pneumococcal vaccination).

All new cases of IPD in children eligible for routine PCV will require follow-up as part of the surveillance of this new vaccination programme.

Contacts

Close contacts of pneumococcal meningitis or other invasive pneumococcal disease are not normally at an increased risk of pneumococcal infection and therefore antibiotic prophylaxis is not indicated. Clusters of invasive pneumococcal disease should be discussed with local health protection teams.

Outbreaks

Outbreaks of pneumococcal respiratory disease in hospitals and residential care homes need prompt investigation. Control measures including vaccination may be appropriate; these should be agreed in discussion with local health protection or infection control teams.

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13

Poliomyelitis

Introduced in 1957

NOTIFIABLE

Introduction

Poliomyelitis is an acute illness which may result from invasion of the gastro-intestinal tract by one of three types of polio virus (1, 2 and 3). The virus has a high affinity for nervous tissue. Inactivated poliomyelitis vaccine (Salk) was introduced to Ireland in 1957 and replaced by attenuated live oral polio vaccine (Sabin) in the early 1960s. Inactivated polio vaccine was reintroduced into the primary immunisation schedule in 2001. Individuals born before 1958 may not have been immunised.

One case of polio can potentially infect up to 5 non-immune contacts.

Epidemiology

Poliomyelitis is endemic in some low-income countries where epidemics of poliomyelitis occur. In countries where the disease incidence is low, but where transmission still exists, polio cases are seen sporadically or as outbreaks among unimmunised individuals. Outbreaks have recently occurred in Afghanistan, Angola, India, Namibia, Nigeria and Pakistan. This shows the ongoing threat of wild polio virus, and the need to maintain high immunisation levels and to report cases of acute flaccid paralysis (AFP).

The most recent case of wild poliomyelitis notified in Ireland was in 1984. If current trends continue, and polio is eradicated in the near future, there will be no need for polio vaccines.

Transmission is through contact with the faeces or pharyngeal secretions of an infected person. The incubation period ranges from 3-21 days, but may be longer. Cases are most infectious from about 10 days before to 7 days after the onset of symptoms. However, carriers and some immunocompromised persons may shed virus in the faeces for longer than 6 weeks.

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Effects of poliomyelitis

Most infections are clinically inapparent. Clinical disease may range in severity from a non-paralytic fever to aseptic meningitis or paralysis. Symptoms include headache, gastro-intestinal disturbance, malaise and stiffness of the neck and back, with or without paralysis. The proportion of inapparent to paralytic infections may be as high as 1,000:1 in children and 75:1 in adults. A case-fatality rate of more than 50% can occur in young adults.

At present an active surveillance system for acute flaccid paralysis is in operation in Ireland. This commenced in September 1998. In any case of acute flaccid paralysis, it is essential to obtain two faecal samples 24-48 hours apart for viral culture, as soon as possible after the onset of paralysis.

Poliomyelitis vaccine

Poliomyelitis vaccine is available in two forms: Inactivated Polio Vaccine (IPV) and live Oral Polio Vaccine (OPV).

1 Inactivated Polio Vaccine (IPV)

IPV contains polioviruses of all three types which have been inactivated by formaldehyde. The primary course consists of 3 injections at least 1 month apart. An up-to-date list of licensed vaccines is contained in Appendix 1, or can be accessed on the IMB website, www.imb.ie

Indications

Recommendations for IPV vaccination

Children

- All children should receive four doses of IPV at 2, 4 and 6 months, and 4-5 years of age.
- The preferred interval between the first 3 doses is 2 months. If accelerated protection is needed, the minimum interval between doses is 4 weeks.
- No additional doses are necessary if more time than recommended elapses between doses.
- Those who started the vaccine series with one or more doses of OPV should receive IPV to complete the series. A minimal interval of 4 weeks should elapse between OPV and IPV but a gap of at least 2 months is preferable.
- IPV can be administered simultaneously with all other routinely recommended childhood vaccines.

These recommendations may differ from recommendations contained in the manufacturer's literature.

Unimmunised adults

Three doses are recommended, the second 1-2 months after the first dose, and the third dose 6-12 months later. If protection is needed more rapidly, doses can be given at 4 weekly intervals. If protection is needed in less than 4 weeks, OPV can be used, as one dose of OPV results in enhanced mucosal immunity when compared with one dose of IPV. The course should be completed as recommended above with IPV.

Incompletely immunised adults

The course should be completed with IPV, regardless of the interval since the last dose or the type of vaccine previously given. Fully vaccinated adults at increased risk of exposure to wild poliovirus should be given a single dose of IPV. Such persons include:

- Those travelling to areas where poliomyelitis is epidemic or endemic
- Those in contact with patients who may be excreting wild poliovirus
- Those in contact with specimens that may contain wild poliovirus.

Contraindications

A previous anaphylactic reaction to IPV, Neomycin or Streptomycin

Precaution

Acute severe febrile illness, defer until recovery.

Even though there is no convincing evidence of an increased rate of adverse events, IPV should not be administered to a pregnant female unless the benefits of vaccination outweigh theoretical risks.

2 Live Oral Polio Vaccine (OPV)

The risks of vaccine-associated paralytic polio (VAPP) following OPV of approximately 1 case per 2.5 million doses are greater than the risks of wild virus poliomyelitis except in those travelling to areas where polio virus is endemic.

Indications

Unvaccinated persons travelling to areas or countries where polio is endemic or epidemic, and who cannot receive a full course of IPV (see Chapter 19).

In the rare instances where OPV is given to children, unimmunised contacts should be vaccinated against polio.

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Contraindications

- 1 An anaphylactic reaction to a previous dose of OPV or any of its constituents, including neomycin.
- 2 Immunodeficiency states (see Chapter 2). Such persons can be given IPV, although a protective response cannot be assured.
- 3 Household contacts of those with immunodeficiency disorders should not be given OPV. They can be given IPV.
- 4 Pregnancy, even though there is no convincing evidence of an increased rate of adverse effects from OPV or IPV in either the pregnant mother or her foetus.
- 5 HIV positive individuals should only be given IPV.

Precautions

- 1 Immunisation should be postponed if the recipient has:
 - (a) Vomiting or diarrhoea
 - (b) An acute febrile illness with a temperature above 38°C.
- 2 OPV should be given **not less than** 3 weeks before or **not less than** 3 months after an injection of normal immunoglobulin (e.g. for hepatitis A). This may not always be possible in the case of travellers going abroad. However, in such cases the OPV is likely to be a booster dose and the possible inhibiting effect of immunoglobulin is less important.
- 3 OPV may be given at the same time as inactivated vaccines and with other live viral vaccines except oral typhoid vaccine unless time constraints exist. If not given at the same time as other live viral vaccines, an interval of 3 weeks is recommended.
- 4 OPV should not be given within 3 weeks of oral typhoid vaccine.

Adverse reactions

Allergic reactions occur very rarely. Vaccine-associated poliomyelitis (VAPP) has been reported in 1 recipient case and 1 contact case per 2 million doses of OPV. The greatest risk of paralysis occurs with the first dose of OPV.

To minimise the risks of VAPP in contact of those recently immunised with OPV, strict hygiene after changing or toileting should be observed for 6 weeks after vaccination.

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Chapter 13 Poliomyelitis

14

Rubella

Introduced in 1971/ MMR introduced in 1988

NOTIFIABLE

Rubella

Introduction

Rubella is a mild disease caused by a toga virus whose only host is humans. Up to 50% of infections are asymptomatic. Its most serious effects are on the foetus, and prevention of the congenital rubella syndrome is the main aim of rubella vaccination.

Epidemiology

The incubation period is 14-21 days, with most individuals developing a rash 14-17 days after exposure. Respiratory transmission occurs by direct or droplet spread. It may be transmitted by asymptomatic cases. Most infections occur in winter or early spring. Individuals with rubella are most infectious from 1 week before to 1 week after onset of the rash. Infants with congenital rubella may shed high titres of virus from their nasopharynx or in the urine for over 1 year.

Since the introduction of Rubella vaccine in 1971, notifications of rubella have decreased (Figure 14.1). There is a longer interval between outbreaks and the numbers infected are smaller. In order to prevent outbreaks 95% uptake of 2 doses of MMR vaccine is required.

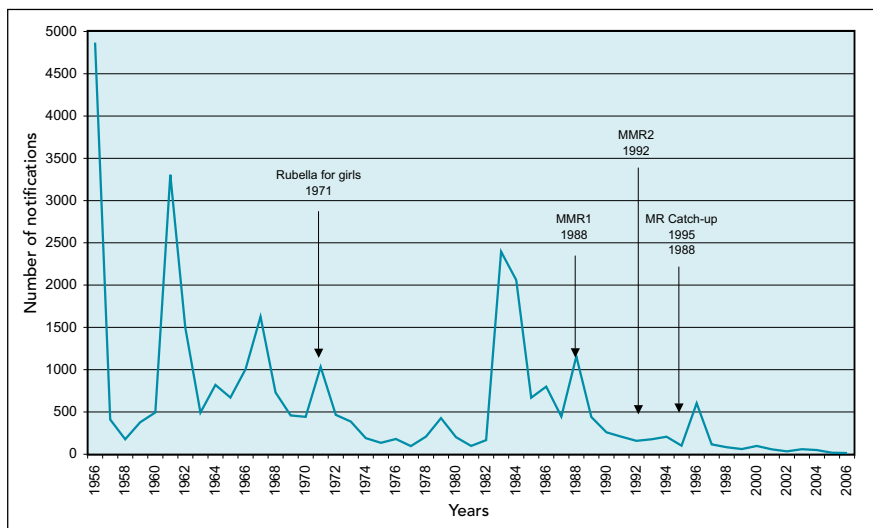
Effects of rubella

Acquired rubella

When symptoms occur they are generally mild. In children, rash is usually the first manifestation and a prodrome is rare. In older children and adults there is often a prodromal illness with low-grade fever, malaise, coryza and mild conjunctivitis. Lymphadenopathy involving post-auricular and sub-occipital glands may precede the rash. The rash is an erythematous maculopapular rash which initially occurs on the face and

Figure 14.1 Number of rubella notifications in Ireland, 1956-2006.

Source: HPSC



neck. The rash is short-lived and is not specific to rubella and therefore laboratory confirmation is recommended.

Arthralgia and arthritis, which may last for up to 1 month, occur frequently in adult females (up to 70%) but are rare in adult males and children. Fingers, wrists and knees are usually affected.

Post-infectious encephalitis occurs in 1 in 6,000 cases, more often in adult females. Haemorrhagic manifestations occur in approx. 1 in 3,000 cases, more commonly in children and are due to thrombocytopenia or vascular damage. Cerebral, GIT or renal haemorrhage may result. Effects may last from days to months, but most patients recover.

Congenital rubella syndrome (notifiable)

Maternal rubella infection in pregnancy may result in foetal loss or major defects affecting almost all organ systems. Manifestations may be delayed for up to 4 years. The congenital rubella syndrome (CRS) comprises eye, ear, heart and CNS defects. Deafness is the most common and sometimes the only manifestation, especially when infection occurs after 16 weeks gestation.

Cardiac defects include patent ductus arteriosus, pulmonary stenosis, septal defects and coarctation of the aorta. Eye defects include cataracts, microphthalmia, pigmentary retinopathy, and glaucoma. Neurological

problems include encephalitis, microcephaly, mental handicap, and behavioural problems. Other abnormalities include hepatitis, splenomegaly, thrombocytopenia, and growth retardation. Diabetes mellitus occurs frequently in later childhood in those with the CRS. Reinfection with rubella may occur, as impaired cell-mediated immunity has been demonstrated in some children with CRS.

The overall risk of defects depends on the stage of pregnancy. If followed up after birth, up to 85% of infants infected in the first 8-10 weeks will be affected. The risk of foetal damage declines to about 10-20%, with infection occurring between 11-16 weeks and with only deafness occurring up to 20 weeks of pregnancy. Defects are rare after 20 weeks.

Preconceptional testing for rubella immunity is recommended.

Assessment of immunity

Satisfactory evidence of protection against rubella would include documentation of having received either 2 doses of rubella-containing vaccine or a positive antibody test for rubella. It has been reported that viraemic infection can occur in vaccinated persons who have low levels of detectable antibody. On rare occasions, clinical reinfection and foetal infection have been reported and CRS has occurred in infants born to women with serological evidence of rubella immunity prior to infection.

Rubella vaccine

Rubella vaccine is only available as MMR (Measles, Mumps and Rubella vaccine). The vaccine contains attenuated measles, mumps and rubella which are cultured separately and mixed before lyophilisation.

The lyophilised powder is reconstituted using the diluent supplied and shaken well to completely dissolve the pellet. The reconstituted vaccine is yellow in colour and should only be used if clear and free from particulate matter.

An up-to-date list of licensed vaccines is contained in Appendix 1, or can be accessed on the IMB website, www.imb.ie.

MMR does not contain thiomersal or any other preservatives. It must be kept refrigerated at 2-8°C, and protected from light. It should be used within 1 hour of reconstitution. Failure to adhere to these recommendations can result in loss of vaccine potency and diminished effectiveness.

Over 90% of individuals develop immunity to measles and rubella after 1 dose of vaccine. Two doses give protection in over 98% of people (see point 1, Indications). Between 61% and 91% are protected against mumps after 1 dose; and 98% are protected after 2 doses. Serological and epidemiological evidence indicates that vaccine-induced immunity is possibly lifelong.

Low rates of seroconversion occur in those under 12 months of age, because of maternal antibodies.

Deferral of MMR following blood or immunoglobulin transfusion

Blood and blood products may contain significant levels of virus-specific antibody, which could prevent vaccine virus replication. Where possible, MMR should be deferred for at least 3 months after receipt of low-dose immunoglobulin, 6 months after red-cell transfusion, and 11 months after high-dose immunoglobulin (as for Kawasaki Disease). If the MMR vaccine is administered within these timeframes, a further dose should be given outside these times.

Laboratory investigation to determine vaccine response is not routinely recommended.

Persons who are tuberculin-positive may have a negative tuberculin test for 3 months after measles infection or MMR vaccine.

Scientific evidence shows no association between the MMR vaccine and autism or inflammatory bowel disease.

Dose and route of administration

The dose is 0.5 ml by deep intramuscular injection. The deltoid is the recommended site of administration. The anterolateral thigh may also be used.

Alcohol swabs are best avoided as alcohol can inactivate the MMR vaccine. If alcohol is used to clean the skin it must be allowed to evaporate completely before the injection is given.

When other injectable vaccines are being given concurrently with MMR, different sites should be used.

MMR may be given at the same time as DTaP, IPV, MenC, Hib and Hep B in situations where the latter are overdue.

Indications

1. All children at 12-15 months of age, with a second dose at 4-5 years of age. For older children who have not received 2 doses, MMR vaccine should be given as soon as possible, and a second dose one month later. Allowing 3 months between doses is likely to maximise the response rate in children aged under 18 months. Where protection against measles is urgently required the second dose can be given 1 month after the first. If children aged under 18 months are given the second dose less than 3 months after the first dose, they need a third dose to ensure full protection. This can be given at 4-5 years.
MMR vaccine can be given to those who have a history of measles, mumps or rubella infection.
2. Measles outbreaks
Outbreaks of measles should be controlled by immunising all susceptible individuals within 72 hours of contact, as vaccine-induced immunity develops more rapidly than natural antibody.
 - If these persons have had no previous measles vaccine, a second dose is given one month later.
 - During an outbreak, particularly if there are high attack rates in younger infants, MMR vaccine may be given to children as young as 6 months of age. However, maternal antibodies may compromise the response to the vaccine. Therefore children vaccinated before their first birthday should have a repeat vaccination at 12-15 months of age, at least 1 month after the first vaccine, with a further dose at 4-5 years of age.
 - Some persons may require HNIG (see below).
3. Children with chronic conditions such as cystic fibrosis, congenital heart or kidney disease, failure to thrive or Down syndrome are at particular risk of measles infection and should be immunised with MMR vaccine.
4. Children coming from low-income countries have probably received measles vaccine but not rubella or mumps vaccine. Therefore, unless there is a reliable history of vaccine administration, these children should be regarded as unimmunised, and given 2 doses of MMR one month apart.
5. Individuals born before 1978 are likely to have had measles infection. MMR vaccine should be offered to such individuals on request if they are considered at high risk of exposure.

6. Health-Care Workers (HCWs) in the following situations (see Chapter 18). Protection is important both for themselves and in the context of their ability to transmit measles to vulnerable groups.
 - Those who do not have evidence either of measles infection or of having received 2 doses of MMR vaccine should be given 2 doses of MMR, separated by at least 1 month.
 - If an outbreak occurs in an institution or an area served by an institution, HCWs should be given 1 dose of MMR.

Antibody response to the mumps and rubella components of the MMR vaccine **does not** develop quickly enough to provide effective prophylaxis after exposure to suspected mumps or rubella. Human normal immunoglobulin is not recommended for the post-exposure protection of pregnant women exposed to rubella. Human normal immunoglobulin is not routinely used as post-exposure protection from mumps.

Contraindications

1. Anaphylaxis following a previous dose of MMR or one of its constituents (e.g. Neomycin, Gelatin)
2. Significantly immunocompromised persons, such as those with untreated malignant disease and immunodeficiency states other than HIV infection, and those receiving immunosuppressive therapy, high-dose x-ray therapy and current high-dose systemic corticosteroids (see Chapter 2)
3. Pregnancy. Furthermore, pregnancy should be avoided for 1 month after MMR

There is no evidence to recommend or support the use of single vaccines against measles, mumps or rubella in place of the combination MMR vaccine.

The following are **NOT** contraindications to MMR vaccine

1. Allergy to egg, even anaphylaxis following egg. If there is a genuine concern regarding serious allergy, a paediatrician may be consulted and the vaccine given in hospital although this is not medically necessary. Currently-used measles and mumps vaccines do not contain significant amounts of egg cross-reacting proteins and recent data suggest that anaphylactic reactions to MMR are not associated with hypersensitivity to egg antigens but

- to other vaccine components (Gelatin or Neomycin)
- 2. Breast-feeding
- 3. HIV-positive patients who are not severely immunocompromised
- 4. Personal or family history of convulsions. Advice regarding the possibility and treatment of pyrexia should be given
- 5. Immunodeficiency in a family member or household contact
- 6. Uncertainty as to whether a person has had 2 previous MMR vaccines
- 7. If women have received anti-RhD immunoglobulin it is not necessary to defer rubella vaccination as the response to the vaccine is not affected

Precautions

- 1. Acute severe febrile illness, defer until recovery
- 2. Injection with another live vaccine within the previous 4 weeks
- 3. Recent administration of blood or blood products (see above)
- 4. Patients who developed thrombocytopenia within 6 weeks of their first dose of MMR should undergo serological testing to decide whether a second dose is necessary. The second dose is recommended if the patient is not fully immune to the 3 component viruses.

Adverse reactions

Soreness and erythema may occur at the injection site (3-8%). Fever (6%), rash (7%), headache, vomiting and salivary gland swelling may occur. A febrile convulsion occurs in 1 in 1,000 children.

