



SLMA
GUIDELINES AND
INFORMATION ON
VACCINES

FOURTH EDITION

SRI LANKA MEDICAL ASSOCIATION

COLOMBO

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ISBN 978-955-9386-24-7

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PREFACE

This is the fourth edition of the series of books on vaccines. The previous editions were published in 2001, 2004 and 2008 respectively. Many specialists have contributed to this book under the review of the Sri Lanka Medical Association (SLMA) Committee on Communicable Diseases. The SLMA wishes to thank the authors for their comprehensive contributions.

As we are well aware infections due to diverse organisms such as bacteria, viruses, parasites, fungi etc., account for innumerable deaths in children and adults. After the introduction of penicillin in the 1940s, several antibiotics have been used to combat bacterial infections which has resulted in a huge burden of resistant bacteria. Anti-viral agents are available only for very few infections such as varicella. Therefore, the most cost-effective way of controlling infections is through immunisation, which has been one of the greatest health success stories in the past.

There are about 70 different microbes causing a variety of infections for which over 30 different vaccines are available. Since 1977 no cases of small pox have been reported. The global eradication programme for elimination of poliomyelitis by the World Health Organization (WHO) has resulted in endemicity of poliomyelitis being confined to just 4 countries at present namely, India, Pakistan, Afghanistan and Nigeria.

In this book comprehensive information has been made available for specific vaccines. In the recent past, as adverse events following immunisation (AEFI) have resulted in disruption of the National Immunisation Programme, a chapter has been devoted to this topic. As more vaccinations are being carried out in the private sector, the importance of maintaining the cold chain has been emphasised in another chapter.

Vaccines do not save lives; vaccination does! Although measles vaccine has been available since 1969, hundreds of thousands of children

continue to die of measles in some African and South East Asian countries (In Sri Lanka measles has been almost eliminated).

In 2009 there were 8.1 million deaths in the under five year age group. Five diseases – pneumonia, diarrhoea, malaria, measles and HIV/AIDS, account for half of all deaths in these children, majority of whom live in developing countries. The 4th Millennium Development Goal of reducing the deaths of children under the age of 5 years by two thirds, by 2015, could be achieved by most developing countries, if vaccines against measles, poliomyelitis, pneumococcus, *Haemophilus influenzae* type b (Hib) and rotavirus are effectively used. Since the inception of the Expanded Programme of Immunization (EPI) in 1974, immunisation programmes have been significantly promoted by the WHO. However, the cost of the newer vaccines against pneumococcus, Hib and rotavirus has delayed their inclusion in the National Immunisation Programme of most developing countries.

The Global Alliance for Vaccines and Immunisation (GAVI) was launched in 2000 to fund the immunisation of children in 75 of the poorest countries. The contributors to GAVI include, WHO, UNICEF, World Bank, NGOs and foundations such as the Bill and Melinda Gates Foundation, governments of developed countries and the vaccine industry. During the last 10 years, through GAVI support, more than 288 million children have been immunized and over 5 million deaths have been prevented, and more and more millions are protected from illness and disability. GAVI has achieved what no single agency could have done on its own. In 2010, civil society organizations have joined GAVI as a constituency to strengthen GAVI's global activities.

The launch of the Advance Market Commitment through GAVI in 2010 and the International Finance Facility for Immunisation brought pneumococcal vaccines against the most deadly forms of pneumonia, the main killer of children under five, within the reach of developing countries.

Vaccines are now recognised to have an impact on non-communicable diseases (NCDs) as well.

The second leading cause of NCD is cancer. One fifth of cancers are caused by chronic infections such as hepatitis B and human papillomavirus (HPV), and vaccines exist to prevent both diseases.

Often at the initial introduction of a vaccine, the costs are prohibitively expensive. However, with wider use of the vaccines and more vaccine manufacturers in developing countries (such as India, China, Indonesia, Brazil) entering the arena, the cost of vaccines has plummeted. The best example is the hepatitis B vaccine which costed over USD 60 per dose when first introduced in the 1980s; thirty years later it costs only few US cents per dose. The sincere hope of third world countries is that the pneumococcal vaccine which is expensive at present, would follow a similar course.

Professor Sanath P Lamabadusuriya MBE

President

Sri Lanka Medical Association

INTRODUCTION

Edward Jenner demonstrated the value of immunisation against smallpox in 1792. Nearly 200 years later, in 1977, smallpox was eradicated from the world through the widespread and targeted use of the vaccine. The global vaccine scene has changed drastically during the past two decades. The most obvious sign of change is a wave of production of new vaccines that began during the last two decades and continues to date. The new vaccines represent a major advance in the science of discovery as well as in production technologies. This period witnessed the production of several conjugate vaccines, *Haemophilus influenzae* type b (Hib) pneumococcal and meningococcal vaccines. The other major development has been in the successful production of combined vaccines which reduces the number of injections without compromising on the efficacy of individual vaccines. The next step forward was utilisation of a new technology, e.g. genetic recombination for production of influenza, rotavirus and human papillomavirus (HPV) vaccines. Vaccines have been useful in preventing malignancies. The hepatitis B virus vaccine prevents chronic liver disease which in some, results in liver cancer. The human papillomavirus vaccine is targeted to prevent cervical cancer, in which the aetiology is confined to persistent HPV infection. This wave of new vaccines also correlated with new pricing policies, such as tiered pricing to make vaccines more affordable for developing countries. Along with these changes, the formation of the Global Alliance for Vaccines and Immunisation (GAVI) and the dedication of new streams of funding led to an emphasis on global vaccination efforts. Thus a number of these new vaccines are already registered for use in Sri Lanka.

With regard to childhood immunisation programmes, the World Health Organization (WHO) established the Expanded Programme on Immunisation (EPI) in 1974. Through the 1980s, WHO and UNICEF worked together to achieve universal childhood immunisation of the six EPI vaccines (BCG, OPV, diphtheria, tetanus, pertussis, and measles) and as a result the current global immunisation coverage is over 80%. New vaccines, pneumococcal conjugate vaccine and rotavirus vaccine

against the leading causes of child deaths, pneumonia and diarrhoea, offer new hope.

Vaccination against smallpox was introduced in Sri Lanka under the Vaccination Ordinance as early as 1886. Subsequently BCG was introduced in 1949 and DPT in 1961. This was closely followed by OPV in 1962. Sri Lanka launched the EPI in 1978 and measles vaccination was included into the EPI in 1984. Sri Lanka's immunisation programme is widely recognized as one of the strongest performers in the region and is among the best in the world. It has effectively controlled or eliminated all traditional childhood vaccine preventable diseases through outstanding levels of sustained infant immunisation coverage. Throughout the last decade, immunisation coverage of infants in Sri Lanka against the six diseases has exceeded 99% as per WHO fact sheet of 2011. In addition the state sponsored, national infant immunisation programme introduced the Hep B vaccine in 2003 which was administered simultaneously with the DPT vaccine. Subsequently with the introduction of the *Haemophilus influenzae* type b (Hib) vaccine in 2008, the pentavalent vaccine (DTwP-Hep B -Hib) replaced the DPT and hepatitis B vaccines requiring only a single injection to administer all five vaccines.

The Communicable Diseases Committee of the Sri Lanka Medical Association reviewed the first edition of this book written by several specialists. It was titled "Guidelines for the use of non EPI vaccines" and was published in 2001. The second edition published in 2004 included the EPI vaccines and was named the "SLMA guidelines on vaccines". The third edition was published in 2008 and was titled "SLMA guidelines and information on vaccines. Work on the fourth edition began in January 2011, with the objective of providing updated information on vaccines to healthcare professionals in Sri Lanka. New vaccines have become available, vaccination schedules have changed and some vaccines have been replaced. The introduction of the live Japanese encephalitis (JE) vaccine has reduced the number of doses required for effective prevention of JE. The MMR vaccine has been introduced to the childhood immunisation programme in 2011 and has replaced the measles and measles-rubella vaccines and is expected to reduce the morbidity due to

deafness, a serious complication of mumps virus infection. Thus the chapter on measles and rubella has been omitted from the current edition.

In addition to the updated information on vaccines included in the previous edition, the revised edition contain new chapters devoted to providing information on 'precautions prior to vaccination' and 'storage and transport of vaccines' that are important additions in the current context where immunisation services are being provided by many Family Practitioners and non state healthcare facilities.

These guidelines are intended to provide assistance to practitioners in their practice and it should be noted that they represent a consensus opinion arrived at, by committee members and authors of chapters. As new information becomes available this edition will be revised. I am grateful to authors of the chapters and the core group who reviewed them, for their dedicated efforts to formulate the revised guidelines. I thank GlaxoSmithKline for their sponsorship during the preparation of the manuscript and for its publication.

This year's theme of the Sri Lanka Medical Association is "Marching Towards Millenium Development Goals". Targets for reduction in the rates of infectious diseases are included in the goals. I earnestly hope and believe that this book will contribute to reducing mortality and morbidity due to infectious diseases by decreasing vaccine preventable diseases.

Professor Jennifer Perera

Chairperson

SLMA Communicable Diseases Committee

ABBREVIATIONS

ACIP	Advisory Committee on Immunisation Practices (of the Centres for Disease Control and Prevention)
AEFI	adverse events following immunisation
AFP	Acute flaccid paralysis
AIDS	Acquired Immunodeficiency Syndrome
ARSN	Asian Rotavirus Surveillance Network
ARV	anti-rabies vaccine
aTd	adult tetanus and diphtheria vaccine
BCG	Bacille Calmette- Guerin
CCID ₅₀	cell culture infective dose 50
CDC	Centres for Disease Control
CD4	cluster of differentiation 4
CMVIG	cytomegalovirus immunoglobulin
CRS	congenital rubella syndrome
DNA	deoxyribonucleic acid
DTP	diphtheria, tetanus and pertussis vaccine
DTaP	diphtheria, tetanus and acellular pertussis vaccine
DTwP	diphtheria, tetanus and whole cell pertussis vaccine
DTP-HepB	diphtheria, tetanus, pertussis and hepatitis B vaccine
DTaP-HepB	diphtheria, tetanus and acellular pertussis and hepatitis B vaccine
DTP-HepB-Hib	diphtheria, tetanus and pertussis, hepatitis B and <i>Haemophilus influenzae</i> type b vaccine
DTaP-HepB-Hib-IPV	diphtheria, tetanus and acellular pertussis, hepatitis B, <i>Haemophilus influenzae</i> type b and injectable polio vaccine

DTP-Hib	diphtheria, tetanus and whole cell pertussis and <i>Haemophilus influenzae</i> type b vaccine
DT	diphtheria and tetanus vaccine
dTpa	reduced antigen, diphtheria, tetanus and acellular pertussis vaccine
EPI	Expanded Programme of Immunisation
ERIG	equine rabies immunoglobulin
EU	enzyme linked immunosorbent assay (ELISA) units
FA	fluorescent antigen
GAVI	Global Alliance on Vaccination and Immunisation
GBS	Guillan Barre Syndrome
HAV	hepatitis A virus
HBV	hepatitis B virus
HBIG	hepatitis B immunoglobulin
HBsAg	hepatitis B surface antigen
HDV	hepatitis D virus
HDC	human diploid cell
HDCV	human diploid cell vaccine (for rabies)
Hep B	hepatitis B
Hib	<i>Haemophilus influenzae</i> type b
Hib-PRP	<i>Haemophilus influenzae</i> conjugated polysaccharide vaccine
PRP-D	with diphtheria toxoid
PRP-T	with tetanus toxoid
PRP-OMP	with meningococcal outer membrane protein
HbOC	<i>Haemophilus b</i> oligosaccharide
HIV	human immunodeficiency virus

HMSO	Her Majesty's Stationery Office	PCEC	purified chick embryo cell vaccine (for rabies)
HPV	human papillomavirus	PCV	pneumococcal conjugate vaccine
HRIG	human rabies immunoglobulin	PET	post exposure treatment (for rabies)
HTIG	human tetanus immunoglobulin	PLHIV	people living with HIV/AIDS
ICV	International Certificate of Vaccination	PVRV	purified vero cell rabies vaccine
ID	intra-dermal	RIG	rabies immunoglobulin
IG	immunoglobulin	RNA	ribonucleic acid
IgA	immunoglobulin A	SC	subcutaneous
IM	intramuscular	SLMA	Sri Lanka Medical Association
IPV	injectable polio vaccine	SLSI	Sri Lanka Standards Institute
ITI	Industrial Technology Institute	ST	sensitivity test
IU	international units		
JAMA	Journal of the American Medical Association	TCV	tissue culture vaccine
JE	Japanese encephalitis	TIG	tetanus immunoglobulin
LAIV	intranasal live attenuated influenza vaccine	TIV	trivalent inactivated vaccine (influenza)
mIU	milli international units	TST	tuberculin skin test
mL	millilitre	TT	tetanus toxoid
MCV4	tetavalent meningococcal conjugate vaccine	UNICEF	United Nations Children's Fund
MPSV4	tetavalent meningococcal polysaccharide vaccine	VAPP	vaccination associated paralytic poliomyelitis
MMR	measles, mumps and rubella vaccine	VZIG	varicella zoster immunoglobulin
NAT	nucleic acid amplification testing	VZV	varicella zoster virus
NCD	non-communicable diseases	WHO	World Health Organization
NGO	non governmental organisation		
N saline	0.9 % sodium chloride		
OCV	oral cholera vaccine		
OPV	oral polio vaccine		

PRECAUTIONS BEFORE VACCINATION

1. Vaccines should not be given;

if there was a severe reaction,

- such as anaphylaxis following administration of that particular vaccine
- to a component of the vaccine

2. Live vaccine should not be given;

- to a person having a malignancy of the reticulo-endothelial system
- if pregnant or pregnancy is planned within three months
- to a person with immune deficiency disorders

3. Postpone vaccination;

- if suffering from an acute infection and/or fever ($>100^{\circ}\text{F}$)
- live vaccine had been administered within one month
- if the person has had blood or blood products including immunoglobulin within three months
- for one month after stopping long-term oral steroids (≥ 2 mg/kg/day prednisolone or equivalent) or 20 mg/kg/day for more than 2 weeks
- for three months after stopping immunosuppressive chemotherapy

4. Be cautious if there is;

- a bleeding disorder
- a history of Guillain Barre Syndrome
- a progressive neurological disorder

5. Vaccination should be given in a hospital if there is a history of severe allergy.

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CHAPTER 1

BCG

Introduction

Tuberculosis is a chronic disease caused by *Mycobacterium tuberculosis*. Primary infection often goes unnoticed clinically; tuberculin sensitivity appears within few weeks and lesions commonly become inactive. It may progress to pulmonary tuberculosis, miliary tuberculosis or meningitis. The only vaccine available for the prevention of tuberculosis is BCG (Bacillus Calmette-Guerin), which was first developed in 1920s.

The coverage of BCG is 99% in Sri Lanka.

Type of vaccine

Live attenuated vaccine

Efficacy

BCG is a relatively weak protective vaccine because only 50% randomised control trials shows it to be effective.

However, childhood immunisation with BCG has caused a remarkable reduction in the incidence of miliary tuberculosis and tuberculous meningitis in children.

Indications

At birth, (including low birth weight babies before discharge from hospital).

Children between 6 months and 5 years of age without BCG scar.

(A tuberculin test is not indicated up to the age of 5 years).

Children over 5 years and adults who are tuberculin negative (less than 10 mm).

Certain strains of BCG may be useful in the treatment of early bladder cancer.

Dosage and administration

Freeze dried vaccine (1 ampoule of 20 doses) is dissolved in 1 mL of solvent.

Dose is 0.05 mL for infants and 0.1 mL for children over 1 year and adults.

When withdrawing doses from a vial, the vaccine should be exposed to light for the shortest period of time possible, and never for more than 4 hours. If it is not used immediately after reconstitution, the vaccine should be stored between 2°C and 8°C and protected from light. Any opened vial remaining at the end of a vaccination session (maximum 4 hours) should be discarded.

The vaccine should be injected by a trained person, strictly via the ID route, avoiding the SC route. For each injection, use one syringe for ID use, fitted with a fine (gauge 27), short (1 cm) beveled needle. No spirit or antiseptic should be applied over the site before injection. Normal saline can be used to clean the area. Hold the arm, and, stretching the skin, introduce the needle with bevel upwards, tangentially to the skin. As soon as the bevel has penetrated the skin, push the plunger gently to introduce the liquid. This injection, administered in the deltoid region of the left arm, should produce an orange-skin papule with a diameter of about 3-4 mm in infants and 6-8 mm in adults, immediately after injection.

Administration of BCG to any other site is not recommended.

Contraindications

Hypersensitivity to any component of the preparation.

Immunodeficiency affecting cell mediated immunity.

HIV infection.

(Infants born to HIV positive mothers could be tested for HIV infection

using HIV RNA test offered by the STDAIDS Control Programme and if results are negative BCG should be administered).

Vaccination need not be postponed in children with common illnesses such as rhinopharyngitis, asthma or eczema, and in children taking antibiotics.

A local reaction is normal after BCG vaccination. A few days after vaccination, an induration develops at the point of injection, gradually changing to a small vesicle and then an ulcer in 2 to 4 weeks. The local reaction usually regresses in 2 to 5 months, leaving a superficial scar.

Adverse effects

In rare cases, an abscess may appear at the point of injection. Axillary or rarely cervical adenitis may occur, leading in exceptional cases to suppuration, requiring treatment with anti-tuberculous therapy.

Faulty injection technique is the most frequent cause of severe injection site reaction.

Storage

2°C-8°C

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CHAPTER 2

CHOLERA VACCINE

Introduction

Cholera is an acute intestinal infection caused by the toxigenic Gram negative bacterium *Vibrio cholerae*. The infection is often asymptomatic or mild and self limited. In severe illness, the patient develops profuse painless diarrhoea with characteristic "rice water stools" associated with vomiting, thirst and muscle cramps. This may lead to rapid volume depletion, sometimes resulting in circulatory collapse. Death may occur in severely dehydrated patients within a few hours after the onset of symptoms. The case fatality rate may exceed 50% among untreated severe cases, but is less than 1% with proper and timely treatment.

Infection is acquired primarily by ingesting contaminated water or food. The incubation period varies from few hours to 5 days, usually 2-3 days.

Increasing frequency of major cholera outbreaks in the world, emergence of new, more virulent strains of *V. cholerae* O1 in parts of Africa and Asia and, emergence and spread of antibiotic-resistant strains have raised serious concerns more recently.

Types of vaccine

Two types of inactivated oral cholera vaccines (OCV) are currently available:

- (1) **WC-rBS**, a monovalent vaccine containing inactivated whole cell *V. cholerae* O1 (classical and El Tor, Inaba and Ogawa) plus recombinant cholera toxin **B** subunit, and
- (2) bivalent vaccines, which contain serogroups O1 and O139.

Live attenuated OCV is no longer available. The use of injectable whole cell cholera vaccine, still produced in a few countries, is not recommended by the World Health Organization due to its low efficacy and limited duration of protection.

Cholera vaccines are not currently available in Sri Lanka.

Efficacy

The currently available OCVs are safe and offer protection of >50% for at least 2 years among endemic populations.

Since immunisation does not provide complete protection against cholera infection, all travellers to a cholera endemic country should be cautioned that the best protection against cholera is to avoid contaminated food and water.

Indications

Oral cholera vaccine is recommended for travellers to endemic or epidemic areas. However, currently there is no mandatory requirement for cholera vaccination as a prerequisite for entry into any country.

Immunisation should be completed at least 1 week before potential exposure.

Dosage and administration

The monovalent vaccine is a 3 ml oral suspension, plus a sachet of effervescent sodium bicarbonate granules (buffer). Vaccine and buffer are mixed in either 150 ml of water (for aged >5 years) or 75 ml (for children aged 2-5 years). One of the bivalent vaccines, which will be available in international market, comes in 1.5 ml single-dose vials.

Product		Primary immunisation	Booster
Monovalent vaccine	Adults & children ≥6 years of age	2 doses, more than 7 days apart (but less than 6 weeks)*	1 dose after 2 years*
	Children 2-5 years of age	3 doses, more than 7 days apart (but less than 6 weeks)*	1 dose every 6 months*
Bivalent vaccine	Adults & children ≥1 year of age	2 oral doses 14 days apart	Booster after 2 years

** If the interval between doses is longer than indicated, restart primary immunisation.*

Food, drink, and other oral medicines should be avoided 1 hour before and after vaccination.

Contraindications

General contraindications for vaccines are applicable (refer chapter 27).

Adverse effects

Adverse effects include headache, diarrhoea, abdominal pain, and rarely, nausea, vomiting, loss of appetite, dizziness, fever, and respiratory symptoms.

Storage

2°C-8°C

Use of cholera vaccine in outbreaks

Vaccination should not be the mainstay of control measures, when an outbreak has already commenced. Pre-emptive vaccination should be considered if the current outbreak is likely to extend to new geographical

areas. Reactive vaccination may become relevant as an additional control measure, depending on the previous and present epidemiological situation, local infrastructure, the logistics associated with its use and the ability to clearly identify target populations. Coverage and rapidity of pre-emptive or reactive vaccination should be as high as and as quickly as possible.

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CHAPTER 3

DIPHTHERIA, TETANUS AND PERTUSSIS VACCINE

Introduction

Diphtheria is a potentially acute disease caused by exotoxin-producing *Corynebacterium diphtheriae*. Morbidity and mortality result from the bacterial toxin that may cause obstructive pseudo-membranes in the upper respiratory tract (croup) or damage to myocardium and other tissues. Devastating diphtheria epidemics affecting mainly children have been described from many countries throughout history. Diphtheria toxoid is one of the oldest vaccines in current use.

Pertussis (whooping cough) caused by *Bordetella pertussis* is an important public health concern even in countries with high vaccination coverage. The clinical outcome of pertussis depends on factors such as age and vaccination status. Although most cases of clinically recognizable pertussis occur in older children, adolescents and adults, pertussis is often unrecognised because of its frequent atypical course. However, older age groups represent an important source of infection for susceptible infants. The main aim of pertussis vaccination is to reduce the risk of severe pertussis in infancy.

Tetanus is an infectious bacterial disease caused by *Clostridium tetani*. Under favourable anaerobic conditions it may produce tetanospasmin, an extremely potent neurotoxin. The disease may affect any age group and protection against tetanus is antibody-dependent and can be achieved only through active (tetanus vaccine) or passive (tetanus-specific immunoglobulin) immunisation. The immunised mother passes antitoxin via the placenta to her fetus, thereby preventing neonatal tetanus.

Combined Diphtheria, Tetanus and Pertussis vaccines (DTwP), has been part of the Immunisation Programme of Sri Lanka from 1961 and in 2004 combined pentavalent DPwT-HepB-Hib vaccine was introduced.

Types of diphtheria, pertussis, tetanus (DPT) vaccines

The following preparations of Diphtheria, Pertussis, Tetanus vaccines are available:

(i) Diphtheria-tetanus-whole cell pertussis vaccine (DTwP)

Diphtheria, tetanus and pertussis adsorbed vaccine is prepared by combining purified diphtheria toxoid, purified tetanus toxoid and suspensions of *B. pertussis* organisms that have been inactivated, usually by formalin. The antigens are adsorbed onto aluminium phosphate adjuvant.

Each DPwT 0.5 ml dose contains diphtheria toxoid ≥ 30 IU, tetanus toxoid ≥ 40 IU and *B. pertussis* ≥ 40 PU adsorbed on aluminium phosphate ≥ 1.5 mg.

(ii) Diphtheria-tetanus-acellular pertussis vaccine (DTaP)

The DTaP vaccine contains purified diphtheria toxoid, purified tetanus toxoid and inactivated pertussis toxin either alone or in combination with other *B. pertussis* components such as filamentous haemagglutinin (FHA), fimbrial antigens and pertactin.

Each DPaT 0.5 ml dose contain diphtheria toxoid ≥ 30 IU, tetanus toxoid ≥ 40 IU and *B. pertussis* toxoid 25 mcg, FHA 25 mcg and pertactin 8 mcg. The antigens are adsorbed onto aluminium salt adjuvants.

(iii) Diphtheria and tetanus vaccine adsorbed (DT)

Diphtheria and tetanus toxoid adsorbed vaccine is prepared by combining purified diphtheria toxoid and purified tetanus toxoid. The antigens are adsorbed on to aluminium phosphate adjuvant.

Each 0.5 ml dose of DT contains diphtheria toxoid ≥ 30 IU and tetanus toxoid ≥ 40 IU and adsorbed on aluminium phosphate ≥ 1.5 mg.

(iv) Diphtheria and tetanus vaccine adsorbed for adults and adolescents (aTd)

Vaccines of lower potency are used for immunisation of children aged over 7 years and adults. This reduction of diphtheria toxoid potency minimises reactogenicity at the injection site but is still sufficient to provoke an antibody response in older children and adults.

Diphtheria and tetanus vaccine adsorbed for adults and adolescents is prepared by combining purified diphtheria toxoid and purified tetanus toxoid. The antigens are adsorbed onto aluminium phosphate adjuvant.

Each 0.5 ml dose of aTd contains diphtheria toxoid ≥ 2 IU and tetanus toxoid ≥ 40 IU adsorbed on aluminium phosphate ≥ 1.5 mg.

(v) Reduced-antigen diphtheria-tetanus-acellular pertussis vaccine (dTpa)

Each 0.5 ml dose of dTpa contains diphtheria toxoid ≥ 2 IU, tetanus toxoid ≥ 20 IU and *B. pertussis* toxoid 8 mcg, FHA 8 mcg and pertactin 2.5 mcg.

(vi) DPaT-HepB vaccine (Please see chapter 6 for more details)

(vii) DPwT-Hib vaccine (Please see chapter 4 for more details)

(viii) DPwT-HepB-Hib (Please see chapters 4 and 6 for more details)

(ix) DTaP-HepB-IPV-Hib (Please see chapter 4 for more details)

Efficacy

Three doses of DPT vaccine, starting as early as 2 months of age and given at least 8 weeks apart at the age of 4 and 6 months are recommended for primary immunisation of infants.

The protection following primary DTP vaccination wanes after 6-12 years. Therefore, the primary vaccination series of 3 doses should be extended

by at least 1 booster dose. To compensate for the loss of natural boosting childhood boosters of DPT should be added to the primary immunisation series of infancy. The optimal timing for and the number of such booster doses should be based on epidemiological surveillance as well as on immunological and programmatic considerations. Boosting at the age of 18 months, at school entry and at 10 to 12 years of age is recommended.

Revaccination of adults against diphtheria and tetanus every 10 years may be necessary to sustain immunity in some epidemiological settings.

High-efficacy levels can be obtained with both DTwP and DTaP vaccines. Available limited data on the interchangeability of pertussis vaccines shows that changing among or within the wP and aP vaccine groups is unlikely to interfere with the safety or immunogenicity of these vaccines.

Indications

- (i) Adsorbed diphtheria, tetanus and pertussis vaccine (DTwP, DTaP)
 1. Primary course of immunisation against diphtheria, tetanus and pertussis is recommended for all infants on completion of 2, 4, 6 and 18 months of age, unless there is a contraindication. If the primary course is interrupted it should be resumed but not repeated, allowing appropriate intervals (minimum of 6-8 weeks) between the remaining doses.
 2. There is no contraindication to vaccination of unimmunised older children up to the age of 7 years.
- (ii) Adsorbed diphtheria and tetanus vaccine (DT)
 1. This vaccine is used for primary immunisation in place of the DTP vaccine, when immunisation against whooping cough is contraindicated.
 2. It is recommended for children immediately before school entry (on completion of 5 years), preferably after at least 3 years from the last dose of the primary course.

- (iii) Diphtheria and tetanus vaccine adsorbed for adults and adolescents (aTd)

For primary vaccination and re-vaccination of adults and adolescents, who are having contraindications for DTP primary vaccination and re-vaccination of children older than 7 years. In order to prevent allergic reactions to the protein of diphtheria toxoid, the quantity of the toxoid has been markedly reduced.

- (iv) Reduced antigen diphtheria tetanus acellular pertussis vaccine (dTpa)

For booster vaccination against diphtheria, tetanus and pertussis of individuals from age of four years onwards.

Dosage and administration

Dose 0.5 ml. DTP vaccine should be administered deep intramuscularly in the anterolateral thigh in infants or in the deltoid muscle in older age groups.

Contraindications

The vaccine should not be given to persons who showed a severe reaction to previous doses of DTP vaccine:

- an extensive area of redness and swelling which becomes indurated and involves most of the antero-lateral surface of the thigh or a major part of the circumference of the upper arm;
- fever equal to or more than 39.5°C within 48 hours of vaccination;
- anaphylaxis;
- bronchospasm; laryngeal oedema; generalised collapse;
- encephalopathy within 7 days;
- prolonged unresponsiveness;
- prolonged inconsolable screaming;
- convulsions occurring within 72 hours,

These reactions may increase in severity with each subsequent injection and in those with severe reactions, DT or DTaP should be used for subsequent vaccinations.

Immediate anaphylaxis to DTP is a contraindication for the use of both DTwP or DTaP.

Progressive neurological disorder (e.g. infantile spasms) is a contra indication.

Precautions

Acute illness is not a contraindication and vaccination should be postponed until the child recovers.

Neither a personal or family history of allergy, nor non progressive neurological conditions such as cerebral palsy or spina-bifida are contraindications to immunisation with DTP.

However, there are certain groups of children to whom the administration of whooping cough immunisation requires special considerations. For these, the risk from vaccine may be higher, but the effects of whooping cough disease could be more severe. The balance of risk and benefit should be assessed in each case. Where there is doubt, appropriate advice should be obtained from a consultant paediatrician before a decision is made to withhold the vaccine.

These groups are:

1. Children with a documented history of cerebral damage in the neonatal period.
2. Children with a history of convulsions.

Adverse effects

While in terms of severe adverse events, DTaP and DTwP vaccines appear to have the same high level of safety, mild adverse reactions are relatively common with DTwP vaccine.

Whole-cell pertussis vaccines are not recommended for use in adolescents and adults due to high reactogenicity. Therefore, vaccine containing acellular pertussis antigen is recommended for them. Vaccines containing lower dose of diphtheria toxoid (aTd, dTpa) are recommended for adolescents and adults to provide satisfactory immune response with lower risk of reactions.

