

The Official Guide to Immunisations

Malta 2011



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Advisory Committee on Immunisation Policy
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Advisory Committee on Immunisation Policy Members

Chair

Dr Charmaine Gauci,

Director Health Promotion and Disease Prevention

Secretary

Dr Victoria Farrugia Sant'Angelo,

Medical Co-ordinator Primary Child Health and National Immunisation Service

Members

Prof. Simon Attard Montalto,

Chairman Department of Paediatrics, Mater Dei Hospital

Dr. Christopher Barbara,

Chairman Department of Pathology, Mater Dei Hospital

Dr. Paul Caruana,

Consultant Pathologist (Microbiology), Mater Dei Hospital

Dr. Tonio Piscopo,

Consultant Physician (Infectious Disease), Mater Dei Hospital

Dr. Tanya Melillo,

Public Health Physician, Disease Prevention Unit

Mr Peter Zarb,

Senior Pharmacist, Infection Control Unit, Mater Dei Hospital

Dr David Pace,

Resident Paediatric Specialist, Mater Dei Hospital and Special Advisor to ACIP

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The National Immunisation Schedule and other vaccine schedules may be altered from time to time depending on continued advances in the field of immunisation. It is therefore important to bear in mind that although every effort has been made for the recommendations in this publication to be precise and up to date at the time of printing, every practitioner is urged to periodically check for updated recommendations with the National Immunisation Centre in Floriana.

Foreword

The Advisory Committee on Immunisation Policy was legally set up in November 2007 following the publication of Legal Notice 253/07.

There have been various developments in the area of vaccination in Malta since the setting up of this committee. These include a revision of the national schedule with phasing out of oral polio and whole cell pertussis vaccines, and replacement with injectable polio and acellular pertussis vaccines. Training of health care professionals was enhanced as was the awareness of the importance of vaccination within the general population. Assessments and recommendations for the introduction of new vaccines on the national schedule and for specific risk groups are also under way. Vaccination results in both a benefit to health and savings in direct and indirect medical care costs. The provision of a publicly funded vaccination programme improves health and results in monetary savings. We encourage parents, guardians, and adults to maintain their children's immunisations up to date and all adults to be immunised according to national recommendations. A reminder here is justified on the obligation of reporting all vaccinations given. This is of paramount importance for compiling national coverage rates which is our obligation to report to World Health Organization and to enable us to seek guidance on further actions. Your role as health care professionals is crucial and hence the Advisory Committee on Immunisation Policy feels the need to present to you the latest information on vaccination in this booklet.

Producing such a publication was possible through the dedication and voluntary time commitment on the part of those involved. I would like to extend my sincere thanks to the members of the committee for completing this very important resource. I would also like to take this opportunity to acknowledge their invaluable contribution and continued commitment in providing ongoing advice and recommendations on vaccine use in Malta.



Dr Charmaine Gauci

Director, Health Promotion and Disease Prevention
Chair, Advisory Committee on Immunisation Policy

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General Information

Legislation

Immunisation has been introduced in legislation through the Prevention of Disease Ordinance since 1908. In 2007, the Public Health Act (Chapter 465 of the Laws of Malta, Public Health Act) was issued and the legislative aspects of immunisation are now covered by this legislation as well as in the Prevention of Disease Ordinance. Article 27 of the Public Health Act gives the power to the Superintendent of Public Health to make, vary or revoke orders:

27(d) *ensuring the protection of the public by immunisation against particular diseases and in particular may by such order:*

- (i) regulate and control the practice of any particular type of immunisation in humans;*
- (ii) prescribe forms, certificates, notices, immunisation certificates and postponement certificates;*
- (iii) prescribe those diseases against which immunisation of humans shall be compulsory;*
- (iv) regulate and control the importation, exportation, manufacture, storage and transport of any type of vaccine;*
- (v) publish schedules regarding compulsory or recommended immunisations.*

Under the same act a legal notice (L.N. 253 of 2007, Advisory Committee on Immunisation Policy Regulations, 2007) was issued on the setting up of the Advisory Committee on Immunisation Policy Regulations. The legislation describes the duties of this committee as to:

- (a) promote the understanding of, and support for, the immunisation programme among professionals and the public at large*
- (b) keep abreast of the latest research in vaccine development*
- (c) advise the Superintendent of Public Health with respect to vaccination programme priorities in the short, medium and long term*
- (d) develop written recommendations for the routine administration of vaccines*
- (e) issue guidelines regarding dosages, periodicity and contraindications applicable to individual vaccines*
- (f) tender advice as may be requested by the Superintendent of Public Health.*

This legislation also describes the composition of the committee as follows:

1. Chairperson nominated by the Superintendent of Public Health
2. A specialist in Public Health Medicine
3. A specialist in Paediatrics
4. A specialist in Virology
5. A specialist in Microbiology/Bacteriology
6. A specialist in Infectious Disease
7. A pharmacist
8. A Secretary to the Committee appointed by the Superintendent of Public Health

The Committee regulates its own procedure.