'Mini-measles' may occur 6-10 days after immunisation and consists of mild pyrexia and an erythematous rash. 'Mini-mumps' with salivary gland swelling may rarely occur during the third week after immunisation. Very rarely, anaphylaxis, erythema multiforme, thrombocytopenia, and nerve deafness have been reported.

The rubella component may occasionally produce a rash, mild arthralgia, and lymph-node swelling 2-4 weeks post-vaccination, particularly in post-pubertal females (up to 25% of recipients). The incidence is lower than after natural disease.

There is no evidence of congenital rubella syndrome or increase in other teratogenic effects in women inadvertently given rubella vaccine before or during early pregnancy, but pregnancy remains a contraindication. Adverse reactions are considerably less common (under 1%) after a second dose of MMR.

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15

Tetanus

Introduced in 1930s (DT) and 1952/3 (DTP)

NOTIFIABLE

Introduction

Tetanus is an acute neurological disease characterised by muscular rigidity with superimposed contractions. It is caused by the neurotoxin produced by *Clostridium tetani* which grows anaerobically in a contaminated wound. Effective protection is provided in 90-95% of children who are fully vaccinated. Protection declines with time; up to 50% of 20-year-olds and up to 70% of 70-year-olds who have not received boosters may be unprotected.

Epidemiology

Tetanus spores are present in the soil, and in the gut and faeces of cattle, sheep, horses, chicken. In agricultural areas a significant number of adult humans may harbour the organism in their gut. The spores may be introduced into the body during injury, often through a puncture wound but also through burns or trivial wounds. Spores may also be found in contaminated heroin.

Worldwide, over 1 million cases occur each year. Between 1988 and 2004, 10 cases of tetanus were reported in Ireland with 2 deaths. Twenty cases occurred among injecting drug users in the UK in 2003-2004.

The incubation period is between 4 and 21 days, commonly around 10 days. The shorter the incubation period, the greater the likelihood of death. Spores germinate in anaerobic conditions, producing toxins that spread via blood and lymphatics. Tetanus is not transmissible from person to person. Those most at risk of developing tetanus are young children and people over 60, many of whom have never had active immunisation.

Effects of tetanus

Local tetanus is manifested by muscle spasms in areas contiguous to the wound. The spasms may continue for several weeks. Local tetanus may precede generalised tetanus but is usually much milder, about 1% of cases being fatal.

Generalised tetanus is the most common type of tetanus. It usually starts with spasms of the jaw and neck muscles, and proceeds distally. Spasms may be frequent, last for minutes, and persist for 3-4 weeks. Complete recovery may take months. Complications include laryngospasm, fractures of the long bones, secondary infections, aspiration pneumonia, and hypertension due to autonomic nervous system dysfunction. Pulmonary embolism is a problem in drug users and the elderly. Mortality rates in recent years are 10-90%, being highest in infants, the elderly, and those who are unvaccinated.

Tetanus vaccine

This is a toxoid, prepared by inactivating tetanus toxin with formaldehyde and adsorbing it onto aluminium. This acts as an adjuvant, to increase immunogenicity. *Bordetella Pertussis* also acts as an effective adjuvant.

Tetanus vaccine is not available as a single vaccine. The currently licensed tetanus vaccines are all combined vaccines. An up-to-date list of licensed vaccines is contained in Appendix 1, or can be accessed on the IMB website, www.imb.ie.

Toxoids should be stored at 2-8°C.

Dose and route of administration

The suspension may sediment during storage and should be shaken prior to administration. The dose is 0.5 ml, given by intramuscular injection into the anterolateral thigh or the deltoid area.

Indications

Immunisation of infants and children under 10 yrs

Primary immunisation

This consists of 3 doses at 2, 4 and 6 months of age.

Booster doses

A booster dose should be given at 4-5 years of age, as DTaP/IPV, ideally at least 3 years after the third primary dose. The booster dose of DTaP/IPV at 4-5 years should be given even though a child may already have

received 4 doses of these vaccines. The risk of Arthus reactions with currently-used vaccines is very small.

A second booster as is given between the ages of 11 and 14. The aim is that each child should be given a minimum of 5 doses of tetanus and diphtheria toxoids. Whenever possible at least 5 years should be left between the first and second boosters.

If the primary schedule has been delayed, the first booster may be given at age 4-5 years, at least 6 months after the third primary dose.

Td is now recommended as a replacement for tetanus-only boosters for those aged over 10 years. For immunised persons who have received 5 doses of tetanus toxoid, booster doses may be unnecessary as they may cause considerable local reactions.

If pertussis vaccine is refused by parents, the only available diphtheria and tetanus vaccines are Td and Td/IPV, which contain insufficient tetanus and diphtheria toxoid for primary immunisation. **They are not intended for use as part of the primary vaccine schedule, may not give a sufficient immune response if so used, and are not licensed for such use.**

Immunisation of persons aged 10 years or over (unimmunised or partly immunised)

Primary immunisation

This consists of 3 doses of tetanus toxoid with intervals of at least 1 month between doses.

Booster doses

A booster dose of tetanus toxoid should be given 5 years after the primary course and again 10 years later.

International travel

Td/IPV should be considered, as it may be difficult to obtain safe and effective booster doses in some countries.

HIV positivity

HIV-positive individuals can be immunised against tetanus unless they had anaphylaxis following a previous dose.

Adverse reactions

Local: Pain, redness, and swelling around the injection site can occur and persist for several days. These reactions are less likely when a 25 mm

needle is used, but are more common after the fourth and subsequent doses. Exaggerated local (Arthus-like) reactions occasionally occur. They begin 2-8 hours after vaccination and are more common in adults. They consist of extensive painful swelling which may involve the entire upper part of the arm. They almost always resolve completely.

General: Headache, malaise, myalgia and fever are uncommon. Rash and lymphadenopathy occasionally occur. Anaphylaxis is extremely rare.

Contraindications

Anaphylaxis to a previous dose of the vaccine or to one of its constituents.

Precautions

Acute severe febrile illness; defer until recovery.

Arthus-type reaction to a previous dose; further tetanus vaccine should be deferred for 10 years.

Prophylaxis for tetanus-prone wounds

The following wounds are considered tetanus-prone:

- Wounds contaminated with soil, faeces, saliva or foreign bodies
- Puncture wounds, avulsions, burns or crush injuries
- Wounds or burns requiring surgical treatment which is delayed for more than 6 hours
- Compound fractures

Note: Occasionally, apparently trivial injuries can result in tetanus.

Table 15.1 Risk assessment of wounds for use of tetanus immunoglobulin (TIG)⁽¹⁾

Age	Immunisation status	Clean wound	Tetanus prone wound
<4 years	<3 doses or unknown	DTaP/IPV+/- Hib ⁽²⁾	TIG, DTaP/IPV +/- Hib ⁽³⁾
	3 or more doses	Nil	Nil Consider TIG ⁽¹⁾
>4 to 9 years	<3 doses or unknown	DTaP/IPV	TIG plus DTaP/IPV
	3 doses only, >5 years since last dose	DTaP/IPV	DTaP/IPV Consider TIG ⁽¹⁾
	3 or more doses, <5 years since last tetanus toxoid	Nil	Nil Consider TIG ⁽¹⁾
	4 or more doses, >5 years since last dose	Nil	DTaP/IPV, consider TIG ⁽¹⁾
10 years and over	<3 doses or unknown	Td	TIG plus Td/IPV
	3 or more doses >10 years since last dose	Td	Td, consider TIG ⁽¹⁾
	3 or more doses, <10 years since last dose	Nil	Consider TIG ⁽¹⁾

(1) Consider TIG if wound contaminated with stable manure, or extensive devitalised tissue.
Give TIG if HIV positive, *irrespective of vaccine status*.

(2) If last tetanus containing vaccine <1 month previously, defer for 1 month.

(3) If child is >1 year, the follow-up vaccine(s) will be DTaP/IPV or DTaP/IPV/Hib (only one dose of Hib is required >1 year).

TIG

DTaP/IPV/Hib

Tetanus Immunoglobulin.

Diphtheria, Tetanus and acellular Pertussis vaccine/Inactivated Polio

Chapter 15 Tetanus

DTaP/IPV	Virus vaccine/ <i>Haemophilus influenzae</i> b vaccine Diphtheria, Tetanus and acellular Pertussis vaccine/Inactivated Polio Virus vaccine
Td/IPV	Tetanus, low-dose diphtheria/ Inactivated Polio Virus vaccine
Tdap	Tetanus, low-dose diphtheria and low-dose acellular pertussis vaccine

IMPORTANT:

If both TIG plus a vaccine are to be given, administer at separate sites.

Refer to GP for follow-up vaccines.

Batch numbers and expiry dates must be recorded for all vaccines given.

This information **MUST** be communicated to the patient's GP so that:

- Duplication of vaccination does not occur.
- Full records may be passed onto the relevant agencies in order that a full nationwide database is kept of batch numbers and expiry dates of vaccines given to children.

Specific anti-tetanus immunoglobulin

Indications

- 1 Those with tetanus-prone wounds who have not received at least 3 doses of tetanus toxoid and their last dose within 10 years (see Table 15.1 above)
- 2 Patients with impaired immunity (see Chapter 2) who suffer a tetanus-prone wound – may in addition require anti-tetanus immunoglobulin
- 3 Patients who have suffered a high-risk wound, regardless of vaccine history

Dose and route of administration

Prevention

250 IU intramuscularly into the anterolateral thigh.

The single dose of TIG is doubled to 500 IU (2ml) when any of the following situations exist:

- The injury occurred more than 24 hours previously.
- The patient weighs more than 90 kg.
- The wound is heavily contaminated.
- The wound is infected or involves a fracture.

Treatment

150 IU/kg given in multiple sites. Specific anti-tetanus immunoglobulin is available in 1 ml ampoules containing 250 IU.

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16

Tuberculosis

BCG introduced in 1950s

NOTIFIABLE

Introduction

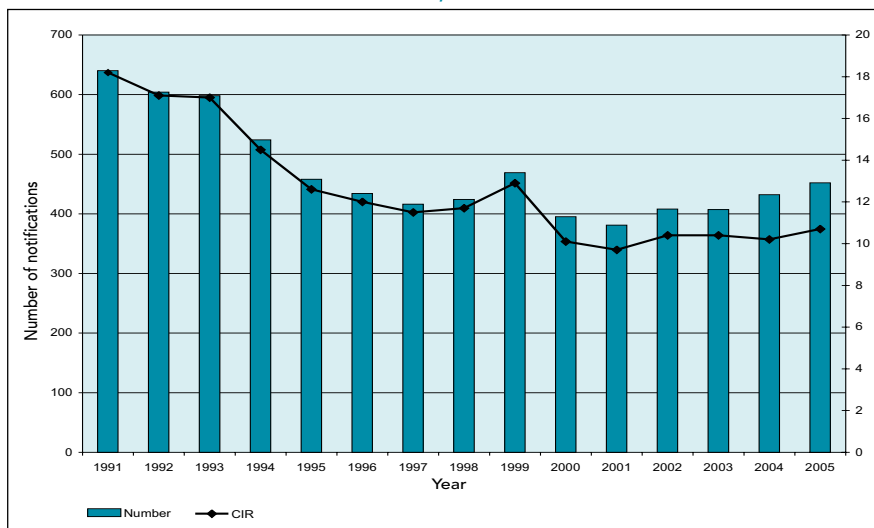
Human tuberculosis is caused by infection with bacteria of the *Mycobacterium tuberculosis* complex (*M. tuberculosis*, *M. bovis*, *M. africanum*, *M. microti* or *M. canettii*, *M. caprae*, *M. pinnipedii*). The organism may infect any part of the body. However, the majority of cases involve the respiratory system.

The World Health Organization (WHO) declared TB a global health emergency in 1993. In 2006 WHO launched the Global Plan to Stop TB 2006-2015 in collaboration with public and private partners. This plan is a comprehensive assessment of the action and resources needed for implementation and to make an impact on the global TB burden. It aims at global elimination of TB by 2050.

Epidemiology

The incidence of tuberculosis in Ireland has declined from a recorded rate of 230 cases per 100,000 in 1952 to a rate of 10.6 per 100,000 in 2005. The number of notified cases declined each year from 1991 to 1997 but increased in 1998 and 1999. The number of cases fell to 9.7 per 100,000 in 2001 with a total of 450 cases. Since 2001 the rate has slowly increased to the current rate of 10.6 per 100,000 (432 cases). Multidrug-resistant (MDR) isolates remain very uncommon, with 1-3 reported per year. Extensively drug-resistant (XDR) isolates remain very uncommon worldwide, with only 1 case reported in Ireland in 2005.

Figure 16.1 Number and crude incidence rates (per 100,000 total population) of tuberculosis notifications in Ireland, 1991-2005. Source: HPSC



Transmission

The infection is usually acquired by the respiratory route through breathing in infected droplets from a person with infectious pulmonary TB. Such transmission is more likely when the index case has sputum, which is smear positive for the bacteria on microscopy, and often occurs after prolonged close contact such as living in the same household as the case.

Effects of tuberculosis

A notified case of tuberculosis refers to clinically active disease due to infection with *M. tuberculosis* complex. Tuberculosis disease is classified as pulmonary, extrapulmonary or both. In Ireland, approximately 70% of all TB cases are pulmonary cases. Non-respiratory forms of TB are more common in those with impaired immunity.

The symptoms of TB are varied and depend on the site of infection. General symptoms may include fever, lassitude, loss of appetite, weight loss and night sweats. Pulmonary TB typically causes a persistent productive cough, which may be accompanied by blood-streaked sputum or more rarely frank haemoptysis.

The initial TB infection may be eliminated or remain latent or progress to active TB disease. Latent TB infection (LTBI) occurs where a person

has no symptoms and no evidence of TB disease but the TB bacteria remain in the body. LTBI may reactivate in later life in approximately 5% of persons particularly if an individual's immune system becomes weakened, e.g. by disease (HIV), due to certain medical treatments such as cancer chemotherapy, corticosteroids, TNF- α antagonists, or in old age. Currently a diagnosis of LTBI is most commonly based on a positive tuberculin skin test (Mantoux test). Interferon gamma release assays (IGRA) may be used (where they are available) as an adjunct to the tuberculin skin test in the diagnosis of LTBI.¹

BCG vaccine

Bacille Calmette Guerin (BCG) vaccine contains a live attenuated strain derived from *Mycobacterium bovis*. BCG Vaccine Statens Serum Institut (SSI) is the only available licensed BCG vaccine in Ireland. It contains the Danish strain 1331. It does not contain thiomersal or any other preservatives.

The efficacy of BCG in preventing tuberculosis has varied in reported studies over the years, but is probably most consistently effective against tuberculous meningitis and miliary TB, with protection lasting approximately 15 years. Two meta-analyses of published clinical trials and case control studies have shown the vaccine to be 70-80% effective against the most severe forms of disease such as TB meningitis in children. International and Irish studies have also indicated a protective efficacy of the vaccine against childhood tuberculosis.

BCG is less effective in preventing respiratory disease, which is the more common form in adults and more important for the transmission of the disease. There are few data on the protection afforded by BCG vaccine when it is given to adults (aged 16 years and older) and virtually no data for persons aged over 35 years.

BCG is not usually recommended for people over 16 years of age unless the risk of exposure is great, e.g. new entrants from areas where the annual rates of tuberculosis are high and those at occupational risk, in which case it is given up to and including age 35 years, except in the case of health-care workers when it is given at any age.

Indications for BCG vaccine continue to be re-evaluated by the National

¹ Interferon Gamma Release Assays (IGRA) are new whole blood tests for screening for latent TB infection (LTBI) and active TB disease. These tests measure the release of interferon-gamma from white blood cells in response to stimulation by the tuberculin antigens ESAT-6 and CFP-10 which are not present in BCG or the vast majority of non-TB mycobacteria. They aim to be more specific by removing false positive results and to be better correlated with LTBI.

TB Advisory Committee. At present it is recommended that universal neonatal BCG be continued.

Dose and route of administration

BCG vaccine may be given concurrently with another live vaccine, but if it is not given at the same time an interval of at least 4 weeks should be allowed between such vaccines. It can also be given at the same time as killed vaccines, e.g. DTaP/IPV/Hib or MenC. When BCG is given to infants there is no need to delay the primary immunisations. No further immunisation should be given in the arm used for BCG immunisation for at least 3 months because of the risk of regional lymphadenitis.

Infants under 12 months of age

The recommended dose is 0.05 ml, by **intra**dermal injection of the reconstituted vaccine at one site over the middle of the deltoid muscle.

Adults and children 12 months and over

The recommended dose is 0.1 ml, by **intra**dermal injection, of the reconstituted vaccine and given at one site over the middle of the deltoid muscle.

Although the protection afforded by BCG vaccine may wane with time, there is no evidence that repeat vaccination offers significant protection and repeat BCG is not recommended. If re-immunisation with BCG is being considered expert advice should be sought.

Indications

The vaccine is indicated for prophylactic immunisation in Mantoux (or interferon-gamma) negative individuals.

Groups in whom BCG vaccine is indicated

- a. Newborn babies
- b. Unvaccinated children aged 1-15 years (i.e. those with no documented evidence of BCG or without a characteristic scar)
 - Children aged 3 months to less than 6 years who are not in an at-risk environment² do not need a Mantoux test prior to receiving BCG vaccine
 - Children in at-risk environments should have a Mantoux test prior to BCG
- c. Unvaccinated Mantoux negative immigrants with a history of ever living in a high incidence country (Appendix 2) and their children who are previously unvaccinated (that is without adequate

² Children in at-risk environments include those who are contacts of a pulmonary TB case, who are from an area of high endemicity or whose parents are from an area of high endemicity.

- documentation or a characteristic scar) and aged younger than 16 years OR aged 16-35 years who ever lived in a sub-Saharan African country or country with a TB incidence of 500 per 100,000
- d. Unvaccinated Mantoux negative contacts aged 35 years and under, of cases with active respiratory tuberculosis. Children under 5 years of age in contact with smear positive tuberculosis should be referred to a contact tracing clinic for investigation and then immunised with BCG as indicated
 - e. Members of special at-risk groups such as the Traveller community – due to the logistical difficulties of providing alternative control measures and follow-up of contacts
 - f. Unvaccinated Mantoux negative persons under 16 years of age intending to live with local people in high-incidence countries for more than 1 month (Appendix 2)
 - g. All health-care workers who are previously unvaccinated (i.e. without adequate documentation or a characteristic scar) and will have contact with patients or clinical materials and are Mantoux (or interferon-gamma, if available) negative should be offered BCG vaccination irrespective of age. Health-care workers include the following:
 - Those who will have contact with patients or clinical materials
 - Laboratory staff who will have contact with patients, clinical materials or derived isolates
 - h. Those more likely than the general population to come into contact with someone with infectious sputum positive TB. Unvaccinated Mantoux negative persons aged 35 years and under in the following occupations should be offered BCG vaccination.
 - Veterinary laboratory staff who handle animal species known to be susceptible to TB and abattoir workers who handle animal species, carcasses and products known to be susceptible to tuberculosis. Agricultural officers and veterinary inspectors may require BCG vaccination based on individual risk assessment
 - Prison staff working directly with prisoners.
 - Staff of facilities for the elderly
 - Staff of hostels for homeless people and facilities accommodating refugees and asylum seekers.