D.P.T.

Local reactions

Pain, redness and swelling at the injection site may occur and persist for several days; persistent nodules at the injection site may arise if the injection is not given deep enough.

Systemic reactions

Headache, lethargy, malaise, myalgia and pyrexia may occur uncommonly; acute anaphylactic reactions and urticaria may occasionally occur and, rarely peripheral neuropathy.

Crying, screaming and fever may occur for the whooping cough component in triple vaccine; these reactions may also occur after vaccines which do not contain the whooping cough component; attacks of high pitched screaming, episodes of pallor, cyanosis, limpness, convulsions as well as local and general reactions have been reported; neurological events including convulsions and encephalopathy may rarely occur after the whooping cough component.

D.T.

Local reactions

Reactions are generally mild and confined to the site of injection. Occasionally a painless nodule may develop at the site of injection but usually disappears without sequelae.

Systemic reactions

Transient fever, headache, malaise and irritability. Severe anaphylactic reactions are rare; neurological reactions have been reported occasionally

Storage

The vaccine should be stored in a dry place and stored and transported at 2°C to 8°C. Vaccines should not be frozen or come into direct contact with ice or ice packs during transport or storage. DTP vaccines can be irreversibly damaged by inadvertent freezing. Pertussis vaccine can be damaged by heat.

Further reading

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CHAPTER 4

HAEMOPHILUS INFLUENZAE TYPE B VACCINE

Introduction

Haemophilus influenzae b (Hib) is a common cause of bacterial meningitis, pneumonia and septicaemia in children. There is evidence that a significant number of cases of meningitis in children in Sri Lanka are due to *Haemophilus influenzae* type b. In industrialised countries and some parts of the developing world, immunisation has greatly reduced the incidence of Hib disease.

Types of vaccine

Hib vaccines consist of polyribosylribitol (PRP) conjugated to a protein carrier. The conjugated protein carrier induces immune response to the PRP polysaccharide.

Currently available Hib vaccines are based on Hib-PRP polysaccharide conjugated to one of the following protein carriers:

- (i) Non toxic mutant diphtheria toxin CRM 197 (PRP-CRM197)
- (ii) Tetanus toxoid (PRP-T)
- (iii) Meningococcal outer membrane protein (PRP-OMP)
- (iv) Haemophilus b oligosaccharide (HbOC)
- (v) Diphtheria toxoid (PRP-D)

Hib vaccine, either monovalent or in combinations with varying antigens, is available in both liquid and lyophilized (freeze dried) preparations. These vaccines induce protective circulating antibodies and immunological memory in all age groups.

The available Hib vaccines in combinations are as follows:

- with diphtheria, tetanus and whole cell pertussis vaccine (DTwP-Hib)

- with diphtheria, tetanus and whole cell pertussis and hepatitis B vaccine (DTwP-HepB-Hib)
- with diphtheria, tetanus, acellular pertussis, hepatitis B and inactivated polio vaccine (DTaP-HepB-IPV/Hib)

Efficacy

Hib vaccines are efficacious even when administered in early infancy. Though the duration of protection following the primary series is poorly defined, in most instances, it is protective during the years of the highest susceptibility to invasive Hib disease. Other than PRP-D, all other conjugate Hib vaccines have demonstrated remarkably high, consistent efficacy and effectiveness against Hib invasive disease in a variety of settings.

Among conjugate Hib vaccines, only PRP-OMP is highly efficacious after a single dose. PRP-T conjugate Hib vaccine has demonstrated that following the initial dose, second and third additional doses given at 2 months intervals are required to induce high levels of immunity. After a third dose, 98-100% immunogenic response has been demonstrated even in younger infants. PRP-T conjugate Hib vaccine has demonstrated an efficacy over 95% against all invasive Hib disease and 100% efficacy against Hib pneumonia.

Partly as a consequence of the effect of herd immunity induced by Hib vaccination, nasopharyngeal colonization has been drastically reduced in populations with high vaccine coverage. As a consequence of these direct and indirect effects, Hib disease has been practically eliminated in many industrialised countries and its incidence has been drastically reduced in some developing countries.

Indications

Infants and children under 5 years of age.

Older children and adults who are at risk of invasive Hib disease due to following conditions:

HIV/AIDS

Partial immunoglobulin deficiency

Hodgkin's disease

Recipients of stem cell transplants

Patients undergoing chemotherapy for malignant neoplasm

Anatomic or functional asplenia

Sickle cell anaemia or thalassaemia

Children with nephrotic syndrome

Children who have had invasive Hib disease

Children under two years of age with Hib disease do not produce antibodies reliably. As such, these children need the full course of immunisation. For others, the number of doses required will depend on the age at which the first dose after the illness is given, ignoring any doses given before the illness. Re-immunisation should be initiated approximately one month after the onset of disease.

Dosage and administration

In general, a three dose primary series is given at the same time as the primary series of DTP. The National Immunisation Programme recommends administration of Hib vaccine at 2nd, 4th, and 6th months of life. The first dose may be given as early as 6 weeks of age and the second and 3rd doses may be given 4-8 weeks intervals along with DTP. In developed countries, a booster dose is given at 12-18 months. If immunisation is started between 6 months and one year of age, the child should receive two doses, 4-8 weeks apart.

For children aged 12-24 months who have not received the primary series of Hib vaccine, one dose is sufficient.

All conjugate Hib vaccines should be injected deep intramuscularly. The standard dose is 0.5 ml.

An immunisation series started with one type of conjugate Hib vaccine may be completed with another formulation of conjugate Hib vaccine.

Hib vaccine, as a separate vaccine, can be given at the same time as other routine vaccines at a different site. However, it should not be mixed in the vial or syringe with any other vaccine.

Contraindications

Other than general contraindications to any vaccine, following are specific contraindications to Hib vaccines:

- Known hypersensitivity or anaphylaxis to any component of the vaccine.
- History of hypersensitivity to a previous dose of Hib vaccine.

Adverse effects

Hib vaccine has not been associated with serious adverse events. In rare reports of severe adverse events, no causal effect of the vaccine has been established. However, some local and systemic reactions have been reported. In general, these reactions appear within 24-72 hours after vaccination, are mild and resolve spontaneously.

Local reactions – redness, pain and swelling at the injection site.

Systemic reactions – fever, loss of appetite, restlessness, irritability, vomiting, diarrhoea and unusual crying.

Storage

2°C-8°C

Further reading

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CHAPTER 5

HEPATITIS A VACCINE

Introduction

Hepatitis A virus (HAV) produces an acute hepatitis after an average incubation period of 28 days (range 15 - 50 days) and it is transmitted by the faeco-oral route. In children <16 years, about 70% of the infections are asymptomatic and they shed the virus for longer periods compared to adults, lasting up to 10 weeks after onset of illness. Viraemia occurs soon after infection, however the concentration in blood is much lower than in stools. A person is most infectious from 14-21 days before the onset of symptoms, through 1 week after the onset of symptoms. Complications of hepatitis A include relapsing hepatitis, cholestatic hepatitis and fulminant hepatitis. Fulminant hepatitis leading to liver failure with high mortality occurs in less than 0.5% but this increases up to 2% in adults over 50 years. Acute liver failure is more common in pregnancy and in alcoholics with liver disease. There are no carriers of the virus. HAV has been transmitted by transfusion of blood and blood products collected from donors during their viraemic phase of infection. Outbreaks of HAV have been reported among intravenous drug users, men who have sex with men and persons who work with nonhuman primates. Globally an estimated 1.5 million clinical cases of hepatitis A occur each year.

In a hospital based study conducted in Colombo in 2002, seroprevalence for hepatitis A virus was 10.8% in children aged 1 to 12 years. However, according to studies in the South East Asia there is about 75% seroconversion by adolescence.

Types of vaccine

Formalin inactivated purified virus adsorbed to adjuvant aluminium hydroxide is used as the vaccine.

Vaccine preparations

Two preparations

1. Viral antigen content is expressed as 1440 ELISA units (EL.U.) /ml 2-phenoxyethanol is the preservative.
2. Viral antigen content is expressed as 50 units (U)/ ml. No preservative.

The two brands of the hepatitis A vaccine are interchangeable.

Combined vaccine: A combination vaccine containing inactivated hepatitis A and recombinant hepatitis B vaccines is available for use in persons over one year countries. The combination vaccine is given as a 3-dose series, using a 0, 1, 6 month schedule.

Efficacy

Efficacy ranges between 94% to 99%.

The duration of protection is at least 25 years or possibly life long.

Post exposure vaccination efficacy is 79%.

Indications

For individuals over 12 months of age.

Recommended for

Travellers to high endemic areas

Armed forces and persons working in natural disaster or war affected areas

High risk groups – day care staff, hospital workers, laundry and cleaning staff

Contacts of patients

Sewage workers

Food handlers

Intravenous drug users
Patients needing repeated transfusions of blood and blood products
Male homosexuals
Persons with chronic liver disease
Persons with developmental disabilities
Children, adolescents and high risk persons during hepatitis A outbreaks

Post exposure prophylaxis

The performance of vaccine, when administered <14 days after exposure, approaches that of immunoglobulin (IG) in healthy children and adults aged <40 years. However, these findings might not be generalisable to all populations and settings.

Healthy persons aged 12 months-40 years who recently have been exposed to HAV and who previously have not received hepatitis A vaccine should be administered a single dose of single-antigen hepatitis A vaccine or IG (0.02 mL/kg) as soon as possible and vaccine is preferred over IG. Vaccine recipients should complete the second dose 6-12 months after the first dose to protect against infections from future exposures.

Post exposure prophylaxis with IG is indicated for:

Children aged <12 months and persons over 40yrs of age, immunocompromised persons, persons who have had chronic liver disease, and persons for whom vaccine is contraindicated. When administered IM before or within 2 weeks after exposure to HAV, IG is >85% effective in preventing HAV infections.

If IG is administered to persons for whom hepatitis A vaccine also is recommended, a dose of vaccine should be administered simultaneously with IG at a separate anatomical injection site. The second vaccine dose should be administered 6-12 months after the first dose to complete the series.

The efficacy of IG or vaccine when administered >2 weeks after exposure has not been established.

Dosage and administration

Two doses IM for both vaccines

0.5 mL at 0, and 6-12 months later in children 1-18 years old

1.0 mL at 0, and 6-12 months later in adults ≥19 years

Contraindications

Hypersensitivity to any component of the vaccine or previous dose.

Acute febrile illness.

The safety data in pregnant women are not available, but the risk is considered to be low or nonexistent because the vaccines contain inactivated purified viral proteins.

Can be administered to immunocompromised patients.

Adverse effects

No serious events attributed to hepatitis A vaccine has been reported.

Local – Transient erythema, soreness and induration at injection site.

Systemic – Headache, malaise, fever, vomiting, nausea in of vaccinees. These usually occur 3-5 days after vaccination and lasts for 1-2 days.

Storage

2°C-8°C. Do not freeze.

Further reading

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CHAPTER 6

HEPATITIS B VACCINE

Introduction

Hepatitis B, is caused by hepatitis B virus (HBV), which produces an illness that is clinically indistinguishable from other forms of hepatitis. It is a significant cause of acute and chronic hepatitis in the world. Acute infection is frequently symptomatic in adults, though usually asymptomatic in young children, particularly infants. Fulminant hepatitis could occur in 0.1-0.6% of acute cases. The sequelae of chronic HBV infection vary from an asymptomatic "health" chronic carrier state, to the development of chronic hepatitis, cirrhosis and hepatocellular carcinoma. The rate of progression from acute to chronic hepatitis B is primarily determined by the age of infection, the rate being approx. 80-90% for those infected during the first year of life, 30-50% for infections between the age of 1-4 years, and 5-10% for adult-acquired infection. By preventing HBV infection, hepatitis B vaccine also protects against HDV infection.

Worldwide an estimated 2 billion people have been infected and it includes 350 million people with chronic hepatitis B infection. Carrier prevalence of HBV differs in different parts of the world, and may be quite variable within countries. Sero-epidemiological studies done in Sri Lanka have shown varying HBsAg prevalence rates ranging from 0.1 to 2.5%.

HBV, though similar to HIV in its primary routes of transmission, is hundred times more infectious than HIV. It is transmitted parenterally, sexually and vertically. However, in a significant proportion of patients the route of transmission cannot be determined.

Types of vaccine

Recombinant hepatitis B vaccine was introduced in 1986 and has gradually replaced the plasma-derived hepatitis B vaccine. The recombinant vaccine contains hepatitis B virus surface antigen

(HBsAg) and alum is used as an adjuvant. In certain preparations thiomersal is present as a preservative. A new recombinant hepatitis B vaccine that is intended for adult patients with renal insufficiency uses alum and lipid A as adjuvants.

The vaccine is available as monovalent formulations or in combination with other vaccines, including DTwP, DTaP, Hib, hepatitis A and IPV. (Please see Chapter 3)

Efficacy

Efficacy as measured by the presence of an anti-HBs antibody titre of >10 mIU/mL measured 1-2 months after the administration of the last dose is >95% for infants, children and young adults. The duration of protection is lifelong in healthy persons. The antibody response rates reduces primarily with ageing, in chronic disease, HIV infection, smoking and obesity.

Indications

- All children and adolescents aged less than 18 years
- Persons at high risk of contracting HBV infection including persons with high-risk sexual behaviour, partners and household contacts of HBsAg-positive persons, injecting drug users, persons who frequently require blood or blood products, recipients of solid organ transplantation, those at occupational risk of HBV infection, including health care workers and emergency care staff, and for international travellers to HBV-endemic countries.
- In addition, vaccine is indicated together with passive immunisation, for babies born to mothers who have had hepatitis B infection during pregnancy or are hepatitis B surface antigen positive.
- Post exposure vaccination following needle stick injuries.

Dosage and administration

The recommended dose varies by product and with the age of the recipient therefore, manufacturer's recommendation for dosage should be followed. In most cases, infants and adolescents receive 50% of the adult dose.

The vaccine is administered by IM route. The anterolateral aspect of the thigh is the preferred site of injection for infants and children aged below 2 years; the deltoid muscle is preferred for older children and adults. Administration in the buttock is not recommended as this is associated with decreased protective antibody levels.

A larger vaccine dose (40µg) is required to induce protective antibody in immunocompromised and haemodialysis patients. Post vaccination testing of protective antibody response is specially recommended in such patients to determine the need for revaccination.

Vaccination schedules

Three doses are given to all infants at 2, 4 and 6 months of age.

3 doses of vaccine can be given at any age, at 0, 1 and 6 month schedule.

The accelerated schedule of 0, 1, 2 months and a booster at 12 months is appropriate for travellers.

Contraindications

Contraindications are known hypersensitivity to any of the vaccine components or anaphylactic reaction to a previous dose of hepatitis B vaccine or allergy to common bakers yeast.

Neither pregnancy nor lactation is a contraindication for use of the vaccine.

Adverse effects

Adverse effects, when they occur, are transient and minor. They include local soreness, redness, nausea, diarrhoea, malaise and fever.

Storage

2°C to 8°C. Do not freeze.

Post-exposure prophylaxis for hepatitis B

Prophylactic treatment to prevent infection after exposure to HBV should be considered in the following situations:

- 1) Perinatal exposure of an infant born to a HBsAg-positive mother.
- 2) Sexual exposure to a HBsAg-positive person.
- 3) Household exposure.
- 4) Inadvertent percutaneous or permucosal exposure to HBsAg-positive blood.

1) Perinatal exposure

For an infant with perinatal exposure to a HbsAg-positive mother, a regimen combining one dose of hepatitis B immunoglobulin (HBIG) at birth with the hepatitis B vaccine series started soon after birth is 85-95% effective in preventing development of the HBV carrier state.

HBIG at birth and HBV vaccine at 0, 1, 2, and 12 months.

Simultaneous administration of HBIG and vaccine should be at two different sites.

2) Sexual partners of person with acute hepatitis B virus infection

Sexual partners of HbsAg positive person are at increased risk of acquiring HBV infection.

All susceptible persons whose sexual partners have acute hepatitis B infection should receive a single dose of HBIG and hepatitis B vaccination should be initiated simultaneously.

3) Household contacts of persons with acute hepatitis B virus infection

Since infants have close contact with mother or baby care-givers and they have a higher risk of becoming HBV carriers after acute HBV infection, prophylaxis of an infant less than 12 months of age with HBIG and hepatitis B vaccine is indicated if the mother or primary care-giver has acute HBV infection.

Prophylaxis for other household contacts of persons with acute HBV infection is recommended

If the index patient becomes an HBV carrier, all household contacts should receive hepatitis B vaccine.

(Please refer manufacturer's instructions for HBIG dosage)

4) Inadvertent percutaneous or permucosal exposure to HbsAg positive blood

Management is as in the table below.

Exposed person Status	Management when source is found to be		
	<i>HbsAg+</i>	<i>HbsAg-ve</i>	<i>HbsAg status unknown</i>
Unvaccinated	HBIG × 1 and initiate HBV vaccination (preferably within 24hrs)	Initiate HBV vaccination	Initiate HBV vaccination

(Continued)

Exposed person Status	Management when source is found to be		
	<i>HbsAg+</i>	<i>HbsAg-ve</i>	<i>HbsAg status unknown</i>
Vaccinated responder (a person with Anti HBs of ≥ 10 mIU/mL)	No treatment	No immunisation	No immunisation
Vaccinated nonresponder [#]	HBIG $\times 2$ one month apart or HBIG 1 dose and initiate revaccination	No immunisation	If high risk source treat as if source was HBsAg+ve
Vaccinated unknown response	Test exposed person for anti-HBs. If inadequate ** HBIG $\times 1$ + hepatitis B vaccine dose If adequate no immunisation	No immunisation	Test exposed person for anti-HBs. If adequate no immunisation If inadequate ** initiate revaccination

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**Anti HBs titre of < 10 m IU / mL

Post vaccination testing of HCW for anti HBs titres should be done 1-2 months after completion of vaccination. If titres are < 10 mIU/mL a second three dose vaccine series should be given or evaluated for HBs antigen positivity. A vaccine non responder is a person who does not develop protective HBs antibodies after completing 2 full series of hepatitis B vaccine and for whom an acute or chronic hepatitis B infection has been ruled out.

CHAPTER 7

HUMAN PAPILLOMAVIRUS VACCINE

Introduction

Cervical cancer is a leading cause of cancer morbidity and mortality in women throughout the world. Persistent infection with oncogenic human papilloma virus (HPV) is associated with the development of cervical cancer. Infection with oncogenic HPV types is also implicated in the development of other malignancies including neoplasms of the vulva, vagina, anus and penis. Of the oncogenic HPVs types, 16 and 18 accounts for some 70% of cervical cancers. Non-oncogenic HPV types 6 and 11 cause genital warts. HPV is a common asymptomatic infection with an estimated 40% of sexually active women becoming infected during life. HPV infection can lead to both squamous and adeno dysplasias, and cancers.

A vaccine to prevent infection with oncogenic HPV types has a potential to reduce the incidence of precursor lesions and cervical cancer. Vaccines prevent the disease by producing high level of neutralizing antibodies which is several folds higher than levels produced by natural infection. HPV vaccine is not therapeutic and is not intended to treat patients with cervical cytological abnormalities or genital warts.

Components of the vaccine

The L1 major capsid protein of HPV is the antigen used for HPV vaccine. Using recombinant DNA technology, the L1 protein is expressed in *Saccharomyces cerevisiae* (yeast).

Types of vaccines

There are two types of vaccines commercially available.

1. Quadrivalent HPV vaccine – This is a mixture of four HPV type-specific virus like particles prepared from the L1 proteins of HPV 6, 11, 16, and 18 combined with an aluminum adjuvant (aluminum

hydroxyphosphate sulfate). The formulation also includes sodium chloride, L-histidine, polysorbate 80, sodium borate, and water for injection. The quadrivalent HPV vaccine contains no thimerosal or antibiotics.

2. Divalent HPV vaccine – This is a mixture of two HPV type-specific virus like particles prepared from the L1 proteins of HPV 16, and 18 combined with an adjuvant AS 04.

Efficacy

HPV vaccine has a high efficacy for prevention of HPV subtypes 16, and 18 related persistent infection and vaccine type-related CIN 1/2/3. In addition quadrivalent HPV vaccine prevents external genital warts. Recent studies have shown the vaccine provides significant cross protection against CIN lesions associated with oncogenic subtypes 31, 33 and 45. Clinical significance of this cross protection is yet to be demonstrated.

Duration of protection

Proof of principle trials has shown the vaccine to be highly immunogenic. Follow up studies after 10 years indicate that the antibody level remains high not requiring booster doses. The need for booster doses can only be determined by further follow up data.

Indications

Ideally the vaccine has to be given before sexual debut. Routine vaccination is recommended for females aged 11 to 18 years. The vaccination series can be started as young as age 9 years. Catch-up vaccination is recommended for females aged 18-26 years who have not been routinely vaccinated.

Quadrivalent is licensed for use in females age 9 to 45 years. It also has been registered for the prevention of vulva and vaginal cancer and their precancerous lesions. Quadrivalent is also approved for use in males aged 9 to 15 years for the prevention of HPV infection.

Bivalent is licensed for use in females from 10 to 45 years of age for the prevention of cervical cancer and its precursor lesions.

Dosage and administration

1. Quadrivalent HPV vaccine – given intramuscularly to the deltoid region as 3 separate 0.5 mL doses. The second dose should be administered 2 months after the first dose and the third dose 6 months after the first dose. The vaccine is available as a sterile suspension for injection in a single-dose vial or a prefilled syringe.
2. Divalent vaccine – given intramuscularly to the deltoid region as 3 separate 0.5 mL doses. The second dose should be administered 1 month after the first dose and the third dose 6 months after the first dose.

Vaccination of the sexually active women

Sexually active women can receive the HPV vaccine. Women with a history of previous HPV infection will most likely benefit from protection against diseases caused by the other HPV vaccine genotypes with which they have not been infected. The need to continue cervical cytology screening according to the recommended national policies should be emphasized. These patients should be counselled that the vaccine may be less effective in women who have been exposed to HPV before vaccination, than in women with no prior HPV exposure at the time of vaccination.

Cervical cytology screening

Current cervical cytology screening recommendations remain unchanged and should be followed regardless of the vaccination status.

Simultaneous administration with other vaccines

As HPV vaccine is a recombinant vaccine it can be given simultaneously with other vaccines using a separate syringe at a different anatomical site.

Pregnancy and lactation

HPV vaccine is not recommended for use in pregnancy. There is no evidence to suggest that administration of the vaccine adversely affect fertility, pregnancy or infant outcomes. Women who become pregnant during the course of vaccination should defer the subsequent doses until the completion of the pregnancy regardless of timing. Vaccination should resume at the appropriate dose interval. There is no need to recommence the completed vaccination programme. For example women who have received one or two doses should receive the second and/or 3rd dose at the completion of the pregnancy.

Lactating women can receive HPV vaccine.

Immunocompromised persons

It can be administered to females who are immunosuppressed as a result of disease or medications. The immune response and vaccine efficacy might be less than that in persons who are immunocompetent.

Precautions and contraindications

1. HPV vaccine can be administered to persons with minor acute illnesses (e.g., diarrhoea or mild upper respiratory tract infections with or without fever). However, for persons with moderate or severe acute illnesses vaccination should be deferred until after the patient improves.
2. HPV vaccine is contraindicated for persons with a history of hypersensitivity.
3. Syncope (i.e. vasovagal or vasodepressor reaction) can occur after vaccination, most commonly among adolescents and young adults. Vaccine providers should consider observing patients for 15 minutes after they receive HPV vaccine.

Adverse effects

Side effects are minimal with the most common side effect seen mainly at the injection site as pain, swelling and erythema. Uncommon side

effects are gastrointestinal symptoms, pleuritis, urticaria, arthralgia, bronchospasms and dizziness.

Storage

At 2°C-8°C and not frozen.

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CHAPTER 8 INFLUENZA VACCINE

Introduction

Annual influenza epidemics among humans affect 5-15% of the population, causing an estimated half million deaths worldwide annually. Vaccination is currently the only effective means of reducing or counteracting this burden of mortality and morbidity in the community.

Influenza vaccine contains three influenza viruses: Two influenza A viruses, A (H3N2) and A (H1N1) virus and one influenza B virus. In 2010 the seasonal A (H1N1) virus was replaced by the 2009 pandemic influenza A (H1N1) virus. The viruses in the vaccine change each year based on international surveillance and scientist's estimations which types and strains of virus will circulate. In contrast to many other vaccines, the viruses in influenza vaccine are updated because circulating influenza viruses evolve continuously. The World Health Organization (WHO) decides on which types and strains of viruses will circulate in a given year depending on the results of global influenza surveillance.

WHO convenes technical consultations in February and September each year to recommend viruses for inclusion in influenza vaccines for the northern and southern hemispheres respectively. For countries in equatorial regions, epidemiological considerations influences which recommendation (February or September) is more appropriate for consideration by national and regional authorities.

Types of vaccine

1. **TIV** – trivalent inactivated vaccine (whole virus / split virus / sub unit vaccine) containing the killed virus. This injectable vaccine is approved for use in persons older than 6 months.
2. **LAIV** – an intra nasal live attenuated influenza vaccine (cold adapted/ genetically re-assorted) made with live, weakened flu virus that do not cause the flu. LAIV is not recommended for individuals under the age of 2 years and over 50 years and during pregnancy.

About 2 weeks after vaccination, antibodies that provide protection against virus infection develop in the body.

Vaccine effectiveness

Efficacy varies with the recipient's age and health status and the antigenic match between the virus strains in the vaccine and those in circulation. The vaccine will prevent the illness in 70-90% of healthy adults provided that there is a good antigenic match.

The vaccine may reduce the number of hospitalisations and overall mortality during influenza seasons. TIVs show high efficacy in children >6 years of age, but are poorly protective in children aged <2 years.

Indications:

1. General population

- a. Anyone who wants to reduce their chances of getting the flu
- b. People who are engaged in essential duty - servicemen
- c. Travellers

2. People at high risk for complications from the flu should be given the vaccine each year

- a. Residents of institutions for the elderly or the disabled;
- b. Elderly, non-institutionalized individuals with chronic conditions, chronic cardiovascular, pulmonary, metabolic or renal disease, or who are immuno compromised;
- c. All individuals > 6 months of age with any of the conditions listed above.
- d. All persons 65years and older (People above nationally defined age limit).
- e. Pregnant women – influenza vaccine containing the killed virus is safe and is recommended for all pregnant women during the influenza season.

3. People who live with or care for those at high risk of complications.

- a. Healthcare workers
- b. Household members who are in close contact with high risk persons

Dosage and administration

1. Inactivated vaccine

- a. Is given intra muscularly to deltoid muscle. Single dose for children over 9 years and healthy adults. (Follow manufacturer's instructions)
- b. Children between 6 and 12 months given to the antero – lateral aspect of thigh. These vaccines should not be given to children aged less than 6 months. Those aged 6-36 months should receive half the adult vaccine dose.
- c. Previously unvaccinated children aged less than 9 years should receive two injections, administered at least one month apart

2. Live attenuated vaccine

- a. Approved for use in healthy people 2-49 years of age, who are not pregnant.
- b. It can be given for healthy children 2-4 years old, with out a history of asthma or recurrent wheezing.
- c. These are currently licensed in Russia and USA. It is safe, efficacious and gives long lasting protection.

Contraindications

1. People who have a severe allergy to chicken eggs.
2. People who have had severe reaction to an influenza vaccine in the past.
3. Children under 6 months of age.

4. Hypersensitivity to any component of the preparation.
5. Acute febrile illness – postpone the vaccination.

Adverse effects

1. Local reactions at the site of the injection – pain, erythema or induration
2. Systemic effects – low grade fever and body aches

If these problems occur, they begin soon after the injection and last for 1-2 days.

3. Risk of Guillain Barre Syndrome (GBS)-rare

Split and sub unit vaccines show reduced systemic reactogenicity, compared with whole virus preparations.

Storage

2°C-8°C

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CHAPTER 9

JAPANESE ENCEPHALITIS VACCINE

Introduction

Japanese encephalitis (JE) is a disease of public health importance in many Asian countries. It is an infection of the central nervous system characterized by coma, seizures, paralysis, abnormal movements and death in one third of cases and serious sequelae in 40% of survivors. This disease primarily occurs in children and most infections are asymptomatic. There is no specific antiviral treatment for JE.

It is caused by a flavivirus transmitted to man through mosquitoes. The virus is transmitted in an enzootic cycle among mosquitoes and vertebrate amplifying hosts chiefly domestic pigs and aquatic birds. *Culex* mosquitoes, primarily *Cx. tritaeniorhynchus* and *Cx. gelidus* are the principal vectors. JE cases have been identified from various parts in Sri Lanka throughout the year. It shows a marked increase with the north-east monsoonal rains (November-February) as a result of increased mosquito breeding, due to water logging of rice fields and ground pools. The incubation period is 5 to 15 days.

Types of vaccine

- **Inactivated – is of 2 types**

1. Vaccine prepared from suspension of mouse brain infected with JE virus.
Freeze dried or liquid (Nakayama strain)
Liquid (Beijing strain)
2. Cell culture derived inactivated JE vaccine based on Beijing P-3 strain. Manufactured and available only in China, this vaccine provides broad immunity against heterologous JE viruses and high viral yields when propagated in primary hamster kidney cells.

- **Live attenuated**

Freeze dried (SA-14-14-2 strain)

The vaccine is prepared in primary hamster kidney cell culture. This vaccine is based on the genetically stable, neuro-attenuated SA 14-14-2 strain of the JE virus, which elicits broad immunity against heterologous JE viruses.

It is administered in the public sector through the MOH clinics in Sri Lanka.

Efficacy

- **Inactivated vaccine**

The proportion of vaccinees retaining detectable neutralizing antibodies and their geometric mean titres decline rapidly in the first year after the primary 2 doses.

78-89% of Nakayama strain vaccine recipients and 88-100% of Beijing - 1 strain vaccine recipients had protective antibody levels before the one year booster.