The Importance of Cold Chain Maintenance

Introduction

What is the Cold Chain?

The cold chain is a temperature-controlled supply chain. An unbroken cold chain is an uninterrupted series of storage and distribution activities which maintain a given temperature range. It is used to help extend and ensure the shelf life of products such as vaccines.

Cold Chain and Vaccines

Vaccines are biological substances that may lose their effectiveness quickly if they become too hot or too cold at any time, especially during transport and storage. Storage outside of the recommended temperature range - including during transport and storage - may speed up loss of potency, which cannot be reversed, resulting in failure of the vaccine to induce protection.

Some vaccines are inactivated even at room temperature in temperate zones, and in hot tropical regions they are not only inactivated, but some may even become toxic. Heat-sensitive vaccines must stay refrigerated while in transit to distribution centres and to peripheral clinics where the target populations are located. During vaccination sessions the stored vaccines must be kept at a suitable low temperature at all times. Vaccines should only be removed from refrigeration at the time of immunisation. When vaccine failure is detected, either by serological studies of vaccinated populations or by the occurrence of breakthrough cases in a previously vaccinated population, the cause is most likely to be a break in the cold chain, which frequently occurs after a vaccine is dispensed.

It is mandatory that all those handling vaccines follow policies to ensure cold chain compliance. The individual Summaries of Product

Characteristics (SPCs) that are supplied by the manufacturers of the vaccines specify the temperature range allowed. Vaccines that have not been properly distributed or stored are not be used.

Maintenance of the cold chain is standard practice for vaccines throughout the pharmaceutical industry (see Figure 1). Maintaining the cold chain ensures that vaccines are transported and stored according to the manufacturer's recommended temperature range of $+2^{\circ}\text{C}$ to $+8^{\circ}\text{C}$ until the point of administration.

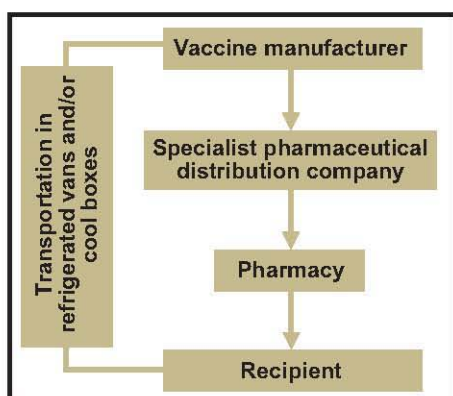


Figure 1:
Cold chain system

Storage

Vaccines must be stored in the original packaging at $+2^{\circ}\text{C}$ to $+8^{\circ}\text{C}$ and protected from light. All vaccines are sensitive to some extent to heat and cold. Heat speeds up the decline in potency of most vaccines, thus reducing their shelf life. Freezing may cause increased reactogenicity and loss of potency of some vaccines. It can also cause hairline cracks in the vials, leading to contamination of the contents.

Vaccines must always be stored in a temperature monitored pharmaceutical refrigerator. Domestic refrigerators are not suitable for storing vaccines and should not be used. Storage of vaccines in the door, in the bottom drawers or adjacent to the freezer plate of the refrigerator leads to temperature variations outside the recommended $+2^{\circ}\text{C}$ to $+8^{\circ}\text{C}$. Sufficient space should be allowed in the refrigerator so that air can circulate freely.

Patients or parents should not normally be asked to store vaccines. Exceptionally, patients may be asked to transport vaccines and to store them for short periods of time. Should this need arise, advice on appropriate storage should be given to the patient.

Domestic cool boxes should not be used to store, distribute or transport vaccines. Validated cool boxes (with maximum - minimum thermometers) and ice packs from a recognised medical supply company should be used. Individual manufacturers' instructions should be strictly adhered to.

Vaccines must be kept in the original packaging, wrapped in bubble wrap (or similar insulation material) and placed into a cool box with cool packs as recommended by the manufacturer's instructions. This will prevent direct contact between the vaccine and the cool packs and will protect the vaccine from any damage, such as may occur with freezing.

The vaccine refrigerator

Specialised refrigerators are available for the storage of pharmaceutical products, and must be used for vaccines and diluents. Ordinary domestic refrigerators must not be used. Food, drink and clinical specimens must never be stored in the same refrigerator as vaccines. Opening of the refrigerator door should be kept to a minimum in order to maintain a constant temperature.