Contraindications

BCG vaccine should not be given to:

- 1 Neonates in a household where an active TB case is suspected or confirmed
- 2 Those receiving systemic corticosteroid therapy (other than as replacement) or other immunosuppressive treatment including x-irradiation. Inhaled steroids are not a contraindication

- 3 Those suffering from blood dyscrasias, lymphoma, or malignant neoplasms involving bone marrow or the lymphoreticular system, or with gamma globulin deficiency or abnormality
- 4 Those with a family history of primary immunodeficiency, e.g. inherited severe combined immunodeficiency (SCID), Chronic Granulomatous Disease (CGD) etc. until evaluation is complete
- 5 Those with pyrexia $\geq 38^{\circ}\text{C}$
- 6 Those with generalised infected dermatosis. The effect of BCG vaccine may be exaggerated in these patients, and a more generalised infection is possible. If the person has eczema, an immunisation site should be chosen that is free from skin lesions. Eczema is not a contraindication
- 7 Those who are pregnant. Breast feeding does not constitute a contraindication to BCG vaccine
- 8 Those with positive tuberculin tests (or gamma interferon tests)
- 9 Those who have had a confirmed anaphylactic reaction to a component of the vaccine.

HIV

BCG should not be given to children known to be HIV positive. However lack of knowledge of maternal HIV status is not a reason to defer routine BCG inoculation in healthy newborns.

Adverse reactions

Local: Side-effects include local induration, pain and occasionally ulceration, enlargement of a regional lymph node greater than 1 cm, abscess formation, lupoid reaction and inflammatory and suppurative adenitis.³

General: Headache, fever, and generalised lymphadenopathy can occur on rare occasions (in less than one in 1,500 vaccinated). Anaphylactic reaction and disseminated BCG complications (such as osteitis, osteomyelitis or disseminated BCG infection) are also very rare. Disseminated BCG infection occurs in approximately 2 per 1 million persons.

Interactions

Administration of blood or plasma transfusions, hepatitis B vaccine, hepatitis B immunoglobulin and normal immunoglobulin are thought not to reduce the effectiveness of BCG vaccine. A baby who has received

³ In extremely rare instances, an accelerated local response to BCG vaccine known as Koch's Phenomenon characterised by induration that is more than 5 mm (within 24-48 hours), early pustule formation (within 3 to 5 days), an ulcer (at day 7) and a scab (within 10-15 days) can occur and indicates concurrent TB.

blood or plasma transfusions can be subsequently immunised with BCG, after the observation period for transfusion reactions has ended (24 hours). A baby who has received hepatitis B vaccine, hepatitis B immunoglobulin or normal human immunoglobulin can be subsequently immunised with BCG without delay.

Administration of BCG vaccination

Detailed instructions including illustrations are available in Chapter 2.

Note: In all cases, BCG must be administered strictly intradermally.

Immunisation reaction and care of the immunisation site

The expected reaction to a successful BCG vaccination seen in 90-95% of recipients is induration at the injection site followed by a local lesion, which starts as a papule 2 or more weeks after vaccination. It may ulcerate and then slowly subside over several weeks or months to heal leaving a small flat scar. It may also include enlargement of a regional lymph node to less than 1 cm.

It is not necessary to protect the site from becoming wet during washing and bathing. The ulcer should be encouraged to dry and abrasion (for example by tight clothes) avoided. Should any oozing occur a temporary dry dressing may be used until a scab forms. It is essential that air is not excluded. If absolutely necessary (e.g. to allow swimming), an impervious dressing may be applied but only for a short period as it may delay healing and cause a larger scar.

Further observation after routine vaccination with BCG is not necessary, other than as part of monitoring of the quality of the programme, nor is further tuberculin testing recommended.

Severe injection site reactions, large discharging ulcers, abscesses and keloid scarring are most commonly caused by faulty injection technique, excessive dosage or vaccinating individuals who are tuberculin positive. It is essential that all health-care professionals be properly trained in all aspects of the process involved in tuberculin skin tests and BCG vaccination.

Management of adverse reactions

Local adverse reactions to BCG vaccine occur in 1-2% of immunisations. Severe local reactions (ulceration greater than 10 mm, caseous lesions, abscesses or drainage at the injection site) or regional suppurative lymphadenitis with draining sinuses following BCG vaccination should be discussed with a respiratory physician or paediatrician.

Most experts do not recommend treatment of draining skin lesions or chronic suppurative lymphadenitis caused by BCG vaccine because spontaneous resolution occurs in most cases. Large needle aspiration of suppurative lymph nodes may hasten resolution. There is little evidence to support the use of either locally instilled anti-mycobacterial agents or systemic treatment of patients with severe persistent lesions.

Disseminated BCG infection should be referred to a respiratory or infectious disease consultant for specialist advice and will normally require systemic anti-tuberculous treatment and mandate a detailed immunological investigation.

Tuberculin testing prior to BCG immunisation

BCG should not be administered to an individual with a positive tuberculin test. It is unnecessary and may cause a more severe local reaction. Those with strongly positive tests should be referred to a respiratory physician for assessment of the need for further investigation and treatment.

A tuberculin skin test (Mantoux test) is necessary prior to BCG vaccination for:

- Children aged 3 months to under 6 years in at-risk environments²
- Persons aged 6 years and older
- Infants and children under 6 years of age with a history of ever having lived or had a prolonged stay (more than 1 month) in a country of high endemicity (Appendix 2)
- Those who have had close contact with a person with known TB
- When there is a history of TB in a household contact in the last 5 years.

BCG can be given up to 3 months following a negative tuberculin test.

The Mantoux test is used as a screening tool for tuberculosis infection or disease and as an aid to diagnosis. The local skin reaction to tuberculin purified protein derivative (PPD) injected into the skin is used to assess an individual's sensitivity to the tuberculin protein. The greater the reaction, the more likely it is that an individual is infected or has active TB disease. The standard test for use in Ireland is the Mantoux 2TU/0.1 ml tuberculin PPD.

² Children in at-risk environments include those who are contacts of a pulmonary TB case, who are from an area of high endemicity or whose parents are from an area of high endemicity.

Administration of the Mantoux test

Detailed instructions are available in Chapter 2.

Care should be taken to store PPD Mantoux tests and BCG vaccine in separate areas of the fridge to ensure that the correct product is administered (see section on cold chain for storage of PPD and BCG).

Mantoux testing can be undertaken at the same time as inactivated vaccines are administered. Live viral vaccines can suppress the tuberculin response and so testing should not be undertaken within 4 weeks of having received a live viral vaccine such as MMR.

Reading the Mantoux test

The results should be read within 48-72 hours of receiving the test but a valid reading can usually be obtained up to 96 hours later. The transverse diameter of the area of induration but not the erythema at the injection site is measured with a ruler and the result recorded using millimetres. As several factors affect interpretation of the test, the size of the induration should be recorded and NOT just as a positive or negative result, see Table 16.1.

There is some variability in the time at which the test develops its maximum response. The majority of tuberculin sensitive subjects will be positive at the recommended time of reading.

Note:

- A delay in reading the Mantoux test if the result is positive i.e. ≥ 6 mm does not affect the validity of the results.
- A strongly positive Mantoux test resulting from inadvertent subcutaneous administration does not affect the validity of the reading.

Table 16.1 Interpretation of the Mantoux test

Diameter of induration	Interpretation	Action
Less than 6 mm	Negative	Previously unvaccinated individuals may be given BCG provided there are no contraindications
6 mm or greater but less than 15 mm	Hypersensitive to tuberculin protein. May be due to previous TB infection, BCG or exposure to atypical mycobacteria	Should not be given BCG*
≥15 mm	Strongly hypersensitive to tuberculin protein Suggestive of TB infection or disease	Refer for further investigation and supervision which may include preventive chemotherapy

* When Mantoux tests are being performed as part of an immunisation programme, no further action is required for people with a reaction in this range (6-<15 mm). In other contexts (e.g. new immigrant screening, contact tracing programmes) where the subject has not been previously vaccinated with BCG and taking account of the precise size of the reaction and the circumstances of the case, referral to a respiratory physician may be indicated for further investigation.

Factors affecting the result of the tuberculin test

The reaction to tuberculin protein may be suppressed by the following:

- 1 Infectious mononucleosis
- 2 Viral infections in general including upper respiratory tract infections
- 3 Live viral vaccines (tuberculin testing should not be undertaken within 4 weeks of having received a live viral vaccine)
- 4 Sarcoidosis
- 5 Corticosteroid therapy
- 6 Immunosuppression due to disease or treatment including HIV infection

Subjects who have a negative test but who may have had an upper respiratory tract or other viral infection at the time of testing or at the time of reading the test should be re-tested 2-3 weeks after clinical recovery before being given BCG. This second test should be done on the other arm; repeat testing at one site may alter the reactivity either by hypo- or more often hyper-sensitising the skin and a changed response may only reflect local changes in skin sensitivity.

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Chapter 16 Tuberculosis

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17

Varicella-Zoster

OUTBREAK NOTIFIABLE

Introduction

Infection with the varicella-zoster virus (VZV) causes two distinct clinical syndromes, chickenpox and shingles (zoster). Primary infection results in varicella, an acute exanthematous disease of childhood. The virus becomes latent in the cells of the dorsal root or cranial nerve ganglia and may reactivate after a latent period, which may be several decades. Reactivation results in the clinical syndrome of zoster.

Epidemiology

In Ireland, the incidence of varicella is seasonal, reaching a peak from January to April. The incubation period is from 14 to 16 days (range 10-21). This may be prolonged up to 28 days in immunocompromised patients and in individuals who have received specific varicella-zoster immunoglobulin (VZIG). VZV enters through the respiratory tract and conjunctiva. Transmission is by inhalation of respiratory droplets, by direct contact with vesicular fluid, or less commonly by contact with fomites. In Ireland ICGP/HPSC sentinel data from 2000-2005 demonstrated that 54% of chicken pox cases occur in children under 5 years of age while 17% of cases occur over age 15 years.

Cases of chickenpox are highly infectious from 2 days before the appearance of the rash until all of the lesions have crusted, typically a total of 7 days. This period may be prolonged in immunosuppressed individuals. In the family setting the secondary attack rate ranges from 60-90% for susceptible hosts.

Zoster is transmissible to non-immune contacts as chickenpox, but is less infectious than chickenpox. Transmission is by direct or indirect contact including inhalation from non-intact vesicles. The period of infectivity,

typically 5 days, is from the appearance of the lesions until all lesions have crusted. In some clinical circumstances, the viral load and/or viral shedding may be increased with increased risk of transmission. Examples are disseminated zoster, exposed lesions (e.g. ophthalmic zoster) or immunosuppressed patients with localised zoster on any part of the body. In the Irish ICGP/HPSC sentinel data 60% of zoster cases occurred in those over 45 years of age, and 9% in those aged under 15 years.

Effects of varicella

Varicella is typically a benign infection of childhood characterised by a generalised, pruritic vesicular rash. Complications of varicella are uncommon in childhood and include superinfection usually with the Group A streptococcus, skin scarring, encephalitis, pneumonia, hepatitis and coagulopathy. The risk of complications varies with age and is higher in infants under 1 year and in persons over 15 years of age. In the USA, the fatality rate of varicella is approximately 1 per 100,000 cases among children aged 1-14 years; this increases to 25.2 per 100,000 cases in adults aged 30-49 years.

Maternal infection in pregnancy carries a greater risk of severe varicella pneumonia in the mother especially late in the second trimester and early in the third trimester.

Risks to the foetus and neonate are related to the time of infection in the mother.

In the first 20 weeks of pregnancy maternal infection can result in the congenital (foetal) varicella syndrome, which includes limb hypoplasia, microcephaly, cataracts, growth retardation and skin scarring. The mortality rate is high. The incidence has been estimated to be less than 1% in the first 12 weeks and around 2% between 13 and 20 weeks of pregnancy. A prospective study published in 1994 found no cases of congenital varicella syndrome among the 477 pregnancies in which maternal varicella occurred after 20 weeks gestation.

In the second or third trimester of pregnancy, infection can cause herpes zoster in an otherwise healthy infant. Occasional case reports of foetal damage comprising chorioretinal damage, microcephaly and skin scarring following maternal varicella between 20 and 28 weeks gestation have been published. The risk is likely to be substantially lower than that of the typical congenital varicella syndrome that occurs after maternal varicella in the first 20 weeks' gestation.

In contrast, **maternal infection in the period from 5 days before to 2 days after delivery is associated with a significant risk of severe neonatal infection, with visceral dissemination or haemorrhagic varicella.**

Other groups at increased risk of severe complications or disseminated infection include immunocompromised patients, especially those who have leukaemia or other disorders in which there is depressed cell-mediated immunity, and transplant recipients.

Effects of zoster

Zoster is usually a unilateral vesicular eruption in the distribution of a single dermatome. Severe pain in the affected area and/or parasthesia is common and may occur prior to the onset of the rash. Post-herpetic neuralgia may be severe and is more common in the elderly. Zoster is typically found in conditions in which cell-mediated immunity is suppressed such as immunosuppressive therapy or HIV infection. Zoster is rare in childhood but can follow intrauterine exposure, congenital or neonatal varicella. Zoster is transmissible to susceptible individuals as chickenpox. There is no evidence that maternal zoster poses a risk to the foetus or neonate.

Passive immunisation: Varicella-zoster immunoglobulin (VZIG)

An intravenous preparation of varicella-zoster immunoglobulin (VZIG) has product authorisation in Ireland.

This product is prepared from pooled plasma of donors with a history of recent chickenpox or herpes zoster, or from those who on screening are found to have high titres of V-Z antibody. It contains specific antibodies (mainly IgG) against varicella-zoster virus. It must be stored at 2-8°C and protected from light. The solution should be used immediately when ampoules or bottles have been opened and any unused solution discarded.

VZIG should ideally be given within 96 hours of exposure. It does not always prevent infection. However, it will typically attenuate the illness. Severe varicella may still occur despite VZIG prophylaxis in high-risk groups including immunosuppressed individuals, adults and neonates.

Indications

Recommendations for VZIG prophylaxis

VZIG prophylaxis is recommended for individuals who fulfil all of the following three criteria:

a Significant exposure (see below) to:

(i) Chickenpox

or

(ii) Disseminated zoster or extensive exposed lesions in immunocompetent individuals

or

(iii) Localised or disseminated zoster in immunosuppressed patients.

PLUS

b A clinical condition which increases the risk of severe varicella (see below).

PLUS

c No antibodies to varicella-zoster virus (see below).

a. Explanation of significant exposure

As a guideline, significant exposure includes the following:

- Household contact
- Contact in the same room* for a significant period of time (usually 1 hour or more)
- Face-to-face contact such as when having a conversation (usually 5 minutes or more)

*An example of 'same room' is a classroom or 2-4 bedded hospital bay. This does not usually include a large hospital ward. However, because airborne transmission at a distance has occasionally been reported in large open wards, in this instance the necessity of giving VZIG to all susceptible high-risk contacts should be considered on a case-to-case basis, particularly in paediatric wards where the degree of contact may be difficult to define.

VZIG should normally be restricted to patients exposed to a case of chickenpox or disseminated zoster between 48 hours before onset of rash until crusting of lesions. In the case of exposure to localised open zoster (e.g. ophthalmic zoster) the relevant time period for exposure is day of onset of rash until crusting of lesions.

Zoster in an unexposed localised site (e.g. thoracolumbar area) in an

immunocompetent patient has a low risk of transmission and contacts do not require VZIG therapy.

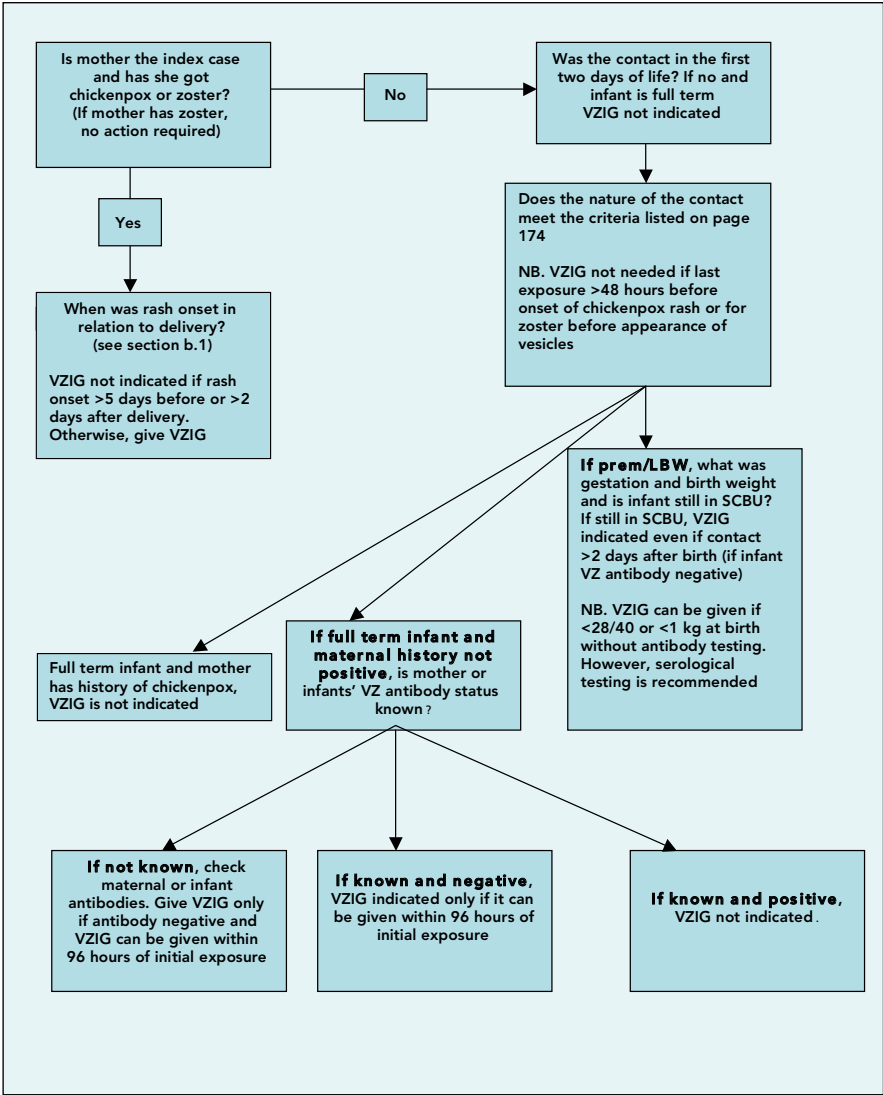
b. Description of clinical conditions that increase the risk of severe varicella

(1) Neonates

Infants whose mothers develop chickenpox (but not zoster) from 5 days before to 2 days after delivery should receive VZIG. Approximately half of these infants may develop varicella despite immunoprophylaxis, but the disease is usually modified. All infants in this group should be carefully monitored; hospitalisation and i.v. acyclovir treatment may occasionally be required.