Given that the most frequent occurrence of JE is in infancy and the likely interference with passively acquired maternal antibodies during the first months of life, vaccination is not recommended for children before the age of 6 months. In people whose immunity is unlikely to be boosted by natural infection, repeated boosters are required for sustained immunity.

- **Live attenuated vaccine**

Efficacy trials in children 1-10 year olds have yielded high protection rates above 98% following a single dose of vaccine after 1 year. Case control and numerous large scale field trials in China have consistently shown an efficacy of at least 95% following 2 doses administered at an interval of 1 year.

Indications

Children above 9 months of age and adults for the prevention of JE.

Dosage and administration.

- **Inactivated vaccine – in JE endemic countries**

Freeze dried or liquid vaccine which contains Nakayama strain, the dose for adults and children above 3 years is 1 mL and administered subcutaneously (SC). Freeze dried vaccine is reconstituted with the diluent provided.

Liquid vaccine (Beijing strain) is a colourless or a slightly turbid preparation. The dose for adults and children more than 3 years is 0.5 mL and administered SC.

For children 1-3 years half the adult dose is recommended. One dose each is administered subcutaneously at an interval of 2 weeks and an additional booster dose given after 1 year.

For travellers visiting JE endemic countries

For travellers aged >1 year visiting rural areas of endemic countries for at least 2 weeks, the established current practice is to administer 3 primary doses at days 0, 7 and 28; alternatively 2 primary doses preferably 4 weeks apart. When continued protection is required, a booster dose should be given after 1 year.

- **Live attenuated vaccine**

Each dose of the vaccine is reconstituted with 0.5 mL of the sterile diluent provided. Vaccine should be used immediately after reconstitution.

The primary immunisation dose 0.5 mL is recommended for children above 9 months of age given SC. A booster dose of 0.5 mL is recommended after 1 year if necessary.

Contraindications

Hypersensitivity to any component of the vaccine

Severe febrile illness (> 38.3° C)

Acute illness

Pregnancy

Immunodeficiency states

Leukemia, lymphoma and other malignancies

History of convulsions/seizures within the past one year

Adverse effects

Local – pain, induration and redness at site of inoculation

Systemic – Headache, fever, malaise, myalgia, urticaria, nausea and vomiting

Most of the adverse reactions occur 12 - 72 hours after the administration of the vaccine. They are more frequent after the 2nd or 3rd doses of inactivated vaccine. These reactions appear to be more common in those with a previous history of urticaria.

Acute encephalitis, shock and anaphylactoid reactions are rare.

Storage

Instructions on the product leaflet should be followed. The vaccine should be stored at +2°C to 8°C. Avoid exposure to direct sun light. The liquid vaccine should not be frozen.

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CHAPTER 10

MEASLES VACCINE

Introduction

Measles is a highly contagious disease which is a leading cause of death among children globally. According to the World Health Organization, there were 297,000 reported cases of measles and 197,000 deaths in the world in 2007. Measles is common in developing countries particularly in parts of Africa, the Eastern Mediterranean and Asia.

Measles is an acute viral illness which is caused by a virus of the paramyxovirus family. It is spread by airborne droplets or direct contact with throat or nasal secretions of infected persons. The illness is characterised by high fever, an erythematous maculopapular rash, coryza, cough, conjunctivitis and Koplik's spots (pathognomic enanthem).

It is the complications of measles that cause death, rather than the disease itself. The measles virus causes a depression in cellular immunity, making secondary infections more likely. Furthermore, severe measles is more likely in poorly nourished children and in immunocompromised patients. Complications of the disease are more common in children under the age of 5 years and in adults over the age of 20 years. These include, pneumonia, diarrhoea, otitis media, blindness and encephalitis (including subacute sclerosing panencephalitis). The leading cause of death in measles is pneumonia. Furthermore, the nutritional status may deteriorate or a dormant tuberculous focus could be activated.

Due to its high infectivity and its predilection for the non immune, poorly nourished and immunocompromised, measles can be a big problem in situations of natural disasters and war, if preventative measures are not taken.

Vaccination for measles has made a major impact on the morbidity and mortality caused by measles. The measles vaccine was introduced in Sri Lanka in 1984. It led to a remarkable reduction in measles. In 2009 there were only 21 laboratory confirmed measles cases reported from the whole country. In 2010 the number was 14, and up to end 2011 it was 04.

Types of vaccine

Live attenuated freeze dried (lyophilized) vaccine.

Vaccine strains: Most of the live, attenuated measles vaccines used now originate from the Edmonston strain of measles virus which has been propagated on human diploid cells.

Schwarz strain grown in chick embryo fibroblasts.

Efficacy

A single dose, administered at 9 months, provides suboptimal immunity due to presence of maternal antibodies. Therefore a repeat dose is required. Those who do not seroconvert after the initial dose almost always seroconvert after the second.

Indications

- Primary and booster immunisation of infants and children against measles.
- To prevent infection in susceptible contacts during measles outbreaks.

The first dose of measles immunisation is given as the MMR vaccine at the completion of 1 year to all children.

EPI offers the second opportunity of measles immunisation to all children in the country at 3 years of age through the 2nd dose of MMR vaccine.

Measles vaccine should be given to children who have had or who are suspected to have had measles.

Antibodies to measles develop faster following vaccination than following the natural infection. Therefore, measles vaccine can be used effectively to protect susceptible contacts during an outbreak. It should be administered within 3 days following exposure to be effective.

Dosage and administration

A single dose of 0.5 mL is administered by deep subcutaneous injection to the upper arm.

The vaccine should be reconstituted only with the supplied diluent using a sterile syringe and a needle. The dried powder is easily dissolved with gentle shaking.

Can be safely and effectively administered with DTP, DT, TT, BCG, OPV, hepatitis B and yellow fever vaccines.

Contraindications

- Acute febrile illness.
- Immunocompromised patients, or patients on long term corticosteroids or other immunosuppressive drugs.
- Hypersensitivity to any component of the vaccine including neomycin.
- Pregnancy.

Precautions

Patients with tuberculosis should be under treatment when immunised as the measles virus administered in the vaccine may exacerbate tuberculosis.

Persons who are tuberculin positive may become tuberculin negative for up to one month after measles immunisation.

Adverse effects

Reactions are generally mild. A slight increase in temperature (37.6°C) may occur in 5-6% of those vaccinated. A rash which usually lasts less than 48 hours is observed in 1-2% of those vaccinated. Both the fever and the rash tend to occur 7-10 days after administration and may last up to 1-2 days. There may be enlargement of cervical and occipital lymph nodes.

Storage

Lyophilized vaccine should be stored at 2°C-8°C and protected from light.

After reconstitution the vaccine should be stored at 2°C-8°C and be discarded after 8 hours.

The diluent should be kept cool but not frozen.

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CHAPTER 11

MEASLES, MUMPS AND RUBELLA VACCINE (MMR)

Introduction

MMR is a live attenuated combined vaccine of a lyophilised formulation which aims to eliminate measles/mumps/rubella (and congenital rubella syndrome).

Measles strains – Schwartz – grown in chick embryo fibroblasts.
– Edmonstan-Zagreb – grown in human diploid cells.

Mumps strains – Jeryl-Lynn; RIT4385 (derived from Jeryl-Lynn) and Urabe.
– All grown in chick embryo tissue culture.

Rubella strain – Wistar RA27/3 grown in human diploid cells.

Measles

Please see Chapter 10

Mumps

The clinical case definition of mumps is an acute onset of unilateral or bilateral, tender, self-limiting swelling of the parotid or other salivary glands lasting more than 2 days and without any other apparent cause.

Mumps is an acute viral illness caused by an RNA virus in the Paramyxoviridae family transmitted by respiratory droplets. After a period of viraemia (3-5 days), the virus spreads to multiple tissues, such as the salivary glands, pancreas, testes, ovaries and the meninges, leading to characteristic symptoms of parotitis, orchitis and aseptic meningitis. Parotitis is the most common manifestation (30%-40%). Parotitis may be unilateral or bilateral, and any combination of single or multiple salivary glands may be observed.

The incubation period of mumps is 14-18 days (range, 14-25 days).

Complications

Asymptomatic occurrence of aseptic meningitis is common (50%-60%). Symptomatic meningitis occurs in up to 10% of patients and resolves without sequelae in 3-10 days.

Adults are at a higher risk for this complication than children, and boys are more commonly affected than girls (3:1). Parotitis may be absent in as many as 50% of such patients. Encephalitis is rare (less than 2 per 100,000).

Orchitis is the most common complication in post pubertal males, but sterility is rare. Other rare complications include arthritis, thyroiditis, mastitis, glomerulonephritis, myocarditis, pancreatitis, cerebral ataxia, transverse myelitis and hearing impairment. Oophoritis occurs in (5%) of post pubertal females. It may mimic appendicitis. There is no relationship to impaired fertility. Deafness caused by mumps virus occurs in approximately 1 per 20,000.

Mumps during the first trimester of pregnancy is associated with an increased incidence of spontaneous abortions. Nevertheless, no evidence has suggested any congenital malformations.

Rubella

Rubella is an acute viral infection which generally results in mild disease in children and adults. It is characterised by low grade fever, a generalised erythematous maculopapular rash and generalised lymphadenopathy (commonly suboccipital, post auricular and cervical). It is caused by a togavirus which is spread by droplets and through direct contact with nasal or throat secretions of infected persons. The incubation period is generally 18 days. 25 to 50% of rubella infections are subclinical.

However, rubella is of great significance if it occurs in a pregnant woman, as it can cross the placental barrier and has teratogenic effects. Rubella infection in pregnancy may lead to miscarriage or still birth. Some infants may be born with congenital rubella syndrome (CRS) which includes, ophthalmologic, cardiac, auditory and neurological abnormalities.

The risk of congenital defects in the first trimester is approximately 80%, with the risk falling to 10-20% by the 16th week of pregnancy.

Immunisation against rubella was introduced to the National Immunisation Programme in 1996.

In Sri Lanka there were 26 laboratory confirmed cases of rubella and 3 cases of CRS in 2010. However, by end June 2011, the respective numbers were 46 and 3.

Immunogenicity and vaccine efficacy

Recipients of a single dose of MMR at 15 months of age develop antibodies to measles in 98%, 97% for mumps and more than 95% for rubella. Studies conducted in the United States (US) during 1973-1989 determined that 1 dose of MMR vaccine was 75%-91% effective. A study from the United Kingdom documented that vaccine effectiveness of 88% with 2 doses. Until recently the duration of vaccine-induced immunity was believed to be greater than 25 years.

Results of recent studies conducted in other countries (Finland, Spain and the US) have revealed that MMR induced immunity showed difficulties in maintaining the achieved seroprotective levels against mumps for a longer period.

The effectiveness of the mumps component of the MMR vaccine is lower than that of the measles or rubella components.

It is strongly suggestive that elimination targets of measles, mumps and rubella can be reached with sufficiently high coverage by the 2-dose MMR vaccination programme. Nevertheless, it is important to realise that although vaccination alone does not prevent all mumps outbreaks, maintaining high measles, mumps, and rubella (MMR) vaccination coverage remains the most effective way to prevent outbreaks and also to limit their extent when they occur.

Indications

- After 12 months of age the first dose is routinely recommended.

- Combined measles-mumps-rubella (MMR) vaccine is recommended to be used when any of the individual components is indicated.

Dosage and administration

A single dose of 0.5 mL reconstituted vaccine is given subcutaneously but can also be given intramuscularly.

The first dose of the vaccine is recommended after 12-15 months of age. A second dose is given before starting school (3-5 years of age).

Children presenting at pre school age who have not received the first dose of MMR can also be given a dose of MMR followed three months later by a second dose. Furthermore, individuals of both sexes at the school leaving age who have never received MMR can also be offered MMR.

According to the revised schedule of the National Programme of Immunisation of Sri Lanka (2011) the MMR is recommended at one year. The second dose of MMR vaccine should also be given routinely at the age of 3-5 years particularly before a child enters kindergarten or the first grade. The age 11-12 years also can serve as a catch-up opportunity to verify vaccination status and administer MMR vaccine to those children who have not yet received two doses of MMR. The second dose of MMR may be administered as early as 4 weeks after the first dose.

Post exposure prophylaxis

MMR vaccine is not suitable for prophylaxis following exposure to mumps, measles or rubella as the antibody response to mumps or rubella components is too slow for effective prophylaxis (for measles please refer Chapter 10). Vaccination after exposure is not harmful and may possibly avert later disease.

Contraindications

- Pregnancy, persons with immunodeficiency, AIDS, pregnancy or immunosuppression.

- Children with a history of allergies to any of the vaccine components (gelatin, neomycin or kanamycin).
- Persons received immunoglobulin injections, receipt of blood or blood products within three months.
- if given to women, pregnancy should be avoided for three months after vaccination.

When pregnancy occurs within three months after MMR vaccination, no teratogenicity has been reported. Therefore, there is no indication to consider termination of the pregnancy. Vaccination should only be deferred in children with acute febrile illnesses.

Adverse effects

Malaise, fever or rash may occur following the first dose of MMR vaccination. Most adverse events reported are attributable to the measles or rubella components.

Parotitis may occasionally occur in the third week after vaccination. Adverse reactions are less common after the second dose of vaccination than the first dose. Thrombocytopenic purpura has been rarely reported within six weeks of the first MMR. However, the risk of developing thrombocytopenia after the MMR vaccination is much less than the risk of developing it after an infection with measles, rubella or mumps virus.

The concerns about the probable associations of MMR vaccine and infantile autism and Crohn's' disease have been evaluated. Many epidemiological studies have firmly disproved the remotest possibility of a cause and effect phenomenon with regard to the MMR vaccine and, pervasive and regressive developmental disorders in children.

Storage

Both lyophilised and reconstituted vaccine should be stored at 2°C-8°C protected from light. Reconstituted vaccine should be used as early as possible and discarded after 8 hours.

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CHAPTER 12

MENINGOCOCCAL VACCINE

Introduction

Neisseria meningitidis meningitis has a case fatality rate of 10-20% in industrialized countries. Invasive meningococcal disease causes substantial morbidity with 11- 19% of survivors having sequelae such as hearing loss, neurological disability, digit or limb amputations and skin scarring.

Most infections are caused by serogroups A, B and C. Serogroup A is responsible for large epidemics. It is endemic and epidemic in the sub-Saharan meningitis belt in Africa. In epidemics attack rates are more than 500 cases per 100,000 population and about 50% of cases are in children less than 4 years. Group B is responsible for approximately 50% of endemic meningitis in developed countries.

Persons who have complement factor deficiencies and those with functional or anatomical asplenia are at increased risk of meningococcal disease.

Meningococcal meningitis is uncommon in Sri Lanka and the cases encountered are almost always imported.

Types of vaccine

The capsular polysaccharide vaccines that are used at present are less immunogenic than the conjugated vaccines. Conjugated vaccines are vaccines containing capsular polysaccharides joined to a protein to enhance immunogenicity. These are currently not available in Sri Lanka.

Unconjugated vaccines (Polysaccharide vaccines)

Bivalent vaccines – containing polysaccharides to serogroups A+C

Tetravalent vaccines – containing polysaccharides to serogroups A, C, W-135, Y (MPSV4).

The vaccine contains 50 µg each of the purified bacterial capsular polysaccharides. Single dose (0.5 mL) vials are available.

The duration of protection is 3-5 years.

A vaccine for serogroup B is not available. Therefore in serogroup B outbreaks chemoprophylaxis is recommended for the close contacts ideally within 24 hours of diagnosis of the primary case. Rifampicin or ceftriaxone or ciprofloxacin are recommended for adults while rifampicin is recommended for children.

Conjugated vaccines

- a) Group C conjugate vaccines (conjugated either to tetanus or diphtheria toxoid)
- b) Tetravalent conjugate vaccine, conjugated to diphtheria toxoid (MCV4)

These are currently not available in Sri Lanka. The duration of protection of conjugated vaccines is longer compared to unconjugated vaccines.

Efficacy

Efficacy varies between 85-93% for both conjugated and unconjugated vaccines. Antibody response to serogroup C is the lowest following vaccination with unconjugated vaccines. With conjugated vaccines, the lowest antibody titres were observed against the Y serogroup.

Indications

Not recommended for routine immunisation

Current vaccines are recommended for use in:

- epidemic or outbreak situations.
- travellers to endemic countries.
- pilgrims to Saudi Arabia during the annual Hajj.
- persons exposed to patients.

- patients undergoing splenectomy.
- patients with terminal complement component (C3, C5 - C9) deficiency.
- laboratory workers handling meningococci.
- Students entering overseas universities in countries where the disease is endemic.

Dosage and administration

Unconjugated vaccine

Dose 0.5 mL subcutaneously.

The lyophilised preparation of purified polysaccharides should be dissolved in the diluent which is sterile saline.

Children >2 years – one dose is adequate. It protects up to 3-5 years.

Meningococcal polysaccharide vaccine is not recommended for children <2 years of age.

Conjugated vaccine

Dose 0.5 mL IM

Children 3 months to 2 years – 2 doses 3 months apart, with meningococcal MCV4 vaccine.

Persons aged 2-55 years – A single dose is adequate for healthy recipients. Persons with functional or anatomic asplenia should receive one booster dose after 5 years.

Currently polysaccharide MPSV4 is preferred for adults >55 yrs. It provides better and longer lasting protection compared to conjugated MCV4.

Contraindications

Acute febrile illness.

Hypersensitivity to any component of the vaccine.

Polysaccharide vaccines are not contraindicated in pregnancy.

A history of Guillain Barre Syndrome (GBS) is a contraindication for receiving MCV4, and MPSV4 can be given for short term protection (3-5 years).

Adverse effects

Local – erythema, slight induration, tenderness or pain at the injection site.

Systemic – Febrile reactions and chills have rarely been observed within 24 hrs of vaccination.

GBS has been reported after MCV4.

Adverse effects are commoner with MCV4 than with MPSV4.

Storage

2°C-8°C

Further reading

1. Prevention and control of meningococcal disease. Recommendations of the Advisory Committee on Immunisation Practices (ACIP) of the Centers for Disease Control and Prevention. *MMWR* 2005; **54** (no RR-7).
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CHAPTER 13 PNEUMOCOCCAL VACCINE

Introduction

Over one third of deaths among children under five, are caused by pneumonia and diarrhoea. Pneumonia is the single largest cause of death in children globally killing more than 1.5 million children every year. According to the WHO, immunisation against pneumococcus, *Haemophilus influenzae* type b (Hib), measles and pertussis is the most effective way to prevent pneumonia. Vaccines are available against all four infections. **Pneumococcal disease (pneumonia meningitis and septicaemia) is recognized as the world's leading vaccine preventable child killer**, which is estimated to cause up to one million deaths in children under 5 years of age annually. There are about 90 distinct serotypes. Globally about 20 serotypes are associated with >80% of invasive pneumococcal disease occurring in all age groups.

The introduction of the 7-valent pneumococcal conjugate vaccine (PCV 7) has changed significantly the epidemiology of pneumococcal infections, including invasive pneumococcal disease. PCV 7 was first introduced to children in 2000 in USA and within a decade, pneumococcal infections were almost eliminated in that age group. Furthermore, herd immunity has significantly reduced the incidence of such infections in the over 65 year age group, as well as in older children. Although there has been some increase in the incidence of pneumococcal infections caused by serotypes not covered by PCV 7, especially serotype 19A, the overall incidence of pneumococcal disease has been significantly reduced.

In 2009, PCV 10 and in 2010, PCV 13 were introduced. Data suggest that changing from the 7 valent vaccine to the 10 valent vaccine would increase the proportion of serotypes covered from 80% to 88% in the USA and from 74% to 84% in Europe. In developing countries, in Africa, the corresponding increase would be from 67% to 81% and in parts of Asia, it would increase from 43% to 66%. Changing from the 10 valent to 13 valent vaccine would further improve coverage of serotypes by 4% to 7% globally. In developed countries the newer vaccines are fast replacing PCV 7 which is being phased out.

Types of vaccine

Two types of vaccine are available – pneumococcal polysaccharide vaccine and pneumococcal conjugate vaccine.

1. Pneumococcal polysaccharide vaccine

It contains purified polysaccharide for 23 capsular types of pneumococci.

Efficacy

It is effective in adults and children over 2 years of age. Efficacy depends on each individual's antibody response to each of the 23 antigens and serotype of subsequent infections.

Indications

- Adults over 65 years
- Persons aged over 2 years who are at increased risk of pneumococcal infection
 - Asplenia or severe dysfunction of the spleen
 - Splenectomy – in elective splenectomy, at least two weeks prior to surgery
 - Patients awaiting cochlear implants, at least two weeks prior to surgery
 - Chronic renal disease or nephrotic syndrome
 - Immunodeficiency or immunosuppression due to disease or treatment, including HIV Infection
 - Chronic heart disease
 - Chronic lung disease
 - Chronic liver disease including cirrhosis
 - Diabetes mellitus
 - Coeliac disease

Dosage and administration

Single dose of 0.5 mL IM. It can be administered simultaneously with

routinely used vaccines. As revaccination in individuals with higher concentration of antibodies can produce adverse reactions, revaccination is not recommended, except every 5 years in individuals in whom the antibody concentration is likely to decline rapidly (eg. asplenia, splenic dysfunction and nephrotic syndrome).

Contraindications

Severe reaction to a previous dose of vaccine.

Precautions

Acute febrile illness. Postpone all vaccinations until the child is well.

Adverse effects

Local reactions such as pain, erythema and induration may occur which lasts 1-3 days.

Storage

2°C-8°C (should not be frozen)

2. Pneumococcal conjugate vaccine (PCV)

PCVs are more immunogenic than polysaccharide vaccines, especially in children under 2 years of age. Currently 3 types of vaccine are available PCV 7, PCV 10 and PCV 13. In developed countries PCV 7 is being replaced by PCV 13, due to its formulation. PCV 10 provides protection against some non-typeable Hib (NTHi) infections such as acute otitis media.

Indications

Recommended routinely (if affordable) for children mainly under 2 years age but could be given up to 5 years.

Efficacy

PCV 7 provides cover against serotypes 4, 6B, 9V, 14, 18C, 19F and 23F

Provides cover against 50% of invasive serotypes globally.

PCV 10 provides cover against serotypes 1, 4, 5, 6B, 7F, 9V, 14, 18C, 19F and 23F.

Provides cover against 70% of serotypes globally and also against non-typeable *Haemophilus influenzae* (NTHi).

PCV 13 provides cover against serotypes 1, 3, 4, 5, 6A, 6B, 7F, 9V, 14, 18C, 19A, 19F and 23F.

It provides cover against serotype 19A which became an important pathogen after the introduction of PCV 7 in 2000, in some countries.

Dosage and administration

0.5 mL IM per dose. In USA a 3 dose primary series at 2, 4, 6 months and a booster dose at 12-15 months.

In Europe a 3 dose schedule at 2, 4 and 12 months

Children between 1-2 years will need 2 doses.

Children between 2-5 years will need 1 dose

Minimum intervals – 4 weeks between doses given before 12 months
– 8 weeks between doses given at/after 12 months

Transitioning from PCV 7 to PCV 10 or PCV 13

Children aged 2 months to 5 years who have not completed the course, complete the course with PCV 10 or PCV 13.

Children under 5 years of age who have completed a PCV 7 series – one dose of PCV 10 or PCV 13 should be administered.

Contraindications

Severe reaction to a previous dose of vaccine or an adverse reaction to the diphtheria toxoid component.

Precautions

Acute febrile illness. Postpone all vaccinations until the child is well.

Adverse effects

Local reactions such as pain, erythema and induration may occur which lasts 1-3 days.

Storage

2°C-8°C (should not be frozen).

Further reading

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2. Hicks LA et al. Incidence of pneumococcal disease due to non-pneumococcal conjugate vaccine (PCV 7) serotypes in the United States during the era of widespread PCV vaccination 1998-2004. *Journal of Infectious Diseases* 2007; **196**(9): 1346-54.
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CHAPTER 14

POLIOMYELITIS VACCINE

Poliomyelitis

Poliomyelitis is an infectious disease caused by the polio virus. The disease which causes paralysis can strike at any age but mainly affects children. Polio virus is an enterovirus. There are three antigenic types, (type 1, type 2, type 3) and all three can cause paralysis. Most cases of paralysis are due to type 1, while paralysis caused by type 3 is less frequent. Paralysis due to type 2 is uncommon. Most epidemics are due to type 1.

The virus enters through the mouth and thereafter multiplies inside the throat and intestines. Once established, polio virus can enter the blood stream and invade the central nervous system spreading along nerve fibres. As it multiplies, the virus destroys motor neurons. Muscle pain, spasms and fever are associated with the rapid onset of acute flaccid paralysis. Paralysis due to poliomyelitis is almost irreversible.

Poliomyelitis occurred world wide in epidemic form in the first half of the 19th century. The Global Polio Eradication Programme has dramatically reduced polio virus transmission throughout the world. By 2010 only 4 countries remain polio-endemic which are India, Afghanistan, Pakistan and Nigeria and they are the current focus of the global programme.

In Sri Lanka poliomyelitis was made a notifiable disease in 1944 and the surveillance of acute flaccid paralysis (AFP) cases commenced in 1990. The last virologically confirmed case of polio was detected in Sri Lanka in 1993.

Types of vaccine – Oral polio vaccine (OPV)
– Injectable (inactivated Salk) polio vaccine (IPV)

Oral polio vaccine (OPV) has been used in Sri Lanka since 1963 to successfully combat the polio outbreaks.

Efficacy

Oral polio vaccine (OPV)

OPV is highly effective in producing immunity to polio virus. Three doses of OPV produces immunity to all 3 polio virus types in more than 95% of recipients. As with other live virus vaccines immunity from oral polio virus vaccine is probably lifelong. OPV produces excellent intestinal immunity, which helps prevent infection with wild virus.

Inactivated poliovirus vaccine (IPV)

IPV is highly effective in producing immunity against polio virus and protection from paralytic poliomyelitis. Ninety percent or more of vaccine recipients develop protective antibody to all three poliovirus after 2 doses and at least 99% are immune following 3 doses.

Indications

Infants at 2, 4 and 6 months

Boosters at 18 months and school entry.

Both OPV and IPV could be used. However, only OPV is used at present in National EPI Programme in Sri Lanka.

IPV is especially recommended for patients with congenital or acquired immunodeficiency and those on systemic steroid therapy or chemotherapy

Dosage and administration

OPV is administered as 2 drops orally

One multi dose vial contains 1 mL and is recommended for 10 children.

Even for those who have received full immunisation additional doses during mass campaigns is beneficial.

Both OPV and IPV could be administered with other vaccines, including, DTP, hepatitis B, measles and Hib.

IPV dosage is 0.5 mL and can be inoculated either subcutaneously or intramuscularly. When given in combination with other vaccines such as diphtheria, tetanus and pertussis or hepatitis B the vaccine should be administered intramuscularly.

Vaccination schedule for OPV and IPV

Age	Vaccine
2 months	OPV/IPV
4 months	OPV/IPV
6 months	OPV/IPV
18 months	OPV/IPV
5 years	OPV/IPV

The minimum interval between two doses is 4 weeks.

Contraindications

Moderate or severe acute illness. However, mild illness, including mild diarrhoea is not a contraindication. Severe allergy to vaccine or component of the vaccine. OPV should not be given to immunodeficient individuals or household contacts of individuals who have immune deficiency diseases or immune depression (due to therapy). IPV must be substituted for OPV in these circumstances.

Adverse effects

Local reactions are uncommon. Allergic reactions are very rare.

Vaccine associated paralytic poliomyelitis (VAPP)

VAPP risk is increased in persons with immunodeficiency. The risk of VAPP in either recipients or contacts of recipients was less than 0.3 per million doses of OPV distributed (<1 case per 3.3 million doses).

Storage

OPV

The vaccine can be stored at minus 20°C (-20°C) in the freezer compartment of the refrigerator or freezer room for up to two years and +2°C to +8°C in the refrigerator compartment up to 6 months.

IPV

The vaccine should be maintained at 2°-8°C Freezing diminishes the potency of IPV and should be avoided. The vaccine should be perfectly clear and colourless. Any vaccine showing particulate matter, turbidity or change in colour should be discarded.

Further reading

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CHAPTER 15

RABIES VACCINE

Introduction

Rabies is an acute encephalomyelitis caused by a rhabdovirus. It is primarily an infection of mammals, spread by bites of infected animals. In many parts of the world especially in South East Asia, dogs are the principal reservoir of rabies. Humans are occasionally infected by wild animals, but domestic dogs and cats are responsible for the majority of cases. In Sri Lanka rabies has been detected in mongoose, cattle, goats, pigs, bandicoots, jackals, pole cats, civet cats, rock squirrels, monkeys, horses and elephants. Domestic rats have not been implicated in the transmission of rabies in Sri Lanka. Human to human transmission also has not been documented.

The virus can penetrate broken skin or intact mucous membranes. Humans are usually infected when virus laden saliva is inoculated through the skin by the bite of a rabid animal. Saliva can also infect if the skin is already broken, e.g. by the claw of the animal. The virus has been isolated in an animal's saliva even up to 14 days before it exhibits the first signs of rabies. Intermittent excretion of the virus in the saliva continues throughout the illness. The incubation period in humans averages 1 to 3 months but can range from 5 days to more than one year.

Infection with rabies virus characteristically produces an acute illness with rapidly progressive central nervous system manifestations, including anxiety, dysphagia and seizures. Illness almost invariably progresses to death. Some patients may present with paralysis.

Types of vaccine

Inactivated anti rabies cell culture vaccine

- Human diploid cell vaccine (HDCV)
- Purified vero cell rabies vaccine (PVRV)*

- Purified chick embryo cell vaccine (PCEC)*

*Vaccines available in Sri Lanka at present.

These freeze dried vaccines have a potency of >2.5 IU/dose

Efficacy

100% seroconversion after a full course of vaccine.

Indications

Pre-exposure immunisation

Pre exposure immunisation is recommended for the following risk groups

Veterinary surgeons, support staff and students

Laboratory staff handling material contaminated with rabies virus

Abattoir workers, animal handlers, vaccinators

Wild life officers, dog catchers

Employees in animal quarantine premises and zoological establishments.