The accidental interruption of the electricity supply can be prevented by using a switchless socket or by placing cautionary notices on plugs and sockets. Refrigerators should not be situated near a radiator, in direct sunlight or any other heat source that could affect their working, and should be appropriately ventilated.

Ice should not be allowed to build up within the refrigerator, as this reduces effectiveness. Records of regular servicing, defrosting and cleaning should be kept. An approved cool box or alternative refrigerator should be used to store vaccines during defrosting of the main refrigerator. Vaccines should only be replaced once the refrigerator has returned to the correct temperature after defrosting.

Refrigerator thermometers

The temperature within the vaccine refrigerator must be continually monitored with a maximum–minimum thermometer. This will identify when the temperature may have varied outside the recommended range. Digital thermometers are the most reliable. More sophisticated temperature-recording devices are now available, including alarmed digital maximum–minimum thermometers.

Thermometers should be reset and replaced according to the manufacturer's guidance. Temperatures in the refrigerator must be monitored and recorded at least once each working day, and documented on a temperature record chart. The calibration of thermometers should be checked annually to ensure that they are working correctly.

Refrigerator failure or disruption of the cold chain

Arrangements should be in place for back-up facilities to be available in the event of the refrigerator failing or breaking down.

Solidarity

The United Nation's Children's Fund (UNICEF) promotes the delivery of safe and effective vaccines especially in developing countries. This UNICEF initiative is partly financially supported by the European football giants FC Barcelona as can be seen in Figure 2.



Figure 2: Barcelona Kit – FC Barcelona donate money to UNICEF for this 'advert' whilst other clubs (with the exception of Aston Villa FC that donates to the ACORNS children's hospice) get paid for adverts on their kit.

Types of Vaccines

While a number of novel vaccine types are currently being investigated, only vaccine types which have been licensed (as of 2011) for general use will be considered herein.

Live attenuated vaccine

The entire live organism (bacterium or virus) is used to induce the immune response. The organism in modified form is capable of replication but with reduced virulence.

Inactivated (killed) vaccine

The entire organism is killed/inactivated prior to its use as an immunogen.

Subunit vaccines

Specific component(s) derived from the organism of interest are used as antigens, for the induction of immunity in the recipient.

This group includes:

- ▶ **Toxoid Vaccines** - Bacterial toxins are rendered non-virulent while maintaining their antigenicity.
- ▶ **Polysaccharide Vaccines** - Purified bacterial capsular polysaccharide
- ▶ **Conjugate Vaccines** - A specific bacterial capsular oligo/polysaccharide is linked to a protein. These conjugate vaccines exhibit a substantially improved immune response when compared to the pure polysaccharide vaccines.
- ▶ **Virus-Like Particle Vaccines** - The viral outer shell is produced and used as the antigen.
- ▶ **Acellular Vaccines** - A variable mixture of antigenic components is selected from the bacterium of interest.

Immunisation Procedures

Vaccine Reconstitution

Freeze dried vaccines must be reconstituted with the diluent supplied and must be used within the recommended period, according to the manufacturer's instructions. In some cases, this might not be longer than 30 minutes.

Single dose containers are preferable; any vaccine left from multi-dose vials must be discarded at the end of a session. The diluent should be added using a sterile syringe with a 21G (green) needle and should be added slowly to avoid frothing.

Administering the vaccine

Most vaccines are given by intramuscular or deep subcutaneous injection. In infants, a 23G (blue) needle should be used, with the vaccine being given into the anterolateral aspect of the thigh. For adults, a 23G needle is also recommended.

BCG is given intradermally, using a 25G (orange) needle.



Figure 3: Intramuscular administration of the influenza vaccine

Contraindications to Vaccination

No one should be denied immunisation without serious thought as to the individual and community repercussions of such denial.

Absolute Contraindications

- ▶ Acute illness: immunisation should be postponed until the individual has recovered. Minor infections without fever or systemic upset are not reasons to postpone immunisation.
- ▶ Severe local and/or systemic reactions to a preceding dose as defined below:

Local - This would include a local extensive area of redness and swelling becoming indurated and involving most of the anterolateral surface or a major part of the circumference of the limb.

Systemic reactions - such as anaphylaxis, convulsions or encephalopathy occurring within 72 hours of vaccination.