- VZIG is not recommended for full-term healthy infants exposed post-natally to varicella, including infants of mothers who develop varicella more than 48 hours after delivery
- In the event of significant exposure in a neonatal intensive care unit (NICU), or special care baby unit (SCBU), VZIG is recommended for infants of non-immune mothers. Infants born before 28 weeks or whose birth weight is less than 1,000 g may not possess VZ antibody despite a positive maternal history or titre and should receive VZIG in the event of significant exposure.

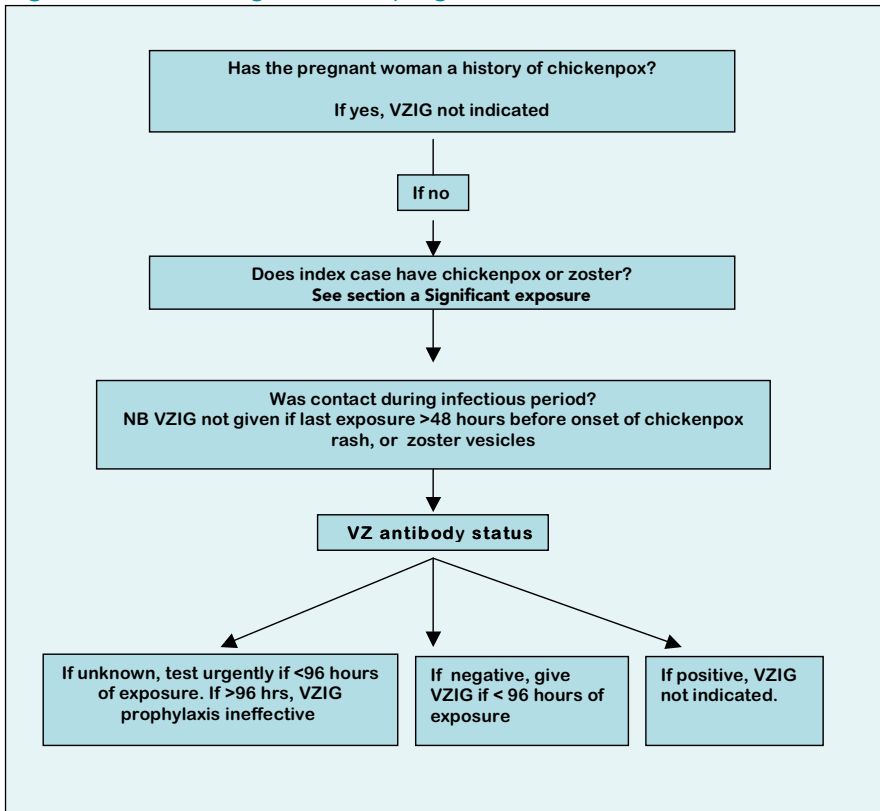
Figure 17.1 VZIG algorithm for neonates



(2) Pregnant women

It is generally recommended that non-immune women who have been significantly exposed to varicella at any stage of pregnancy should be offered VZIG as soon as possible and within 96 hours of the contact. The primary aim of VZIG immunoprophylaxis is to modify the illness in the mother, but severe maternal varicella may still occur despite prophylaxis. There is little evidence that VZIG will prevent the congenital varicella syndrome following significant exposure of a non-immune mother in the first 20 weeks. Management of varicella in pregnancy should be discussed urgently with an obstetrician/microbiologist/ID consultant and consideration given to the use of acyclovir.

Figure 17.2 VZIG algorithm for pregnant women



(3) Immunosuppressed patients

Immunosuppressed patients in whom VZIG is recommended include:

- Patients being treated with chemotherapy or generalised radiotherapy, or within 6 months of completing such treatments
- Patients who have received an organ transplant and are currently receiving immunosuppressive treatment
- Patients who have received a bone marrow transplant until at least 12 months after finishing all immunosuppressive treatment, or longer where the patient has developed graft-versus-host disease. Further advice can be found in current guidance produced by the European Group for Blood and Marrow Transplantation (www.ebmt.org)
- Children who within the previous 3 months have received prednisolone, orally or rectally, at a daily dose (or its equivalent) of 2 mg/kg/day for at least one week, or 1 mg/kg/day for one month. For adults, an equivalent dose is harder to define but immunosuppression may be present in those who have received a dose of around 40 mg prednisolone per day for more than one week in the previous 3 months
- Patients on lower doses of steroids, given in combination with cytotoxic drugs
- Patients with evidence of impaired cell mediated immunity, e.g. severe primary immunodeficiency or those with symptomatic HIV infection. There is no evidence of any increased risk of severe varicella in asymptomatic HIV-positive individuals with normal CD4 counts; hence VZIG is not indicated in this group
- Patients with immunoglobulin deficiencies who are receiving replacement therapy with intravenous normal immunoglobulin do not require VZIG.

c. **Description of conditions where there are no antibodies to varicella-zoster virus**

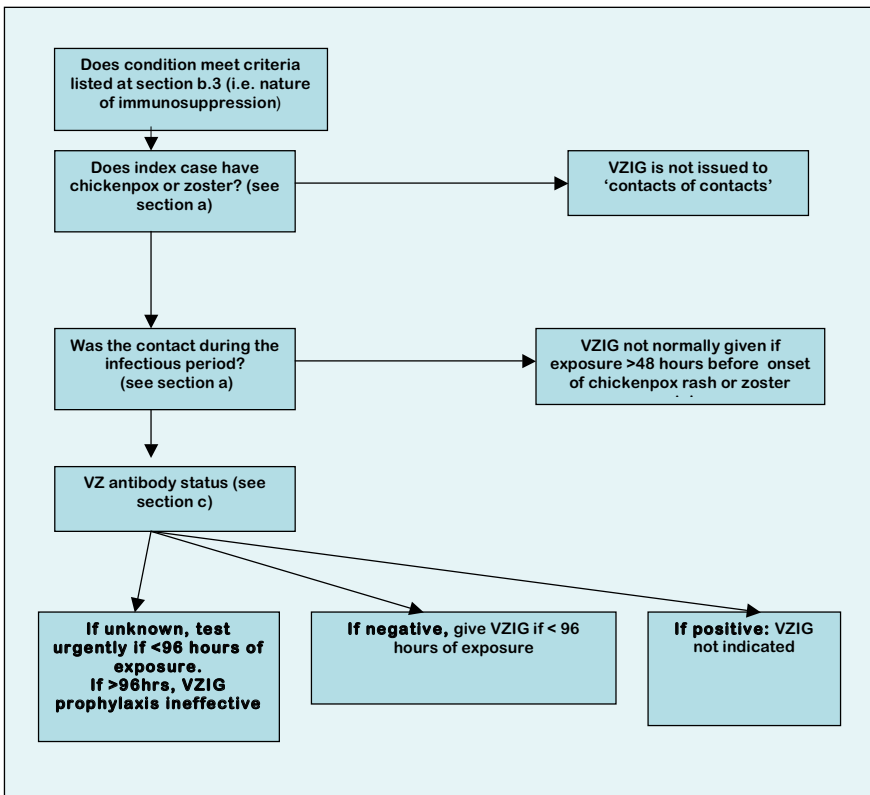
Normal immunocompetent contacts with a definite history of chickenpox are immune; serology or immunoprophylaxis are not necessary and they can be reassured.

The majority of adults and a substantial proportion of children without a definite history of chickenpox are VZ antibody positive. In all individuals without a definite history or of unknown status who are being considered for VZIG, a serum sample should be tested for VZ antibody; only those without antibody require immunoprophylaxis. However, immunosuppressed contacts should be tested for VZ antibody regardless of history of chickenpox. When antibody is not detected, VZIG is indicated. To arrange urgent testing for VZ antibody local laboratories

should be contacted. Testing will rarely be required outside normal working hours.

VZ antibody detected in patients who have been transfused, or who have received intravenous immunoglobulin in the previous 3 months, may have been passively acquired. Although VZIG is not indicated if antibody from other blood products is detectable, re-testing in the event of a subsequent exposure is required, as the patient may have become antibody negative.

Figure 17.3 VZIG algorithm for immunocompromised patients exposed to varicella



Dose of VZIG for prophylaxis

VZIG is administered by intravenous infusion and is most effective when given within 96 hours of exposure. The dose is 25IU(1 ml) per kg, at a rate of 1 ml per minute. The solution must be inspected for particulate matter and discolouration prior to administration; cloudy or discoloured solutions or those that have deposits must not be used.

Adverse reactions to VZIG

Nausea, chills, fever, headache, vomiting, allergic reactions, arthralgia and mild back pain may occasionally occur. The efficacy of live attenuated virus vaccines may be impaired for at least 6 weeks and possibly up to 3 months.

Active immunisation: Varicella Vaccine

Varicella zoster vaccine is a live attenuated viral vaccine, derived from the Oka strain of VZV.

Indications

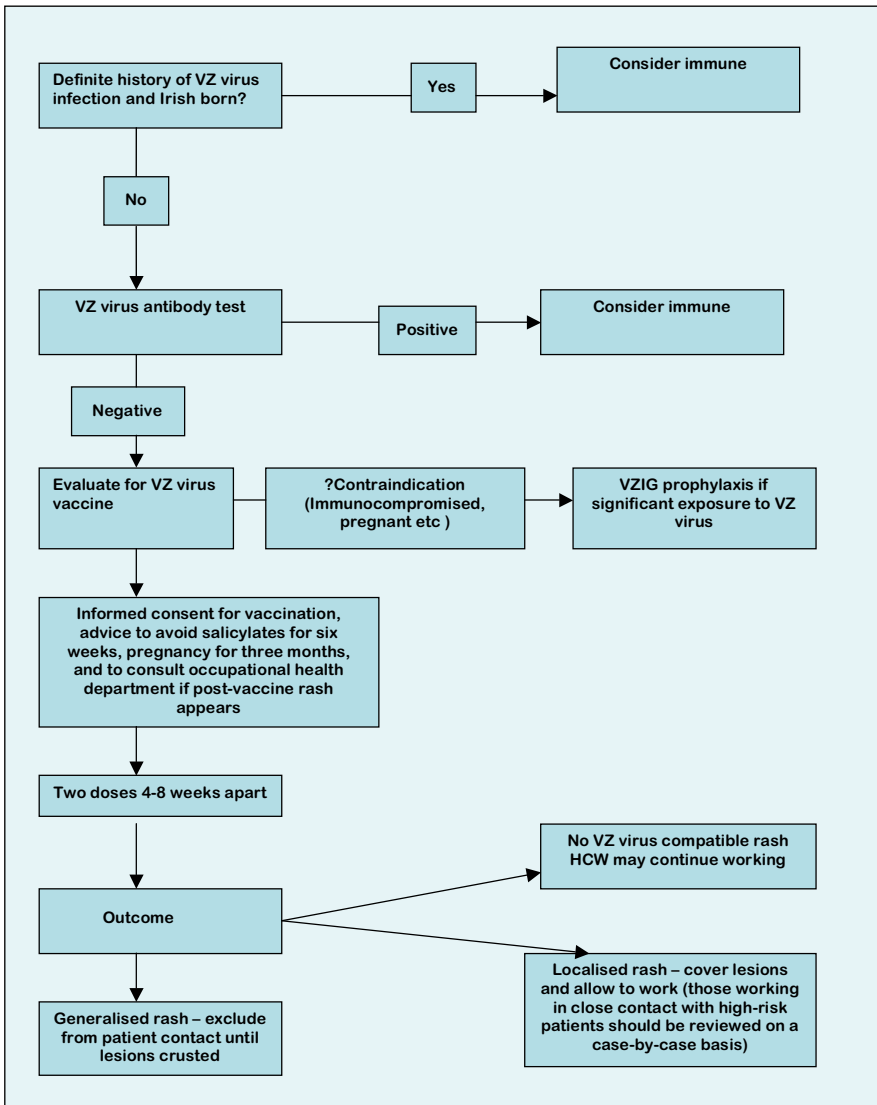
Recommendations for use of the vaccine

Two doses at least 4 weeks apart are required in both children and adults in the following risk groups:

- Non-immune health-care workers. HCWs without a definite history of chickenpox, proof of immunity or vaccination status, particularly those working with haematology, oncology, obstetrical, general paediatric or neonatal patients should be routinely screened for VZ antibody. A history of chickenpox is a less reliable predictor of immunity in individuals born and raised overseas, and therefore routine testing should be considered in this group of HCWs. In addition, HCWs from outside Ireland and Western Europe are less likely to be immune. Vaccination should be offered to non-immune staff. Testing for varicella immunity following 2 doses of vaccine is not recommended because 99% of persons have adequate response following the second dose
- Laboratory staff who may be exposed to varicella virus in the course of their work
- Healthy susceptible close household contacts of immunocompromised patients
- Children with asymptomatic or mildly symptomatic HIV infection with age specific CD4+ T-lymphocyte percentage more than 25% should be considered for varicella vaccination. Two doses with a 3-month interval are required
- Under specialist hospital supervision and protocols certain categories of immunocompromised patients may be vaccinated, e.g. cases of lymphocytic leukaemia in remission and organ transplant recipients
- Children in residential units for severe physical disability
- All women of childbearing age without a history of varicella infection should have their immunity checked. Women with negative serology should be vaccinated prior to pregnancy, if

no contraindications exist. Pregnancy should be avoided for 3 months following the last dose of varicella vaccine. Alternatively, on completion of their pregnancy women who do not have evidence of varicella immunity should receive the first dose of varicella vaccine before discharge from the health-care facility. The second dose should be administered 4-8 weeks later.

Figure 17.4 Procedure for vaccinating health-care workers



Contraindications

- Anaphylactic reaction to a preceding dose or any of the constituents including neomycin or gelatin.
- Immunosuppression due to leukaemia, lymphoma, generalised malignancy, immunodeficiency disease or immunosuppressive therapy should not be vaccinated (see above for exceptions under hospital supervision).
- Pregnancy. Pregnancy should be avoided for 3 months following the last dose of varicella vaccine. Inadvertent vaccination during pregnancy should be reported to the immunisation division in HPSC where surveillance of these events is being established.

Precautions

- Recent (less than 11 months) receipt of antibody containing blood product (specific interval depends on product See Chapter 1).
- Acute severe febrile illness, defer until recovery.
- Vaccine recipients should avoid salicylates for 6 weeks after vaccination (because of the association between aspirin use and Reye syndrome following chickenpox although this has not been reported following the vaccine)
- Persons known to have active untreated tuberculosis, although there is no evidence that either varicella or VZV exacerbates tuberculosis.

Persons whose immunosuppressive therapy with steroids has been discontinued for a month (3 months for chemotherapy) can be vaccinated.

The following are NOT contraindications

- Pregnancy of recipient's mother or other close or household contact
- Immunodeficient family member or household contact*
- Treatment with low dose (less than 2 mg/kg/day) alternate-day, topical, replacement, or aerosolised steroid preparations
- Asymptomatic or mildly symptomatic HIV infection
- Humoral immunodeficiency (e.g. agammaglobulinemia)
- Breast feeding. A study has shown no evidence of transmission of vaccine virus in breast milk. Non-immune breast-feeding mothers should be given varicella vaccine.

* If a vaccinee experiences a presumed vaccine-related rash 7-25 days after vaccination, avoid direct contact with immunocompromised persons for the duration of the rash, if possible.

Presentation and storage

Varicella vaccine is available as lyophilised preparations for reconstitution with a diluent. VZV is less stable than other live virus vaccines and the storage temperature requirements are critical. The unreconstituted vaccine and its diluent should be stored in the original packaging at +2°C to +8°C and protected from light. After reconstitution the vaccine should be used immediately. **Discard any vaccine unused after 30 minutes. Varicella vaccines do not contain thiomersal or any other preservatives.**

The vaccine should be administered by deep subcutaneous injection.

Immunogenicity and vaccine efficacy

After one dose of vaccine, 97% of children 12 months to 12 years of age develop detectable antibody titres. Vaccine efficacy is estimated to be 80-90% against infection, and 85-95% against moderate or severe disease.

As 10-20% of children who have received 1 dose of the vaccine are not fully protected, 2 doses are now advised for all ages. Vaccine efficacy is lower (~75%) in those aged 13 years and older. Immunity appears to be long lasting, probably permanent in the majority of vaccinees. However, approximately 1% of vaccinees per year have developed breakthrough infections. Breakthrough infection is significantly milder, with fewer lesions many of which are maculopapular rather than vesicular. The incidence of breakthrough infections may be less in those receiving 2 doses.

Post-exposure prophylaxis

Data from the USA and Japan indicate that varicella vaccine is effective in preventing illness or modifying the severity of illness if used within 3 days, and possibly up to 5 days of exposure. Post-exposure vaccine prophylaxis is indicated for those listed in the risk groups for vaccination, but who have not yet been vaccinated or had the disease (subject to the listed precautions and contraindications).

Adverse reactions

Local reactions (pain redness or swelling) occur in 7-30% of vaccinees. Fever over 39°C occurs in 15% of children and 10% of adolescents and adults.

A localised or generalised maculopapular or papulovesicular rash may develop. Most varicelliform rashes that occur within 2 weeks after

vaccination are due to wild type varicella-zoster virus with median onset 8 days after vaccination (range 1-24 days), while rashes caused by vaccine strain occur at a median of 21 days after vaccination (range 5-42 days). About 50% of vaccinated leukaemic patients develop a rash after the first dose and some may need antiviral therapy.

Transmission of vaccine virus from a vaccinated person can occur but the risk is very low and primarily occurs in the presence of a post-vaccination rash.

Zoster in vaccinated children has rarely been reported, and is usually a mild illness without complications.

Management of hospital exposure

Non-immune staff who have had a significant exposure to VZV (see above) should be excluded from contact with high-risk patients from 8-21 days after exposure.

HCWs with localised herpes zoster on a part of the body that can be covered with a bandage and/or clothing may be allowed to continue working unless they are in contact with high-risk patients, in which case an individual risk assessment should be carried out.

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18

Immunisation and Health Information for Health-Care Workers and Other 'At Risk' Occupations

Workers in many occupations may be exposed to infectious agents. A complete risk assessment should be carried out to determine which, if any, vaccinations are recommended for workers. This is required under the Health and Safety at Work Biological Agents Regulations. It should ideally take place before employment. Routine review of general immunisation status may also be appropriate. Persons whose work involves international travel should consider the recommendations given in the chapter on travel vaccinations.

Immunisation is one of the most effective health-care interventions. Nonetheless, it must be seen as just one part of a wider policy to prevent transmission of infection in health-care workers and their patients. Immunisation should never be regarded as a substitute for good infection control practices, such as hand washing and universal precautions for the prevention of transmission of blood-borne viruses.

Decisions about vaccination(s) recommended should be based on the duties of the individual rather than on job title alone. These guidelines may change as the prevalence of disease changes.

Categories of workers

Category A

Frontline health-care workers (both clinical and non-clinical), whose work may expose them to blood-borne virus infections and other infectious

diseases, e.g.