Dosage and administration

Freeze dried vaccine should be reconstituted with the diluent provided.

Administration by IM or SC route.

Primary immunisation

Day 0 1 dose administered IM or SC in the deltoid

Day 7 „ „ „ „

Day 28 „ „ „ „

One booster to be taken 01 year later.

Further boosters to be taken every 5 years for maintenance of rabies protective antibody levels.

Administration of rabies immunoglobulin is contraindicated in persons on pre-exposure therapy. They should only be given additional doses of anti-rabies vaccine IM one dose each on day 0 and day 3 as boosters, even in the case of major exposure.

Post-exposure immunisation

Patients on pre exposure immunisation should not be administered rabies immunoglobulins. If an exposure takes place medical advice should be sought immediately regarding boosters.

Choice of therapy depends on the screening of the person exposed and also the animal involved in the incident.

If an animal who bites a person is healthy and alive for 14 days following the bite it is considered that the animal has not infected that person.

It is essential to screen the patient and the animal before the decision is made regarding post exposure treatment (PET).

Screening the patient – Categorisation of the exposure

Major exposures:

- a. Single or multiple bites with bleeding on head, neck, face, chest, upper arms, palms, tips of fingers and toes, and genitalia.
- b. Multiple deep scratches with bleeding on the head, neck and face.
- c. Single or multiple deep bites on any part of the body.
- d. Contamination of mucous membranes with saliva.
- e. Bites of wild animals with bleeding.

Minor exposures:

- a. Single, superficial bite or scratch on the lower limbs (excluding tips of toes), upper limbs (excluding upper arms, palms and tips of fingers), abdomen and back.
- b. Nibbling of uncovered skin.

- c. Contamination of open wounds with saliva.
- d. Drinking of raw milk of rabid cow or goat.

Screening the animal

In case of **major** exposure to dogs and cats:

- If the animal is apparently healthy, observable and has had a minimum of 2 consecutive rabies vaccinations, with the last vaccination given within 1 year of the incident, PET can be delayed while observing the animal for 14 days.
- When the animal is suspected to have rabies or is sick, but observable, initiate PET while observing the animal. Discontinue treatment if the animal is apparently healthy after 14 days.
- If the animal is having rabies (confirmed by laboratory diagnosis) or unobservable (animal dead, missing or stray animal) initiate PET and continue the full course.

In case of **minor** exposure to dogs and cats:

- If the animal is apparently healthy, observable and has had a minimum of 1 rabies vaccination:
 - within 1 year of the incident
 - at an age above 3 months
 - incident occurring at least 1 month after the vaccination

PET can be delayed while observing the animal for 14 days.

- When the animal is suspected to have rabies or is sick, but observable, initiate PET while observing the animal. Discontinue PET if the animal is healthy after 14 days.
- If the animal is having rabies (confirmed by laboratory diagnosis) or unobservable (animal dead, killed, missing or stray animal) initiate PET and continue the full course.

The patient must be clearly advised that the animal should be put in a cage or leashed during the observation period. If the animal dies, becomes sick or develop any abnormal behaviour, the patient should be advised to report to the hospital immediately. In case of death of the animal patient should be encouraged to send the head of the animal for laboratory confirmation of rabies.

The following are not considered as exposures:

- Contamination of intact skin with saliva of a suspected rabid animal.
- Petting, bathing or coming in contact with utensils of a suspected rabid animal.

Anti rabies PET: when indicated :

1. All patients in the major category should be given rabies immunoglobulin (equine or human) followed by a course of anti rabies vaccine (ARV).
2. Patients in the minor category should be given only a course of ARV.

Rabies immunoglobulin (RIG)

RIG available in Sri Lanka at present:

- Equine rabies immunoglobulin (ERIG)
- Human rabies immunoglobulin (HRIG)

Rabies immunoglobulins should be given immediately after the incident. However, if the patient reports late, RIG could be given up to 3 months after exposure, if he has not taken more than 2 doses of anti rabies vaccine.

It is essential to test for sensitivity before administering ERIG. HRIG does not require sensitivity testing prior to its administration.

Method of sensitivity testing (ST) for ERIG

Control: Inoculate 0.1 mL of sterile N saline ID on flexor aspect of the forearm.

Test: Prepare a 1:10 dilution of rabies equine serum with sterile N saline and inoculate 0.1 mL ID on flexor aspect of the opposite forearm.

Initial diameter of the indurated area should be measured in mm and recorded.

Patient is kept under observation and the ST should be read after 20 minutes. Examine for itching, induration or urticaria or any systemic effects of anaphylaxis. If the initial diameter of the induration is less than 6 mm and the induration after 20 minutes is over 10 mm or if there is any systemic reaction ST should be considered as a positive.

Separate fixed needle-syringes should be used for each patient.

The drug of choice in anaphylaxis is 1:1000 adrenaline 0.5 mL given IM immediately. (Please refer Chapter 24)

Mild sensitivity reactions could be managed with antihistamine therapy. Oral or parenteral steroids should be best avoided as it could depress the immune response.

If a patient with a major exposure is ST positive for all available products of ERIG, HRIG should be considered.

However, in a situation where HRIG is not available:

1. If the animal is **apparently healthy and observable**, the modified 4 site ID ARV schedule could be considered while observing the animal for 14 days and report to hospital immediately, if the animal falls sick, dies or goes missing during this period.
2. If the animal is **suspected of having rabies or is not observable**, WHO recommended method of using ERIG under adrenaline and antihistamine in an ICU setup should be considered.

Please note: In a patient with a major exposure, modified 4 site ID ARV should not be considered as equivalent for RIG and a course of ARV.

Dosage and administration of RIG

HRIG 20 IU/kg body weight

ERIG 40 IU/kg body weight

Part of the dose (as much as possible depending on the site) should be infiltrated in and around all wounds. After infiltration if there is any remaining RIG, it should be given deep SC or IM on the thighs. Deltoids should be spared for ARV when giving RIG. Vaccine should be administered preferably on the same day after RIG, but at a different site.

Anti rabies vaccines (ARV)

Patients with major exposures should be given rabies cell culture vaccine IM or deep SC according to the following schedule.

One dose to be given in the deltoid on days 0, 3, 7, 14 and 30.

Patients with minor exposures should be given a total of 4 doses of rabies cell culture vaccine IM or deep SC on the following days.

Day 0 – 2 doses to be given IM or deep SC, one in each deltoid.

Day 7 – 1 dose IM or deep SC

Day 21 – 1 dose IM or deep SC

Intradermal inoculation of rabies cell culture vaccine

ID vaccination schedule has been recommended by the WHO to be used in developing countries where cost is a major limiting factor.

Recommended ID dose is 0.1 mL per site for both PCEC and PVRV

2 site ID schedule

One dose (0.1 mL) given ID at each of 2 sites in the deltoids on days 0, 3, 7 and 30.

2 site schedule is routinely used in all patients irrespective of the use of rabies immunoglobulins.

Example: Severe exposure – rabies immunoglobulin + 2 site ID schedule of anti rabies vaccine.

Minor exposure – 2 site ID schedule of anti rabies vaccine only.

Modified 4 site ID schedule

One dose of (0.1 mL) given ID at each of 4 sites on day 0 (both deltoids and lateral thighs) and 0.1 mL given at 2 sites on days 3, 7 and 30.

The modified 4 site schedule is helpful in patients with low risk exposure who are sensitive to ERIG, patients with a minor exposure who come late for treatment or when rabies immunoglobulin is not available in the country. It gives an earlier antibody response than the 2 site schedule.

Precautions that should be taken when using ID ARV schedules

All ID injections should be **administered only by trained staff** under supervision of a medical officer. Once the vaccine is reconstituted the contents should be used as soon as possible (preferably within 8 hours stored at 2°-8°C). Separate disposable syringes and needles should be used for each patient to prevent contamination.

Management of patients following a full course of rabies PET previously

For both major and minor exposures: If the animal is apparently healthy and observable, PET could be delayed while observing the animal for 14 days.

If the animal is **proven rabid, suspected of rabies or unobservable:**

- a. Up to 6 months from the last dose of ARV – PET is not indicated.
- b. From 6 months - 5 years from the last dose of ARV – 2 site ID ARV 2 doses each or IM ARV one dose each should be given on days 0 and 3. As an alternative to this regimen, the patient may be offered a single visit 4 site ID regimen on day 0, consisting of 4 injections of

0.1 mL, equally distributed over left and right deltoids or prescapular areas.

- c. Up to 5 years from the last dose of ARV, RIG is not indicated.
- d. After 5 years, a full course of ARV with or without RIG (depending on the category of exposure and animal screening) is recommended.

Contraindications

In view of the gravity of the disease, all contraindications are secondary in cases of exposure to suspected rabies infections.

Adverse effects

Local – pain, tenderness, erythema.

Systemic – malaise, headache, nausea, mild fever, urticaria

Storage

2°C-8°C

Further reading

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CHAPTER 16

ROTAVIRUS VACCINE

Introduction

Globally, rotavirus is the leading cause of acute gastroenteritis in children less than 5 years of age. Each year it causes 138 million diarrhoeal episodes, 2 million hospitalisations and an estimated 527,000 deaths. More than 80% of the deaths occur in the developing world. Worldwide it is estimated that almost every child has had at least one episode of diarrhoea due to rotavirus by the age of 5 years.

The incidence of rotavirus infection is comparable in the developing and developed world showing that increased disease awareness, improved sanitation and hygiene and safe water supply is not effective in controlling the spread of the disease.

Rotavirus infection in Sri Lanka is a significant cause of morbidity. Several studies and the ongoing rotavirus surveillance studies show that rotavirus causes about 24% of the watery diarrhoeal infections. Of this, 80% of the infections occurred in the age group < 2 years. But the mortality due to rotavirus infection in Sri Lanka is low.

Virology and transmission

Rotavirus infection is caused by rotavirus which is a member of the genus reoviridae. It is divided into 7 groups A-G out of which only group A infects humans. The virus has 2 surface glycoproteins G and P. The genotypes of rotavirus are based on these glycoproteins. There are 15 G types and 26 P types. Out of this 5 G types are seen commonly G1-4 and G9. The common P types are 8, 6 and 4. The most common genotype seen in the developed world is G1 while the developing countries show a more varying scenario.

Rotavirus is shed in very high numbers during acute infection (10^{12} viral particles per gram of stools). It is transmitted from person to person by the faecal-oral route via contaminated fomites. Transmission by contaminated food and water is not common. Transmission via the

respiratory route has been suggested. It is infectious in low doses (about 100 viral particles). The virus can survive in the environment for days and in stools for months.

The incubation period is 1-4 days and a child will be excreting the virus a few days before and after the clinical illness. The clinical illness which lasts for 3-7 days, is of sudden onset, with fever, vomiting and explosive watery diarrhoea up to 10 times a day. There is no blood in the stools but might be mucoid. About 50% of the infections might be subclinical.

The first infection which occurs around 3 months of age, is the most likely to cause severe gastroenteritis with dehydration. The primary infection confers protection for rotavirus gastroenteritis in 77% of patients and against severe gastroenteritis in 87% of patients. The subsequent infections confer a broader heterotypic immunity while the primary infection confers homotypic immunity.

Types of vaccine

Two types of vaccines are available. One is a human monovalent vaccine against G1P[8] and the other is a bovine-human reassortant pentavalent vaccine against G1-4 and P[8]. Both are oral vaccines.

Efficacy

The vaccine will prevent about 73% of all rotavirus gastroenteritis, about 93% of severe cases, and about 96% of hospitalisations due to rotavirus.

Indications

Prevention of childhood gastroenteritis due to rotavirus.

Dosage and administration

- **Human monovalent vaccine**

Lyophilised vaccine to be reconstituted with a diluent (supplied with the vaccine), 1 mL/dose at 2 and 4 months of age. The minimum age for the first dose is 6 weeks and the minimum interval between the

doses is 4 weeks. It is not recommended for children over 24 months of age.

- ***Bovine-human reassortant pentavalent vaccine***

Liquid vaccine (ready to use), 2 mL/dose at 2, 4 and 6 months. The minimum age for first dose is 6 weeks and the minimum interval between the doses is 4 weeks. It is not recommended for children over 32 months of age.

Rotavirus vaccine can be given safely with other childhood vaccines including DTaP, Hib, IPV, hepatitis B and OPV.

Contraindications

Life-threatening allergy to any component of the rotavirus vaccine. Children with severe allergy to latex should not receive the monovalent vaccine.

Children who are moderately or severely ill. This includes children who have acute moderate to severe gastroenteritis.

Precautions

Both types of vaccines have not been associated with intussusception. It is suggested that children who have had one episode of intussusception should not get rotavirus vaccine as they are at a higher risk for getting a recurrence. However, no data is available on rotavirus vaccine in children with a history of intussusception.

No safety or efficacy data are available for the administration of rotavirus vaccine to infants with known or suspected altered immunocompetence.

Adverse effects

Diarrhoea, vomiting, otitis media and nasopharyngitis was seen among 1-3% of children more than normal children.

Storage

2°C-8°C, protected from light. The diluent may be stored at 20°C-25°C.

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CHAPTER 17
TETANUS VACCINE
(Tetanus toxoid)

Introduction

(Please refer Chapter 3)

Type of vaccine

Toxoid

Aluminium absorbed liquid vaccine (tetanus toxoid) is a markedly turbid white suspension. If the product contains clumps of material that cannot be resuspended with vigorous shaking, it should not be used.

Indications

To prevent tetanus in all age groups

To prevent neonatal tetanus by immunising pregnant women.

Vaccines containing tetanus toxoid

	Diphtheria	Tetanus	Pertussis
Diphtheria, tetanus and pertussis vaccine DTP (DPT)	≥30 IU/dose	≥40 IU/dose	≥40 IU/dose
Diphtheria, tetanus and acellular pertussis vaccine DTaP	≥30 IU/dose	≥40 IU/dose	≥25µg pertussis toxoid ≥25µg filamentous haemagglutinin ≥8µg pertactin per dose

	Diphtheria	Tetanus	Pertussis
Diphtheria and tetanus vaccine DT	≥30 IU/dose	≥40 IU/dose	-----
Low antigenic diphtheria, tetanus and acellular pertussis vaccine dTpa	≥2 IU/dose	≥20 IU/dose	≥8µg pertussis toxoid ≥8µg filamentous haemagglutinin ≥2.5µg pertactin per dose
Diphtheria and tetanus vaccine for adults aTd	≥2 IU/dose	≥40 IU/dose	-----
Tetanus toxoid vaccine TT	-----	≥40 IU/dose	
Diphtheria, tetanus, pertussis, HiB and Hepatitis B vaccine (penta) DTP-HiB-Hep B	≥30IU/dose	≥40IU/dose	≥40IU/dose
Diphtheria, tetanus, and acellular pertussis vaccine. hepatitis B vaccine, HiB vaccine, and injectable polio vaccine DTaP-HepB-IPV-Hib	≥30 IU/dose	≥40 IU/dose	≥25µg pertussis toxoid ≥25µg filamentous haemagglutinin ≥8µg pertactin

Active immunisation with tetanus toxoid is indicated for all persons who have not been adequately immunized. In children, initial tetanus immunisation is administered with DTP, DT, DTaP, DTP-HepB, DTP-HepB-Hib, or DTaP-HepB-Hib-OPV, DtaP-HepB-Hib-IPV (total of 5 doses).

The primary series of 3 doses of a tetanus toxoid containing vaccine should be given in infancy (age <1 year) with a first dose of booster at 18 months of age followed by the second booster before school entry so that the school going child is completely immunised against tetanus.

However, the WHO suggests that in addition to the childhood vaccination programme, an extra tetanus toxoid or tetanus toxoid containing vaccine dose to adults, as it has been found that immunity after 5 doses wanes in adult life. This will provide additional assurance of long lasting, possibly lifelong protection against tetanus. Therefore a sixth dose is recommended for adolescents at age 10-15 years as aTd or dTpa and for young adults as TT. which can be routinely and conveniently given eg. at the time of, the first pregnancy, induction to military service, the medical examination before first employment, admission to universities and higher centres of training, wound management. Those who receive their first tetanus vaccine doses as adolescents or adults require a total of 5 appropriately spaced doses to obtain the same long-term protection.

Dosage and administration – for infants and children See Chapter 3

Dosage and administration – for adolescents and adults

Dosage - 0.5 mL of tetanus toxoid

3 injections as follows – 1 stat, 2nd 6 weeks later, 3rd 6 months later.

A history regarding tetanus immunisation should always be taken before tetanus toxoid is given for wound prophylaxis. Tetanus toxoid need not be given to children with a history of complete immunisation with 5 doses of tetanus toxoid. Adults with a history of immunisation with only 5 doses of tetanus toxoid in childhood need 1 dose. Adults with a history of immunisation with 6 doses of tetanus toxoid including the 5 received in childhood do not need tetanus toxoid for wound prophylaxis. Persons who have had initial tetanus immunisation in adolescence or adulthood with 5 doses of toxoid do not need any doses for prophylaxis. One dose given to a person not immunised against tetanus will not produce effective immunity

Administration – Deep intramuscularly into deltoid or antero-lateral aspect of thigh.

Subcutaneous injection can cause local irritation, inflammation, granuloma formation and necrosis

Tetanus toxoid in pregnancy – (Please refer Annexure 1 National Immunisation Schedule). Pregnant women with an inadequate or unknown immunisation history should always receive 2 doses of tetanus vaccine: the first dose administered after completion of 12 weeks of pregnancy and the second dose at least 4 weeks later. The second dose should be given at least 2 weeks prior to delivery. Effort should be made to complete the recommended series of 5 immunisations while respecting the minimum intervals between doses.

Contraindications

Hypersensitivity to any component of the vaccine.

Adverse effects

Anaphylactic reactions, Guillain-Barre syndrome, and brachial neuritis attributable to tetanus toxoid have been reported but are rare.

Storage

2°C-8°C. Do not freeze.

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CHAPTER 18

TYPHOID VACCINE

Introduction

Enteric fever (typhoid and paratyphoid fever) is an acute febrile illness, endemic in developing countries with occasional outbreaks. The prototype of this syndrome is typhoid fever caused by *Salmonella enterica* serotype Typhi. However, paratyphoid fever due to *Salmonella enterica* serotype Paratyphi A is replacing typhoid fever in many South Asian countries including Sri Lanka.

Transmission is by food and water contaminated by faeces. The incubation periods are 7-14 days for typhoid and 1-10 days for paratyphoid.

Typhoid and paratyphoid fever cannot be differentiated clinically. Clinical features include continued fever, headache, abdominal pain, constipation or diarrhoea and splenomegaly. Bacteraemia is present and blood cultures are positive in 50-70% of cases. Resistance to the commonly used antimicrobials is emerging worldwide increasing the urgency to control the disease.

Vaccines are available only to prevent typhoid fever.

Types of vaccine

Two safe and moderately efficacious vaccines against typhoid fever have been licensed.

Ty21A (oral): A live-attenuated vaccine, manufactured from the *S. Typhi* Ty21a strain, is available as an enteric-coated capsule. The capsule is licensed for persons over 5 years. The liquid formulation, which was licensed for children over 2 years, is currently not commercially available.

Vi polysaccharide (parenteral): purified Vi capsular polysaccharide vaccine (ViCPS) licensed for persons over 2 years of age.

Efficacy

Vaccine protective efficacy can be overcome by the high inocula seen in food borne exposure. Therefore vaccination is only an adjunct to avoidance of high risk food and drink. Protection lasts only for a limited period.

Oral Ty21A vaccine:

Efficacy for 3 years is around 51%. Protection commences 10-14 days after taking the third dose and lasts 5-7 years. However, those living in endemic areas should be revaccinated every three years and travellers from non-endemic areas need annual revaccination.

Herd protection of non-vaccinated population and moderate cross protection against Paratyphi B is also seen.

Vi polysaccharide vaccine:

Efficacy for 3 years is around 55%. Protection occurs 7 days after vaccination and lasts for 3 years. Revaccination is recommended every 3 years.

The efficacy of the Vi and Ty21a vaccines in children aged <2 years has not been demonstrated and neither of the vaccines is licensed for use in this age group.

There are currently no licensed vaccines against paratyphoid fever.

Indications

1. WHO recommends vaccination targeting high risk groups and populations especially where typhoid is a significant public health problem and when drug resistant strains are prevalent. For each country, data on sub-populations at risk should be obtained and such groups targeted.
2. Vaccination is also recommended for outbreak control.
3. Travellers visiting typhoid endemic areas (e.g. Indian subcontinent),

especially if travelling into areas where sanitation and food hygiene are likely to be poor.

4. Household contacts of typhoid carriers.
5. Laboratory personnel who may handle *Salmonella* Typhi in the course of their work.

Dosage and administration

Oral Ty21A vaccine:

Primary course

The schedule comprises a total of three doses, given every other day. One capsule, to children over 5 years of age and adults, on days 1, 3, and 5.

The vaccine should be taken at least one hour before a meal with 100-200 mL of cold or lukewarm water (temperature should not exceed body temperature, i.e. 37°C). It should not be taken with milk or other beverage with acid or basic pH as this may kill the bacteria, preventing the appearance of an immune response and thereby decreasing the vaccine's efficacy. Stored capsules must be refrigerated between doses.

No antibiotics should be taken from 3 days before to 3 days after immunisation with oral live bacterial vaccines. People on antibiotics could be immunised with Vi polysaccharide vaccines given parenterally. In the case of foreseen malaria prophylaxis, the interval between the last vaccine dose and beginning of the malaria prophylaxis should generally be 3 days.

Some authorities recommend a 4th dose of the enteric capsule for better efficacy.

Boosters

Booster series is recommended every 3 years for people residing in endemic areas. Travellers from non-endemic areas to endemic areas should be revaccinated annually.

Vi capsular polysaccharide vaccine:

Single 0.5 mL (25µg) dose IM or SC. Booster doses every 3 years.

Contraindications

Previous severe hypersensitivity reaction to any component of the vaccine

Precautions

Oral Ty21A vaccine:

- Immunodeficiency
 - Pregnancy
 - Treatment with antibiotics
 - Acute febrile illness
 - Acute gastroenteritis
- } postpone vaccination

Adverse effects

Local reactions such as pain, induration and erythema may be seen 48 to 72 hours after administration of the Vi capsular polysaccharide vaccine. The oral Ty21a vaccine is remarkably well tolerated and has low rates of adverse events.

Storage

2°C-8°C. Do not freeze.

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CHAPTER 19

VARICELLA VACCINE

Introduction

Chickenpox in childhood is characterised by fever and a pruritic vesicular rash of generalised distribution. Although in temperate climates, the majority of the population is immune to the varicella zoster virus (VZV) by 5 years of age, the epidemiology is remarkably different in Sri Lanka. In Sri Lanka, only 50% of those living in rural areas had had chickenpox by the age of 60 years. In addition, 56.2% of women of child bearing age were not immune to chickenpox¹.

Complications such as pneumonia are 25 times commoner in adults than in children and mortality rates are far higher. VZV infection associated viral pneumonia has an incidence of 0.3% to 50% and a reported mortality of 2% to 20% in adults. Primary varicella infection during pregnancy may cause serious complications in mother and baby and infection in the first or second trimester may cause congenital infection. Chickenpox is prolonged (more than 10 days) in the immunosuppressed and many have complications. Visceral dissemination and multi organ failure subsequently leading to death has been reported in many. Following chickenpox, the lifetime risk of zoster is estimated to be 10-30% and the incidence increases markedly with age affecting up to 50% of people aged >85 years.

Types of vaccines

All varicella vaccines contain the Oka strain of live attenuated VZV, lyophilized vaccine supplied with sterile diluent.

Efficacy

Two doses of vaccine are effective in preventing any form of clinical disease in 98% of recipients and 100% effective against severe disease, 10 years after vaccination. Immune responses are influenced by the number of doses given, immune status and age of receiving the vaccine.

- **Age of receiving the vaccine:** seroconversion rates are between 77-96% in adult vaccinees, which is lower than the seroconversion rates in children.
- **Immune status:** seroconversion rates are lower in children with malignancies.
- **Number of doses:** Protective antibody levels in children after one dose are 85.7% and after 2 doses is 99.6%. The 2 dose schedule reduces breakthrough chickenpox, i.e. chickenpox that develops >42 days after vaccination).

Indications

- Susceptible children over 1 year of age, adolescents and adults.
- Those at a higher risk of contracting chickenpox: health care workers, family contacts of immunocompromised persons, teachers of young children, day care employees and residents and staff in institutional settings, hostels, school children, university students, inmates and staff of correctional institutions and military personnel, those going for studies in temperate climates.
- Non-pregnant women of childbearing age. They should be advised to avoid pregnancy for 3 months following each dose of vaccine.
- Patients with human immunodeficiency virus (HIV) infection, if CD4 > 200 cells/ μ L, or if CD4 counts >25% of the total lymphocyte count (in children).

Dosage and administration

- 0.5 mL given subcutaneously.

Aged 12 months to 12 years

- First dose of varicella vaccine could be given at age 12--15 months. A second dose of varicella vaccine is recommended routinely for all children aged 4-6 years. (booster dose).
- The booster dose may be administered at an earlier age provided

that the interval between the first and second dose is more than 3 months.

- Those who have received only one dose of the vaccine during childhood based on earlier guidelines are recommended another dose of the vaccine.

Persons aged ≥13 years

- should receive two 0.5 mL doses of varicella vaccine, 4-8 weeks apart.

Post exposure prophylaxis

The varicella vaccine is effective in preventing illness or modifying the illness if given to children within 3 days following exposure to a rash. Vaccination within 3 days of exposure to rash was ≥90% effective in preventing varicella whereas vaccination within 5 days of exposure to rash was approximately 70% effective in preventing varicella and 100% effective in modifying severe disease. Therefore, the varicella vaccine is recommended for post exposure administration for unvaccinated persons without other evidence of immunity (please see chapter on passive immunisation for more details).

Herpes zoster

The incidence of herpes zoster (HZ) among persons older than 75 years of age is >10 cases per 1000 person-years and the lifetime risk of HZ following chickenpox is estimated to be 10-20%. The incidence is significantly higher in individuals with impaired cell mediated immune responses such as those with malignancy, organ transplant recipients and persons on immunosuppressant treatment. The most common complication of HZ, particularly in older persons, is postherpetic neuralgia (PHN). PHN is the persisting debilitating pain weeks to months after resolution of HZ.

As the VZV vaccine is a live attenuated vaccine, the vaccine virus also establishes latency similar to the wild type virus. In a study of leukaemic children, the rate of HZ was 2% in VZV vaccine recipients and 15% in children following natural infection. Data is not available in HZ risk after

vaccination in healthy individuals. However, studies suggest that the risk for HZ following the varicella vaccine is lower than that after wild-type varicella infection.

Absolute contraindications

- Those suffering from cellular immune deficiencies including individuals who have any malignant condition.
- Persons receiving high-dose systemic immunosuppressive therapy, including persons on oral steroids ≥2 mg/kg of body weight.
- Patients with human immunodeficiency virus (HIV) infection, can receive the vaccine if CD4 > 200 cells/μL, or if CD4 counts >25% of the total lymphocyte count.
- Pregnancy. Although pregnancy is an absolute contraindication, no adverse effects have been reported in instances where the vaccine has been mistakenly administered.

Relative contraindications

- Impaired humoral immunity: can be given after obtaining specialist opinion.
- Patients on steroids <2mg/kg of body weight per day.
- Those with leukemia, lymphoma, or other malignancies whose disease is in remission and when chemotherapy has been terminated for at least 3 months.

Adverse effects

- Mild pain, redness at site of administration.
- Causes a vesicular rash in 5% of recipients.
- The virus is able to establish latent infection in the vaccinated host and reactivation may occur, although less frequently than in those following natural infection.

Storage

At 2°C-8°C. Please refer to manufacturers instructions.

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CHAPTER 20 YELLOW FEVER VACCINE

Yellow fever

Yellow fever is a viral haemorrhagic fever which is endemic in the tropics of Africa and South America. It poses a significant hazard to unvaccinated travellers to these areas. The case fatality rate may reach 20% to 80%. Yellow fever is transmitted in a cycle involving monkeys and mosquitoes but human beings can also serve as the viraemic host for mosquito infection. Although the vector mosquito *Aedes aegypti* is found in Sri Lanka, yellow fever has not been reported. The emphasis is on preventative vaccination as there is no specific treatment.

Types of vaccine

Live attenuated vaccines

The French neurotropic vaccine from human virus passaged in mouse brain.

The 17D vaccine from human virus passaged in embryonated chicken eggs.

Only the latter is available in Sri Lanka.

Efficacy

Neutralising antibodies develop between the 7th and 21st day after immunisation.

95% of recipients develop antibodies. Immunity lasts for 10 years.

Indications

Those >6 months who are travelling to countries where yellow fever vaccination is required.

e.g. Africa and South America

Travellers are expected to get immunised two weeks prior to departure. They are advised to keep the immunisation records while travelling, as they may have to show such record on arrival to a country with yellow fever.

Because of the risk of serious adverse events that can occur after yellow fever vaccination, clinicians should only vaccinate people who 1) are at risk of exposure to YFV or 2) require proof of vaccination to enter a country.

Dosage

Reconstitution

Once reconstituted with the diluent provided the vaccine should be used immediately, as at 37°C the vaccine loses all potency within 1 hour. The reconstituted vaccine could be stored for a maximum of 3 hours at 2°C to 8°C.

Administration

0.5 mL subcutaneously.

The only authorized place for administration of this vaccine for the travellers to countries with risk, is the office of the Assistant Port Health Officer in the premises of the Medical Research Institute, Colombo 8.

Contraindications

Allergy to one of the vaccine components, notably egg albumin.

Congenital or acquired immunodeficiency (asymptomatic HIV infection is not a contraindication).

Active malignant disorders.

Patients on cytotoxic agents.

Infants below the age of 6 months.

Pregnancy.

Adverse effects

A) Common adverse reactions

Reactions to yellow fever vaccine are generally mild; reported events typically include low-grade fever, headache, and myalgias that begin within days after vaccination and last 5-10 days.

B) Severe adverse reactions

Hypersensitivity

Immediate hypersensitivity reactions, are uncommon. Anaphylaxis after yellow fever vaccine is reported to occur at a rate of 1.8 cases per 100,000 doses administered.