False Contraindications

Persons may still be vaccinated in the following situations:

- ▶ Family history of any adverse reaction following immunisation
- ▶ Family history of convulsions
- ▶ Previous history of pertussis, measles, rubella or mumps infection
- ▶ Prematurity: immunisation should proceed along the established schedule according to the chronological age of the child
- ▶ Stable neurological conditions such as cerebral palsy and Down's syndrome
- ▶ Contact with an infectious disease
- ▶ Asthma, eczema, allergic rhinitis or "snuffles"
- ▶ Treatment with antibiotics or topical steroids
- ▶ Pregnancy in the mother or a close contact
- ▶ Breast feeding
- ▶ Low birth weight or failure to thrive
- ▶ Recent or imminent surgery
- ▶ Treatment with inhaled corticosteroids

Immunisation with Live Attenuated Vaccines

Live vaccines should not be administered to pregnant women, persons suffering from specific immunocompromising conditions, or persons suffering from malignant conditions of the reticuloendothelial system, such as leukaemia or lymphoma.

If it is necessary to administer more than one vaccine at the same time, with at least two of them being a live attenuated type, they should be given either simultaneously in different sites (unless a combined preparation is used), or be separated by a period of at least 28 days.

It is also recommended that a four (when given at different sites) or twelve week interval (when given at the same body site) should be allowed between the administration of a live vaccine and BCG inoculation.

Immunisation of HIV positive individuals

The risk and complications of some vaccine-preventable diseases is higher in HIV-infected individuals. However, the immune response following vaccination is generally impaired and shorter lasting in HIV-infected individuals, especially in those with low CD4+ T-lymphocyte counts and detectable HIV viral load. Even in patients responding to antiretroviral treatment, an impaired immune response may persist despite normalisation of the CD4+T-cell count.

Apart from this, vaccines other than the live attenuated types can be used in HIV-positive individuals similar to the general population. Caution with live-attenuated vaccines is warranted in HIV-infected individuals with low CD4+T-lymphocyte counts. Decisions regarding administering a live-attenuated vaccine should be made after weighing the risks and benefits on an individual basis and only under expert supervision.

BCG is specifically contraindicated in all HIV-positive individuals. MMR and varicella-zoster vaccines are generally considered safe if the CD4+T-lymphocyte count is greater than 25% in children. Yellow fever vaccination appears safe and effective in HIV-infected adults with a median CD4+T-cell count greater than 500 cells/ μ l, while the risk of complications from this specific vaccine given to HIV-positive patients with a lower CD4+T-cell count is unclear. Furthermore, it has been hypothesised that the use of this vaccine might not be safe in patients treated with CCR5 inhibitors.

Therefore, the indication for Yellow fever vaccination should be carefully made - visitors to other countries should consider, as an alternative, a letter of exemption where a certificate of vaccination is required for entry into the country.

The Vaccines

Diphtheria

Introduction

Diphtheria is an acute infectious disease caused by toxigenic strains of *Corynebacterium diphtheriae*, a rod shaped, gram positive bacterium. It usually affects the upper respiratory tract, or less commonly the skin. Respiratory obstruction is the resultant life-threatening complication of upper respiratory tract diphtheria. In addition, the toxin produced spreads systemically, and may adversely affect the function of myocardial, nervous and adrenal tissues.

The incubation period is around 2 to 5 days. Cases are infectious until the virulent bacilli have disappeared from the site of infection (usually less than 2 weeks and seldom more than 4 weeks from disease onset). Rarely, chronic carriers may shed organisms for 6 months or more; however appropriate antibiotic treatment rapidly stops shedding.

Active Immunisation

Diphtheria immunisation is carried out by using diphtheria toxoid. This is the toxin, responsible for causing the disease, extracted from toxigenic strains of *C. diphtheriae*, which is treated with formaldehyde to render it non toxic while retaining its antigenic properties, and then purified for use in human vaccination. One should note that the vaccine thus protects against the development of the disease – it does not prevent colonisation.

This toxoid is usually available as one of the components in several different types of combined vaccines, which when administered would simultaneously stimulate a protective immune response to various infectious diseases.

The diphtheria toxoid present in these various combined vaccines is available in two different strengths, which are denoted either by capital letter D, which contains the higher concentration of toxoid (usually 30IU of purified and adsorbed diphtheria antigen), or small letter d, which contains a lower concentration of toxoid (usually 2 IU).

The higher D concentration should always be used to vaccinate children up to the age of 6 years. Children and adults above this age should be vaccinated using the d concentration, to reduce the incidence of adverse effects.

Recommendations

This vaccine is usually included as part of the early immunisation schedule in infancy, when it should be given as follows:

Dose 1 - At six to eight weeks of age

Dose 2 - At three months of age

Dose 3 - At four months of age

Dose 4 - At eighteen months of age

Following this, a booster dose (using the d strength vaccine) should be given at 16 years of age. Further booster doses may be given at 10 year intervals and in combination with the tetanus vaccine.