- Medical, nursing and paramedical staff
- Medical and nursing students
- Dentists and dental staff
- Hospital porters and cleaners
- Ambulance personnel
- Other health-care personnel deemed vulnerable following risk assessment
(This may include all persons working 'on-site' whether paid or unpaid)

Hepatitis A

- Hepatitis A immunisation may be occasionally advisable in some of the above categories, e.g. paediatric hospital staff, workers who culture hepatitis A, or during local outbreaks of hepatitis A.

Hepatitis B

- All workers in this category should be offered hepatitis B vaccination if not previously vaccinated.
- All workers in this category should have anti-HBs levels checked if previously vaccinated against hepatitis B and response not known (see hepatitis B chapter for adequate response levels).
- Please refer to hepatitis B chapter for new recommendations re anti-HBc testing in frontline health-care workers.

BCG (Bacillus Calmette Guerin)

- Please refer to tuberculosis chapter.
- Health-care workers should have pre-employment base-line Mantoux tuberculin testing performed if there is no BCG scar present, or no documented evidence of having received BCG vaccination.
- If there is an inadequate Mantoux response (defined as skin induration less than 5 mm in diameter) then the health-care worker should be referred to their public health clinic or occupational health department, where BCG should be offered.
- Any health-care worker who has been in close contact with a case of smear-positive tuberculosis should be assessed by an occupational health department.

Varicella

- Health-care workers without a definite history of chickenpox, proof of immunity or vaccination status, particularly those working with haematology, oncology, obstetrical, general

paediatric or neonatal patients should be routinely screened for VZ antibody. A history of chickenpox is a less reliable predictor of immunity in individuals born and raised overseas, and therefore routine testing should be considered in this group of HCWs. In addition HCWs from outside Ireland and Western Europe are less likely to be immune. Vaccination should be offered to non-immune staff.

- Laboratory staff who may be exposed to varicella virus in the course of their work should be offered vaccination.
- Post-vaccination serological testing is not recommended. Where exposure occurs in a susceptible HCW, advice should be sought from Occupational Health on further management and possible exclusion from the workplace.

Influenza

- Health-care workers should be offered vaccination against influenza on an annual basis each autumn.

Measles, mumps, rubella

- Health-care workers should have serological proof of immunity or evidence of having received 2 doses of MMR. Those who are non-immune should receive 2 doses of MMR. Post-vaccination testing is not recommended.
- Where exposure occurs in a susceptible HCW, advice should be sought from Occupational Health on further management and possible exclusion from the workplace.

Category B1

Non-healthcare workers who share the occupational risk of exposure to blood borne viral infection:

- Members of security and rescue services
- Members of An Garda Síochána
- Members of the fire brigade
- Members of the armed forces
- Employees of security companies
- Staff of institutions for persons with learning difficulties
- Any other workers who may be exposed to 'blood to blood' injuries.

Hepatitis B

- All workers in this category should be offered hepatitis B vaccination if not previously vaccinated (see hepatitis B chapter for immunisation schedule).
- All workers in this category should have anti-Hbs levels

checked if previously vaccinated against hepatitis B and response not known (see hepatitis B chapter for adequate response levels).

Category B2

Prison Officers

Hepatitis A

- Immunisation against hepatitis A may be considered if there is an ongoing outbreak in a prison.

Hepatitis B

- All workers in this category should be offered hepatitis B vaccination if not previously vaccinated (see hepatitis B chapter for immunisation schedule).

BCG

- Prison Officers aged 35 years and under should have pre-employment base-line Mantoux tuberculin testing performed if there is no BCG scar present, or no documented evidence of having received BCG vaccination.
- If there is an inadequate Mantoux response, BCG vaccination should be offered.

Category C

Workers in contact with raw faecal material, e.g.

- Sewage workers
- Crèche workers.

Hepatitis A

- All workers in this category may be checked for hepatitis A immunity (see Chapter 5).
- Workers in this category who are not immune to hepatitis A may be offered hepatitis A vaccination (see Chapter 5 for immunisation schedule).
- Crèche workers may be immunised against hepatitis A, especially if there is evidence of an ongoing outbreak of hepatitis A.

Category D

Scientists dealing with human body fluids, e.g.

- Medical laboratory technicians
- Research scientists.

Hepatitis A

- All workers in this category who culture hepatitis A virus should be checked for hepatitis A immunity, and if not immune, should be offered hepatitis A vaccine (see Chapter 5 for immunisation schedule).

Hepatitis B

- All workers in this category should be offered hepatitis B vaccination if not previously vaccinated (see Chapter 6 for immunisation schedule).
- All workers in this category should have anti-HBs levels checked if previously vaccinated against hepatitis B and response not known (see Chapter 6 for adequate response levels).

Polio

- Workers in this category who culture enterovirus should give a history of polio vaccination and may need to be offered immunisation.

Diphtheria

- Workers in this category who handle material that may contain pathogenic corynebacteria may require immunisation. This includes most laboratory staff (see Chapter 3 for immunisation schedule).

BCG

- Immunisation may be required in certain instances. Workers in this category who culture mycobacteria may require immunisation.

Other organisms

- Medical laboratory staff working in higher risk settings (e.g. reference laboratories or infectious disease units) or those conducting research into specific organisms should be considered for immunisation against these organisms (e.g. Japanese B encephalitis, cholera, meningococcal ACW₁₃₅Y, typhoid, influenza, varicella, rabies).

Category E

Personnel who work with animals and have exposure to animal tissues, e.g. veterinary staff, abattoir workers, zoological workers, veterinary inspectors, agricultural officers and poultry workers.

BCG

- This may be recommended to those thought to be at particular risk, (see Chapter 16, for immunisation schedule).

Rabies

- This may be recommended to those thought to be at particular risk, (see Chapter 20, for immunisation schedule).

Tetanus

- This may be recommended to those thought to be at particular risk, (see Chapter 15, for immunisation schedule).

Influenza

- Poultry workers, veterinary inspectors, agricultural workers, park rangers and those with likely contact with water fowl (as this puts them at risk of co-infection with avian influenza).

Occupational blood exposures

Occupational blood exposures (e.g. through needle stick or sharp injuries) may occur in the health-care sector. Some of these may leave a person at risk of getting hepatitis B, hepatitis C or HIV. Such exposures should be assessed by a competent person, e.g. Occupational Medicine Consultant or Infectious Diseases Consultant, or a member of their team.

In the first instance, the wound should be washed and all appropriate first aid given. Health-care workers should attend their occupational health department or A&E depending on local arrangements. A risk assessment will then be carried out. If appropriate, the Occupational Medicine Consultant or Infectious Diseases Consultant should be contacted. Such risk assessment includes details of the source patient's risk status (if known). A blood sample from the source patient should be taken (with consent) and tested for viruses.

If the exposed person has not been adequately vaccinated against hepatitis B, then hepatitis B prophylaxis should be considered. Specific hepatitis B immunoglobulin is available for passive protection and may be used in addition to hepatitis B vaccination to confer passive/active immunity after exposure. If they have had a previous needle stick injury, or recent hepatitis B vaccination, it may not be necessary to give hepatitis B immunoglobulin as the results of any previous hepatitis B test should be available within 72 hours.

If the occupational blood exposure was from a source believed to be HIV positive, then post-exposure prophylaxis with antiviral therapy should also be considered. *This should be undertaken urgently, ideally within 1-4 hours.* As the drug regime for such antiviral prophylaxis changes regularly, it is not possible to go into the details of such therapeutic protocols in these guidelines. The local Occupational Medicine Consultant/ Infectious Disease Consultant, or a member of their team, can provide up-to-date details on this.

19

Immunisations and Health Information for Travel

This chapter has the following sections:

- Introduction
- Vaccines for global travellers
 - Yellow fever
 - Meningococcal Infection
 - Cholera
 - Typhoid
 - Japanese B encephalitis
 - Tick-borne encephalitis
 - Rabies
 - Diphtheria
 - Poliomyelitis
 - Hepatitis A
 - Influenza
 - Tuberculosis
 - Hepatitis B
 - Other immunisations
- Travel health general information
 - Diarrhoea
 - Malaria
 - AIDS
 - Prolonged travel
 - Visiting friends and relations
- Bibliography

Chapter 19 Immunisations and Health Information for Travel

Introduction

The increase in international travel has continued to grow over the past 20 years and current projections suggest that this pattern will be maintained for the foreseeable future. Data released by the World Tourism Organisation in 2002 showed international tourist arrivals amounted to 693 million despite economic downturns and terrorist attacks. The figures of 150 million arrivals in 1970 and 500 million in 1993 illustrate how rapidly the numbers in international passengers are growing.

Changes in travel patterns that have become apparent include a trend for visiting ever more remote destinations. Many young people travel to several countries or continents for months at a time either as part of their summer holiday or as a gap year. International corporations place travellers in diverse destinations for short visits on international assignments. Travel for medical care is a relatively new phenomenon and is likely to increase over the coming years. Other specialised groups are those seeking to adopt children abroad and immigrants who wish to return to their country of origin in order to visit family and friends.

Many people are unaware that exotic destinations include potential exposure to infections that are rare in their home environment and other infections such as malaria that they will never have encountered previously. The resurgence of malaria in many parts of the world, with an increasing pattern of drug resistance, has led to an increase in the number of cases of malaria presenting in non-endemic areas. The emergence of new infections such as SARS and the spread of dengue fever and West Nile Virus place an ever-increasing responsibility on the doctor to remain up-to-date with current practice. The advent of new chemoprophylactic agents and of new vaccines also presents exciting challenges in dealing with the traveller.

A pre-travel consultation needs to address what immunisations are recommended, their potential side-effects and suitability for each traveller. Knowledge of relative risks to particular destinations is essential, as is an assessment of the patient's overall medical health and current medications. Additional recommendations and advice for those with pre-existing chronic illness should be included. Patients who are very young, those who are pregnant and the elderly also warrant special considerations in many areas of the usual consultation.

The determinates of advice and immunisations to travellers depend on:

- Duration of visit

- Destination
- Purpose of visit
- Standards of accommodations and food hygiene
- Behavioural or lifestyle patterns of the traveller

Many major urban centres and well-developed tourist destinations pose small risks to the short-term tourist or business traveller. Travel to areas where water supplies are difficult, the general standard of hygiene is poor and medical services are difficult to access or non-existent can pose serious risks to travellers. Any special occupation or activity should also be taken into account, e.g. contact with fresh water in areas where schistosomiasis is endemic.

While immunisations represent an important part of the travel consultation it should be emphasised that advice on risk avoidance, chemoprophylaxis and in some cases methods of self-treatment all constitute an important role in the travel medicine consultation. Ideally short-term travellers should present for advice 4-6 weeks before travel; those travellers who are travelling for long periods or going to very remote regions may require 6-12 weeks for the full series of immunisations.

Travellers should be aware that many conditions may present after they have returned from their trip abroad. In general patients who encounter problems within 1 year of returning should inform a doctor that they have been abroad. Check-ups for disease should be considered in those who have suffered from any serious problem abroad, i.e. any medical problem that has not been self-limiting, potential exposure to a known medical risk or development of problems within a year of return.

It is also of note that tour operators, travel agents and airline and shipping companies have a responsibility to advise travellers to consult a travel medicine clinic as soon as possible after booking a trip to any destination where significant health risks may be encountered.

There are also responsibilities that any traveller needs to accept before travel, including seeking advice in good time, compliance with recommended vaccines and other medications and general health measures. They should also consider carrying a medical kit and obtain adequate health insurance cover. Regulations regarding entry requirements such as the need for yellow fever certificates can be obtained from organisations such as WHO whose website address is given at the end of the chapter.

Chapter 19 Immunisations and Health Information for Travel

Immunisations should be arranged at least several weeks before travel, where possible.

Vaccination is a highly effective way of preventing disease. However, not all vaccinations offer 100% protection against disease and all additional recommendations in preventing disease should be followed. In general travel vaccinations are both safe and effective. As most vaccines take some time to become fully effective they should be administered at least 2 weeks before travel, although the late-presenting traveller may still benefit from having vaccinations even at the last minute.

Multiple vaccines can be administered at different sites on the same day. However, certain vaccines commonly cause local reactions that may be accentuated if a number of these vaccines are given simultaneously. If possible these should be given on separate occasions unless time constraints dictate otherwise. This is important in aluminium-containing vaccines such as hepatitis A, hepatitis B, tetanus, diphtheria toxoids, IPV, and conjugate meningococcal C vaccines. Various combined vaccinations are now available and these offer travellers considerable advantage by reducing the number of injections involved and improving compliance.

Vaccines for global travellers

- 1 Those that are used routinely particularly in children
- 2 Those that may be advised before travel
- 3 Those that are mandatory

Many childhood vaccinations require periodic boosting to maintain immunity throughout life. Pre-travel precautions should include booster doses of routine vaccines if the regular schedule has not been followed or where travel occurs to countries where boosters, e.g. tetanus, may not be readily available should the need arise. Older travellers may never have received primary courses of routine vaccines. Immunisation history should be checked to confirm adequate protection, including need for appropriate booster doses. **It is recommended that each traveller should be up to date with his/her routine vaccine schedule including vaccines against influenza and pneumococcal vaccines for travellers who are in the appropriate age group or those who have indications for vaccines due to underlying medical conditions.** Other vaccines will be advised depending on the area visited, the type of travel, any special identified risks, and on age, health and vaccination history of each individual. Please note that some vaccines can appear in more than one group.

Table 19.1 Vaccines for travellers

Category	Vaccine
1. Routine vaccination – check status and update	DTaP/IPV or Td/IPV for adults
	Hepatitis B
	Hib
	MMR
	Influenza
	Pneumococcal
2. Recommended vaccines depending on itinerary, type and duration of travel	Cholera
	Hepatitis A
	Hepatitis B
	Japanese encephalitis
	Meningococcal ACWY
	Rabies
	Tick-borne encephalitis
	BCG
	Typhoid fever
	Yellow fever
3. Mandatory vaccination	Yellow fever
	Men A,C,W,Y (for Hajj, Umra)

Table: WHO, International Travel and Health 2006

Yellow fever vaccine should not be given to infants less than 9 months of age unless the risk of yellow fever is very high, as the vaccine may cause encephalitis.

Yellow fever (notifiable)

Yellow fever is an acute haemorrhagic fever spread by mosquitoes that occurs in Tropical South America and in many countries in sub-Saharan Africa. Generally presenting as an acute fever with jaundice and

Chapter 19 Immunisations and Health Information for Travel

haemorrhage its mortality rate can be up to 50% in outbreaks. The risk of acquiring disease increases in patients who travel to jungle areas but also in urban centres reporting outbreaks. Areas where yellow fever occurs far exceed those officially reported.

The risk of infection can be reduced by taking precautions against mosquito bites. The species that transmits yellow fever also bites during day time. Vaccination is recommended for all travellers (for exceptions see below) who visit countries or areas within countries where there is a risk of yellow fever transmission. For in-country travel, vaccination is recommended outside urban areas of the endemic zone (see current WHO maps) even if these countries have not officially reported the disease. Vaccination for personal protection is not mandatory.

Mandatory vaccination against yellow fever is carried out to prevent the importation of yellow fever virus in countries where the potential for yellow fever exists because the vectors and primate hosts to support transmission are already present. In such cases vaccination against yellow fever may be an entry requirement for all travellers arriving from countries where there is a risk of yellow fever transmission. It does not generally apply to passengers from European countries unless the host country states that **all** travellers must have yellow fever as an entry requirement.

If yellow fever is contraindicated for medical reasons (see below) a certificate of exemption may be provided.

A yellow fever certificate only becomes valid after 10 days and is valid for 10 years from that date.

Vaccine

Yellow fever is a live viral vaccine. The dose is 0.5 ml subcutaneously, for both children and adults. One dose provides 10 years protection.

Tolerance of the vaccine is generally good; 2-5% of recipients have mild reactions including myalgia and headache. Up to 20% may report influenza like symptoms. Rarely encephalitis can occur at any age but has a higher incidence in infants under the age of 9 months. Infants less than 6 months should never receive yellow fever vaccine.

Contraindications to the vaccine include egg protein allergy, a confirmed serious reaction to a previous dose of any vaccine component, congenital or acquired cellular immunodeficiency, and symptomatic HIV infection. In cases where patients are under specialist care for immunodeficiency,

consultation with the patient's doctor may clarify matters for the travel advisor. Pregnant women should be advised not to travel where exposure to yellow fever may occur. There is a theoretical risk of harm to the foetus if the vaccine is given in pregnancy but that risk must be weighed against the serious risk of the mother travelling unvaccinated to a high risk zone.

Recently there have been reports of a small number of serious adverse reactions, including deaths, following yellow fever vaccine. This syndrome has been described as yellow fever vaccine associated viscerotropic disease (YEL-AVD); post-vaccinal encephalitis has been renamed as yellow fever associated neurotropic disease (YEL-AND). Most cases occurred in elderly people being vaccinated for the first time for yellow fever and there was an association with a history of thymectomy or disorders of the thymus. The risk to individuals travelling to areas where transmission is occurring is far higher than the risk of vaccination but it is important that yellow fever vaccination is not prescribed for individuals who are not at risk of exposure to infection.

Meningococcal infection (notifiable)

Meningococcal vaccine (see Chapter 9).

Indications

1. Travel to high-risk areas, particularly for those visitors who live or travel 'rough' such as hitchhikers or 'trekkers'. These areas include the meningitis belt of Africa (Southern sub-Saharan parts of Senegal, Mali, Niger, Chad and Sudan; all of Gambia, Togo and Benin; Northern parts of Sierra Leone, Liberia, Ivory Coast, Nigeria, Cameroon, Central African Republic, Uganda and Kenya) where epidemics of Group A infections occur in the dry season (December-February)
2. Travel to areas where epidemics of meningococcal disease are occurring
3. Long-term and rural travellers to countries where outbreaks can occur. In the past these outbreaks have usually been due to Group A disease, especially in areas of Africa as above. Outbreaks have occurred in Saudi Arabia due to meningococcal A and to W₁₃₅ in association with the Hajj and have led to mandatory requirements for meningococcal vaccine before entry to Saudi Arabia. W₁₃₅ has also been reported from Burkina Faso. ACWY quadrivalent vaccine is the recommended vaccine for travellers.

Vaccine

The ACWY vaccine is a purified heat-stable lyophilised capsular

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polysaccharide from meningococci of the respective groups. Efficacy levels of 85-100% have been documented in older children and young adults but it is not as effective in children under the age of 2 years. The meningococcal C conjugate vaccine (MenC) is not suitable for travel to areas where group A types are dominant. There is no available vaccine against type B strains.

Adverse reactions

Local: Injection site reactions occur in approximately 10% of recipients and last for about 24-48 hours.

General: Generalised reactions are rare but pyrexia occurs in up to 2% of vaccines.

ACWY vaccine does not elicit a protective immune response to meningococcal serotype C antigen in children under the age of 2 years. Response to A, W and Y antigens may be achieved in children under the age of 2 years but are likely to be short-lived.