Yellow fever vaccine-associated neurologic disease (YEL-AND)

YEL-AND, include meningoencephalitis, Guillain-Barré syndrome, acute disseminated encephalomyelitis, bulbar palsy, and Bell palsy and are seen among people of all ages. 4-6 cases occur per 1 million doses distributed. The illness occur 3-28 days after vaccination, and almost all cases were in first-time vaccine recipients. YEL-AND is rarely fatal and commoner in people aged ≥ 60 years.

Yellow fever vaccine-associated viscerotropic disease (YEL-AVD)

YEL-AVD is a severe illness similar to wild-type disease, with vaccine virus proliferating in multiple organs and often leading to multisystem organ failure and death. YEL-AVD appears to occur after the first dose of yellow fever vaccine, rather than with booster doses. The onset of illness for YEL-AVD cases averaged 3 days (range, 1-8 days) after vaccination. The case-fatality ratio for reported YEL-AVD cases is 65%. The rate is higher for people aged ≥ 60 years. The frequency is 3-5 cases per 1 million doses distributed.

Precautions

- Infants aged 6-8 months as the incidence of YEL-AND is higher.

- Adults 60 years of age or older when receiving the vaccine for the first time as incidence of YEL-AND and YEL-AVD is higher.
- Breast feeding as YEL-AND is reported from breast fed babies less than one month.

Storage

2°C-8°C. Do not freeze.

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CHAPTER 21

IMMUNISATION OF HIV INFECTED PERSONS

Introduction

Immunisation is an important measure to protect people living with HIV/AIDS (PLHIV) against certain vaccine preventable diseases. Compared to healthy individuals, PLHIV may have an increased risk of infection or experience more severe disease following exposure to vaccine-preventable diseases. The antibody response, which is associated with the CD4 T cell count, is frequently impaired. They need higher or more frequent vaccine doses and more frequent testing for serological response. Certain vaccines enhance virus replication and transiently increase HIV viral load. Theoretically, vaccination should be given before the immune status of the patients is suppressed. Persons with severe immunodeficiency* may have impaired humoral response, and may not respond to vaccines, or they may require supplemental doses to develop serological evidence of protection. If possible, vaccines should be administered before the CD4 count decreases to <200 cells/μL.

All inactivated vaccines can be administered safely to persons with altered immunocompetence whether the vaccine is a killed whole organism or a recombinant, subunit, toxoid, polysaccharide, or polysaccharide protein-conjugate vaccine. The usual doses and schedules are recommended. However, the effectiveness of such vaccinations might be suboptimal.

*HIV-infected persons >6 years of age with CD4 counts <200 cells/μL, history of an AIDS-defining illness, or clinical manifestations of symptomatic HIV are considered to have severe immunosuppression. Children <5 years of age with CD4 percentage <15% are considered to have severe immunosuppression. Asymptomatic HIV-infected persons with CD4 counts from 200-500 cells/μL are considered to have limited immune deficits.

General principles of immunisation in HIV-infected children

- Vaccines may be less effective in HIV infected children. However,

these children also have an increased risk of vaccine preventable diseases and may have more severe illness if they are infected. Completing immunisation is thus important, but consideration should be given to the most appropriate time for immunisation, as vaccination is more likely to be effective after immune reconstitution in the severely immunocompromised.

- The HIV antibody test is the currently available serological test to diagnose HIV infection in Sri Lanka. HIV antibodies are passively transferred from the infected mother to the baby and these may last up to 18 months in the baby. Hence it is difficult to diagnose HIV infection early in the baby especially if asymptomatic.

General principles of immunisation in HIV-infected adults

- Persons with symptomatic HIV infection or CD4 counts <200/μL should not be given live vaccines. Vaccination may be reconsidered when immune restoration occurs with antiretroviral therapy.
- Transient increases in plasma HIV RNA load have been reported after administration of several vaccines to HIV-infected persons. Available evidence indicates that these transient increases do not have clinical significance and should not prevent the use of any vaccine.

Schedule for pre-exposure vaccination in HIV-infected adults

Vaccine	Indication	Primary course	Boosting	CD4 count	Comments (cells/μL)
Hepatitis A	RS	Two or three doses	5 years	*	Three doses if CD4 count <300 cells/μL
Hepatitis B	R	Three or four doses	HBsAb <10 IUL	*	HBsAb levels yearly
Haemophilus influenzae type b (Hib)	RS	Single dose	None	*	

Vaccine	Indication	Primary course	Boosting	CD4 count	Comments (cells/μL)
Human papilloma virus	RS	3 doses	none	*	
Influenza-parenteral	R	Single dose	Repeat yearly	*	
Measles, mumps, rubella (MMR)	RS	One or two doses	None	>200	Two doses if measles IgG negative
Meningococcal (ACWY)	RS	Single dose	5 years	*	
Pneumococcal (polysaccharide)	R	Single dose	5 years	*	
Tetanus-diphtheria	R	One to five doses	10 years	*	
Injectable poliomyelitis (IPV)	R	One to five doses	10 years		
Typhoid (Vipolysaccharide)	RS	Single dose	2-3 years	*	Boosting after 2 years if CD4 count <200 cells/μL
Varicella	RS/CS	Two doses	None	>400/ >200	
Yellow fever	CS	Single dose	10 years	>200	Contraindicated if aged >60

*Vaccinations can be given irrespective of the CD4 count.

CS – consider in selected persons; HBsAb – Hepatitis B surface antibody; R – recommended; RS – recommended in selected persons

Inactivated polio vaccine (IPV)

The IPV is recommended for HIV-infected children. This gives good antibody titres in most patients with CD4 counts of >200 cells/ μ L, but a small number of patients with CD4 counts of <200 cells/ μ L may fail to respond.

OPV

However, as there has been no data to suggest increased risk of immunodeficiency-associated vaccine-derived poliovirus (iVDPV) in HIV infection or AIDS, OPV can be used in HIV infected children as in the usual immunisation schedule of Sri Lanka.

Measles, mumps and rubella (MMR) vaccine

Measles vaccine is recommended for all HIV-infected children who are not severely immunosuppressed (with severe immunosuppression defined as a CD4 percentage of <15%). Serological response may be poor in HIV infection.

BCG

A delayed approach is recommended, in which vaccination is delayed in infants known to have been exposed to HIV in utero or during birth, until HIV infection is ruled out. The child should be closely followed for ascertainment of HIV status and BCG vaccination given after HIV infection is excluded.

If the mother is HIV positive, the baby should be tested for HIV virus prior to administration of the vaccine. If infection status can be established with early virological testing, BCG may then be administered once HIV infection has been ruled out.

Varicella vaccine

Varicella vaccine is contraindicated in severe immunodeficiency. It is regarded as safe in children with asymptomatic or minimally symptomatic

HIV infection and an age-specific CD4 cell count of >15%. 2 doses should be given with an interval of 3 months. It is also recommended for susceptible close contacts of HIV-infected persons because of risk of transmission of varicella.

***Haemophilus influenzae* type b (Hib) vaccine**

HIV-infected children aged ≤ 5 years should receive the Hib conjugate as per routine vaccination schedule. It should be considered among HIV-infected children >5 years old who have not previously received Hib vaccine. For these older children, two doses of conjugate Hib vaccine, should be administered at least 1-2 months apart.

Pneumococcal conjugate vaccine

HIV-infected children aged <2 years should receive the pneumococcal conjugate vaccine. Children aged >2 years should receive the 23-valent pneumococcal polysaccharide vaccine with a single booster dose 5 years later.

Meningococcal vaccine

HIV infection is not a contraindication to receiving meningococcal vaccine.

Live attenuated Japanese encephalitis vaccine

Immunosuppression is a contraindication at present.

Inactivated Japanese encephalitis vaccine

The inactivated JE vaccine can be given safely to HIV infected patients. The WHO recommends that the inactivated JE vaccine should be given for immunocompromised patients until further studies regarding live JE vaccine is available.

Rabies vaccine

Rabies vaccine can be given safely in HIV infected patients who are

exposed to the rabies virus. They should be administered both rabies immunoglobulin and rabies vaccine. The vaccine has to be given by the IM route and not the intra-dermal route. The immune response is affected by the CD4 cell count and low or absent antibody responses have been reported in some persons with CD4 counts <200 cells/ μ L.

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CHAPTER 22

PASSIVE IMMUNISATION

Introduction

Passive immunisation involves administration of preformed antibodies to individuals in order to prevent or reduce the severity of infection. This may be carried out either as post exposure prophylaxis to individuals who are likely to develop severe disease or complications following exposure to an infectious agent, or if the infection is already present antibodies may be used to ameliorate or suppress the infection (e.g. botulism, tetanus etc.).

Several types of products have been used in passive immunisation. These include immunoglobulins and specific immunoglobulins (hyperimmune) given intramuscularly, specific immunoglobulins given intravenously (botulism immunoglobulin), intravenous immunoglobulins, monoclonal antibodies and antibodies of animal origin. Immunoglobulins are a sterile solution, derived from the pooled plasma from adults that has been tested negative for hepatitis B surface antigen, antibodies to HIV and HCV, HCV RNA, syphilis, HTLV-1 and HTLV-2. It is prepared by an alcohol fractionation procedure. This procedure inactivates any viruses (e.g. HBV, HCV and HIV) present in the preparation.

The main immunoglobulins are of the IgG type (96%) with trace amounts of IgM and IgA. Hyperimmune immunoglobulins are prepared from donors who have high antibody titres to the specific organism. Serum concentrations of antibodies are usually achieved 3-5 days after IM administration.

Administration

Intramuscular: Immunoglobulin for passive immunisation (to be used for the prevention of infection) is licensed to be administered intramuscularly. It should be administered into a large muscle mass such as the gluteal region (upper outer quadrant) in an adult or the anterior thigh region in a child. No more than 5 mL should be administered at one

site in an adult, and an adolescent; a lesser volume per site (1-3 mL) should be given to small children and infants.

Subcutaneous: This route is safe and effective in adults and children with primary immune deficiencies. It is used to administer smaller amounts of immunoglobulins at weekly intervals. Immunoglobulins should not be administered intradermally.

Intravenous: This route is used in the replacement of immunoglobulins in monthly intervals in patients with primary immune deficiency states. IV route is also used in certain diseases such as Kawasaki disease, immune mediated thrombocytopenia (ITP), autoimmune diseases (e.g. Guillain-Barré syndrome, myasthenia gravis), paediatric HIV infection, prevention of graft versus host disease and infection in patients who receive bone marrow transplants.

Indications for use pooled human immunoglobulins (given IM)

1. **Hepatitis A prophylaxis:** Indicated as post exposure prophylaxis of infants (<12 months old), individuals older than 40 years, in immunocompromised individuals and in individuals with chronic liver disease. In individuals from 12 months to 40 years old, hepatitis A immunisation is preferred to administration of immunoglobulins in post exposure prophylaxis.
2. **Measles prophylaxis:** Used as post exposure prophylaxis. Will prevent or attenuate infection if given within 6 days of exposure. The usual recommended dose is 0.25 mL/kg given intramuscularly; immunocompromised children should receive 0.5 mL/kg intramuscularly.
3. **Rubella prophylaxis:** If administered to pregnant women who have not received the vaccine or are non-immune to rubella after exposure may decrease the risk of foetal infection

Indications for specific (hyperimmune) immunoglobulins (given IM)

1. **Hepatitis B immunoglobulin:** should be administered as soon as possible after an exposure and preferably within 24 hours. The

hepatitis B vaccine should be administered at the same time as immunoglobulins (different sites). Indications are as follows:

- Neonate of HbSAg positive mother: HBIG (0.5 mL) should be given intramuscularly (IM), preferably within 12 hours of birth.
 - Percutaneous (bite or needle stick) or mucosal exposure to HbSAg positive blood or body fluids.
 - Victim of sexual abuse (perpetrator who is HBsAg positive).
2. **Varicella zoster immunoglobulin:** should be administered within 96 hours exposure for the following group of individuals.
- Immunocompromised individuals.
 - Newborn infant whose mother had onset of chickenpox within 5 days before delivery or within 48 h after delivery.
 - Hospitalized preterm infant (28 wk or > of gestation) whose mother lacks a reliable history of chickenpox or serologic evidence of protection against varicella.
 - Pregnant women without evidence of immunity.

It should be given intramuscularly. Please refer manufacturer's instructions for dosing. IGIV is given intravenously at the dose of 400 mg/kg. As administration of VZV-immunoglobulin may result in asymptomatic infection, testing for VZV-specific antibodies 2 months after administration is recommended for subsequent management of the patient (e.g. in immunocompromised patients). Incubation period of varicella can be prolonged following administration of immunoglobulins.

Please see chapter on the varicella vaccine for details on postexposure prophylaxis in immunocompetant individuals.

3. **Rabies immunoglobulin:** please see chapter on rabies
4. **Tetanus immunoglobulin:** Human tetanus immunoglobulin should be given at a single dose intramuscularly as soon as possible. Please refer manufacturers' instructions for dosing. Part of the recommended dose should be infiltrated locally.

5. **Botulism immunoglobulin:** Antitoxin can arrest the progression of paralysis and decrease the duration of paralysis and dependence on mechanical ventilation. Antitoxin should be given early in the course of illness, ideally <24 h after onset of symptoms because antitoxin neutralises only toxin molecules that are yet unbound to nerve endings.

Subsequent administration of other vaccines

When immunoglobulins are given intramuscularly for the prevention of infectious diseases (post exposure prophylaxis), other vaccines can be administered at the same time, but at a different site. E.g. in the use of rabies hyperimmune serum, rabies vaccine can be administered at the same time but at a different site.

However, use of immunoglobulins is known to interfere with immune responses to subsequent vaccines if given very soon after administration of immunoglobulins. For instance, after the use of immunoglobulins or other blood products, immune responses to vaccines such as the measles vaccine have been shown to be inhibited even 3-4 months after the use of these products. Therefore, use of live vaccines should be delayed at least for 3 months after the use of immunoglobulin preparations.

Precautions

- Caution should be used when administering immunoglobulins to individuals with a past history of adverse reactions.
- The intramuscular route should not be used in individuals with thrombocytopenia and coagulation disorders.

Adverse effects

- Many experience pain and discomfort at the site of administration. Flushing, headache, nausea and vomiting may occur less frequently.
- Serious reactions: these are uncommon but chest pain, constriction, dyspnoea and anaphylaxis may occur.

- In individuals with IgA deficiency: the trace amounts of IgA present in immunoglobulins may induce an anaphylactic reaction.

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CHAPTER 23

SURVEILLANCE AND PREVENTION OF ADVERSE EVENTS FOLLOWING IMMUNISATION

Introduction

Immunisation can be followed by adverse events due to the inherent properties of the vaccine (vaccine reaction), or an error in the immunisation process (programme error). The event may be unrelated to the immunisation, but have a temporal association (coincidental event). Anxiety-related reactions may occur due to fear or pain of the injection not the vaccine. In some cases the cause of the Adverse Events Following Immunisation (AEFI) remains unknown.

It is difficult to be sure of the exact frequency of true adverse reactions (vaccine reactions). Vaccines are mostly administered to infants and young children who are in the period of their lives when they are experiencing many illnesses. Many events which occur after vaccination may well have occurred whether or not the child had been vaccinated. These events are "coincidental". When two sets of events can both be expected to occur frequently, it may be difficult to determine whether they are causally linked. As disease incidence declines due to effective immunisation programmes, the occurrence of AEFIs will receive more attention. AEFIs due to coincidence and programme errors in storage, handling, or administration of vaccine are more common than AEFIs due to the properties of vaccines (vaccine reactions).

Therefore, AEFI could be defined as a medical event, which occurs after an immunisation and believed to be caused by the immunisation. Temporal relationship and suspicion of the cause and effect relationship is sufficient to label the event as an AEFI. Exclusion is based on the case investigation.

Hence, monitoring of AEFIs is important for the success of the immunisation programme, since such events can influence community acceptance of immunisation. Careful surveillance and investigation of

AEFIs are necessary to identify causes of these events and to take appropriate actions.

Prevention of AEFIs

The most common programme errors linked with immunisation are listed below.

- Exceeding the recommended amount of the dose
- Incorrect immunisation site
- Incorrect immunisation route.
- Inadequately sterilised syringes and needles.
- Vaccine reconstituted with incorrect diluent.
- Incorrect volume of diluent
- Drug inadvertently substituted for vaccine or diluent
- Incorrectly prepared vaccine, e.g. an adsorbed vaccine not being shaken properly before use.
- Contaminated vaccine or diluent
- Incorrectly stored vaccine such as freezing of liquid vaccines
- Contraindications not complied.
- Reconstituted vaccine used beyond six hours.

A significant proportion of AEFIs reported can be linked to improper handling of reconstituted vaccines, e.g. measles, MR, MMR, BCG and some other polyvalent lyophilized vaccines. The vaccines should be reconstituted only with the diluent supplied by the manufacturer.

Contamination of reconstituted vaccine with *Staphylococcus aureus* has been documented in several countries. Children immunised with contaminated vaccines become sick within a few hours; local tenderness and tissue infiltration, vomiting, diarrhoea, cyanosis and high temperature are the frequent signs and symptoms. These incidents, which result in

needless deaths or life threatening illness may damage confidence on immunisation, are preventable if proper reconstitution of vaccines and proper handling procedures are followed.

In some vaccination centres and hospitals many potentially dangerous medications are stored in the same refrigerator in which vaccines are stored. These medications are packed in vials or ampoules with similar appearance to vaccines or their diluents and may be used by mistake for reconstitution of vaccines.

Health personnel who administer vaccines should be trained and closely supervised to ensure that proper procedures are being followed. This is essential for the prevention of AEFIs. A comprehensive investigation should be carried out in the event of an AEFI.

Reporting of AEFIs

According to the decisions taken by the Expert Committee on AEFI of the Ministry of Health, all health personnel in both government and private sector institutions should be made aware of the AEFI reporting system and AEFI reporting forms should be made available to them.

According to the national AEFI surveillance guidelines, information on every reportable AEFI should be reported to the Medical Officer of Health (MOH), where the patient resides using Notification Form for Adverse Events Following Immunisation (AEFI Form 1). The MOH will consolidate all AEFI data received and send a monthly consolidated AEFI Return to the Epidemiology Unit.

The MOH, Regional Epidemiologist or the Epidemiology Unit will initiate an investigation for all severe AEFIs, all deaths following AEFIs and AEFI clusters. Therefore it is prudent to carry out pertinent laboratory and postmortem investigations in all serious AEFI cases and deaths following immunisation. All deaths and serious AEFIs such as anaphylaxis, need to be informed to the Epidemiology Unit as soon as possible.

The format of Notification Form for Adverse Events Following Immunisation (AEFI Form 1) with the list of reportable AEFIs and definitions are given in Annex V.

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CHAPTER 24

MANAGEMENT OF ANAPHYLAXIS

Introduction

Anaphylaxis is an acute, life-threatening systemic reaction with varied mechanisms, clinical presentations, and severity that results from the sudden systemic release of mediators from mast cells and basophils. Although a precise definition of anaphylaxis is not important for the emergency treatment of an anaphylactic reaction with adrenaline, experts in the field of allergy and immunology have developed a definition of anaphylaxis as one of three clinical scenarios as described in Box 1.

Box 1. Definition of anaphylaxis

- 1) Acute onset of a reaction (minutes to hours) with involvement of the skin, mucosal tissue or both and at least one of the following:
 - a) respiratory compromise: airway and breathing (refer Box 2)
 - b) reduced blood pressure (BP) or symptoms of end-organ dysfunction (refer Box 2)
- 2) Two or more of the following that occur rapidly after exposure to a likely allergen for that patient:
 - a) involvement of the skin/mucosal tissue (refer Box 2)
 - b) respiratory compromise
 - c) reduced blood pressure or associated symptoms
 - d) persistent gastrointestinal symptoms (refer Box 2)
- 3) Reduced age specific blood pressure after exposure to a known allergen for that patient (minutes to several hours) or greater than 30% fall from baseline or less than 90 mmHg for adults

Note: age specific BP is defined in Box 5.

Anaphylaxis following vaccination is rare but recognition of signs and symptoms of anaphylaxis (Box 2) is crucial for prompt treatment and to prevent confusion with more frequent acute events that may occur after vaccination such as vaso-vagal collapse, and sudden onset rash without anaphylaxis.

Box 2. Diagnostic features of anaphylaxis	
Respiratory	<p>Airway</p> <ul style="list-style-type: none"> • Throat and tongue swelling (pharyngeal/laryngeal oedema) – the patient has difficulty in breathing and swallowing and feels that the throat is closing up • Hoarse voice • Stridor <p>Breathing</p> <ul style="list-style-type: none"> • Bilateral wheeze (bronchospasm) • Respiratory distress – 2 or more of the following: <ul style="list-style-type: none"> ○ Tachypnoea ○ Increased use of accessory respiratory muscles ○ Recession ○ Cyanosis • Grunting • Respiratory arrest
Cardiovascular	<ul style="list-style-type: none"> • Feeling faint or collapse with measured hypotension

Cardiovascular <i>(Continued)</i>	<ul style="list-style-type: none"> • Clinical diagnosis of uncompensated shock, indicated by the combination of at least 3 of the following: <ul style="list-style-type: none"> ○ Tachycardia ○ Capillary refill >3 times ○ Reduced central pulse volume ○ Decreased level of consciousness or loss of consciousness • Cardiac arrest <p>Note</p> <ul style="list-style-type: none"> • Anaphylaxis can cause myocardial ischaemia and electrocardiograph (ECG) changes even in individuals with normal coronary arteries. • Bradycardia (a slow pulse) is usually a late feature, often preceding cardiac arrest
Disability (because of decreased brain perfusion)	<ul style="list-style-type: none"> • Confusion • Agitation • Headache • Feeling of impending doom • Loss of consciousness
Dermatologic or mucosal	<ul style="list-style-type: none"> • Tingling of lips • Generalized urticaria or generalized erythema

	<ul style="list-style-type: none"> • Angioedema, localized or generalized (angioedema is similar to urticaria but involves swelling of deeper tissues, most commonly in the eyelids and lips, and sometimes in the mouth and throat) • Generalized itching of skin especially hands, forehead and eyes in children <p>Note</p> <p>Although skin changes can be worrying or distressing for patients and those treating them, skin changes alone without life-threatening airway, breathing or circulation problems do not signify an anaphylactic reaction</p>
Gastrointestinal	<ul style="list-style-type: none"> • Diarrhoea • Colicky abdominal pain • Vomiting • Incontinence
Ocular	<ul style="list-style-type: none"> • Pruritus • Conjunctival injection • Lacrimation

The limited available data from Sri Lanka indicates that in 86% of documented vaccine /drug induced anaphylaxis cases fitted into category three where hypotension was the only manifestation. Increased vascular permeability, a characteristic feature of anaphylaxis, allows transfer of as much as 35% of the intravascular fluid into the extravascular space

within 10 minutes. As a result, haemodynamic collapse may occur rapidly with little or no cutaneous or respiratory manifestations. Respiratory compromise and cardiovascular collapse are of greatest concern, since they are the most frequent causes of fatalities.

Anaphylaxis often produces signs and symptoms within minutes of exposure to the vaccine but some reactions may develop later (e.g., greater than 30 minutes even up to 12 hours after exposure). Late phase or "biphasic" reactions, which occur 1 to 72 hours (most within 10 hours) after the initial attack, have also been reported. Protracted, severe anaphylaxis may last up to 32 hours despite aggressive treatment.

During vaccination older children and adults may faint (Box 3) or have a panic attack due to fear or pain mimicking anaphylaxis. Fainting attacks in the younger child may be due to anaphylaxis.

Box 3. Differences between a fainting, anaphylaxis and panic attack		
Clinical features	Fainting	Anaphylaxis
Timing	Before, during or few minutes after immunisation	Generally within minutes after immunisation. Could occur, up to several hours.
Skin and mucous membranes	Generalized pallor, cold clammy skin	Itching of the skin (in children especially forehead, hands and ears), tingling around lips, generalised erythema, urticaria, swelling of lips and face.

Respiratory system	Normal breathing Shallow breathing	Tachypnoea, difficulty in breathing, wheezing, cough, stridor, hoarseness of voice, cyanosis of finger tips and lips, recession of intercostal spaces.
Cardiovascular	Bradycardia, weak pulse, carotid pulse felt, hypotension may occur - reversed by supine position	Tachycardia, weak pulse, carotid pulse may be weak, hypotension - not reversed by supine position
Gastrointestinal	Vomiting	Vomiting, diarrhoea, abdominal cramps
Central Nervous System	Faintishness, light headedness relieved by supine posture	Anxiety and distress, loss of consciousness not relieved by supine posture
Panic attack – No hypotension, pallor, wheeze, or urticarial rash or swelling. May have flushing or blotchy skin.		

Management of anaphylaxis

Adrenaline (epinephrine) and oxygen are the most important life saving therapeutic agents administered in anaphylaxis. If there is any doubt regarding diagnosis, it is advisable to administer adrenaline intramuscular (IM). The more rapidly anaphylaxis develops; the more likely the reaction is to be severe and potentially life-threatening. Any delay before the administration of adrenaline or a history of asthma is significant risk factors for anaphylactic death. Death due to anaphylaxis usually occurs as a result of respiratory obstruction or cardiovascular collapse, or both.

A life threatening reaction requires immediate treatment; do not refer the patient during the acute phase without resuscitation. Stocking and maintaining supplies for the treatment of anaphylaxis with regular written documentation of supplies and expiration dates and ready availability of the items in Box 4 are bare essentials. Regular anaphylaxis practice drills are strongly recommended.

<p>Box 4. Pharmaceuticals and other item needed for emergency tray</p> <ol style="list-style-type: none"> Clearly labeled adrenaline vials (adrenaline must be kept in the dark and below 25°C but not refrigerated). Hydrocortisone vials Chlorphenamine vials 0.9% sodium chloride intravenous solution Water for injection Syringes Airways (small, medium, and large) ET tubes Oxygen Sphygmomanometer (adult and child cuffs) Stethoscope Alcohol swabs Tourniquet Tongue depressors Flashlight with extra batteries

1. Initial management

- Reassure patient /parents/guardian. The patient is usually anxious and can experience a "sense of impending doom". Do not leave the patient alone.
- Use the ABCD (Airway, Breathing, Circulation, Disability) approach (Box 2) to recognize clinical problems. It will also help in the differential diagnoses. Rapid assessment of systolic blood pressure is critical to guide treatment. As auscultation may be difficult or misleading, measure systolic blood pressure by simple palpation.

Box 5. Assessment of blood pressure and pulse rate in anaphylaxis

Age	Systolic blood pressure (mm Hg) for diagnosis of hypotension	Pulse rate / minute (count the patient's pulse rate for 1 minute)
Term neonates (0 - 28d)	<60	>140
Infants (1 - 3 months)	<70	>140
Infants (3 - 12 months)	<70	>130
1 - 2 years	< [70 mmHg + (2 × age)]	>130
>2 to 10 years		>80
> 10 yrs	Sudden drop below 90	>75
Adults		> 100

Adults: Treatment should aim for a systolic blood pressure above 100 mm Hg. In older adults, who are normally hypertensive, a blood pressure of 100 mm Hg

may constitute severe hypotension and a higher target may be required to maintain neurological function. Child: A child cuff should be used for measurement of BP.

2. Patient positioning

- Place the patient in a recumbent position and elevate the lower extremities, as tolerated symptomatically.
- If the patient feels faint, do not sit or stand them up (can cause cardiac arrest).
- Patients with airway and breathing problems may prefer to sit up as this will make breathing easier.
- Patients who are breathing and unconscious should be placed on their left lateral position.
- Pregnant patients should lie on their left side to prevent caval compression
- Patients who are hypotensive should be kept in the recumbent position until stabilized, and asymptomatic.

3. Pharmacologic treatment

If anaphylaxis is suspected management in order of importance is: adrenaline, oxygen, intravenous fluids, nebulized therapy, vasopressors, antihistamines, corticosteroids, and other agents. The basic principles of treatment are the same for children and adults. Any differences will be highlighted.

- **Adrenaline** (epinephrine)

Give **adrenaline 1: 1000 dilution via the intramuscular (IM) route** at the first suspicion of anaphylaxis (Box 6). Do not delay treatment as it is the most effective, safe and life saving treatment and works best when given early after the onset of the reaction. Adrenaline has a rapid onset of action after IM administration and a greater margin of safety. The time to highest blood concentration (C_{max}), when studied in asymptomatic subjects, is shorter when

injection is given intramuscularly in the vastus lateralis muscle (lateral thigh) than when it is administered intramuscularly in the deltoid muscle of the arm. Do not inject into hands, ears, buttock or other parts of the body.

Box 6. Adrenaline in the INITIAL management of acute anaphylaxis

Drug, site and route of administration	Frequency of administration	Dose (adult)	Dose (child)*
Adrenaline (epinephrine) 1:1000, IM to the midpoint of the antero-lateral aspect of the middle third of the thigh immediately, then every	5-15 min as needed until there is resolution of the anaphylaxis or signs of hyperadrenalisms: palpitation, tremor, uncomfortable apprehension and anxiety occur. Persisting or worsening cough associated with pulmonary oedema is an important sign of adrenaline overdose and toxicity.	0.3 - 0.5 mL (300 - 500 mcg) 0.3 mL for smaller adults (30- 50 kg) 0.5 mL (<50 kg)	0.01 mL/kg (up to 0.3 mL) According to age <ul style="list-style-type: none"> • <1 yr-0.05 mL • 1-3 yrs (10-15 kg) – 0.10-0.15 mL • 3-5 yrs (15-20 kg) – 0.15-0.20 mL • 5-7 yrs (20-25 kg) – 0.20-0.25 mL • 7-12 yrs (25-30 kg) – 0.25-0.30 mL

Note: The needle used for injection needs to be sufficiently long to ensure that the adrenaline is injected into muscle. A 25 mm needle is best and is suitable for all ages. In pre-term or very small infants a 16 mm needle is suitable for IM injection. In some adults, a longer length (38 mm) may be needed. Give IM injections with the needle at a 90° angle to the skin. The skin should be stretched, not bunched.