Adverse reactions

Swelling and redness at the injection site are common. Malaise, transient fever and headache may also occur. A small painless nodule may form at the injection site but usually disappears without sequelae. Severe anaphylactic reactions are rare.

Tetanus

Introduction

Tetanus is caused by a toxin produced by the bacterium *Clostridium tetani*. *C. tetani* is an anaerobic bacterium that produces spores that are very difficult to kill as they are resistant to heat and many chemical agents. *C. tetani* spores can be found in the soil and in the intestines and faeces of many household and farm animals and humans. The bacteria usually enter the human body through a deep puncture wound. Tetanus is not spread from person to person. The incubation period varies from 3-21 days, with an average of 8 days.

The symptoms of tetanus are caused by the tetanus toxin acting on the central nervous system. In the most common form of tetanus, the first sign is spasm of the jaw muscles, followed by stiffness of the neck, difficulty in swallowing, and stiffness of the abdominal muscles. Other signs include fever, sweating, elevated blood pressure, and tachycardia. Spasms often occur, which may last for several minutes and continue for 3-4 weeks. Complete recovery, if it occurs, may take months. Tetanus has a high fatality rate.

The diagnosis of tetanus is based on the clinical signs and symptoms only. Laboratory diagnosis is not useful as the *C. tetani* bacteria usually cannot be recovered from the wound of an individual who has tetanus, and conversely, can be isolated from the skin of an individual who does not have tetanus. The most dangerous kind of injury involves possible contamination with dirt, animal faeces, and manure. People can also get tetanus from splinters, self-piercing, and self-tattooing. Injecting drug users are also at risk for tetanus.



Figure 4: Spasms 2° to tetanus infection

Active Immunisation

Immunisation with tetanus toxoid protects by stimulating the production of antitoxin which provides immunity against the effects of tetanus toxin.

The recommended vaccines for immunisation are:

- 1. Tetanus/diphtheria (low-dose diphtheria - Td)**
- 2. Tetanus/diphtheria/polio (low-dose diphtheria - Td/IPV)**
- 3. Diphtheria/tetanus/pertussis/polio/Hib - DTaP/IPV/Hib**
- 4. Diphtheria/tetanus/pertussis/polio/Hib/hepatitis B - DTaP/IPV/Hib/HepB**
- 5. Diphtheria/tetanus/acellular pertussis - (low-dose diphtheria, low-dose pertussis - dTap)**

Recommendations

Active immunisation is indicated for all persons above six weeks of age. For primary immunisation, the following schedule with preparation 3 or 4 is recommended:

Dose 1	0.5ml i.m.	from 6 weeks of age
Dose 2	0.5ml i.m.	3 months of age
Dose 3	0.5ml i.m.	4 months of age
Dose 4	0.5ml i.m.	18 months of age

If the course is interrupted, it may be resumed; there is no need to start again, irrespective of the time interval.

Booster Doses

A reinforcing dose using preparation 2 is recommended for those aged 16 years of age, according to the National Immunisation Schedule. Preparation 5 is an alternative to the school-leaving booster dose against tetanus.

In adults, a reinforcing dose 10 years after the primary course and every 10 years thereafter, using preparation 1 should maintain a satisfactory level of protection against tetanus.

For people who were never vaccinated or who may have started but not completed the recommended series of tetanus doses, a 3-dose series of Td (preparation 1) should be given with a 1 to 2 month interval between dose 1 and 2, and a 6 to 12 month interval between dose 2 and 3. If someone experiences a deep or puncture wound, or a wound contaminated with dirt, an additional booster dose may be given if the last dose was more than 10 years previously. It is important to keep an up-to-date record of all immunisations so that repeat doses are not given unnecessarily. Although it is recommended to be adequately protected, receiving more doses than recommended can lead to increased local reactions, such as painful swelling of the limb.

Adverse Reactions

Following DTaP/IPV/Hib and DTaP/IPV/Hib/HepB, local reactions such as fever, redness and swelling at the injection site, and soreness and tenderness where the vaccine was given, are not uncommon in children. These minor local and systemic adverse reactions are much less common now with the vaccine containing acellular pertussis (preparations 3 and 4).

Side effects following Td or Td/IPV in older children and adults include redness and swelling at the injection site. Older children and adults who received more than the recommended doses of Td or Td/IPV vaccine can experience increased local reactions, such as painful swelling of the arm. This is due to the pre-existent high levels of tetanus antibody.