In adults and children over the age of 5 years immunity will persist for up to 5 years. Children who are vaccinated under the age of 5 years should receive boosters at 2-3 years. The mandatory booster interval for those travelling to Saudi Arabia is 3 years.

Cholera (notifiable)

Cholera is an acute diarrhoeal disease caused by an enterotoxin of *Vibrio cholera* which has infected the small bowel. The illness is characterised by the sudden onset of profuse watery stools and occasionally vomiting. Dehydration, metabolic acidosis and circulatory collapse may follow rapidly.

Two main serogroups occur: 01 and 0139. Cholera occurs mainly in countries where there is inadequate sanitation and where clean drinking water is difficult to obtain. The risk for most travellers is very low even in travellers where cholera epidemics occur. Simple precautions are usually sufficient to prevent cholera in most travellers. Workers in disaster areas and in refugee camps are at the highest risk. Cholera is easy to treat; the vast majority of patients will recover if adequate hydration is supplied. Vaccination is only advised for those at increased risk of the disease, particularly emergency relief and health workers in poor conditions.

Vaccine

Parenteral cholera vaccine is no longer recommended by WHO. Modern oral cholera vaccines have now been produced and are now the only recommended vaccines. The killed oral vaccine contains a heat-

inactivated *V. Cholerae* strain of both the Classic and el Tor biotypes but is not effective against 0139 strains. It gives some cross-protection vaccine against some strains of enterotoxigenic *E. coli* by preventing a sub-unit from attaching to intestinal mucosal sites. The vaccine is two doses at 1-6 weekly intervals. It should be kept in a refrigerator and food should be avoided for an hour before and after a dose is taken. The level of protection is much higher than that of previous vaccines (85-90%) in the first 6 months, with antibodies persisting up to 3 years after the original vaccination.

Only evidence of a previous allergic reaction precludes administration of cholera vaccine (killed). Post-vaccine reactions are generally mild and of short duration.

Contraindication

Previous anaphylactic reaction to any component of the vaccine.

An EU licensed oral cholera vaccine has been added to the IMB list of vaccines that are authorised and marketed for use in Ireland.

Typhoid (notifiable)

Typhoid fever is a systemic infection caused by *Salmonella typhi*. Only humans carry salmonella typhi. Most of the approximately 2,000 serotypes in the genus salmonella cause only local infection of the gastro-intestinal tract (gastro-enteritis or 'food poisoning'). *S. typhi*, *S. paratyphi* A, B and C and occasionally other salmonella species may invade systemically to produce a serious illness with prolonged pyrexia and prostration. The likelihood of becoming a chronic carrier increases with age.

Typhoid/paratyphoid fevers are acquired mainly through food or drink contaminated with the excreta of a human case or carrier. It is therefore predominantly a disease of countries with poor sanitation and poor standards of personal and food hygiene. All travellers to endemic areas are at potential risk of typhoid fever; the risk of typhoid fever is lowest in tourist and business centres and rises as travellers enter more rural areas where standards of accommodation and food hygiene are not high. As typhoid vaccine is only partially effective, travellers should be advised to take precautions against eating or drinking potentially contaminated food and drink. Typhoid is particularly prevalent in the Indian sub-continent.

Vaccine – parenteral

Vi polysaccharide vaccine: parenteral capsular polysaccharide typhoid

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vaccine is available. Each 0.5 ml dose contains 25 mcg of the Vi polysaccharide antigen of *S. typhi* preserved with phenol. A single dose gives 70-80% protection for at least 3 years.

Typhoid vaccine should be stored at 2-8°C.

Dose and route of administration

Adults

- Vi polysaccharide vaccine: a single intramuscular or subcutaneous dose (0.5 ml) is given. Reimmunisation with a single dose every 3 years is recommended for those who remain at risk of infection.

Children

- Vi polysaccharide vaccine: the risk for children developing typhoid under one year is low. Children under 2 years may show a suboptimal response to polysaccharide antigen vaccines. Use of the vaccine in this age group should therefore be governed by the likely risk of exposure to infection. Children over the age of 2 years may receive the normal adult dose.

Indications

Typhoid immunisation is required for:

- Laboratory workers handling specimens which may contain typhoid organisms
- Travellers to countries in Africa, Asia, Central and South America and South East Europe, and to other areas where hygiene is likely to be poor. Vaccination is generally less important in areas where typhoid is not highly endemic and where visits are confined to urban centres with good accommodation
- Typhoid immunisation is not recommended for contacts of a known typhoid carrier or for controlling common-source outbreaks.

Contraindications

Previous anaphylactic reaction to any component of the vaccine.

Precautions

- 1 Acute febrile illness; defer until recovery.
- 2 As with other vaccines, typhoid vaccine should only be given to a pregnant woman if a clear indication exists.

Adverse reactions

Vi polysaccharide vaccine: Local reactions are reported to be mild and transient and systemic reactions are less common than with the older whole cell vaccine.

Japanese B encephalitis (notifiable)

This is predominantly a rural disease causing a potentially fatal encephalitis that is endemic in a large expanding swathe from northern Australia to India and Nepal. Epidemics are associated with the monsoon season. The majority of people who contract Japanese encephalitis virus will remain asymptomatic or suffer from a short acute viral illness. In 1 in 200 people the disease causes encephalitis that has a mortality rate of about 30%; many survivors have long-lasting severe neurological sequelae. The chance of permanent neurological disease increases with increasing age. The case fatality rate can reach 50%.

This *Culex* mosquito-borne viral disease is a zoonosis infecting pigs and wading birds, and humans are infected incidentally. The mosquito is a night feeder, biting especially in the cooler hours of dusk and dawn. Rice paddies are important breeding sites.

The risk of contracting the disease is estimated at 1:5,000 per month of travel in highly endemic areas. The risk to short-term tourists is low. The vaccine should be offered to expatriates who plan to reside in endemic areas and travellers spending more than 30 days in such areas or those whose type of activity places them at risk. If indicated, further detailed information should be sought from specialised centres or the WHO website.

Vaccine

The current vaccine is available on a named patient basis only. The vaccine is a solution of inactivated Nakayama-NH strain of the virus incubated with mouse brain. This produces a highly efficacious vaccine. The vaccine is administered at 0, 7 and 28 days using 1.0 ml of vaccine subcutaneously. Shorter, 2-dose schedules (day 0 and 14) can be used but efficacy is usually reduced in these cases to about 80%.

Localised pain and erythema occur in about 20% of recipients, with fever and pruritis occurring in 10%. Due to a number of cases of hypersensitivity reactions in the past it is advisable to keep patients for at least 30 minutes post-vaccine and advise them of potential late-onset allergic reactions up to 10 days post-vaccination. Patients should not travel abroad for at least 10 days after the last vaccination.

Tick-borne encephalitis (notifiable)

This viral disease occurs sporadically through parts of eastern and central Europe and the Asian part of the former USSR. Disease transmission primarily occurs during the spring and summer months in those exposed to tick bites. Travellers planning to camp or trek through forests or

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to walk along nature trails should consider having vaccination before travelling as currently no therapy exists for this disease. If indicated, further detailed information should be sought from specialised centres or the WHO website.

This flavivirus belongs to the same family as Japanese encephalitis, dengue and yellow fever viruses. The virus is transmitted by ticks that feed on wild and domestic animals that constitute the natural reservoirs for TBV. Once infected, the tick can then transmit the virus to humans. They are mainly to be found in spring and summer. The ticks wait for their prey on the underside of vegetation and attach themselves to passing animals or humans. After attachment the tick may not feed for up to 12 hours. Early removal of ticks can, therefore, prevent disease. The tick should be removed with tweezers, care being taken not to leave the head or mouth parts attached to the skin.

The disease is also transmitted by unpasteurised goat's milk or goat's milk products. It occurs in many countries in Central Europe and has spread to areas in Scandinavia and Switzerland. In Russia and across the former USSR it is known as Russian spring-summer fever. There is an initial viraemic phase, with a minority of those affected going on to develop encephalitis in about 20-30% affected. Similarly post-encephalitic sequelae are common and the disease has a mortality rate of 1%.

Vaccine

The vaccine is a suspension of purified inactivated TBV propagated on chick embryo cells. Three doses of 0.5 ml are given, the first two at an interval of 1 month with a booster at 12 months. A booster is given every 3 years for those who are exposed to the disease regularly. A shorter course of a 14-day interval can be used for rapid protection. The vaccine is currently unlicensed but is available in adult and junior forms.

Occasional local reactions may occur such as erythema and induration at the site of injection. In a small number of cases fever occurs and may persist. Contraindications include sensitivity to thiomersal, hypersensitivity to egg protein and severe reaction to a preceding dose.

Rabies (notifiable) (see Chapter 20)

Rabies, a viral disease transmitted by bites licks or scratches from infected mammals, is a very important cause of viral encephalomyelitis in many parts of the world. Travellers can be bitten in parts of the world where access to treatment is difficult and sometimes unavailable. For a

full discussion of rabies pre- and post-exposure vaccines see Chapter 20.

Diphtheria (notifiable) (see Chapter 3)

It should be re-emphasised that children aged 10 years and over and adults should not be given the higher strength childhood vaccine due to the possibility of anaphylactic reaction. An up-to-date list of licensed vaccines is contained in Appendix 1, or can be accessed on the IMB website, www.imb.ie.

Poliomyelitis (notifiable) (see Chapter 13)

Transmission of poliomyelitis in many regions of the world has been significantly lessened during the past 20 years and so the risk of infection for the international traveller is small. In most cases vaccination is no longer recommended for those visiting any region in the Americas and it is likely that the recommendations for SE Asia will also change during the next few years. Most disease risk currently occurs through the Indian and African Subcontinents.

Hepatitis A (notifiable)

Gammaglobulin provides passive immunity against Hepatitis A and has been used for this purpose since the early 1940s. Declining levels of hepatitis A antibodies in donor patients and the production of an effective vaccine mean that it is no longer used for routine protection against hepatitis A in travellers. If its use is indicated gammaglobulin is sometimes available. Current internationally accepted advice suggests that active vaccination against Hepatitis A (even at short notice before potential exposure) provides adequate protection. Travellers presenting within 10 days of travel should be advised of the potential risk of vaccine failure and the need to exercise extra precautions during this initial period.

Influenza (notifiable) (see Chapter 7)

All travellers are at some risk of acquiring a seasonal influenza during an outbreak. Tourists are at increased risk because they often travel in crowded conditions and visit very crowded locations. All groups at special risk due to age or chronic illness are at increased risk as per the chapter on influenza. Health-care workers are also at high risk.

Vaccine

Each year influenza vaccines change according to the change in their antigenic pattern. The vaccine contains 3 strains, with the composition changing each year to protect against the strains prevalent in any one season. There may be, in any given year, a significant difference between strains during the influenza seasons of the northern and southern

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hemispheres, which occur at different times of the year (November to March in the north and April to September in the south). Therefore influenza vaccine administered in one hemisphere may only offer partial protection to travellers to a different hemisphere. At-risk travellers who are going to another hemisphere just before or early on in the influenza season should arrange to have influenza vaccine as soon as possible after arriving at their destination.

Tuberculosis (notifiable)

See Chapter 16 for a full discussion on TB and the recommendations for BCG.

Tuberculosis occurs worldwide and the risk of infection varies from country to country (see map available on WHO website). BCG should be considered in the following groups of travellers. (Note: Mantoux testing should have been performed within the previous 3 months if BCG is to be recommended.)

1. Unvaccinated Mantoux negative persons intending to live or work with local people in high-incidence countries for more than 1 month. Vaccine may also be considered for shorter-stay travellers who are likely to be at increased risk.
2. Health-care workers who are Mantoux negative and have no history of vaccination and no scar to indicate previous vaccination and who have contact with patients or infectious material.

The degree of protection afforded to those over 16 years is not well documented but for the above groups it is considered to offer some protection. Individuals who are already vaccinated do not need repeat vaccination.

For travel purposes, the vaccine should be given at least 6 weeks before departure. Please note that live vaccines should be separated by at least 4 weeks and further vaccination in the arm in which BCG is given is not recommended for at least 3 months.

Travellers should avoid unpasteurised dairy products. If in doubt boil milk before drinking it.

For information on contraindications to BCG vaccine refer to Chapter 16.

Hepatitis B (notifiable)

Hepatitis B vaccine can be given as an accelerated course if the time to departure is short. The dose is 1.0 ml of vaccine given intramuscularly on

days 0, 7 and 21 or 28. A booster dose should be given 12 months after an accelerated schedule. Accelerated doses of the combined hepatitis A and B vaccine have also been shown to be effective. Other accelerated schedules are indicated in the main text.

Other Immunisations

Advice about other immunisations will always be tempered by the length of time to be spent abroad, the location, and if camping/trekking is intended. If more than 1 live vaccine is required, they should either be given at the same time in different sites, or at an interval of four weeks. (Check relevant Chapters within this book.)

Travel health: general information

It is important to remember that the commonest illnesses acquired abroad are preventable by measures other than vaccines.

Diarrhoea

Traveller's diarrhoea is one of the commonest problems in people travelling abroad. It is estimated that between 20-50% of travellers are affected by this self-limiting condition. The average duration of an attack is 2-5 days. Diarrhoea that continues for longer than 2 weeks is deemed to be persistent traveller's diarrhoea and is more likely to have an underlying parasitic cause. The main cause of acute traveller's diarrhoea is bacterial, although viruses may also be implicated. Organisms causing dysentery can present in well-fed travellers without blood appearing in the stool. The main causative bacterium tends to differ between the areas visited, and variation in the organisms most likely to cause diarrhoea can be seasonal.

All travellers should be made aware to avoid untreated water, avoid ice in their drinks and stick to hot, fresh, well-cooked food preferably eaten in well-maintained restaurants. Statistics do show that travellers rarely adhere to this regime. Apart from advice, most travel advisors will prescribe anti-motility agents and an appropriate anti-microbial for travellers as emergency self-treatment. The use of antibiotics as prophylaxis for diarrhoea is reserved for special cases where chronic disease may make the risk of diarrhoea considerably more serious for such individuals.

Malaria (notifiable)

Malaria is a common and life-threatening disease in many tropical and sub-tropical areas of the world. In general the number of malaria cases is

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increasing due to the increasing drug resistance of the parasite itself, the increasing resistance of mosquitoes to insecticides and the breakdown of public health measures against malaria in many parts of the world due to social and civil disruption.

Malaria is caused by a protozoan *plasmodium*. Four varieties are recognised of which *P. falciparum* is the most serious form. Malaria can be rapidly fatal and is especially serious in pregnant women and children under the age of 5 years. Small children and pregnant women are advised not to travel to areas where falciparum malaria occurs unless travel is essential.

There is ample evidence that strict adherence to mosquito bite precautions and taking appropriate malarial prophylaxis can considerably reduce the risk of acquiring malaria. All travellers to regions where malaria occurs should be informed of the level of risk involved and the types of malaria that occur. Appropriate chemoprophylaxis should be prescribed. Patients should be educated on how to take their medication and advised of any potential side-effects. It is also important to stress that travellers should take precautions against mosquito bites such as the use of repellents and of impregnated bed-nets. Anti-mosquito-bite protection regimes have been shown to provide a significantly cumulative protective effect with chemoprophylaxis.

No anti-malarial regime is 100% effective and travellers should be informed of the need to investigate any unexplained 'flu-like illness occurring more than 7 days after entering a malarious area and for up to a year after return from that area.

For long-term travellers to areas where medical care may be inaccessible, emergency stand-by medication may be appropriate.

It should also be noted that many arthropod viruses are also mosquito-borne and appropriate advice about mosquito avoidance is very pertinent in these diseases, some of whom have no available vaccine, e.g. dengue fever.

Acquired Immune Deficiency Syndrome (AIDS)

Travellers should be told that there are no AIDS-free areas of the world and advised of the dangers of unprotected casual sex. They should also be advised to be accident-wise because of the risk of AIDS transmission in many countries through blood transfusion. Tattoos, acupuncture, unsterile needles and body piercing can place travellers at risk from blood-borne viruses including HIV, hepatitis B and C. Sexually-transmitted

diseases are also an area where considerable risks are taken by travellers. All travellers should be made aware of the dangers of many diseases including bacterial and viral conditions, caused by having unprotected casual sexual intercourse and that the use of condoms while offering some protection is not always reliable.

Prolonged travel

Those planning to live overseas for prolonged periods of time should attend for medical advice regarding immunisations and general health-care advice in sufficient time before their departure. Generally periods up to 3 months may be required and this should be considered when booking their itinerary.

A dental check before travelling is recommended and it may be wise to carry sterile syringes/needles in case an injection is necessary.

Visiting friends and relations

This category of traveller is a new entity for Irish practitioners. Generally these patients will be visiting family and friends in their country of origin and in many cases they will be in rural regions where the risk of disease is high. If visiting highly endemic countries, they may also be resistant to the suggestion that malaria prophylaxis and vaccination cover will be required.

It should be remembered that natural immunity against a number of diseases drops rapidly once an individual is not continuously exposed. Thus following a stay in Ireland of over 6 months it should be assumed that an individual will have lost all natural protection against malaria and diarrhoeal diseases. Generally malaria prophylaxis and vaccination cover for this group should be the same as that suggested for any other traveller. Statistics show that this group is much less likely to seek advice and is many times more likely to present with malaria post-travel. Evidence also shows they are more likely to suffer from other preventable diseases such as typhoid.

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Bibliography

World Health Organization (2006). International Travel and Health.

Further Information

The World Health Organization produces a yearly guide **International Travel and Health, Vaccination Requirements and Health Advice for the International Traveller**. Supplies are available through local medical bookstores or directly from WHO in Geneva (Tel +4122 791 2476 e-mail publications@who.ch). The WHO guidelines are available online and can be downloaded.

Useful websites

- Irish Travel Medicine Society www.istm.ie
- Centre Disease Control, www.cdc.gov
Atlanta Georgia,
USA
- WHO www.who.int
Geneva
Switzerland

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Rabies

NOTIFIABLE

Introduction

Rabies is an acute progressive viral infection, which, if left untreated leads to an almost invariably fatal encephalomyelitis, death resulting from respiratory paralysis. Members of the lyssavirus genus cause rabies. Rabies has traditionally been associated with the Genotype 1 form (classical or sylvatic rabies); another six genotypes are known to produce disease.

In recent years, rabies has become recognised as an emerging zoonosis originating in bats; rabies-related bat lyssaviruses implicated in human disease include European Bat Lyssaviruses (EBLV) and Australian Bat Lyssavirus (ABLV). These variants present in humans in ways that are clinically indistinguishable from classical rabies.

Epidemiology

The WHO records between 40,000 and 70,000 cases of human rabies annually, most in less-developed countries. All continents except Antarctica report animal cases, although individual countries are reported to be rabies-free. Any warm-blooded animal may be infected but amongst domestic animals, dogs and cats are most commonly infected. Globally, over 90% of all human infections result from dog bites. The main source of human rabies in developing countries is from stray or feral dogs and cats and in developed countries the risk arises mainly from wild animal sources. In endemic areas, children are at particular risk.