Reassess the pulse rate and BP regularly: every 5 min, (essential to monitor the response to adrenaline) aiming for the patient's normal BP. If this is unknown, in adults aim for a systolic BP greater than 100 mmHg, for children aim at BP higher than the values given in the text 2.1. Repeat IM adrenaline every 5 minutes as determined by BP and bronchospasm. If the clinician deems it appropriate, more frequent injections of adrenaline can be given.

Do not routinely administer adrenaline via the intravenous (IV) route because of the risk of potentially lethal arrhythmias. The IV route should only be considered in profoundly hypotensive patients or who have not respond adequately to several IM doses of adrenaline or patients in cardio/respiratory arrest. If it has to be given IV, administer as an infusion (Box 7). Intravenous bolus injections of adrenaline have a high risk of potentially lethal arrhythmias and are generally recommended only for imminent cardiac arrest. For IV bolus use only 1: 10,000 dilute adrenaline (dilute 1 ml of 1:1,000 with 9 mL of 0.9% sodium chloride to make a 1:10,000 solution) and give in boluses (0.05 mL/kg or 5 mcg/kg) over at least 5 minutes into the side arm of a fast flowing IV infusion, stopping when a response is obtained.

Continuous haemodynamic monitoring is recommended if adrenaline is given via the IV route even as an infusion. However, use of IV adrenaline should not be precluded in a scenario where such monitoring is not available, if the specialist deems its administration is essential after several IM adrenaline injections. In these special circumstances, monitoring by available means (e.g. every-minute blood pressure and pulse measurements and ECG monitoring, if available) should be considered.

Child: Hypotension and the pulse rate can be difficult to assess in small children and this fact should be taken into consideration before giving escalating intravenous doses of adrenaline in error. Absorption of adrenaline from the IM site is good in children. IV route should be considered mainly for persistent shock or cardio/respiratory arrest (Box 7).

Box 7. Intravenous infusion of adrenaline for life-threatening anaphylaxis-induced hypotension who have failed to respond to intravenous volume replacement and several IM doses of adrenaline.

Adrenaline strength: **1:100,000 (0.1 mg [1 mL of a 1 in 1,000] in 100 mL sodium chloride 0.9% (10 mcg /mL)**

Continuous monitoring (ECG, SpO₂, BP every 3 to 5 minutes) is important

- 1:100,000 solution of adrenaline (0.1 mg [1 mL of 1:1000] in 100 mL saline) intravenously by infusion pump at an initial rate of 30-100 mL/hr (5-15 mg/min), titrated up or down depending on clinical response or adrenaline side effects (toxicity).
- **If an infusion pump is not available and life threatening situation is considered likely without intervention:** Give through a dedicated intravenous line.
- **adrenaline 1mL of 1:1,000 in 100 mL sodium chloride 0.9% IV, at approximately 100 mL/hour, which is 1 drop every 2 seconds for most standard drip sets.**

OR

If you only have a 500 mL bag of infusion fluid use:

- **adrenaline 1 mL of 1:1,000 in 500 mL sodium chloride 0.9% IV, at approximately 500 mL/ hour, which is 2 drops per second for most standard drip sets.**

OR

If you only have a 1000 mL bag of infusion fluid use:

- **adrenaline 1 mL of 1:1,000 in 1000 mL sodium chloride 0.9% IV, at approximately 1000 mL/hour, which is 5 drops per second for most standard drip sets.**

(Continued)

Children with cardiac arrest or profound hypotension: adrenaline 0.1 mcg/kg/min (0.1 mL/kg of a 1:10,000 solution up to 10 mcg/min; maximum dose, 0.3 mg) OR calculate as $(0.6 \times \text{body weight (in kg)}) = \# \text{ of mg diluted to total 100 mL saline; rate of 1 mL/h delivers 0.1 mcg/kg/min}$

- Titrate up or down according to response, aiming for lowest effective infusion rate.
- Wait for 5 to 10 minutes after a change in the infusion rate to assess the response.
- Reduce the rate immediately if signs of adrenaline toxicity (tachycardia, tremor and pallor in association with a normal or raised blood pressure) develop. Reduce the infusion rate (if toxicity is severe, stop the infusion briefly before recommencing at a lower rate). Persisting or worsening cough associated with pulmonary oedema is an important sign of adrenaline overdose and toxicity.
- As the reaction resolves, an infusion that was previously therapeutic can quickly start to have toxic effects. Therefore when features of anaphylaxis improve, begin reducing the infusion, aiming for around half the starting rate if possible.
- One hour after the resolution of all symptoms and signs, wean the infusion over another 30 minutes and stop.

- Establish airway.
- Give high flow oxygen, (6 - 8 L/minute) and airway/ventilation support if needed. Measure oxygen saturation with pulse oximeter.
- Give sodium chloride 0.9% solution infusion via a wide bore access (i.e. 14G or 16G in adults). One to 2 L of normal saline may need to be administered to adults at a rate of 5-10 mL/kg in the first 5 minutes.

If hypotension continues repeat normal saline boluses: sodium chloride 0.9% solution 10 to 20 mL/kg IV bolus, up to total of 50 ml/kg over the first 30 minutes. Children should receive up to 30 mL/kg in the first hour. Adults receiving colloid solution should receive 500 mL rapidly, followed by slow infusion.

- Monitor the patient for adverse effects of adrenaline

Adrenaline is a drug with a narrow toxic/therapeutic ratio. Transient pharmacologic effects such as pallor, tremor, anxiety, palpitations, headache, and dizziness are common after the correct therapeutic dose. If the patient develops a persisting or worsening cough associated with pulmonary oedema the administration of adrenaline should be stopped and the patient assessed as it is an important sign of adrenaline overdose and toxicity.

4. After initial resuscitation with adrenaline and oxygen (Box 8)

- Antihistamines: These agents have a much slower onset of action than adrenaline and should never be used alone in the treatment of anaphylaxis. A combination of chlorphenamine and ranitidine is superior to chlorphenamine alone. The doses are given in Box 8. Do not use two H1 receptor blockers such as chlorphenamine and promethazine as they will only potentiate the hypotension. Intravenous promethazine should not be used as it is highly caustic to the intima of blood vessels, and serious tissue reactions including thrombosis, nerve damage, tissue necrosis and gangrene have been reported. Deep IM is the preferred route of administration if chlorphenamine is not available.
- Steroids: they are of secondary value in the initial management of anaphylactic shock because the onset of action is delayed for several hours. Steroids are given to prevent further deterioration in severely affected patients and continued for 24 to 48 hours according to clinical response. Administer only ONE of the corticosteroids slowly intravenously or intramuscularly, taking care to avoid inducing further hypotension.

- Hydrocortisone: Box 8.
- Oral prednisolone 1 mg/kg up to 50 mg maybe sufficient for milder attacks.
- Dexamethasone IV 0.1-0.4 mg/kg every 6 hours.

Box 8. Pharmacologic treatment once patient's condition is stabilized with adrenaline and fluids			
Drug, and route of administration	Frequency of administration	Dose (adult)	Dose (child)
Chlorphenamine IM or slow IV over 1 min once patient's condition is stabilized with adrenaline and fluids. Child: IM/Slow IV over 1 minute (If small dose is required, dilute with 0.9% sodium chloride) For doses of promethazine refer text. Do not administer both to the same patient.	continue orally every 4 hours for 48 hours.	10 mg	1 month-1 year: 250 mcg/kg (maximum 2.5 mg) 1- 6 years: 2.5 mg 6-12 years: 5 mg

(Continued)

Drug, and route of administration	Frequency of administration	Dose (adult)	Dose (child)
Hydrocortisone Once patient's condition is stabilized with adrenaline and fluids, administer IM or IV slowly For doses of other corticosteroids refer text	repeat every 6 h as needed	Adults and >12 years: 200 mg follow up with prednisolone 50 mg orally daily for 4 days	Child: 2 mg/kg every 6 hours <6 months: 25 mg >6 months - 6 years: 50 mg >6-12 years: 100 mg follow up with xmg/kg up to a maximum of 50 mg orally daily for 4 days
Ranitidine Once patient's condition is stabilized with adrenaline and fluids if given IV: dilute in 5% dextrose to a total volume of 20 ml and give over 5 minutes. Repeat every 4 - 6 hours	Repeat every 8 h as needed	Adult 1mg/kg IV	1mg/kg IV (maximum 50mg) or 2 mg/kg orally

5. Other therapeutic options:

- **Persistent bronchospasm:**

Continuous salbutamol to be nebulized (3 - 5 mg by nebuliser, driven by oxygen at least 8 L/minute), or continuous actuations of metered dose 2-6 puffs salbutamol into ventilation circuit if intubated.

- **Severe bradycardia**

If present consider atropine 0.02 mg/kg IV.

- **If refractory to volume replacement and adrenaline infusion**

Dopamine (400 mg in 500 ml of 5% dextrose) administered at 2-20 mg/kg/min and titrated to maintain systolic blood pressure greater than 90 mmHg, should be administered if adrenaline and volume expansion fail to alleviate hypotension. Dopamine will usually increase blood pressure while maintaining or enhancing blood flow to the renal and splanchnic circulation. It has been shown that a dose of dopamine > 10 mg/kg/min is usually required to produce peripheral vasoconstriction which would be required to maintain systolic blood pressure. In cases of intractable hypotension vasopressin 10 to 40 units IV maybe considered.

Child: Dopamine 2-20 mg/kg/min. Calculate as $6 \times \text{body weight (in kg)} = \# \text{ mg diluted to total 100 mL saline}$; then 1 mL/h delivers 1 mg/kg/min.

- **For continuing respiratory deterioration**

Further treatment with bronchodilators including intravenous salbutamol, inhaled ipratropium, intravenous aminophylline or intravenous magnesium sulphate can be tried.

- **For upper airway obstruction,**

There is anecdotal evidence that nebulised adrenaline may provide some relief. Adrenaline 5 mg in 5 ml (= 5 ml of 1:1000 solution) via nebuliser.

- **Preparation for surgical airway**

If anaesthesia is required for intubation use fentanyl 1-10 mcg per kg IV. Do not use thiopentone or propofol. Suxamethonium 1-2 mg/kg maybe used to facilitate intubation, provided the doctor is sure of being able to intubate.

- Tranexamic acid has been used to treat anaphylactic episodes associated with disseminated intravascular coagulation.

6. **Treatment of cardiopulmonary arrest occurring during anaphylaxis**

- Start cardiopulmonary resuscitation and advanced cardiac life support measures.
- Rapid escalation to high-dose IV adrenaline may be tried for adults. A common sequence is 1 to 3 mg (1:10,000 dilution) IV slowly administered over 3 to 5 minutes, 3 to 5 mg (1:10,000 dilution) IV over 3 minutes, and then 4-10 mcg / minutes infusion.
- Child: 0.01 mg/kg (0.1 mg/kg of a 1 in 10,000 solution up to 10 mcg/minute rate of infusion) repeated every 3 to 5 minutes for ongoing arrest.
- Higher subsequent dosages (0.1-0.2 mg/kg; 0.1 mL/kg of a 1:1000 solution) maybe considered for unresponsive asystole or pulseless electrical activity (PEA).
- Rapid volume expansion.
- Atropine if asystole or PEA is present.
- Prolonged resuscitation is encouraged if needed since a successful outcome is more likely in anaphylaxis.

7. **Patients taking beta adrenergic antagonists**

They are more likely to experience severe anaphylactic reactions; these features may include severe hypertension and cerebral

haemorrhage, to unresolving hypotension, bradycardia and bronchospasm. If adrenaline is ineffective in these patients, both glucagon administration and isotonic volume expansion might be necessary.

Glucagon: 1- 5 mg (child 20-30 mcg/min, maximum dose 1 mg) IV over 5 minutes followed by infusion 5-15 mcg/min titrated to clinical response. Protection of the airway is important, as glucagons may cause emesis and aspiration in drowsy patients. The left lateral position may be sufficient in most patients.

8. **Observation and discharge from hospital**

Patients who have had a suspected anaphylactic reaction (i.e. an airway, breathing or circulation (ABC) problem) should be treated and then observed for at least 6-8 hours in a clinical area with facilities for treating life-threatening ABC problems. They should then be reviewed by a senior clinician and a decision made about the need for further treatment or a longer period of observation. Patients with a good response to initial treatment should be warned of the possibility of an early recurrence of symptoms and in some circumstances should be kept under observation for up to 24 hours. This caution is particularly applicable to:

- Severe reactions with slow onset.
- Reactions in individuals with a history of severe asthma or with a severe asthmatic component in the current episode.
- Reactions with the possibility of continuing absorption of allergen such as vaccines.
- Patients with a previous history of biphasic reactions.
- Patients presenting in the evening or at night, or those who may not be able to respond to any deterioration.
- Patients in areas where access to emergency care could be delayed.

Biphasic reactions occur in 1-23% of patients, up to 72 hours; however, in most instances, it is within 10 hours. There are no clinical criteria to predict the risk of a biphasic reaction, and the observation period should be individualized.

9. Laboratory studies

Serum tryptase can sometimes be helpful in establishing the diagnosis of anaphylaxis. Serum tryptase levels peak one to one and half hours after the onset of anaphylaxis and can persist for as long as five hours after the onset of symptoms. The best time to measure serum tryptase is between one to two hours but no longer than six hours after the onset of symptoms.

10. Reporting

It is mandatory that all vaccine associated anaphylaxis be reported to the Epidemiological Unit. As global experience indicates that the AEFI reports often do not contain sufficient detail to allow for the classification of adverse events make sure that the features described in Box 1 are included in the report.

Further reading

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CHAPTER 25

IMMUNISATION FOR INTERNATIONAL TRAVEL

Introduction

In considering immunisation for travellers the following information is important.

- (a) Current information on vaccine preventable diseases at travel destination.
- (b) Activities planned during travel and at travel destination.
- (c) Traveller's previous immunisation history.
- (d) Traveller's general health (age, allergies, medication, pregnancy, chronic disease conditions).
- (e) Amount of time available before departure.

Immunisation for travellers fall into 3 categories

- (a) Routine immunisation – should be up-to-date regardless of travel
- (b) Immunisation which are required to enter host countries
- (c) Recommended immunisations.

Required immunisation

Most vaccines take time to become effective and ideally should be given 4 - 6 weeks before travel.

a) Yellow fever vaccine

Yellow fever vaccination is the only vaccine required by the International Health Regulations. It is needed for travel to certain countries in sub-Saharan Africa and tropical South America.

Infants under 9 months of age should be vaccinated only if the risk of yellow fever is unavoidable because there is a small risk of

encephalitis. Vaccinating people with diseases of the thymus should be avoided as there is a higher risk of adverse reactions. Alternate means of prevention should be recommended to these travellers.

The International Health Regulations allow countries to require proof of vaccination, International Certificate of Vaccination (ICV), for entry for travellers arriving from endemic countries. Travellers arriving without a completed ICV may be quarantined or refused entry unless submitting to onsite vaccination. For purposes of international travel, yellow fever vaccine produced by different manufacturers worldwide must be approved by WHO and administered at an approved yellow fever vaccination centre. Vaccinees should receive a completed ICV, signed and validated with the centre's stamp where the vaccine was given. This certificate is valid from 10 days after vaccination and for 10 years.

(Please see Chapter 20)

Contraindications to vaccination

If a physician concludes that a particular vaccination should not be administered for medical reasons, the traveller should be given a signed and dated statement of the reasons on the physician's letterhead. Under these conditions, the traveller should obtain specific advice from the embassy or consulate of the country or countries he/she plans to visit.

Personal protection measures

In addition to vaccination, travellers should take adequate measures against exposure to mosquito bites.

b) Meningococcal vaccine

Vaccination against meningococcal disease is required by the government of Saudi Arabia for travellers arriving during the Hajj or for employment. The vaccine should be administered at least 10 days before arrival in Saudi Arabia. It is effective for 3 years.

Children over the age of 2 years and adults should be immunised with the quadrivalent vaccine (serogroups A, C, Y and W135). Children between 3 months and 2 years of age should receive two doses of the serogroup A conjugate vaccine with a 3-month interval between the two doses. (This vaccine is not available in Sri Lanka).

(Please see Chapter 12)

c) Polio vaccine

Some polio-free countries may also require travellers from polio-endemic countries to be immunised against polio in order to obtain an entry visa, e.g. Saudi Arabia (proof of oral poliovirus vaccination is required 6 weeks before application for an entry visa for visitors arriving from countries reporting poliomyelitis cases).

Recommended immunisations

These vaccines are administered to protect travellers from illnesses present in other parts of the world and to prevent the importation of infectious diseases across international borders. The vaccinations depend on the travel destination, age, health status, and previous immunisation. Most immunisation for travel fall into the recommended category.

Varicella vaccine

Varicella infections in adults result in severe disease and is often accompanied by complications. Long distance travellers, expatriates and those whose interests or activities are likely to bring them into close contact with children in schools and day care centres, healthcare settings, refugee camps and orphanages should be immunised before travel if no history of varicella is available. Protection occurs 14 days after the first dose. It is not given to pregnant women and immunocompromised persons.

(Please see Chapter 19)

Hepatitis B vaccine

Hepatitis B is highly endemic in South America, Africa, Asia and the South Pacific.

Immunisation is recommended for people who will experience close contact with residents in countries visited. The accelerated schedule of 0, 1, 2 months and a booster at 12 months or 0, 7, 21 days and a booster at 12 months is recommended for travellers.

(Please see Chapter 6)

Pneumococcal vaccine

Recommended for adults more than 65 years old and adults with chronic cardio-pulmonary conditions or chronic disease. Penicillin resistant pneumococci are prevalent throughout the world and access to effective alternative antibiotics may be limited. Protection occurs 14 days after vaccination.

(Please see Chapter 13)

Hepatitis A vaccine

All susceptible persons travelling to or working in countries that have high or intermediate hepatitis A endemicity should be vaccinated or receive human immunoglobulin (HNIG) before departure. (HNIG is not available at present in Sri Lanka). Hepatitis A vaccine at the age-appropriate dose is preferred to HNIG. The first dose of hepatitis A vaccine should be administered as soon as travel is considered and second dose should be administered 6-12 months after for life long protection.

One dose of single-antigen hepatitis A vaccine administered at any time before departure can provide adequate protection for most healthy persons. Older adults, immunocompromised persons, and persons with chronic liver disease or other chronic medical conditions planning to depart to an area in <2 weeks should receive the initial dose of vaccine and also simultaneously can be administered IG (0.02 mL/kg) at a separate anatomic injection site.

Travellers who are pregnant, aged <12 months, or are allergic to a vaccine component should receive a single dose of IG (0.02 mL/kg), which provides effective protection for up to 3 months.

(Please see Chapter 5)

Typhoid vaccine

Immunity is obtained 2-3 weeks after parenteral (Vi capsular polysaccharide) vaccination or 14 days after completion of the oral (Ty21a) vaccination.

The typhoid vaccines currently available do not offer protection against *S. paratyphi* infection.

(Please see Chapter 18)

Rabies vaccine

Recommended for travelers to rabies endemic areas. Three doses at 0, 7 and 21/28 days are recommended for pre-exposure vaccination. A booster should be given after one year.

If all three doses are not completed, the traveller will not be considered previously vaccinated and will require full post exposure prophylaxis, if an exposure occurs.

Rabies immune globulin (RIG) is not recommended following a rabies exposure to persons who have completed the rabies pre-exposure vaccination series. Previously vaccinated persons who are exposed to rabies require two boosters of a WHO recommended cell culture rabies vaccine on days 0 and 3.

(Please see Chapter 15)

Japanese encephalitis vaccine

The risk of Japanese encephalitis is highest in pig farming areas of China, Korea and South East Asia. Immunisation should be completed 10 days

before travel. Immunisation schedule with the killed vaccine is 0, 7 and 28 days.

(Please see Chapter 9)

Influenza vaccine

The risk for exposure to influenza during international travel depends on the time of year and destination. In the tropics, influenza can occur throughout the year, while in the temperate regions disease activity occurs during the winter. The vaccine that the traveller receives should be active against the strains of influenza virus prevalent in the country he visits. Every year the WHO recommends which strains should be included. The vaccine should be administered 2 weeks prior to travel. These vaccines should not be given to children under the age of 6 months.

(Please see Chapter 8)

General measures

- 1) A number of vaccines, both live and inactivated may be required prior to travel. All commonly used vaccines are relatively safe and can be given simultaneously, at different sites, without impairing antibody responses or increasing rates of adverse reactions. Inactivated vaccines generally do not interfere with the immune response to other inactivated or live-virus vaccines. It could be given at any time before or after a different inactivated vaccine or a live-virus vaccine. If two injected live-virus vaccines are not administered on the same day, the second vaccine should be administered at least 4 weeks later.
- 2) In the case of immunocompromised travellers the vaccination must be considered from the following perspectives: 1) safety in the context of the underlying illness and concurrent medication; and 2) the possibility of decreased effectiveness of the intervention. The doctor should explain to the traveller the risks and benefits of immunisation.

Because the situation is evolving, travellers can stay abreast of new developments by checking the official U.S. government website for

travel (<http://www.cdc.gov/travel>) and the WHO website www.who.int.

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CHAPTER 26

IMMUNISATION IN SPECIAL CLINICAL CIRCUMSTANCES

Preterm and low birth weight infants

Preterm infants born at less than 37 weeks of gestation and infants of low birth weight (lower than 2500 g) should receive all routinely recommended childhood vaccines at the same chronological age as term infants and vaccine doses should not be reduced when given to preterm and low birth weight infants.

Before pregnancy

Rubella and varicella vaccines should be given 3 months prior to pregnancy.

Pregnancy

Immunisation during pregnancy poses theoretical risks to the developing foetus. Pregnant women should receive a vaccine when the vaccine is unlikely to cause harm, the risk of disease exposure is high and the infection would pose a significant risk to mother or foetus. When a vaccine is to be given during pregnancy, it should be postponed if possible to the second or third trimester of pregnancy to minimize the theoretical concern about teratogenicity. Routine vaccinations considered safe in pregnancy are inactivated influenza, diphtheria and tetanus toxoid. Hepatitis A and B vaccines can be given if indicated. Inactivated polio virus (IPV) vaccine can be given to pregnant women who have never received polio virus vaccine or are partially immunised.

Pregnancy is a contraindication to administration of live vaccines. Therefore measles, mumps, rubella, varicella, BCG, live attenuated influenza, oral polio and yellow fever vaccinations should be avoided during pregnancy.

Pregnant women at risk of exposure to pathogens liable to cause certain serious illnesses should be considered for immunisation. These include

pneumococcal and meningococcal infections, Japanese encephalitis, typhoid and rabies. To prevent such infections the relevant inactivated vaccines are recommended. Human papilloma virus (HPV) vaccine contains no live virus but data on immunisation during pregnancy are limited.

Immunocompromised patients

Safety and effectiveness of vaccines in persons with immune deficiency are determined by the nature and degree of immunosuppression. Such people will vary in their susceptibility to infection.

Immune deficiency conditions are grouped into primary and secondary (acquired) immune deficiency disorders.

Primary immune deficiencies

These are usually inherited and involve a part of the immune defenses such as B-lymphocyte (humoral) immunity, T-lymphocyte (cell mediated) immunity, complement or phagocytic function.

Live vaccines are contraindicated for severe B-lymphocyte defects but not for selective IgA deficiency and IgG subclass deficiencies.

Live vaccines are contraindicated for all T-lymphocyte mediated immune disorders. Live bacterial vaccines are contraindicated in phagocytic function disorders, such as chronic granulomatous disease.

Most experts are of the opinion that live virus vaccines are safe to administer to children with complement deficiencies and disorders of phagocytic function.

Secondary (acquired) immune deficiencies

Secondary or acquired immune deficiency disorders occur in people with HIV/AIDS, malignant neoplasms, splenectomy, organ transplantation and in persons on immunosuppressive drugs or radiation therapy. It may also occur in people with severe malnutrition or protein loss, e.g. nephrotic syndrome.

Live viral vaccines are generally contraindicated because of the increased risk of adverse events.

After immunosuppressive therapy for cancer, live virus vaccines are withheld for a minimum of 3 months after discontinuation of therapy. After corticosteroid therapy, the interval of 3 months is based on the assumption that the disease is in remission or under control and that the immune response has been restored. The interval until immune reconstitution varies with the intensity and type of immunosuppressive therapy and the underlying disease. Therefore it is not possible to make a definite recommendation when live virus vaccines can be given safely and effectively.

Patients on corticosteroid therapy

Persons on high dose corticosteroid therapy (2 mg/kg/day of prednisolone) for more than one month can become immunosuppressed. They should receive live vaccines only after 3 months of cessation of therapy.

Solid organ transplant recipients

Children, adolescents and adults being considered for solid organ transplants should receive immunisations recommended for their age prior to transplantation. Vaccines will be more immunogenic before transplantation because medications given after, may be immunosuppressive by adversely affecting the number and function of B- and T-lymphocytes. All patients awaiting transplants should be immunised with hepatitis B and varicella vaccines before transplantation. Live virus vaccines should be given at least 1 month prior to transplantation. Killed vaccines should not pose a risk for solid organ transplant recipients.

Haemopoietic stem cell transplant

Many factors can affect immunity to vaccine preventable diseases for a person recovering from a successful haemopoietic stem cell transplantation or bone marrow transplantation. These include:

1. Donor's immunity.

2. Type of transplant (i.e. autologous or allogenic, blood or haemopoetic stem cell).
3. Time interval since transplantation.
4. Receipt of immunosuppressive medications.
5. Presence of graft versus host disease.

Although many will acquire donor's immunity, some will lose serological evidence of immunity. Therefore it is advisable to facilitate retention of donor immunity by antigenic stimulation soon after transplantation. Inactivated vaccines such as diphtheria, tetanus, pertussis, Hib, hepatitis A and B, IPV and pneumococcal and meningococcal vaccines are recommended immediately after transplantation.

Persons with asplenia or functional asplenia

This results from the following:

1. Surgical removal of the spleen in trauma, in Hodgkins disease, in treatment of haemolytic conditions such as hereditary spherocytosis and in idiopathic thrombocytopenic purpura.
2. Sickle cell disease (functional asplenia).
3. Congenital asplenia.

Such children have an increased risk of fulminant bacteremia and need immunisation with pneumococcal, Hib and meningococcal vaccines. When surgical splenectomy is planned, immunisation status for Hib, pneumococcus and meningococcus should be ascertained and the needed vaccines should be administered 2 weeks prior to splenectomy, if possible. If splenectomy is urgent, immediate administration of vaccines is recommended.

Immunisation of HIV infected persons

Please see Chapter 21.

Immunisation of renal dialysis patients and patients with chronic renal disease

Patients with renal failure have an increased risk of infection with a variety of pathogens particularly hepatitis B and pneumococcus.

Hepatitis B vaccination is recommended for pre-end-stage renal disease before they become dialysis dependent. Patients with uraemia who were vaccinated before they required dialysis have been shown to have higher seroconversion rates and antibody titres. For patients undergoing haemodialysis, higher vaccine doses or increased number of doses are required. Clinically significant hepatitis B infection has been documented in patients who have not maintained anti-HBs concentrations equal to or greater than 10 mIU/mL. A booster dose should be administered when the level is less. (Please see Chapter 6)

Pneumococcal vaccine – Patients with renal failure have an increased risk for pneumococcal infections. The efficacy of pneumococcal vaccination may be lower for some of these patients. Their antibody levels may be low. They may require repeat vaccinations or an increased dose of vaccine. Because secondary antibody responses are less affected than primary antibody responses, immunisation strategies should be formulated early in the course of progressive renal disease. This approach is particularly important if transplantation and immunosuppressive therapy are being considered.

DTaP, Hib, hepatitis A, Japanese encephalitis, MMR, meningococcal, polio (IPV), rabies, typhoid, varicella, yellow fever and inactivated influenza vaccines may be administered prior to commencement of dialysis, if indicated.

Patients requiring repeated blood transfusions

A large number of infections can be transmitted by blood transfusions. These include HIV, hepatitis B&C, syphilis, malaria, human T cell lymphotropic virus types 1&2, cytomegalovirus, Epstein Barr virus and parvovirus B19. Since immunisation is at present available only for hepatitis, donor blood screening is essential before blood transfusion. Nucleic acid amplification testing (NAT) identifies viral genes in the

window period before antibodies develop and is available for infections such as HIV and hepatitis C.

Patients with chronic diseases

Some chronic diseases make people susceptible to severe manifestations and complications of common infections. In general, immunisations recommended for healthy people should be given to such persons with the exception of persons with immunological disorders.

Children with history of seizures

Infants and children with a history of seizures could be given routine immunisations except Japanese encephalitis vaccine. The inactivated Japanese encephalitis vaccine can be given 1 year after the last seizure, provided there is no progressive neurological disorder. If a seizure follows the first dose of any vaccine, that vaccine should not be repeated.

Healthcare personnel

Healthcare personnel should protect themselves by receiving appropriate immunisations specially hepatitis B vaccine.

Active immunisation after exposure to disease

Since not all susceptible persons receive vaccines before exposure, active immunisation may be considered for a person who has been exposed to a specific disease and has not had prior immunisation.

The following situations are the most commonly encountered.

- **Tuberculosis** If the person has received BCG at birth and has a positive Tuberculin Skin (Mantoux) Test, BCG is not required. BCG immunisation should be considered for infants and children whose Mantoux test is negative.
- **Measles** Live virus measles vaccine given to susceptible immunocompetent children twelve months of age or older, adolescents and adults, within 72 hours of exposure will provide protection against measles in some. Determining time of exposure may be difficult

because measles can be spread from 4 days before the appearance of the rash to 4 days after the onset of the rash. Immune globulin (IG) administered intramuscularly within 6 days of exposure, can prevent or attenuate measles in immunocompetent or immunocompromised susceptible persons. Administration of IG is recommended for children less than 1 year of age and for immunocompromised people of any age.