Contraindications

► General contraindications to vaccination

Note: Tetanus vaccine can be administered to an individual suffering from an acute febrile illness in the presence of a tetanus-prone wound.

Tetanus vaccine can be safely given to pregnant women even in early pregnancy.

Passive Immunisation

Passive immunisation using anti-tetanus immunoglobulin should be given to individuals with a tetanus-prone type of wound who either give no history of having been previously immunised or who have had their last dose of the primary course or booster dose more than 10 years prior to the time of injury. Anti-tetanus immunoglobulin should be administered intramuscularly together with a full course or a booster dose of vaccine, injected at different sites.

If the wound is less than 24 hours old, a dose of 250 IU should be used. For wounds older than 24 hours, a dose of 500 IU is used.

Storage

The vaccine should be stored and kept at temperatures between +2°C and +8°C. Opened multi-dose vials should be discarded within 48 hours of opening.

Pertussis

Introduction

Bordetella pertussis, a Gram negative cocco-bacillus, is an obligate human pathogen which causes whooping cough (pertussis), a disease that is endemic worldwide. Pertussis is characterised by a sequential progression from an initial catarrhal, through a subsequent paroxysmal, and a final convalescent stage. The duration of each stage is affected by age and immunisation status but, in general, lasts for 2 weeks. *B. pertussis* specifically infects the ciliated epithelium of the respiratory tract and symptoms are a result of the several exotoxins produced by this bacterium. The paroxysms of uninterrupted coughing are typically followed by a loud whoop, except in infants <3 months of age who often lack a whoop and whose presenting features may be apnoea and cyanosis. Apnoea (which may lead to cerebral damage from hypoxia), superimposed bacterial pneumonia, otitis media and respiratory failure are the major complications of pertussis. Complication and mortality rates are highest in infants <6 months old, especially those <2 months of age. Older children and adolescents may have an atypical presentation and a persistent cough for >2 weeks may be the sole presenting symptom. A resurgence of pertussis has been noted over the last 10 years in several countries, with adolescents and adults being most frequently affected.

Pertussis is an extremely contagious disease, with secondary attack rates approaching 100% in susceptible individuals. Transmission occurs through aerosolised droplets. Adolescents and adults are an important source of transmission of *B. pertussis* to unimmunised infants.

Active Immunisation

Whole cell pertussis vaccines, containing killed *B. pertussis* pathogens, have been used effectively to control the morbidity and mortality associated with pertussis, and are still widely used globally.

However, the reactogenicity of whole cell pertussis vaccines has limited their acceptance and in industrialised countries acellular pertussis vaccines have replaced their use. Acellular pertussis vaccines contain purified components of *B. pertussis*, including pertussis toxoid, filamentous haemagglutinin, fimbrial proteins and pertactin. Most available preparations contain between 3-5 pertussis components. Formulation of acellular pertussis vaccines is in combination with other antigens, such as tetanus toxoid, diphtheria toxoid, inactivated poliomyelitis viruses and conjugate *Haemophilus influenzae* type b polysaccharide, with the choice of antigens varying widely between different preparations and manufacturers.

Recommendations

Active immunisation is recommended from the age of 6 weeks as follows:

- Dose 1 - at 6-8 weeks of age
- Dose 2 - at 3 months of age
- Dose 3 - at 4 months of age
- Dose 4 - at 18 months of age

The recommendation of an adolescent boost against pertussis varies between countries and depends on the epidemiology of the disease in this age group. In Malta, the benefit of introducing an adolescent boost against pertussis is still being studied.

Adverse Reactions

Acellular pertussis vaccines are associated with much less adverse events when compared to whole cell pertussis vaccines, with erythema and swelling being the most common local reactions and mild fever and drowsiness being the most frequently observed systemic reactions.

Poliomyelitis

Introduction

The Poliovirus is classified within the family Picornaviridae, genus Enterovirus. It causes an acute illness following invasion of the gastrointestinal tract by any of three types of polio virus, designated type 1, 2 or 3.

The virus has a high affinity for nervous tissue and the primary changes are in neurons. The infection may be asymptomatic, or range in severity from a non paralytic fever to aseptic meningitis or paralysis. Symptoms include headache, gastrointestinal disturbance, malaise and stiffness of the neck and back, with or without paralysis.

The incubation period ranges from 3 to 21 days. Cases are most infectious from 7 to 10 days before and after the onset of symptoms, while the virus may be shed in the faeces for up to six weeks or longer. Transmission is through contact with faeces or pharyngeal secretions of an infected person.

Active Immunisation

As part of the WHO Global Polio Eradication Plan and in conjunction with most other EU countries, vaccination with the live attenuated oral polio vaccine (OPV) has been phased out and replaced with the inactivated polio vaccine (IPV).