In the United States, amongst wild animals, skunks, racoons and bats

account for 85% of animal cases of classical rabies; the incidence has been rising there since the 1950s. In Latin America, vampire bats carry classical rabies. Elsewhere, monkey bites have been known to transmit the virus. The development of international travel, and the capacity for greater numbers of people to travel to more exotic and remote locations, puts many more people at risk now than was the case in the past.

It should be emphasised that any bite, lick or scratch from any warm-blooded animal in an endemic area must be considered as a high risk and further specialised advice should be sought as soon as possible. In Europe, foxes have been the primary host but there has been extensive infection among dogs and cats. Vaccination of foxes (and certain domestic species) has led to the dramatic decline in vulpine rabies in Western Europe in the last 20 years, although foxes remain a significant source of rabies in Eastern Europe and Turkey.

Certain countries that are declared rabies-free have rabies-related viruses (bat lyssaviruses) in their bat populations, e.g. Australia and the UK. In the UK, rabies-related viruses have only been detected in Daubenton's bats but not in the commonest UK bat species, the Pipistrelle.

The issue of EBLV has become a concern recently; an ongoing survey in the UK has demonstrated that four bats have been identified as having been infected with EBLV. In addition, in 2002 an unvaccinated bat handler in Dundee in Scotland died of EBLV, having been bitten by a bat. Only 3 other cases of EBLV infection (all fatal) have been reported in the past 30 years in Europe. In order to assess the risk of EBLV in Ireland, the Department of Agriculture and Food is undertaking a survey of Daubenton's bats for EBLV. This survey was initiated in 2002 and is ongoing.

Transmission

Infection is usually transmitted by the bite (or scratch) of a rabid animal. The virus may also be passed when infected saliva comes in contact with broken or grazed skin, with mucous membranes and with the cornea. In addition, laboratory workers manipulating the virus or clinical specimens containing the virus are at potential risk of occupational contact or inoculation. Aerosol transmission is considered possible (possibly accounting for certain lab-acquired cases; this method may also be important in rabies-infected bat caverns). Human-to-human transmission is rare and the only documented cases involve corneal and solid organ transplantation.

Effects of rabies

The incubation period of rabies is generally between 2 and 12 weeks but may range from 9 days to 2 years or even longer. The wide variation in incubation is thought to depend, in part, on the site of inoculation, the severity of the wound, and the amount of virus introduced. The factors that tend to reduce the incubation period include inoculation occurring closer to well-innervated parts of the body (including primary nerve bundles and the brain) and deeper and more extensive wounds (which will tend to allow an increased viral load into the wound). The duration tends to be shorter in children than adults.

Rabies has the highest case-fatality ratio of any infectious disease. Untreated, symptomatic disease is almost invariably fatal; the majority of the half dozen or so documented cases of survival from rabies had had some form of pre- or post-exposure treatment.

Initial virus replication takes place in the tissues at the point of entry, persisting for between 48 and 72 hours. It progresses along the axonal sheaths in peripheral nerves towards the central nervous system. Viral spread then occurs to the peripheral nerves, largely out of reach of circulating antibody; there is no antibody response until the onset of clinical symptoms.

The symptoms of rabies are highly variable. Early symptoms are non-specific and include pain and paraesthesiae at the inoculation site. Low-grade fever, malaise, anorexia, headache, nausea and vomiting and even sore throat are all commonly reported. Depending on the parts of the CNS affected, the patient may be excitable, irritable with more classical hypoglossal spasm associated with water (hydrophobia) or blowing in the face (aerophobia) or more obtunded with an ascending paralysis. Rising intracranial pressure leads to the decreased level of consciousness and the development of focal convulsions. Central and peripheral nervous impairment will lead to progressive respiratory distress. A wide variety of cardiac dysrhythmias can occur.

Other causes of viral encephalitis, Guillain-Barré syndrome, tetanus, poliomyelitis and the toxic effects of drugs and poisons are among the differential diagnoses.

A. PRE-EXPOSURE PROPHYLAXIS

Rabies vaccines

Rabies vaccine is used for pre-exposure protection of those at risk. One type of rabies vaccine, human diploid cell rabies vaccine (HDCV), is a

freeze-dried suspension of Wistar rabies virus strain PM/W1 38 1503-3M cultured on human diploid cells and inactivated by beta-propiolactone. The potency of the reconstituted vaccine is not less than 2.5 IU per 1 ml dose. The freeze-dried vaccine should be stored at 2-8°C. It should be used immediately after reconstitution with the diluent supplied and any unused vaccine discarded after 1 hour. It may be given by intramuscular injection, usually in the deltoid region or anterolateral region of the thigh (never in the buttocks). The manufacturer's recommendations should be consulted prior to administration. The vaccine contains traces of neomycin and human albumin.

An alternative vaccine that may be used is purified chick embryo cell vaccine. This contains inactivated rabies virus (Flury LEP). The potency of 1 ml is greater than or equal to 2.5 IU. The vaccine should be kept refrigerated. The recommended dose is 1 ml intramuscularly. The vaccine should be given in the deltoid or antero-lateral part of the thigh. Intra gluteal injection is not recommended. Patients with a history of severe hypersensitivity to eggs or egg products should not receive this vaccine for pre-exposure prophylaxis. This vaccine may also contain trace residues of polygeline, amphotericin B, chlorotetracycline or neomycin.

Ideally a pre-exposure course should be completed using one type of cell culture vaccine throughout the primary course, but if one type of cell culture vaccine is unavailable then another may be substituted.

Indications

Pre-exposure prophylaxis should be offered to those in the following categories:

- Laboratory workers handling or potentially handling the virus
- Those, who by the nature of their work are likely to be in direct contact with imported animals:
 - Staff at animal quarantine centres
 - Staff at zoos
 - Staff at research and acclimatisation centres where primates and other imported animals are housed
 - 'At-risk' staff at sea and airports, e.g. Dept of Agriculture and Food Inspection Staff
 - Authorised carrying agents for imported animals
- Selected National Parks and Wildlife Staff who may handle bats, based on risk assessment
- Dog wardens and other relevant staff in the Local Authorities
- Workers in enzootic areas abroad at special risk (e.g. veterinary staff, zoologists)
- People who regularly handle bats

- Health-care workers who have, or are about to, come into close contact with a patient (or their clinical specimens) with probable or confirmed rabies
- Those living or travelling in endemic areas who may be exposed to the risk of being infected or are undertaking journeys in remote parts where medical treatment may not be immediately available
- Staying in highly endemic areas for more than 4 weeks (particularly in the case of children).

Dose and route of administration

For primary pre-exposure protection, three 1.0 ml doses of HDCV should be given, one each on days 0, 7, 21 **OR** 28 by intramuscular injection in the deltoid region or anterolateral region of the thigh. The same dose is used for adults and children. All travellers to areas of risk should be informed by their medical advisors to seek immediate medical aid if an animal bite or scratch is sustained. They should be given advice on wound toilet – see *Standard Operating Procedure for Risk Assessment and Management of Non-Indigenous Rabies Exposure* available at www.hpsc.ie.

Contraindications

Anaphylactic reaction to a preceding dose or any of the constituents.

Precautions

Pre-exposure vaccine should only be given to pregnant women if the risk of exposure to rabies is high.

Adverse reactions

Local: HDCV may cause local reactions such as redness, swelling or pain at the site of injection within 24-48 hours of administration.

General: Systemic reactions such as headaches, fever, muscle aches, vomiting and urticarial rashes have been reported. Anaphylactic shock has been reported from the USA and Guillain-Barré Syndrome from Norway, although no causal relationship between Guillain-Barré syndrome and rabies vaccine has been established. Reactions to the vaccine may become more severe with repeated doses.

The initial primary dose pre-exposure course produces protective antibody in virtually 100% of recipients and makes routine post-immunisation serological testing unnecessary.

Rabies vaccine will induce long-lasting memory giving rise to an accelerated immune response when a booster dose of vaccine is administered.

- Periodic booster injections are therefore not recommended for general travellers.
- In the event of a significant animal exposure, persons who have previously been immunised should receive 2 further doses of rabies vaccine.

B. CONTINUED OCCUPATIONAL EXPOSURE

The following groups are managed as outlined below:

For those people who have continuous occupational exposure and where exposure is likely to go unnoticed, e.g. rabies research laboratory workers and rabies vaccine production workers, serological testing should be carried out at 6-monthly intervals and boosters administered when the antibody level goes below a predetermined level – less than 0.5 IU/ml.

For those who have frequent episodic exposure, e.g. rabies diagnostic workers, veterinary surgeons and staff, wildlife rangers who are conducting bat research, serology should be carried out every 2 years and boosters administered as necessary.

For those who are at greater risk than the population but have only potential episodic exposure and can report exposures, e.g. dog bites. In the absence of an exposure, these staff do not require further booster doses/ serological testing once primary immunisation has been completed.

The current best advice is that boosters should not be administered more frequently than every 2-3 years to minimise the possibility of localised reactions to the vaccine.

Serological testing is otherwise only advised for those who have had a severe reaction to a previous dose of vaccine to determine the necessity of a booster dose.

Further information on rabies vaccine and post-exposure treatment is available from the Irish Medicines Board, Cherry Orchard Hospital, Health Protection Surveillance Centre and from the Health Service Executive.

C. POST-EXPOSURE TREATMENT

Travellers who have been exposed to the possibility of rabies while abroad should seek immediate medical attention. On return to Ireland they should contact their General Practitioner or specialised vaccination centre or infectious diseases department to receive further advice. Similarly, anyone having received a bat bite in Ireland or the UK should seek immediate medical attention.

Treatment, including wound toilet, must not be delayed, and should be started as soon as possible while enquiries are made about the local epidemiology of rabies in the country concerned (see above) and, where possible, the ownership and condition of the biting animal and the vaccination status of the animal should be determined.

The immediate steps to be taken are as follows:

- 1 **Wound toilet:** As soon as possible after the incident, the wound or site of exposure (e.g. mucous membrane) should be thoroughly cleaned with water under a running tap for at least 10 minutes. The wound should be **initially** washed thoroughly (with soap or detergent and water) and then rinsed completely. It is important not to mix disinfectant with soap during washing, as detergents can negate the effects of disinfectant. A suitable disinfectant (e.g. povidone-iodine solution or 70% alcohol) should be applied and the wound covered with a simple dressing. Tetanus prophylaxis and measures to control bacterial infection should also be administered as indicated. Suturing should be delayed where at all possible (taking into account cosmetic factors and the potential for bacterial infections).
- 2 **Risk assessment:** Each case of possible exposure requires a careful and thorough risk assessment along the lines laid out below:
 - **Country of exposure (or the country of origin of the animal):** Depending on the country of exposure, the patient will be considered to be at 'No Risk', 'Low Risk' or 'High Risk'. (Up-to-date information on rabies by country can be found in World Health Organization, Rabies Bulletin Europe: www.who-rabies-bulletin.org/ or Centre for Disease Control and Prevention, USA: www.cdc.gov/ncidod/dvrd/rabies/epidemiology/epidemiology.htm).
 - **The type, severity and site of the wound:** Highest risk wounds involve piercing and breaking of the skin or involvement of mucous membranes.
 - **Circumstances of bite:** Unprovoked bites are more worrying and carry a much higher risk than provoked bites.

- **The species, behaviour and appearance of the animal:** Crazed or frantic animals pose a very significant risk. Bat rabies may be suspected if the bat is sick, grounded without injury or if an uninjured bat is found dead. Apparently healthy bats may have rabies. That said the risk of bat rabies in Ireland is likely to be very small. Table 20.1 shows the assessment of post exposure treatment requirements from significant bat bites sustained in Ireland and UK.
- **Vaccination status of the animal (if known):** Regularly vaccinated animals are much less likely to have rabies.
- **Immune status of the individual involved:** Fatal rabies encephalomyelitis is extremely unlikely in a fully immunised individual and is virtually certain to be prevented by an effective course of post-exposure treatment, if given sufficiently early.

Table 20.1 Assessment of post-exposure treatment requirements from significant bat bites (Ireland and UK)

Rabies risk	Unimmunised /incompletely immunised individual ¹	Fully immunised individual
Insignificant Contact, but no lesions; indirect contact; No contact.	None	None
Minor significance Licks of the skin; Scratches or abrasions; Minor bites (covered areas of arms, trunk, and legs)	Five doses (each 1.0 ml) rabies vaccine on days 0, 3, 7, 14 and 30	Two doses (each 1.0 ml) rabies vaccine on day 0 and day 3
Major significance Licks of mucosa; Major bites (multiple or on face, head, finger or neck)	Five doses (each 1.0 ml) rabies vaccine on days 0, 3, 7, 14 and 30, plus HRIG on day 0 only	Two doses (each 1.0 ml) rabies vaccine on day 0 and day 3

¹Persons who have not received a full course of pre- or post-exposure tissue-culture rabies vaccine

- 3 Post-exposure immunisation and immunoglobulin.** Specialist advice should be sought when post-exposure immunisation and immunoglobulin seems indicated. All immunosuppressed subjects

should be given HRIG following exposure. Table 20.2 provides guidance on the administration of HDCV and HRIG depending on the level of risk as dictated by the country of exposure.

Table 20.2 Post-exposure treatment requirement by country of exposure (for overseas exposure or by exposure to overseas animal)

Rabies risk	Unimmunised /incompletely immunised individual ¹	Fully immunised individual
No risk	None	None
Low risk	Five doses (each 1.0 ml) rabies vaccine on days 0, 3, 7, 14 and 30	Two doses (each 1.0 ml) rabies vaccine on day 0 and day 3
High risk	Five doses (each 1.0 ml) rabies vaccine on days 0, 3, 7, 14 and 30, plus HRIG on day 0 only	Two doses (each 1.0 ml) rabies vaccine on day 0 and day 3

¹Persons who have not received a full course of pre- or post-exposure tissue-culture rabies vaccine

Rabies-specific immunoglobulin

Human rabies immunoglobulin (HRIG) is obtained from the plasma of immunised human donors. It is used after exposure to rabies to give rapid protection until rabies vaccine, which should be given at the same time, becomes effective. After thorough wound cleansing, HRIG should be infiltrated into the depth of the wound and around the wound as much as anatomically feasible. Any remainder should be injected at an intramuscular site distant from that of the vaccine inoculation, e.g. anterior thigh (not gluteal region). The dosage is calculated based on body weight (20 IU/kg body weight).

Adverse reactions

HRIG may cause local reactions and low-grade fever but no serious adverse reactions have been reported.

Vaccine and HRIG suppliers

Post-exposure prophylaxis with the HDCV is currently available free of charge through the National Fever Hospital in Cherry Orchard. A supply of Human Rabies Immunoglobulin (HRIG) will also be maintained at this centre. Contact Dr. O'Dea, Tel. (01) 620 6000

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HRIG is also available from CDSC HPA, 61 Colindale Avenue, London NW9 5EQ, Tel. (00 44) 181 2006868.

It is essential that post-exposure treatment is started as soon as possible after exposure. Moreover, treatment should be considered, irrespective of the period between exposure and presentation unless the individual is previously vaccinated and rabies antibodies can be detected. The decision to administer HRIG should be based on a risk assessment and specialist advice should be sought.

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World Health Organization website. www.who-rabies-bulletin.org/

6a

Human papillomavirus

NOTIFIABLE

Introduction

Human papillomavirus (HPV) is a double stranded DNA virus that infects squamous epithelia including the skin and mucous membranes of the upper respiratory and anogenital tracts. HPV targets basal cells in the stratified squamous epithelium and metaplastic cells at the squamocolumnar junction of the cervix and can, over time, lead to cervical cancer. Infection of the glandular epithelium of the endocervix can lead to adenocarcinoma. There are more than 100 different types of HPV. Some types are responsible for common warts (verrucae). Around 40 types can infect the genital tract. Genital infection is associated with genital warts and various cancers such as cancer of the cervix, vulva, vagina, anus, and penis. HPV infection is also associated with various oropharyngeal cancers in men and women. The types that cause genital warts (low-risk types e.g. HPV 6 and 11) are not those associated with cancer (high-risk types e.g. HPV 16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, 66).

Epidemiology

Genital HPV infection is the most common sexually transmitted disease worldwide. Transmission occurs during vaginal, oral or anal sexual intercourse or genital contact with an infected person. Non-

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sexual routes of HPV transmission include vertical transmission from mother to newborn baby. The clinical spectrum of disease ranges from asymptomatic infection, to benign warts, to invasive cancer.

Genital warts are highly contagious; two-thirds of people who have sexual contact with an infected partner will develop warts. Risk factors associated with genital HPV infection include younger age at sexual initiation, number of sexual partners, and the sexual history of the partner (number of previous sexual partners). In the United States, it is estimated that approximately 1% of sexually active adults have visible genital warts and that at least 15% have subclinical infection, as determined by HPV DNA assay. The highest rates of HPV infection occur in the 18-28 year age group. An estimated 80% of sexually active women become infected with at least one type of HPV by age 50 years.

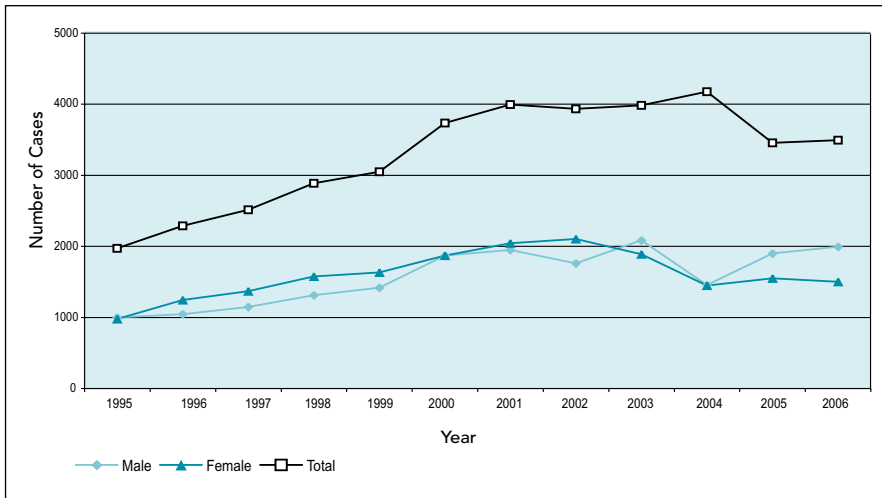
Most genital HPV infections are asymptomatic and transient. However, although 70% of new genital HPV infections clear within one year, and 91% within two years, high-risk types are more persistent than low-risk types. Persistent infection over a number of years may lead to grade 2 or 3 cervical intraepithelial neoplasia (CIN) and cervical cancer. In one study approximately 27% of women with an initial HPV 16 or 18 infection progressed to CIN2/3 within 36 months. Persistent infection by high-risk types is detectable in more than 99% of cervical cancers. Types 16 and 18 are responsible for over 70% of cervical cancers. Types 6 and 11 are associated with over 90% of genital warts.