- **Varicella** Susceptible immunocompetent children more than 1 year of age and susceptible household contacts exposed to a person with varicella, should be given varicella vaccine within 72 hours of appearance of the rash in the patient. Immunisation is safe even if the exposure results in clinical varicella disease. Susceptible immunocompromised children should receive passive immunoprophylaxis with varicella zoster IG as soon as possible and within 96 hours after contact with a patient with varicella.
- **Hepatitis B** Post exposure immunisation is highly effective if combined with administration of HBIG. The latter does not inhibit active immunisation with hepatitis B vaccine. For post exposure prophylaxis in a new born infant whose mother is a HBsAg carrier, administration of HBIG and hepatitis B vaccine are essential. Persons with sexual contact with HBsAg carriers should also be immunised with hepatitis B vaccine. (Please see Chapter 6)
- **Hepatitis A** People recently exposed to hepatitis A virus and who have not had the hepatitis A vaccine should receive a single dose of the vaccine followed by a second dose 6 months later. If the exposed person cannot be given the vaccine, IG 0.02 ml/kg should be administered within 2 weeks.
 - For healthy persons 1 year to 40 years old, hepatitis A vaccine at age appropriate dose should be administered.
 - For those over 40 years, IG is preferred. Vaccine can be used if IG is not available.
 - For infants (younger than 1 year), immunocompromised individuals, and persons with chronic liver disease, IG should be administered. (Please see Chapter 5)

- **Tetanus** In wound management, unimmunised or incompletely immunised persons should be given tetanus toxoid immediately.

Guidelines for immunising patients against tetanus in patients who have open wounds.

*The susceptibility to tetanus is determined by the type of wound.

- Mild – uncontaminated wounds
- Moderate – puncture wounds and contaminated wounds
- High – heavily contaminated wounds

History	Susceptibility to tetanus/ immunisation recommended		
	*Mild	*Moderate	*High
1. Fully immunised <5 yrs since booster	0	0	0
2. Fully immunised 5-10 yrs since booster	0	T	T
3. Fully immunised >10 yrs since booster	T	T	T
4. Incompletely immunised or uncertain	T	T & TIG	T & TIG

T – tetanus toxoid TIG – tetanus immunoglobulin

All patients should be given metronidazole or penicillin for a period of 10 days, to eliminate vegetative forms. In patients of category 3 and 4 above, a booster dose at 6 weeks and a second booster at 6 months is recommended.

The Australian immunisation guidelines say that complete immunisation (5 doses) induces protective levels of antitoxin lasting throughout childhood but, by middle age, about 50% of vaccinees have low or undetectable levels. A single dose of tetanus toxoid produces a rapid anamnestic response in such vaccinees.

An adult who has received 5 doses of tetanus vaccine during adolescence or adult life is likely to have lifelong immunity.

- **Rabies** Thorough local cleansing of the wound and post exposure active and passive immunisation for rabies are essential after proven or suspected exposure to rabid animals.

(Please see Chapter 15)

- **Mumps and rubella** Exposed susceptible people are not necessarily protected by administration of the live virus vaccines. However administration of the vaccine is recommended so that permanent immunity will be provided, even if mumps or rubella does not result from the current exposure.

Further reading

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CHAPTER 27

STORAGE AND TRANSPORT OF VACCINES

Introduction

Vaccines are sensitive to heat and freezing and therefore should be stored and transported at the correct temperature from the time they are manufactured until they are used. The system used for keeping and distributing vaccines in the recommended condition is called the cold chain.

Non adherence to the recommended cold chain conditions results in reduction of vaccine efficacy leading to vaccine failure. It can also lead to an increased risk of adverse reactions following immunisation, particularly after the use of unduly frozen vaccines. Depending on the nature of the product, vaccines can be damaged either by exposure to heat or freezing. In addition there are certain vaccines which are sensitive to light.

The tables 1 and 2 illustrate the degree of sensitivity of different vaccines to heat and freezing.

Table 1. Heat sensitivity of different vaccines

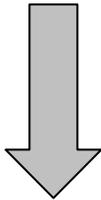
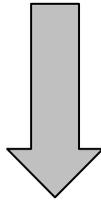
Range	Vaccine
most sensitive  least sensitive	OPV
	Measles, MR, MMR
	DTP, DTP-Hep B, DTP-Hib, DTP-HepB+Hib, YF
	BCG
	Hib, DT
	Td, TT, HepB, JE

Table 2. Freeze sensitivity of different vaccines

Range	Vaccine
most sensitive  least sensitive	HepB
	Hib (liquid)
	DTP, DTP-Hep B, DTP-Hib, DTP-HepB+Hib, YF
	DT
	Td
	TT, Hib lyophilised

Exposure to heat over time can be monitored using vaccine vial monitors (VVM) and the change in colour will guide decisions on the suitability of vaccines for use (Figure 3).

During storage and transportation of freeze-sensitive vaccines (e.g. DTP, TT, DT, Td, hepatitis B and Hib) the risk of freezing is greater than the risk of heat exposure. If exposure to freezing temperature is suspected the shake test should be done as VVM does not indicate exposure to freezing (Figure 4).

Storage of vaccines in a refrigerator: (refer Figure 1)

- Food, drinks and other medications should not be stored in the refrigerator used for storing vaccines.
- The refrigerator door shelves should not be used for storing vaccines and the door should not be opened frequently.
- If a domestic type of refrigerator is used the vaccines that are sensitive to freezing should not be stored on the shelf immediately below the freezing compartment and should be kept away from side and bottom linings of the refrigerator where freezing could occur.

- Freeze and store ice-packs in the freezer compartment.
- Arrange the boxes of vaccines in stacks so that air can circulate.
- The temperature of the main compartment of the refrigerator should range between +2°C to +8°C and the freezer compartment should have a temperature range between -5°C to -15°C.
- Every vaccine containing refrigerator should have a thermometer.
- In case of a power failure do not open the fridge and take immediate steps to restore power.
- If the power failure is likely to last more than 8 hours, vaccines should be moved to another storage site.

Storage of opened multi-dose vials.

Opened multi-dose vials of liquid vaccines from which one or more doses have been removed, following standard sterile procedures, may be used in the next immunisation session, if all of the following conditions are met:

- The expiry date has not passed; **and**
 - The vaccine has not been contaminated; **and**
 - The vials have been stored under appropriate cold chain conditions; **and**
 - The VVM on the vial, if attached, has not reached the discard point.
- Liquid vaccines to which the statement above applies include OPV, DPT, TT, DT, Td, hepatitis B, and liquid formulations of Hib.
 - Freeze-dried vaccines, which include BCG, measles, yellow fever, and freeze dried formulations of Hib, must be discarded six hours after reconstitution or at the end of the immunisation session, whichever comes sooner, and therefore opened vials of these vaccines cannot be stored for future use.
 - Keep opened multi-dose vials of OPV, DPT, TT, DT, Td, hepatitis B, and liquid formulations of Hib that meet the conditions above in a

special box in the main section of the refrigerator, so that you remember to use them first in the next session.

- Discard opened vials of any vaccine (including single dose and multi dose, liquid and freeze dried) immediately, if any of the following conditions apply:
 - Sterile procedures have not been followed when handling the vaccine vials; or
 - If there is evidence of contamination, such as floating particles in the vaccine; or
 - When you suspect that the vaccine has been contaminated.

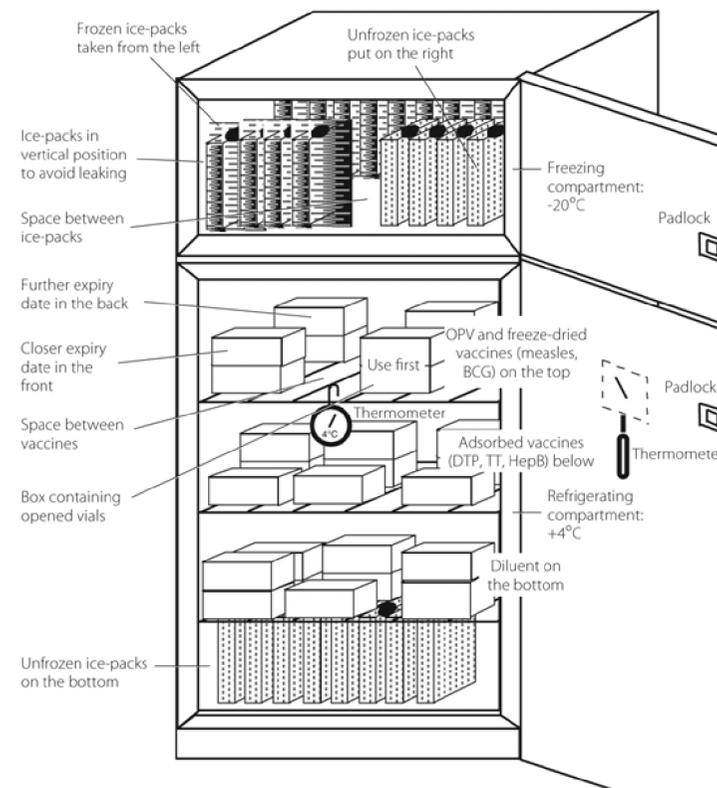


Figure 1. Storage of vaccines in a refrigerator.

Diluent

Diluent vials must NEVER be frozen. If the manufacturer supplies a freeze-dried vaccine packed with its diluent, ALWAYS store the product between +2°C and +8°C. Diluents supplied separately from vaccine may be stored in the cold chain between +2°C and +8°C or left at room temperature. However prior to use store the diluent between +2°C and +8°C for one day so that both the vaccine and diluent are at the same temperature prior to reconstitution.

Temperature monitoring systems

Regular temperature monitoring is vital to proper cold chain management.

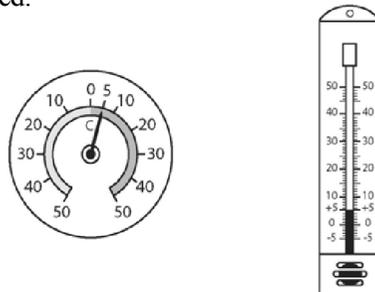
A) Thermometers

Temperatures in the refrigerator should be read twice each day, once in the morning and once before leaving at the end of the day. A temperature log should be posted on the door of the storage unit where the twice daily temperature readings are recorded. A log similar to what has been shown in Table 3 can be used. Use only calibrated thermometers with a Certificate of Traceability and Calibration. Calibration of thermometers is carried out at the Sri Lanka Standards Institute (SLSI) or the Industrial Technological Institute (ITI) in Colombo.

Prior to storing vaccines in a refrigerator, the temperature should be allowed to stabilize. New refrigerators may need 2 or more days of operation to establish a stable operating temperature.

If at any time it is discovered that stored vaccines have been exposed to temperatures outside the recommended ranges, these vaccines should remain properly stored, but segregated and marked "Do NOT Use" until guidance can be obtained.

Figure 2. Dial thermometer and stem thermometer.



B) Data loggers

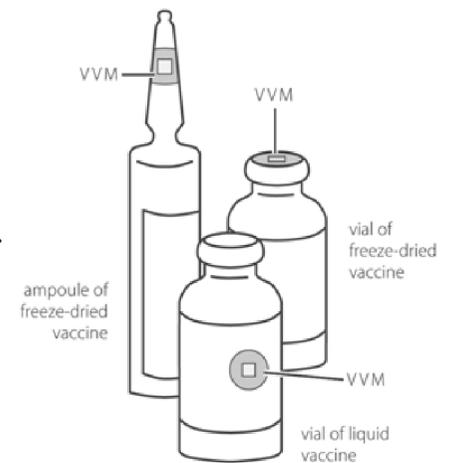
Data loggers (data recorders) are electronic, automatic, continuous, temperature monitoring devices and can provide assurance of temperature maintenance during periods when the clinic is closed. One of the primary benefits of using data loggers is the ability to automatically collect data on changes in temperature on a 24-hour basis. They measure the temperature using sensors. They generally are small, battery powered, portable, and equipped with a microprocessor and an internal memory for data storage. Some data loggers utilize software to activate the data logger and view and analyze the collected data, while others have a local interface device (keypad, LCD) and can be used as a stand-alone device. Due to reports of automatic electronic monitoring system failures and undetected, unresolved vaccine temperature excursions using these systems as the sole equipment temperature monitor, it is recommended that twice daily manual temperature recording has to be continued irrespective of the use of data loggers.

Cold chain monitoring systems

A) Vaccine vial monitors (VVM)

VVM will measure exposure to heat, but not exposure to freezing temperatures.

Figure 3a. Location of vaccine vial monitors.



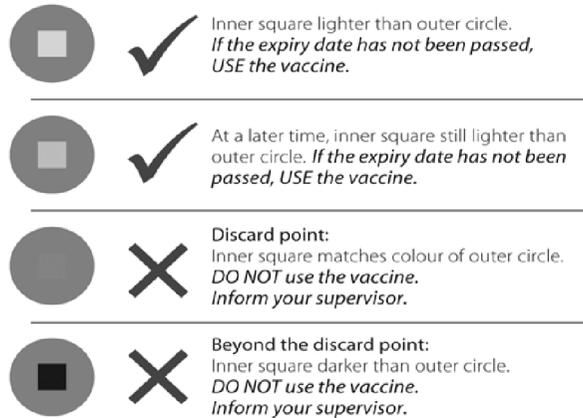


Figure 3b. Interpretation of the vaccine vial monitor.

B) Freeze-tag™

The Freeze-tag™ consists of an electronic temperature measuring circuit with associated LCD display. If the indicator is exposed to a temperature below 0°C ± 0.3°C for more than 60 minutes ± 3 minutes the display will change from the "good" status into the "alarm" status as indicated on the picture below



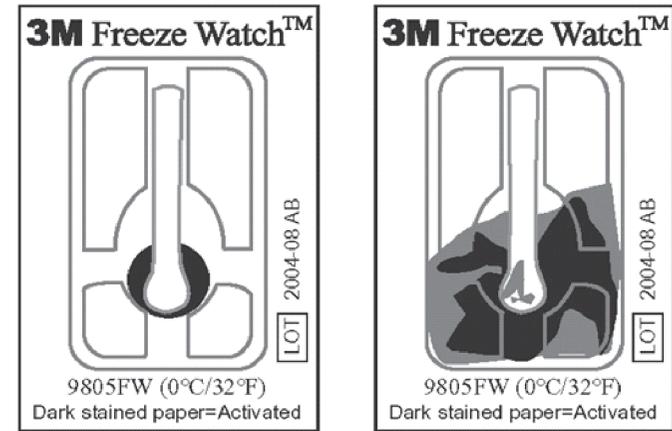
Vaccine can be used



Do shake test prior to use

C) Freeze Watch™

If the freeze indicator (Freeze Watch™) is exposed to temperatures below 0°C for more than one hour, the vial bursts and releases the coloured liquid, staining the white backing card.



The shake test

The "shake test" can help in determining whether adsorbed vaccines (DTP, DT, Td, TT or hepatitis B) have been subjected to freezing temperatures likely to have damaged them. Shake test should not be done when a solid frozen vaccine vial(s) has been found or with a vial for which a homogeneous solution cannot be obtained after vigorous shaking. Discard the vials without any further testing.

The shake test procedure:

- Obtain a vial of vaccine of the same batch from the same manufacturer and freeze it at solid state for at least 10 hrs at -10°C and then let it thaw. This is the control vial.
- Choose your test vial from the batch suspected as having been frozen.
- Shake the test and control vials together in one hand for 10-15 seconds.

- Allow to rest on a table.
- Compare the sedimentation rates of deliberately frozen control vial with the suspect vial.
- If the test vial has a sedimentation rate similar to or faster than the control vial the batch of vaccines should not be used

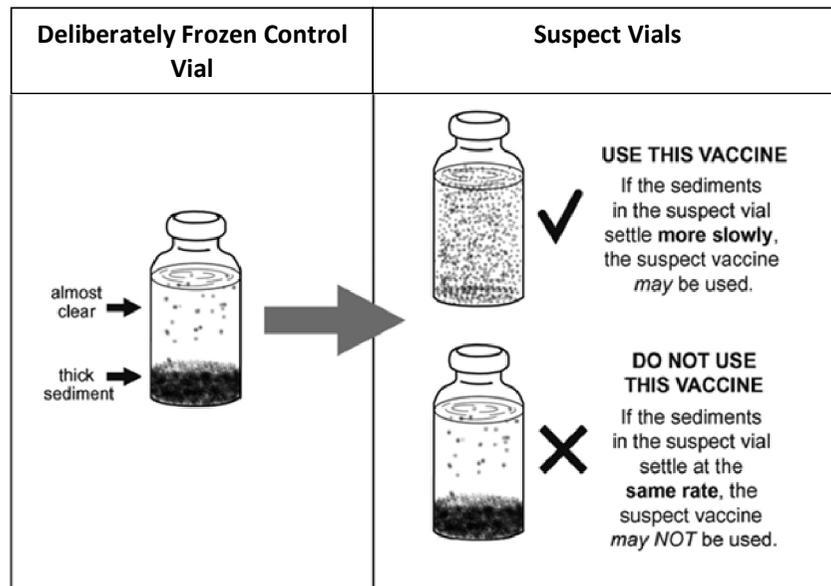


Figure 4. Interpretation of the shake test to determine damage due to freezing of DTP, DT, Td, TT or hepatitis B vaccines.

Light sensitivity

Some vaccines are very sensitive to strong light and their exposure to ultraviolet light (sunlight or fluorescent light) causes loss of potency. BCG, measles, MR and MMR vaccines are sensitive to light. Normally, these vaccines are supplied in vials made of dark brown glass, which gives them some protection against light damage, but care should be taken to keep them protected from strong light at all times.

Transport of vaccines to outreach health centres

Vaccine carriers are used for this purpose. They are insulated containers that, when lined with frozen ice-packs, keep vaccines and diluents cold during transportation. These are also used for temporary storage of vaccines when the refrigerator is being defrosted.

Placing adsorbed vaccine vials such as, tetanus and hepatitis B in direct contact with ice cubes is not recommended as this could damage the potency of vaccines. The floatation of open vials on melting ice will also lead to contamination of contents in vials.

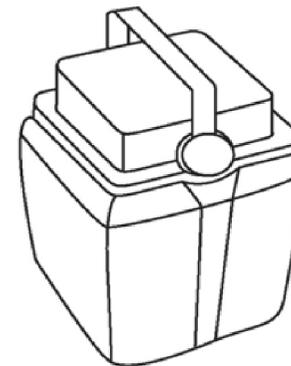


Figure 5. Vaccine carrier

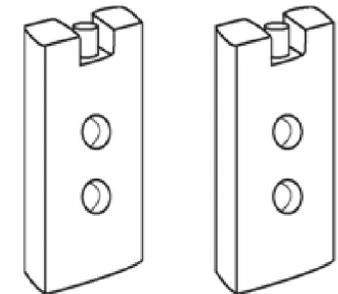


Figure 6. Ice-packs

Procedure for packing the vaccine carrier

- Remove the icepacks from the freezer.
- Wait for them to be free of frost (approximately 10-15 minutes).
- Place the frost free ice-packs around the inside walls of the carrier.
- Stack live vaccines near the frozen ice packs at the bottom.
- Take precautions to prevent vulnerable vaccines from being frozen (by keeping them in their packaging or wrapping a sheet of paper around or placing them in a plastic container).

- Place a layer of frozen ice-packs on top.
- Secure the lid tightly.

Further reading

1. Temperature sensitivity of vaccines. WHO/IVB/06.10. /2006.
2. Immunisation in Practice: Module 3 – Cold Chain. WHO/EPI/TRAM/98.01-11
3. Immunisation Safety Surveillance. Immunisation Focus, Western Pacific Regional Office (WPRO). World Health Organization. WPRO/EPI/99.01.
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CHAPTER 28

GENERAL INFORMATION ON VACCINES

Interchangeability of vaccines

Similar vaccines made by different manufacturers may differ in their components and formulations and may elicit different immune responses. However, such vaccines have been considered interchangeable when administered according to their licensed indications, although data documenting interchangeability sometimes are limited.

Lapsed immunisations

A lapse in the immunisation schedule does not require starting of the entire series. If a dose of vaccine is missed, immunisations should be given at the next visit as if the usual interval had elapsed. The immunisation charts of children in whom immunisations have been missed or postponed should be flagged to remind health care professionals to complete immunisation schedules at the next available opportunity.

Unknown or uncertain immunisation status

A physician may encounter some children with an uncertain immunisation status. Many young adults and some children do not have adequate documentation of immunisations, and recollection by the parent or guardian may be of questionable validity. In general, these persons should be considered disease susceptible, and appropriate immunisations should be administered. There is evidence that administration of measles, rubella, MMR, varicella, Hib, hepatitis B, or polio virus vaccine to already immune recipients is not harmful; dTpa, rather than DTP should be given to those 5 years of age or older.

Simultaneous administration of vaccines

Most vaccines can be safely and effectively administered simultaneously. Infants and children have sufficient immunological capacity to respond to multiple vaccines. Simultaneous administration of IPV, MMR, varicella,

or DTaP vaccines results in rates of seroconversion and of adverse effects similar to those observed when the vaccines are administered at separate visits. When vaccines are administered simultaneously, separate syringes and separate sites should be used, and injections into the same extremity should be separated by at least 1 inch so that any local reactions can be differentiated. Individual vaccines should never be mixed in the same syringe unless they are specifically licensed and labeled for administration in one syringe. If live-virus vaccines are not administered concurrently, 4 weeks should elapse between sequential immunisations. Exception is yellow fever vaccine given less than 4 weeks after measles vaccine. There is no required interval between administration of a live-virus vaccine and an inactivated vaccine or between inactivated vaccines. If an inactivated vaccine and an immunoglobulin product are indicated concurrently (e.g. hepatitis B vaccine and HBIG, rabies vaccine and RIG), they should be administered at separate anatomical sites. Live vaccines administered by the oral route [oral polio vaccine (OPV), oral typhoid, and rotavirus] are not believed to interfere with each other if given simultaneously. These vaccines may be given at any time before or after each other.

The following combined vaccines are currently available in Sri Lanka

1. DTaP and DTwP
2. DT
3. MMR - measles, mumps and rubella vaccine
4. DTP-HepB – diphtheria, tetanus, pertussis, and hepatitis B vaccine
5. DTP-Hib – diphtheria, tetanus, pertussis, and Hib vaccine
6. DTwP-HepB-Hib (pentavalent) – diphtheria, tetanus, whole cell pertussis, hepatitis B and Hib vaccine
7. DTaP-HepB-IPV-Hib (hexavalent) – diphtheria, tetanus and acellular pertussis, hepatitis B, inactivated polio and Hib vaccine

8. dTpa – reduced antigen diphtheria, tetanus and acellular pertussis vaccine for adolescents and adults
9. Hepatitis A and hepatitis B vaccine

DTP Hep B vaccine can be used as a solvent for Hib vaccine and both can be given from the same syringe (both preparations must be from the same manufacturer. Please see manufacturer's recommendations).

Allergy to egg protein

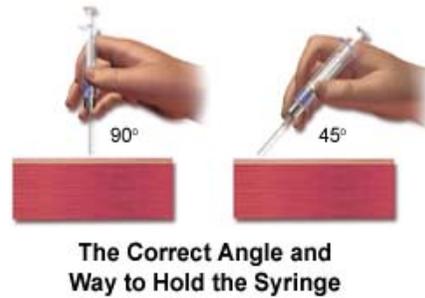
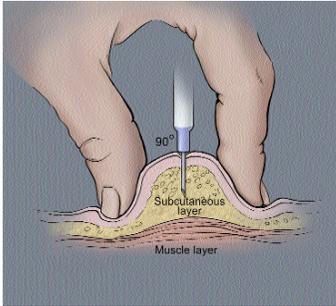
Influenza and yellow fever vaccines should be avoided by persons who have a history of allergy to egg protein. Persons who have developed hives, had swelling of the lips or tongue, or have experienced acute respiratory distress or collapse after consuming eggs should consult a physician for appropriate evaluation to determine whether to proceed with vaccination or defer. Persons with documented immunoglobulin E (IgE)-mediated hypersensitivity to eggs – including those who have had occupational asthma or other allergic responses from exposure to egg protein – may also be at increased risk for reactions from these vaccines, and similar evaluation should be considered. Protocols are available for vaccination of persons who have egg allergies and are at high risk of acquiring diseases or its complications. Egg allergy is not common in Sri Lanka.

Vaccine injection techniques

If administration of a particular vaccine is recommended through the intramuscular route, it should not be administered subcutaneously. All parenteral live vaccines are administered subcutaneously.

1. Subcutaneous injections

Subcutaneous shots can be given straight in at a 90 degree angle, or at a 45 degree angle. Give the shot straight in at a 90 degree angle if 2 inches of skin can be grasped between your thumb and first (index) finger. If only 1 inch of skin can be grasped, give the shot at a 45 degree angle.



Needle size

Subcutaneous injections go into the fatty tissue below the skin and require a smaller, shorter needle. A needle that is 1/2 inch to 5/8 of an inch long with a gauge of 25 to 30 is usually sufficient to administer the medication.

Sites recommended for subcutaneous injections:



Figure. Sites on Body where a sub-cutaneous injection can be given

Upper Arm: Find the area in the middle part of the arm, halfway between the elbow and shoulder. Gently grasp the skin at the back of the arm between your thumb and first 2 fingers. You should have 1-2 inches of skin.

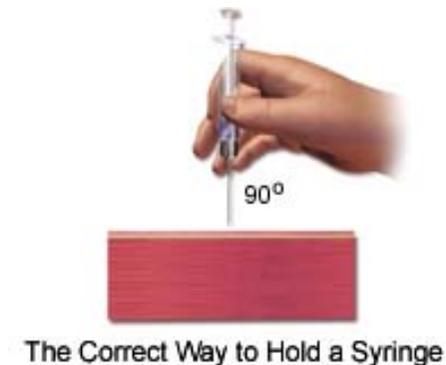
Abdomen: Area below the waist, to just above the hip bone, and from where the body curves at the side to about 2 inches from the middle of the abdomen. Avoid the bellybutton. Use the natural line in the middle of the body as a marker.

Thigh: Find the area between the knee and hip. The middle of the thigh, from mid-front to mid-side, on the outside part of the thigh is a safe site. Gently grasp the area to make sure you can pinch one to two inches of skin.

2. Intramuscular (IM) injections

All adjuvanted vaccines should be given IM. Depress and pull the skin a little with your free hand. Keep holding the skin a little to the side of where you plan to put the needle. Use your wrist to inject the needle at a 90 degree angle (straight in). Let go of the skin.

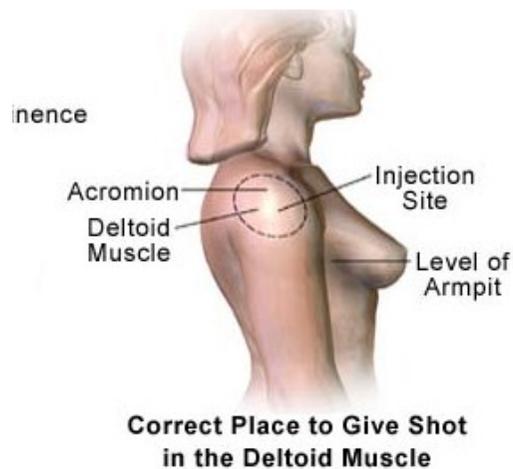
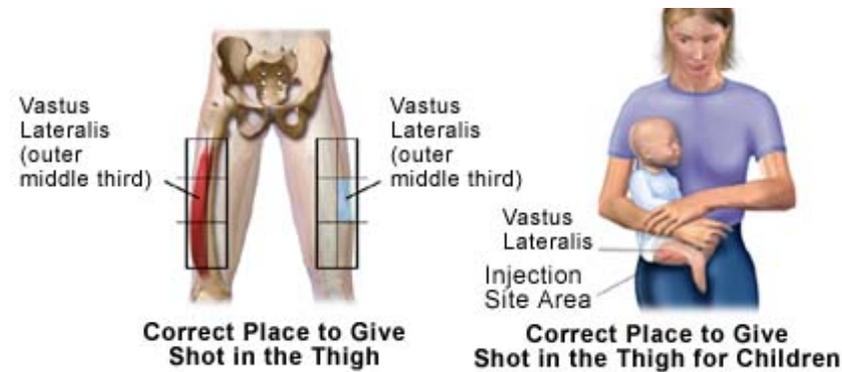
The needle will want to jerk sideways. As you let go of the skin, hold the syringe so it stays pointed straight in. Pull back on the plunger just a little to make sure you aren't in a blood vessel. Push down on the plunger and inject the medicine slowly, to reduce the pain.



Needle size

Intramuscular injections go into the muscle below the subcutaneous layer, so the needle must be thicker and longer to ensure that the medicine is being injected into the proper tissue. 23-25 G needles that are an inch or an inch and a half long are usually appropriate for this type of injection. For a person who is thin, with very little fatty tissue one can use the inch long needle; a heavier person may require the inch and a half long needle.

Sites recommended for IM injections



3. Intradermal (ID) injections

For intradermal injection, a short thin needle of 25 or 27 gauge and 3/8 to 3/4 inch (1-2 cm) is inserted into the skin parallel to the skin surface, with the bevel of the needle facing upward (Figure 1). A wheal should appear immediately after injection, at the site where the medication is deposited (Figure 2). The same sites recommended for subcutaneous injections can be used for administering intradermal injections.

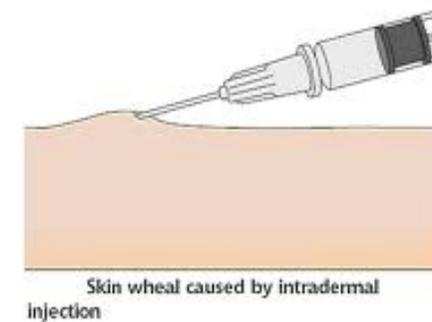


Figure 1. Injected parallel to the skin.



Figure 2. Appearance of the wheal.

Further reading

1. Epidemiology and prevention of vaccine-preventable diseases. The Pink Book: Course Text Book. 12th Edition (2011). Centre for Disease Control and Prevention. Department of Health and Human Services. Atlanta, GA 30333, USA.
2. Practice Parameter. Administering influenza vaccine to egg allergic recipients: a focused practice parameter update. Greenhawt MJ, Li JT eds, 2010 American College of Allergy, Asthma and Immunology.
3. Workman B. Nursing Procedures, Royal College of Nursing. Safe injection techniques. Article 498. *Nursing Standard* 1999; **13**: 39, 47-53.