Recommendations

IPV is usually administered as an intramuscular injection as part of a combination vaccine. As part of the primary immunisation programme during childhood, it should be given at ages 6-8 weeks, 3 months and 4 months, with a fourth dose to be given at 18 months of age a fifth dose is recommended at 16 years of age.

Routine vaccination of adults is not necessary because most are already immune and have little risk of being exposed to wild polio virus. However, it may be considered for travellers to areas where polio is still endemic, laboratory scientists who handle specimens that might contain polioviruses, and workers in close contact with individuals who might be excreting wild polioviruses in their stool (such as immigrants from endemic countries).

If an adult is at increased risk of exposure and has never been vaccinated against polio, he or she should receive three doses of IPV, the first two doses given 1-2 months apart, and the third 6-12 months after the second dose. If an adult at risk previously received only one or two doses of polio vaccine (either OPV or IPV), he or she should receive the remaining dose(s) of IPV, regardless of the interval since the last dose.

If an adult at increased risk previously completed a primary course of polio vaccine (three or more doses of either OPV or IPV), he or she may be given another dose of IPV to ensure protection. Only one "booster" dose of polio vaccine in a person's lifetime is recommended. It is not necessary to receive a booster dose each time a person travels to an area where polio is still endemic.

Adverse Reactions

Local reactions such as fever, redness and swelling at the injection site, and soreness and tenderness where the vaccine was given, are not uncommon in children and adults.

Storage

The vaccine should be stored and kept at temperatures between +2° and +8°C.

Haemophilus influenzae type b (Hib)

Introduction

Haemophilus influenzae is a gram negative cocco-bacillus with an outer capsule that allows it to be typed (from a-f). The capsular forms of *H. influenzae* cause most invasive disease. Hib colonises around 2-5% of preschool children and is responsible for both upper and lower respiratory tract infections, epiglottitis and meningitis. Prior to the advent of an effective vaccine against Hib, these infections were responsible for significant morbidity and mortality in childhood with up to 10% of affected children below the age of 5 years succumbing to the disease. Survivors of Hib meningitis commonly developed significant hearing loss (around 6%), as well as delayed speech, ataxia, hydrocephalus, learning disability and convulsions.

H. influenzae lacking a capsule is non typeable and, although it may colonise the upper respiratory tract in 60-90% of asymptomatic individuals, it may still cause disease, particularly acute otitis media, sinusitis, upper respiratory infections in children and exacerbations of bronchitis in adults.

All children are at risk of Hib, especially those below the age of five years (>90% of cases), with the peak prevalence of both Hib meningitis and epiglottitis occurring in those below the age of three years. Children with sickle cell disease, asplenia and immunosuppression are especially at risk. In Malta, prior to the Hib vaccine, approximately 14 cases with invasive Hib were documented per annum, with Hib meningitis and epiglottitis both averaging 4-5 cases/year. This translated into an annual incidence of 30-37/100,000 in those under 5 years of age.

Hib is spread by droplet aspiration and inhalation following close contact, sneezing and coughing. Some affected individuals may be asymptomatic.

It is difficult to establish the incubation period precisely but this is thought to be around 1-5 days.

Diagnosis and Management

This is based on the clinical picture, together with Gram stain and bacterial culture of the appropriate body fluid, as well as Hib antigen detection. One third of Hib isolates may be resistant to ampicillin/amoxicillin and macrolides (except azithromycin), 3% are resistant to amoxicillin-clavulanic acid but resistance against third generation cephalosporins has not been demonstrated. Invasive infection in children over the age of one month should be treated with ampicillin and cefotaxime or ceftriaxone for a minimum of 10 days. Localised infections (e.g. otitis media) can be treated with amoxicillin-clavulanic acid or, in the case of resistant strains, co-trimoxazole or a cephalosporin.

Cases of invasive Hib should be notified.

Active Immunisation

A conjugate vaccine comprising capsular antigens derived from the b capsule was developed in 1988 and resulted in a dramatic reduction in invasive Hib infection in those countries that introduced the vaccine. This was observed in Malta after the introduction of the Hib vaccine, initially in the private sector in the mid-nineties, followed by national vaccination in 1996-7.

The Hib vaccine is available as a separate vaccine or, more commonly, in combination with others including diphtheria, tetanus, pertussis, polio (5 in 1) and hepatitis B (6 in 1). It is administered intramuscularly to all infants from 6 weeks of age.

Recommendations

Infants should receive 3 doses and a booster as per Table 1. The same schedule should be followed in infants starting their Hib vaccination after 4 months of age. Those aged 13 months - 4 years require a single dose.