The prevalence of cervical HPV infection varies worldwide. The International Agency for Research on Cancer (IARC) population-based studies found that overall HPV DNA prevalence varied 20-fold from 1.4% (95% CI 0.5-2.2) in Spain to 25.6% (95% CI 22.4-28.8) in Nigeria. The most common type was 16, followed by type 42, 58, 31, 18, 56, 81, 35, 33, and 45. HPV 16 was twice as common as any other high-risk type in all regions except sub-Saharan Africa where HPV 35 was equally common. Infection by multiple types was common.

Ireland

Ano-genital warts are notifiable in Ireland. They accounted for 35% of all sexually transmitted infection notifications in 2006. The trend in notifications is similar in males and females (Figure 1). The largest proportion of cases occurs in young adults in the 20-29 year age group.

Figure 1 Ano-genital wart notifications in Ireland by gender, 1995-2006.
Source: HPSC



Note: The total also includes notifications where gender was unknown

A recent study of 996 cervical cytology samples in an Irish urban female, opportunistically screened population, found an overall HPV prevalence of 19.8%, varying from 31% in women under 25, to 23% in women aged 25-35 and 11% in women over 35 years of age. HPV 16 at 20% and HPV 18 at 12% were the commonest high-risk types detected.

Effects of human papillomavirus

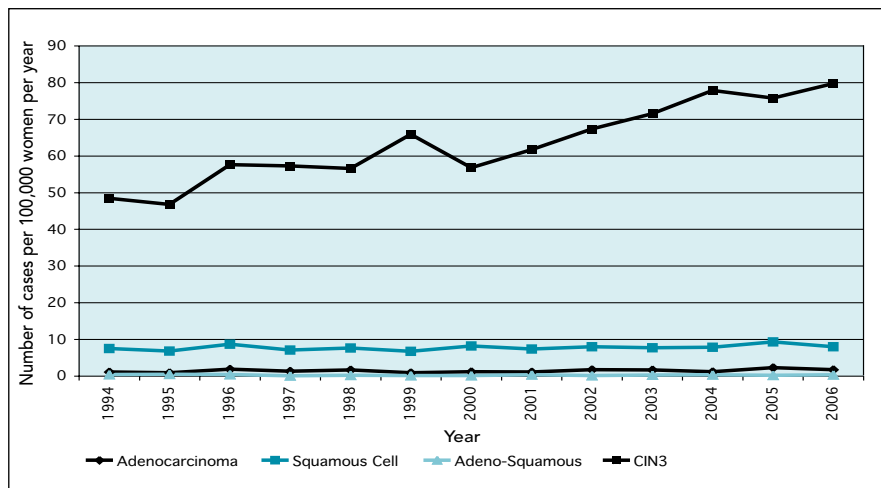
HPV is responsible for 5.2% of the cancer burden worldwide. Cervical cancer is the second most common cancer in women worldwide with an estimated 493,000 new cases in 2002 and 274,000 deaths. Most cases occur in countries without effective screening programmes.

In Ireland, on average 180 women develop cervical cancer each year with 73 deaths from cervical cancer. The average age at diagnosis is 46 years and of death is 56 years. Recent trends in the incidence of squamous cell carcinoma, adenocarcinoma, CIN3 and adeno-squamous carcinoma in Ireland are shown in Figure 2. The incidence of CIN3 has increased significantly from 1999 to 2006 while the incidence of carcinoma has remained unchanged.

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Figure 2 Rate of invasive and in situ cervical cancer per 100,000 population in Ireland, 1994-2006.

Source: Irish Cancer Registry



Individuals can reduce their risk of getting genital HPV infection by changes in sexual behaviour including abstinence from any sexual activity or lifelong monogamy. Reducing the number of sexual partners and the frequency of new partners will also reduce the risk. Condom use reduces but does not eliminate the risk of sexual transmission of HPV.

Cervical screening can detect pre-cancerous lesions and cervical cancer at an early stage when treatment can be successful. In countries where there is an organised cervical cancer screening programme there has been a marked reduction in the incidence of invasive cervical cancer.

Human papillomavirus vaccines

Currently available HPV vaccines contain virus-like particles (VLPs) produced from the major capsid protein L1 of each HPV type using recombinant DNA technology. These vaccines are not live vaccines, contain no viral DNA and are not infectious or oncogenic. An up-to-date list of vaccines that are licensed and marketed in Ireland is contained in Appendix 1, or can be accessed on the IMB website at www.imb.ie. Full prescribing information relating to the HPV vaccines is available at www.medicines.ie.

Two HPV vaccines are licensed for use in Ireland, a bivalent vaccine containing VLPs for two HPV types (16 and 18) and a quadrivalent vaccine containing VLPs for four HPV types (6, 11, 16 and 18). The VLPs used in

the bivalent vaccine are adjuvanted by ASO4 containing 3-O-desacyl-4'-monophosphoryl lipid A (MPL) adsorbed on aluminium hydroxide. The VLPs used in the quadrivalent vaccine are adsorbed on amorphous aluminium hydroxyphosphate sulphate adjuvant.

Immunogenicity and vaccine efficacy

Both HPV vaccines are highly effective at preventing infection of susceptible women with the HPV types covered by the vaccines. Both vaccines were also found to be over 99% effective in preventing pre-cancerous lesions associated with HPV types 16 and 18 in young women. Efficacy of the quadrivalent vaccine against HPV 6, 11, 16 or 18-related genital warts was 99%. Vaccination provides less benefit to females if they have already been infected with one or more of the HPV vaccine types. Protection lasts for at least five years and is likely to be long-lasting. The need for a booster has not yet been determined for either vaccine. Partial cross-protection has been demonstrated for both vaccines against infection with several non-vaccine oncogenic HPV types, including HPV 45 and 31 the commonest non-vaccine oncogenic types.

The vaccines will reduce but not eliminate the risk of cervical cancer since at present they target only two oncogenic HPV types (16 and 18) which account for 70% of cervical cancer risk. Therefore, cervical cancer screening programmes will continue to be important even in vaccinated populations.

Dose and route of administration

There is no evidence that the HPV bivalent and quadrivalent vaccines are interchangeable. If an individual has started a course of one vaccine then the vaccination series should be completed with that vaccine.

The bivalent vaccine is licensed for females aged 10-25 years for the prevention of premalignant cervical lesions (CIN2/3) and cervical cancer causally related to HPV types 16 and 18. Three doses (0.5ml) are recommended to be given at 0, 1 and 6 months by IM injection in the deltoid region.

The quadrivalent vaccine is licensed for females aged 9-26 years for the prevention of premalignant genital lesions (cervical, vulvar and vaginal), cervical cancer and external genital warts causally related to HPV types 6, 11, 16 and 18. Three doses (0.5ml) are recommended to be given at 0, 2 and 6 months by IM injection in the deltoid region. An alternative vaccination schedule may be used such that the second dose is given at least one month after the first dose and the third dose at least three months after the second dose with all three doses given within one year.

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The vaccines are currently not licensed for women over 26 years of age or for males.

HPV vaccines should be stored at 2°C to 8°C in the original packaging and protected from light. If the vaccine has been frozen, it should not be used.

Indications

Recommendations for HPV immunisation:

- All girls 12 years of age should receive the vaccine
- It may be given to girls aged 9-12 years in accordance with the vaccine licence and at the discretion of the physician
- Females aged 13-26 years who would not have had the opportunity to receive the vaccine at age 12 may also be given the vaccine.

Ideally, the vaccine should be administered before potential exposure to HPV through sexual contact. However, as it is not possible to determine which females have been exposed to any or all of the HPV types contained in the vaccines, women in the appropriate age group with a history of sexual contact may also benefit from the vaccine. Those who are sexually active should be advised that the vaccine has not been shown to have a therapeutic effect on existing HPV infection or cervical lesions.

Contraindications

Anaphylactic reaction to a preceding dose or any of the constituents.

Precautions

Acute severe febrile illness; defer until recovery. The response may be impaired in those who are immunocompromised. Syncope has been reported among adolescents who received HPV or other vaccines. Recipients should be seated during vaccine administration. Where possible, patients should remain in the vicinity of the place of vaccination for up to 15 minutes.

Pregnancy and breastfeeding

HPV vaccine is not at present recommended during pregnancy, although there is no known risk associated with using recombinant viral vaccines during pregnancy. If a woman becomes pregnant during the vaccination series, remaining doses should be delayed until after completion of the pregnancy.

The quadrivalent vaccine can be given to breastfeeding mothers. The effect on breastfed infants of giving the bivalent vaccine to the mother has not been evaluated, although there is no known risk associated with using recombinant viral vaccines whilst breastfeeding.

Use of HPV vaccine with other vaccines

The vaccines can be given at the same visit as other vaccines recommended for persons of this age group (e.g. Tdap, MMR, hepatitis B, IPV), preferably in a different limb.

Adverse reactions

Local: Localised pain, swelling and erythema are very common at the injection site.

General: Fever ($\geq 38^{\circ}$), myalgia, fatigue and headache have been commonly reported. Fainting can uncommonly occur.

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APPENDICES

- Appendix 1.** List of licensed vaccines provided by the Irish Medicines Board which are authorised and marketed in Ireland.
- Appendix 2.** Table of countries with TB Notification Rates $\geq 40/100,000$ Population, 2005 (WHO figures).

Appendix 1 List of licensed vaccines provided by the Irish Medicines Board which are authorised and marketed in Ireland.

VACCINES AUTHORISED AND MARKETING IN IRELAND Feb 2008		
Marketing Authorisation Holder	Product Name and Authorisation number	Common Name
Baxter Healthcare Limited	Ticovac 0.5ml (PA 935/1/3)	Tick Borne Encephalitis Vaccine (inactivated)
	Ticovac 0.25ml Junior (PA 935/1/2)	Tick Borne Encephalitis Vaccine (inactivated)
	NeisVac-C (PA 167/107/001)	Meningococcal Group C Polysaccharide Conjugate Vaccine (adsorbed)
GlaxoSmithKline Ltd.	Engerix B Adult (PA 1077/23/2)	Recombinant Hepatitis B (adsorbed)
	Engerix B Paediatric (PA1077/23/1)	Recombinant Hepatitis B (adsorbed)
	Fendrix (EU/1/04/299/1-3)	Hepatitis B vaccine (adjuvanated, adsorbed)
	Fluarix (PA 1077/25/1)	Influenza vaccine (split virion, inactivated), Seasonal
	Havrix Junior Monodose (PA 1077/26/1)	Hepatitis A Vaccine (inactivated, adsorbed)
	Havrix Adult Monodose (PA 1077/26/2)	Hepatitis A Vaccine (inactivated, adsorbed)
	Hepatyrix (PA 1077/99/1)	Hepatitis A Vaccine (inactivated, adsorbed) and Typhoid Polysaccharide vaccine
	Hiberix (PA 1077/27/1)	Haemophilus Influenzae type B conjugate Vaccine
	IPV Infanrix (PA 1077/108/1)	Diphtheria, Tetanus, Acellular Pertussis and Poliomyelitis (inactivated) Vaccine

VACCINES AUTHORISED AND MARKETING IN IRELAND Feb 2008		
Marketing Authorisation Holder	Product Name and Authorisation number	Common Name
	Infanrix IPV Hib (PA 1077/29/2)	Diphtheria, Tetanus, Acellular Pertussis, Poliomyelitis (inactivated) and Haemophilus Influenzae type B conjugated Vaccine (adsorbed)
	Priorix (PA 1077/36/1)	Measles / Mumps/ Rubella live Vaccine
	Poliomyelitis Vaccine (Oral) Ph. Eur., Live. (Monodose) (PA 1077/35/1)	Poliomyelitis Vaccine (Oral, live)
	Twinrix Paediatric (EU/1/97/029/009)	Hepatitis A and Hepatitis B Surface Antigen vaccine
	Twinrix Adult (EU 1/96/20/7)	Hepatitis A and Hepatitis B Surface Antigen Vaccine
	Typherix (PA 1077/38/1)	Typhoid polysaccharide vaccine
	Rotarix (EU/1/05/330/001)	Oral Rotavirus Vaccine (Live)
	Cervarix (EU/1/07/419/004)	Human Papillomavirus vaccine [Types 16, 18] (Recombinant, adjuvanted, adsorbed).
Novartis Vaccines and Diagnostics GmbH & Co.KG	Begrivac- Influenza Vaccine (PA 877/1/1)	Influenza Vaccine (split virion, inactivated) (seasonal)
	Rabipur (PA 877/3/1)	Rabies Virus Inactivated
Novartis Vaccines and Diagnostics S.r.l.	Menjugate Kit (PA 919/4/2)	Meningococcal group C oligosaccharide conjugate vaccine

VACCINES AUTHORISED AND MARKETING IN IRELAND Feb 2008

Marketing Authorisation Holder	Product Name and Authorisation number	Common Name
Sanofi Pasteur MSD Ltd	Gardasil (EU/1/06/357/015)	Human Papillomavirus Vaccine [Type 6,11,16,18]
	HBVAXPRO 5 (EU/1/01/183/024)	Hepatitis B (recombinant) Vaccine
	HBVAXPRO 10 (EU/1/01/183/028)	Hepatitis B (recombinant) Vaccine
	HBVAXPRO 40 (EU/1/01/183/015)	Hepatitis B (recombinant) Vaccine
	Rabies Vaccine (PA 544/14/1)	Rabies Vaccine (inactivated)
	Pneumovax II Vial (PA 544/21/3)	Pneumococcal polysaccharide vaccine
	Avaxim (PA 544/29/1)	Hepatitis A (inactivated, adsorbed)
	Stamaril (PA 544/31/1)	Yellow Fever Vaccine (live)
	Pentavac (PA 544/32/1)	Diphtheria, tetanus, acellular, pertussis, inactivated poliomyelitis and haemophilus type b conjugate vaccine (adsorbed)
	Tetravac (PA 544/33/1)	Diphtheria, tetanus, acellular, pertussis, and inactivated poliomyelitis vaccine
	Typhim Vi (PA 544/7/1)	Typhoid polysaccharide Vaccine
	Inactivated Influenza Vaccine (split virion)BP (PA 544/34/1)	Influenza Vaccine (split virion, inactivated) (seasonal)
	Revaxis (PA 544/35/1)	Diphtheria, tetanus and poliomyelitis(inactivated) vaccine
	Varivax (PA 544/38/1)	Varicella Vaccine(live)

VACCINES AUTHORISED AND MARKETING IN IRELAND Feb 2008		
Marketing Authorisation Holder	Product Name and Authorisation number	Common Name
	Viatim (PA 544/37/1)	Typhoid polysaccharide and Hepatitis A (inactivated) Vaccine
SBL Vaccine Ab	Dukoral (EU/1/03/263/001-003)	Oral Cholera vaccine
Solvay Healthcare	Influvac Sub-unit PA 108/17/4	Influvac Sub-unit, suspension for injection (Influenza vaccine, surface antigen, inactivated)
Statens Serum Institute	BCG Vaccine (PA 798/2/1)	BCG Vaccine
	diTeBooster (PA 798/3/1)	Diphtheria and Tetanus vaccine (adsorbed)
Wyeth Lederle Vaccines SA JOHN WYETH & BROTHER	Prevenar pre-filled syringe 0.5ml singles pack with separate needle (EU/1/00/167/006)	Pneumoccal polysaccharide Conjugate Vaccine (adsorbed)
	Meningitec suspension for injection in prefilled syringe PA 22/78/2	Meningococcal Group C polysaccharide Conjugate Vaccine (adsorbed)

Appendix 2 Table of countries with TB Notification Rates $\geq 40/100,000$ Population, 2005 (WHO figures).

Western Pacific Region

Country	Rate/100,000 population
Brunei	44
Cambodia	253
China	68
China, Hong Kong SAR	81
China, Macao SAR	77
Kiribati	334
Lao PDR	64
Malaysia	61
Marshall Islands	179
Micronesia	89
Mongolia	174
Nauru	81
Northern Mariana Islands	71
Palau	50
Papua New Guinea	231
Philippines	165
Rep. of Korea	80
Solomom Islands	83
Tuvalu	115
Viet Nam	113
Wallis & Futuna	45

South-East Asia

Country	Rate/100,000 population
Bangladesh	87
Bhutan	47
DPR Korea	190
India	105
Indonesia	114
Myanmar	212
Nepal	123
Sri Lanka	45
Thailand	90
Timor-Leste	398

Europe

Country	Rate/100,000 population
Armenia	73
Azerbaijan	72
Belarus	54
Bosnia & Herzegovina	54
Bulgaria	42
Georgia	101
Kazakhstan	174
Kyrgyzstan	120
Latvia	61
Lithuania	62
Rep. of Moldova	122
Romania	120
Russian Federation	89

Tajikstan	84
Turkmenistan	66
Ukraine	85
Uzbekistan	81

Eastern Mediterranean

Country	Rate/100,000 population
Afganistan	73
Djibouti	392
Morocco	83
Pakistan	87
Qatar	40
Somalia	157
Sudan	76
Yemen	43

The Americas

Country	Rate/100,000 population
Bolivia	106
Brazil	43
Dominican Rep.	56
Guyana	85
Haiti	168
Honduras	46
Panama	51
Peru	119

Africa

Country	Rate/100,000 population
Algeria	65
Angola	233
Botswana	570
Burundi	87
Cameroon	132
Cape Verde	58
Central African Rep.	79
Chad	65
Congo	246
Cote d'Ivoire	108
DR Congo	169
Eritrea	81
Ethiopia	160
Gabon	182
Gambia	134
Ghana	55
Guinea	73
Guinea-Bissau	112
Kenya	300
Lesotho	602
Liberia	105
Madagascar	102
Malawi	198
Mauritania	70
Mozambique	168
Namibia	735
Niger	56

Nigeria	48
Rwanda	80
Sao Tome & Principe	87
Senegal	84
Sierra Leone	122
South Africa	570
Swaziland	781
Togo	41
Uganda	142
UR Tanzania	159
Zambia	425
Zimbabwe	388

Routine childhood immunisation schedule

Age	Immunisations	Comment
Birth	BCG	1 injection
2 months	DTaP/Hib/IPV/Hep B + PCV	2 injections
4 months	DTaP/Hib/IPV/Hep B + MenC	2 injections
6 months	DTaP/Hib/IPV/Hep B + PCV + MenC	3 injections
12 months	MMR + PCV	2 injections
13 months	MenC + Hib	2 injections ¹
4 to 5 years	DTaP/IPV + MMR	2 injections
11 to 14 years	Tdap + BCG ²	1 injection

¹ If a combined MenC/Hib vaccine is available only one injection is required.

² Only for those who are known to be tuberculin negative and have no previous BCG (see Chapter 16).

BCG	Bacille Calmette Guerin vaccine
DTaP	Diphtheria, Tetanus and acellular Pertussis vaccine
Hib	<i>Haemophilus influenzae</i> b vaccine
IPV	Inactivated Polio Virus vaccine
Hep B	Hepatitis B vaccine
PCV	Pneumococcal Conjugate Vaccine
MenC	Meningococcal C vaccine
MMR	Measles, Mumps and Rubella vaccine
Tdap	Tetanus, low-dose diphtheria and low-dose acellular pertussis vaccine