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CHAPTER 29

FREQUENTLY ASKED QUESTIONS

1. Sri Lanka has achieved the highest immunisation coverage in the region. Therefore, can we reduce the number of expensive vaccines in use and take steps to prevent infections through measures such as better hygiene, sanitation and breastfeeding?

Despite indirect associations between improved socio-economic status and a decrease in certain diseases, vaccination is still crucial to prevent serious infectious diseases. Breastfeeding offers transient, rather than a long-lasting protection against some of the infections. It is important to realize that even if the disease has been eliminated from the country the possibility of resurgence is always there. At any given time an imported case can lead to a disease outbreak. Therefore, routine immunisation should be continued. Furthermore, even in the developed countries where there is a low prevalence of infectious diseases, routine immunisation is still continued.

2. In the National Immunisation Programme (NIP) of Sri Lanka many vaccines are given routinely and most such diseases are well controlled. There are other vaccines available outside the NIP such as rotavirus, chickenpox, hepatitis A, human papilloma virus and pneumococcal. Who should receive such vaccines?

The decision to vaccinate should be taken in consultation with the health care professional based on individual needs.

3. Can children who have begun the vaccination with DTwP continue their remaining doses with DTaP and even interchange between different DTP brands?

There is no clinical data to support switching from one type of DTwP to another type of DTwP vaccine and DTaP vaccine within the primary vaccination programme, but there is no contraindication to do so. DTaP has comparable efficacy to DTwP and has the advantage of a lower incidence of local reactions, fever and other systemic adverse effects.

4. Is an interval of 4 weeks mandatory between immunisations?

This is true regarding injectable live vaccines, because the desired antibody response may not be achieved if a second live vaccine is given before four weeks.

5. Is local massage recommended immediately at the site of injection in IM, SC and intradermal immunisations?

Local massage or fomentation is not recommended.

6. What is your advice for a child who has not developed a scar after BCG vaccination?

It depends on the age of the child. If the child is less than 5 years of age, repeat the BCG. If the child is more than 5 years, do the Mantoux test and if it is negative give the BCG.

In general it takes about 10-12 weeks to produce a scar and non-formation of a scar does not mean that BCG has not been taken up. In 10-12% of vaccinees, scar formation may not take place at all.

7. Can the BCG vaccine be given to children with HIV /AIDS?

BCG vaccination is contraindicated in children infected with HIV.

8. Which age group is affected by *Haemophilus influenzae* type b infections?

The highest risk of infection is between 6-24 months and it declines gradually by 5 years. The higher the incidence of *Haemophilus influenzae* type b in the community, greater the chance of developing meningitis, pneumonia, otitis media and rarely epiglottitis.

9. Why is a booster dose of Hib vaccine given during the 2nd year of life?

More than 90% of vaccinees achieve a titre of $>1.0 \mu\text{g/ml}$ after 3 doses giving protection till 15-18 months of age. In more than 50% of them, the titre falls to less than $0.15 \mu\text{g/ml}$ (the minimum protective level) by 18 months. If a booster dose is given at 15-18 months of

age the titre rises by 30-90 fold in all of them and reaches levels as high as $40 \mu\text{g/ml}$. Hence a booster dose is recommended at 18 months of age.

10. When 2 doses of MMR are to be given to adolescents what should be the minimum interval?

A minimum of 4 weeks interval is needed.

11. How long should a female avoid pregnancy, after rubella and chickenpox containing vaccinations?

The minimum interval should be 3 months for chickenpox vaccine and 28 days for rubella containing vaccines, because of the theoretical risk to the developing foetus.

However, pregnancy within this period is not an indication for termination.

12. If a child has received only one dose of vaccine, is it necessary to restart the schedule again?

No. The vaccine schedule can be safely continued as if there has been no delay. The recommended intervals between further doses should be maintained.

13. Should low birth weight babies have their vaccinations delayed?

Low birth weight babies should receive BCG when they are fit to be discharged from the hospital. They should also receive their routine vaccination at the recommended age.

14. What precautions should be taken when vaccinating preterm babies?

It is important that preterm infants have their immunisations at the appropriate chronological age.

The potential risk of apnoea and the need for respiratory monitoring for 48-72 hours should be considered when administering the primary immunisation series to infants who were born extremely premature

(born ≤ 28 weeks of gestation) and particularly for those with a history of respiratory immaturity.

It is advisable that the 2 months' vaccination of a child born extremely premature is administered in hospital and for further advice to consult a paediatrician.

15. Should vaccination be postponed if a child has a common cold or cough?

No. Babies with minor coughs and colds (without fever) can be safely immunised.

16. Can children with acute respiratory tract infections be immunised?

The vaccination should only be postponed if a child is seriously ill or has high fever $\geq 100^\circ\text{F}$ or $\geq 38^\circ\text{C}$ at the time of immunisation.

17. Does natural immunity produce better protection than vaccine induced immunity?

Although acquiring natural immunity by contracting the disease is long lasting, the disease may be fatal or cause permanent disability. Vaccination is safer than contracting the disease and re-vaccination can be carried out if or when necessary.

18. When one member of a family has developed chickenpox is it justifiable to vaccinate the rest of the family?

The varicella vaccine, if administered within 3-5 days of exposure $>80-90\%$ effective in preventing the disease and complications or modifying the severity of illness. In addition, it is important to protect susceptible immunocompromised persons with varicella zoster immunoglobulin (VZIG) as soon as possible, after exposure.

19. Sometimes we find that certain vaccines have been administered abroad according to different schedules. What schedule should we follow?

Vaccination schedules are based on the disease prevalence in

countries. It would be appropriate to continue with the schedule of the country where the person is going to live. For example, if a person is on holiday, it is not rational to restart or reschedule his future vaccination. On the other hand, for persons who have returned from abroad and are going to live in this country it would be advisable to have their subsequent vaccinations re scheduled according to the local schedule.

20. What action should be followed if you find any of your liquid vaccines frozen?

Safety and effectiveness of vaccine is affected by extreme temperature changes and such should be discarded safely. However, an open oral polio vaccine can be stored below 0°C .

21. Students going for overseas studies are recommended a number of vaccines within a short period. Is it safe to give all of them?

It is advisable to plan an overseas stay well in advance enabling adequate time intervals for vaccinations. Please refer to the accelerated schedules under respective chapters.

Most vaccines can be given as accelerated schedules with the exception of cholera and yellow fever vaccines. Two live vaccines such as, MMR and varicella can be concurrently administered or at 4 weeks interval. Delaying the other vaccines depend on the travel plan. The killed and subunit vaccines can be given over intervals of 1 - 2 weeks.

22. Why is it important to give two doses of MMR vaccine?

Two doses will provide the recipient and the community with better protection.

With the first dose of MMR vaccine 5-10% children will remain vulnerable to these diseases. However, after the 2nd dose, only 1% will remain unprotected.

23. Can the HPV vaccine be given to women who are already sexually active?

Ideally HPV immunisation should be completed before the onset of sexual activity. However, women who have begun sexual activity will benefit from vaccination if they have not yet become infected with the vaccine preventable HPV serotypes. Vaccination will also prevent re-infection from the specific serotypes.

24. Does the HPV vaccine protect against all types of cervical cancers?

No. There are two types of vaccines commercially available as quadrivalent (oncogenic serotypes 16 and 18 and non oncogenic 6,11) and divalent (oncogenic serotypes 16 and 18). 16 and 18 accounts for nearly 70% of cervical cancers. As other oncogenic serotypes are not covered by the vaccines, it is still important to attend cervical screening every three years. This combination of immunisation and cervical screening offers the best possible protection against cervical cancer.

25. How long does the HPV vaccine protection last?

Current studies have shown that the HPV vaccine results in a high antibody level not requiring booster doses up to even 10 years. Studies will continue and more details regarding the effectiveness of the vaccine will become available in the future.

26. Will women who have been vaccinated with HPV still need cervical cancer screening?

Yes. There are three main reasons why women will still need regular cervical cancer screening. Firstly, the vaccine will not provide protection against all types of HPV that may cause cervical cancer. Secondly, some women may not get all the required doses of the vaccine. Thirdly, women may have already acquired HPV before they complete the immunisation schedule.

27. Does the HPV vaccine interfere with the efficacy of contraceptive pill?

There is no evidence to suggest that the vaccine affects the efficacy of the contraceptive pill.

28. If full DTP vaccinations were completed during childhood vaccination, is it still possible for an adult to get whooping cough?

The immunity acquired from either natural pertussis infection from immunisation is not lifelong. Epidemiological evidence suggests that routine immunisation of adolescents and adults can significantly result in lowering the incidence and severity of the disease. Pertussis vaccinations for adults (DTaP) may be given at intervals of ten years.

29. When there is a reaction to DTwP vaccine in routine EPI schedule, is it better for the patient to go for DTaP vaccine for the next dose or use DT ?

As the reactogenicity is less with DTaP vaccine, it can be used when there is a reaction to DTwP vaccine. The DT can also be given, as the DTaP is only available in the private sector.

30. What is the duration of protection of the hepatitis A ?

One dose of hepatitis A vaccine will protect the recipient for at least 1 year. A second dose given after 6 to 12 months will usually confer lifelong protection.

31. Chickenpox in children is usually not serious. Why not allow children to get the disease?

It is not possible to predict who will have a mild or serious disease, which could even be fatal. When there is an effective vaccine, it is not worth taking this risk. Even a patient with a mild disease could transmit the disease to the susceptible persons in the community.

32. What is the currently recommended schedule of chickenpox vaccination with regard to different age groups?

- All those aged >1 year and above without evidence of immunity should receive two doses of the vaccine.
- Children aged 1-12 years should receive their first dose routinely at age 12-15 months and the second dose is recommended routinely at 4-6 years of age. (2nd dose may also be given earlier as long as it has been >3 months since the first dose).
- Children aged ≥13 years and adults should receive two doses of the vaccine 4 to 8 weeks apart. If >8 weeks have lapsed after the first dose, the second dose may be given without restarting the schedule.
- A second dose catch-up chickenpox vaccination is recommended for all those who previously received only one dose. The second dose can be given any time at least 3 months after the first dose for children <13 years of age and at least 4 weeks after the first dose for persons ≥13 years of age.

33. Is there 100% assurance that a person is protected from chickenpox if 2 doses of vaccine have been administered?

No vaccine is 100% effective in preventing any disease. For chickenpox vaccine, about 90% of vaccines with two doses are completely protected from chickenpox infection and almost 100% from severe disease. On the other hand, if a vaccinated person does get chickenpox, it is usually a very mild form with fewer (<50) skin lesions (breakthrough disease).

34. When a mother has chickenpox at the time of delivery, can the neonate be given the vaccine ?

No. The vaccine is only recommended after infancy. To reduce the risk of severe disease in infants, it is recommended that neonates born to mothers who have signs and symptoms of varicella from 5 days before to 2 days after delivery should receive VZIG, regardless of whether the mother received VZIG.

35. Is the interval of 4 weeks only applicable to live vaccines?

Yes, it is not applicable to killed vaccines.

36. Some vaccines contain aluminum adjuvants. Will this cause reactions or long term problems for recipients?

No. Serious adverse effects attributable to the aluminum adjuvants are rare. However, local reactions such as redness, swelling and/or tenderness at the injection site are not uncommon. More severe local reactions such as large areas of swelling, sterile abscesses, subcutaneous nodules and allergic responses are much less common. Reactions can be minimized by the use of correct IM injection techniques.

37. Is a history of seizure or febrile convulsion contraindicated for JE vaccination?

Yes. Within one year of any seizure including febrile convulsions.

Further reading:

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24. Klein NP, Massolo ML, Greene J, et al. Re-vaccination of 421 children with a past history of an adverse reaction in a specialised service. *Arch Dis Child* 2008; **83**: 28-31.
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NATIONAL IMMUNIZATION PROGRAMME OF SRI LANKA 2011

Annex. I

VACCINE	AGE										Comments	
	Birth	Month 2	Month 4	Month 6	Month 9	Month 12	Month 18	3 years	School entry	10-15 years		Pregnancy
BCG	•											Before leaving hospital within 24 hours of birth. To be given to children between 6 months and 5 years of age, with no evident BCG scar.
Polio	•	•	•	•		•	•		•			
DTP-Hep B-Hib	•	•	•	•		•						
DTP						•						
JE live vaccine					•							
MMR						•	•		•	*		*Females only. (One dose at 15-44 years for all females who have not been immunized earlier)
DT									•			
aTd (adult tetanus & diphtheria)										•		
Tetanus											•	First Pregnancy – 1st dose after the 12th week of pregnancy. 2nd dose: 6 - 8 weeks after the first dose. One dose of tetanus toxoid should be administered during every subsequent pregnancy, upto a maximum of five doses.

VACCINES OUTSIDE THE NATIONAL IMMUNISATION PROGRAMME OF SRI LANKA 2011

Annex. II

VACCINE	AGE										Comments	
	Birth	Month 2	Month 4	Month 6	Month 12	Month 18	2nd year of life	School entry	Over 10 years	Pregnancy		
DTaP-Hep B-IPV-Hib		■	■	■		■						DTP-Hep B and Hib when provided by the same manufacturer can be mixed together and administered as one dose.
DTP-Hib			■	■		■						
Hib		■	■	■		■						
Pneumococcal conjugate		■	■	■								
Rotavirus		■	■	■								To infants from 6 weeks to 24 weeks of age
JE killed vaccine					■		■					2 doses, 2 weeks apart and 3rd dose one year later.
Varicella												1 yr to 12 yrs of age 1st dose at 12-15 months & 2nd dose 4-6 yrs or > 13 yrs 2 doses 4-8 weeks apart.
dTpa (reduced antigen DTP)									■			Adolescents and adults
Human papillomavirus										■		Females > 10 years of age, 3 doses at 0,1, 6 months

INDIVIDUAL

Hepatitis A	For those who have not previously received Hep A vaccination – 2 doses at 0 & 6 to 12 months later (over 2 years)
Hepatitis B	For those who have not previously received Hep B vaccination – 3 doses at 0,1 & 6 months
Hepatitis A + B	For those who have not previously received Hep A & B vaccination – 3 doses at 0, 1 & 6 months later (over 2 years)
Typhoid	Injectable: 1 dose every 3 years

SPECIAL CIRCUMSTANCES

Meningococcal	Rabies
Pneumococcal	Yellow fever
Cholera	

COMBINED SCHEDULE OF ALL VACCINES 2011

Annex. III

VACCINE	Birth	AGE												COMMENTS		
		Month 1	Month 2	Month 4	Month 6	Month 9	Month 12	Month 18	2nd year of life	3 year	School entry	Over 10 years	10-15 years		Pregnancy	
BCG	●															Before leaving hospital, within 24 hours of birth. To be given for children between 6 months and 5 years of age, with no evident BCG scar.
Polio		●			●						●					
DTP-Hep B-Hib or DTP-Hep B or DTaP-Hep B-IPV-Hib or DTP/DTP + Hib		●	●	●	●		■	■	■	■	■	■	■			DTP - Hep B or DTP + Hib when provided by the same manufacturer can be mixed together and administered as one dose.
Hib		■	■	■	■		■	■	■							
Pneumococcal conjugate		■	■	■	■											
Rotavirus		■	■	■												To infants from 6 weeks to 24 weeks of age.
JE						●	■	■	■	■	#					#2 doses, 2 weeks apart and 3rd dose one year later. A booster dose 3-4 yrs later.
MMR							●	●	●	●	●					* Females only. (one dose at 15-44 years for all females who have not been immunized earlier).
DT											●					One dose between 10 and 15 years
aTd (adult Tetanus & Diphtheria) or dTpa (reduced antigen DTP)											■					Adolescents and adults
Varicella																1 yr to 12 yrs of age 1st dose at 12-15 months & 2nd dose 4-6 yrs or > 13 yrs 2 doses 4-8 weeks apart.
Human Papillomavirus																Females > 10 years of age
Tetanus															●	First pregnancy – 1st dose after the 12th week of pregnancy, 2nd dose, 6 - 8 weeks after the first dose. One dose of tetanus toxoid should be administered during every subsequent pregnancy, upto a maximum of five doses.

INDIVIDUAL BASIS

Hepatitis A	■	For those who have not previously received Hep A vaccination – 2 doses at 0 & 6 to 12 months later (over 2 years)
Hepatitis B	■	For those who have not previously received Hep B vaccination – 3 doses at 0, 1 & 6 months
Hepatitis A + B	■	For those who have not previously received Hep A & B vaccination – 3 doses at 0, 1 & 6 months (over 2 years)
Typhoid	■	Injectable: 1 dose every 3 years)

SPECIAL CIRCUMSTANCES

Meningococcal	■	Rabies	■
Pneumococcal	■	Yellow fever	■
Cholera	■		

- National Immunisation Programme
- Vaccines outside National Immunisation Programme
- x Live vaccine
- # Killed vaccine

RECOMMENDATIONS FOR ROUTE AND SITE OF IMMUNIZATION

Annex. IV

VACCINE	TYPE	ROUTE	SITE
Adult Tetanus & Diphtheria (aTd)	Toxoids	IM	Deltoid
BCG	Live bacteria	ID	Deltoid of left arm
Cholera	Live bacteria	Oral	-
Diphtheria – Tetanus Toxoids & Pertussis (DTP)	Toxoids & inactivated Bacteria	IM	Anterolateral aspect of the thigh
Diphtheria – Tetanus Toxoids – Pertussis & Haemophilus influenzae type b (DTP-Hib)	Toxoids and inactivated bacteria	IM	Anterolateral aspect of the thigh
Diphtheria – Tetanus Toxoids – Pertussis & Hepatitis B (DTP-Hep B)*	Toxoids & inactivated bacteria and inactivated virus.	IM	Anterolateral aspect of the thigh
Diphtheria – Tetanus Toxoids – Pertussis – Hepatitis B & Haemophilus influenzae type b (DTP-HepB-Hib)	Toxoids & inactivated bacteria and inactivated virus.	IM	Anterolateral aspect of the thigh
Diphtheria – Tetanus Toxoids – Pertussis – Hepatitis B – Haemophilus influenzae type b – Injectable Polio Virus (DTP-Hep B-Hib-IPV)	Toxoids & inactivated bacteria, polysaccharide protein conjugate with toxoids and inactivated viruses.	IM	Anterolateral aspect of the thigh
Diphtheria – Tetanus Toxoids – Pertussis reduced antigen (dTpa)	Toxoids & inactivated bacteria	IM	Deltoid

* As recommended by the manufacturer, these two vaccines can be mixed and administered as one dose.

RECOMMENDATIONS FOR ROUTE AND SITE OF IMMUNIZATION

Annex. IV (Contd.)

VACCINE	TYPE	ROUTE	SITE
Diphtheria & Tetanus (DT)	Toxoids	IM	Deltoid
H. Influenzae type b (Hib)*	Polysaccharide protein conjugate with toxoids & inactivated bacteria	IM	< 2 years - anterolateral aspect of the thigh > 2 years - deltoid
Hepatitis A + Hepatitis B (combined vaccine)	Inactivated viral antigens	IM	Deltoid
Hepatitis A	Inactivated viral antigen	IM	Deltoid
Hepatitis B	Inactivated viral antigen	IM	< 2 years - anterolateral aspect of the thigh. >2 years - deltoid.
Human papillomavirus	Inactivated viral antigen	IM	
Japanese Encephalitis (JE)	Inactivated virus	SC	Deltoid
Measles	Live virus	SC	Deltoid
Measles, Mumps & Rubella (MMR)	Live viruses	SC	Deltoid
Meningococcal	Polysaccharide	SC	Deltoid
Oral Polio Virus (OPV)	Live virus	Oral	-
Pneumococcal	Polysaccharide Conjugate	IM or SC	Deltoid
Rotavirus	Live virus	Oral	-

* As recommended by the manufacturer, these two vaccines can be mixed and administered as one dose.

RECOMMENDATIONS FOR ROUTE AND SITE OF IMMUNIZATION

Annex. IV (Contd.)

VACCINE	TYPE	ROUTE	SITE
Rabies	Inactivated virus	IM/SC	Deltoid
Tetanus	Toxoid	IM	Deltoid
Typhoid Parenteral Oral	Capsular polysaccharide Live bacteria	SC Oral	Deltoid -
Varicella (Chickenpox)	Live virus	SC	Deltoid
Yellow Fever	Live virus	SC	Deltoid

ID – Intradermal

IM – Intramuscular

SC – Subcutaneous

Definitions of adverse events following immunisation

All of the following adverse events should be reported if temporally related to immunisation. Unless otherwise specified this includes all such events occurring within four weeks of a vaccine administration.

1. Local adverse events

Injection-site abscesses

Occurrence of a fluctuant or draining fluid-filled lesion at the site of injection with or without fever.

Bacterial – Existence of purulence, inflammatory signs, fever, positive Gram stain, positive culture, or finding of neutrophils.

Predominance of content will support a bacterial site abscess, but the absence of some of these signs will not rule it out.

Sterile – There is no evidence of bacterial infection following investigation.

Lymphadenitis (includes suppurative lymphadenitis)

Occurrence of either:

1. at least one lymph node, 1.5 cm in size (one adult finger width) or larger: or a draining sinus over a lymph node.

Almost exclusively caused by BCG and then occurring within 2 to 6 months after receipt of BCG vaccine, on the same side as inoculation (mostly axillary).

Severe local reaction: redness and/or swelling centered at the site of injection and one or more of the following:

1. swelling beyond the nearest joint: 2. pain, redness and swelling for more than 3 days duration: or 3. requires hospitalization.

2. Central nervous system adverse events

Acute paralysis

Vaccine-associated paralytic poliomyelitis

Acute onset of flaccid paralysis within 4-30 days of receipt of oral poliovirus vaccine (OPV), or within 4-75 days after contact with a vaccine recipient, with neurological deficits remaining 60 days after onset, or death.

Guillain-Barre Syndrome (GBS)

Acute onset of rapidly progressive, ascending, symmetrical flaccid paralysis, without fever at onset of paralysis and with sensory loss. Cases are diagnosed by cerebrospinal fluid (CSF) investigation showing dissociation between cellular count and protein content. GBS occurring with 30 days after immunisation should be reported.

Encephalopathy: cases occurring within 72 hours after

Vaccination should be reported. Encephalopathy is an acute onset of major illness temporally linked with immunisation and characterized by and two of the following three conditions:

Seizures: Severe alteration in level of consciousness lasting for one day or more, and distinct change in behaviour lasting one day or more.

Encephalitis (any encephalitis occurring within 1-4 weeks following immunisation should be reported)

Encephalitis is characterized by the above mentioned symptoms and signs of cerebral inflammation and, in many cases. CSF pleocytosis and/or virus isolation.

Meningitis

Acute onset of major illness with fever, neck stiffness/positive meningeal signs (Kerning, Brudzinski). Symptoms may be subtle or similar to those of encephalitis, CSF examination is the most important diagnostic measure, CSF pleocytosis and/or detection of microorganism (Gram stain or isolation).

Seizures

Seizures lasting for several minutes to more than 15 minutes and not accompanied by focal neurological signs or symptoms. Seizures may be febrile seizures or afebrile.

3. Other adverse events

Allergic reaction: characterized by one or more of the

Following:

- 1) Skin manifestation (e.g. hives, eczema);
- 2) wheezing;
- 3) facial or generalized oedema.

Anaphlactoid reaction (hypersensitivity reaction)

Exaggerated acute reaction, occurring within 2 hours after

immunisation, characterized by one or more of the following:

- 1) wheezing and shortness of breath due to bronchospasm;
- 2) laryngospasm/laryngeal oedema;
- 3) one or more skin manifestations,
 - e.g. hives, facial oedema, or generalized oedema.

Anaphylactic shock – Circulatory failure (e.g. alteration of the level of consciousness, low arterial blood pressure, weakness or absence of peripheral pulses, cold extremities secondary to reduced peripheral circulation, flushed face and increased perspiration) with or without bronchospasm and/or laryngospasm. Laryngeal oedema leading to respiratory distress occurring immediately after immunisation.

Arthralgia: Persistent joint pain lasting longer than 10 days.

Transient: Joint pain lasting up to approximately 10 days.

Disseminated BCG itis

Disseminated infection occurring with 1 to 12 months after BCG vaccination and confirmed by isolation of *Mycobacterium bovis* **BCG strain**.

Fever – A. Fever, mild

Temperature 38°C - 38.9°C (rectal)

B. Fever, high

Temperature 39°C - 40°C (rectal)

C. Fever, extreme (hyperpyrexia)

Temperature higher than or equal to 40.5°C (rectal)

D. Fever, unspecified

Temperature presumed to be high but not measured. (Only high and extreme fever should be reported)

Hypotensive-hyporesponsive episode (shock collapse): Sudden onset of paleness, decreased level or loss of responsiveness, decreased level or loss of muscle tone (occurring within 24 hours of vaccination). The episode is transient and self-limiting.

Osteitis/osteomyelitis: Inflammation of the bone either due to BCG immunisation (occurring within 8 to 16 months after immunisation) or caused by other bacterial infection.

Persistent screaming: Inconsolable continuous crying lasting at least 3 hours accompanied by high-pitched screaming.

Sepsis: Acute onset of severe generalized illness due to bacterial infection and confirmed by positive blood culture.

Toxin-shock syndrome: Abrupt onset of fever, vomiting and watery diarrhoea within a few hours of immunisation, often leading to death within 24-48 hours.

4. Other severe and unusual events occurring within 4 weeks after immunisation and not covered under no. 1, 2, or 3.

Any death of a vaccine recipient temporally linked (within 4 weeks) to immunisation, where no other clear cause of death can be established, should be reported.

In addition, any unusual events should be reported.

FORM TO REPORT ADVERSE EVENTS FOLLOWING IMMUNIZATION (AEFI)

(Identities of reporter, patient and institution
will remain confidential)

Demographic details:							
Name (optional)				Identification number:			
Address:				Age:			
Region:		District		Sex:			
Health centre <input type="checkbox"/> / MOH office <input type="checkbox"/>				Reporter:			
Details of vaccine							
Vaccine	Route	Site of injection	Vaccine Lot number	Diluent Lot number	Manufacturer	Expiry date Vaccine	Expiry date Diluent
Date of reporting			Date and time of vaccination			Date and time AEFI started	
Details of dates							
Description of event: (Please tick the box, and give the description in the open space).							
Severe local reaction <input type="checkbox"/>	Anaphylactic shock <input type="checkbox"/>						
Sterile abscess <input type="checkbox"/>	Other allergic reaction <input type="checkbox"/>						
Bacterial abscess <input type="checkbox"/>	Non-allergic rashes <input type="checkbox"/>						
Sepsis <input type="checkbox"/>	Fever <input type="checkbox"/>						
Toxic shock syndrome <input type="checkbox"/>	Febrile seizures <input type="checkbox"/>						
Encephalopathy <input type="checkbox"/>	Prolonged crying <input type="checkbox"/>						
Thrombocytopenia <input type="checkbox"/>	Seizures <input type="checkbox"/>						
Arthritis/Arthralgia <input type="checkbox"/>	Guillain Barré syndrome <input type="checkbox"/>						
Hypotonic-hypo-responsive event <input type="checkbox"/>	Bradycardia <input type="checkbox"/>						
Apnoea <input type="checkbox"/>	Any other <input type="checkbox"/> -----						

Please describe in detail the adverse event:

Outcome:

Recovered fully Recovered partially Continuing Unknown

Hospitalized Date of admission Date of discharge

Died Date of death

Details of past medical and drug history (including history of similar reactions or other allergies) and any other relevant information

Details of reporter:

Name & designation:

Contact details (address and TP number):

Signature:

Complete and send the form to INFO_VIG Dept. of Pharmacology Faculty of Medicine, P.O. Box 271, Kynsey Rd, Colombo 08; Telephone 2695300 Ext 194-198 or Direct line 5677244/2697483; Fax: 2697483; and Epidemiological Unit, Ministry of Health, De Saram Place, Colombo 10. Telephone 2695112
Photocopies of the above are accepted.

Book review

SLMA Guidelines and Information on Vaccines 2008

“SLMA has published a booklet with revised and updated guidelines and information on vaccines.”

“The booklet starts with a useful preface by Professor Lalitha Mendis that recalls the focal points in the history of immunisation and the current global status of communicable diseases. The introduction by Dr. Iyanthi Abeyewickreme summarises the evolution of this book since its last publication, stressing its new features. The joint editors have successfully moulded the chapters into a clear, readable format, happily devoid of jargon.”

“This publication can be considered in two parts. The first gives information on individual vaccines and the second consists of a miscellany of chapters ranging from vaccination in special circumstances such as in HIV infected persons to adverse effect reporting.”

“SLMA Guidelines and Information on Vaccines 2008 offers a full coverage on EPI and non-EPI vaccines in Sri Lanka. The chapters on individual vaccines are conventional, starting with a brief description of the disease, going on to describe the type, efficacy, indications, dosage and administration, contraindications, adverse effects and storage of vaccines. The chapters on hepatitis B vaccine and rabies vaccine deserve commendation for their concise yet comprehensive presentation. The new features include chapters on human papilloma virus vaccine, influenza vaccine and rotavirus vaccine. Chapters on surveillance and prevention of adverse events following immunisation and frequently asked questions are the other notable improvements since the previous edition.”

“For anyone after who may wish for extra information, there are excellent bibliographies at the end of each chapter. A closer look at these lists will strengthen confidence in the accuracy of information provided.”

“I have a few minor criticisms. There is redundancy of information in some chapters which could have been avoided easily. For example in the chapter on DTP vaccine, efficacy and indications overlap. The impression of “overcrowding” in some chapters is actually due to poor formatting.”

“These guidelines should be made available in all the immunisation clinics and libraries of medical schools and hospitals. All postgraduate trainees, medical students and general practitioners will benefit from the expertise offered in this excellent compilation.”

Fernando D. *Ceylon Medical Journal* 2008; **53 (4)**: 159.

ISBN 978-955-9386-24-7

Barcode 9 789559 386247