Table 1: Hib vaccination schedule

Dose	Administration	Age
1	0.5ml i.m	6 weeks - 2months
2	0.5ml i.m	3 months
3	0.5ml i.m	4 months
Booster	0.5ml i.m	12-24 months

Adverse Reactions

Minor effects are common but generally last less than 24 hours. They include swelling, induration and pain at the vaccine site, and fever. Serious events are extremely rare.

Contraindications and Precautions

As with other vaccines, Hib should only be administered to children who are well and afebrile. It should be avoided in those with previous serious adverse events including severe local or generalised reactions. Hib vaccine can be given to HIV-positive individuals.

Storage

Dry, dark refrigeration at +2°C to +8°C and not frozen.

Measles

Introduction

Measles is a highly contagious viral illness spread mainly by droplets, contaminated nasal or throat secretions or contaminated fomites.

The clinical features include a characteristic morbilliform (maculopapular) rash as well as fever, and the three Cs - cough, coryza and conjunctivitis. Complications include bronchitis, pneumonia, diarrhoea, subacute sclerosing panencephalitis, corneal ulceration, nephritis and myocarditis. Measles is probably the most deadly of all childhood febrile/exanthematous illnesses.

The incubation is on average 10 days with a communicability of 1-2 days before the symptoms to 4 days after the appearance of the rash.



Figure 5: Rash of measles infection

Active Immunisation

Most vaccines are derived from the original Edmonston virus strain (Shwarz, Connaught, Moraten, Edmonston-Zagreb strains); the Moraten strain is now the only strain used in the US, the Schwarz or Edmonston strains are the predominant strains used in many other countries.

Several different measles vaccine strains have been developed in Russia (Leningrad-16 strain), Japan (CAM-70 and TD 97 derived from Tanabe strain) and China (Shangain strain). Most measles vaccines are attenuated and produced in chick embryo fibroblasts with a few attenuated in human diploid cells.

Measles vaccine is available in combination with mumps and rubella (MMR) and with varicella (MMRV) vaccines.

Recommendations

Many countries recommend a two-dose immunisation schedule with the first dose at 12-15 months of age and the second dose at 3-4 years (but at least 4 weeks after dose 1).

The second dose intends to produce measles immunity in individuals who failed to respond to the first dose (primary vaccine failure).

The second dose may boost antibody titres in some persons. There is no age restriction for measles immunisation.

In many countries measles cases also occur in adolescents and adults and emphasis must be placed on identifying and appropriately immunising susceptible adolescents and adults.

It is important that health care personnel should be immune to measles.

The duration of immunity after 2 doses of MMR vaccine is life-long.

Adverse Reactions

Fever may develop 5 - 10 days following vaccination and in 5% of vaccinees a mild self-limiting rash is observed. This is not contagious and will not transmit measles infection to susceptible persons.

Contraindications and Precautions

The vaccine should not be given in cases of:

- ▶ A severe allergic reaction to a vaccine component or following a prior dose
- ▶ Moderate or severe acute illness
- ▶ Pregnancy
- ▶ Immunosuppression

Individuals with HIV-infection should be immunised (measles in HIV-infected persons can be severe and often fatal) except if severely immunocompromised (low CD4+ T-lymphocyte counts).

Studies have demonstrated safety of the MMR vaccine in egg allergic individuals.

Pregnancy should be avoided for at least 4 weeks following any dose of the MMR vaccine.

Passive Immunisation

Children and adults with compromised immunity who come into contact with measles should be given human normal immunoglobulin by intramuscular injection (HNIG) as soon as possible after exposure.

Children under 12 months in whom there is a particular reason to avoid measles, (such as recent severe illness), can also be given immunoglobulin; the MMR vaccine should then be given after an interval of at least three months, at around the recommended age of vaccination.

Table 2: Use of Immunoglobulin in Measles Contacts

Use of Immunoglobulin in Measles Contacts		
	Age	Dose
For prevention	<1yr	250mg
	1-2 years	500mg
	3 years and over	750mg
For attenuation	<1 year	100mg
	1 year and over	250mg

Mumps

Introduction

Mumps presents as an unspecific prodrome which includes low grade fever, malaise, headache and myalgias. Swelling of the parotid glands classically develops in 30-40% of cases. Up to 20% may be asymptomatic. Complications include meningitis, orchitis, pancreatitis, deafness and sometimes oophoritis.

The mumps virus is transmitted by droplets or direct contact with infected secretions. The infection is communicable 6-7 days before and up to 9 days after onset of the disease.

The incubation period is 14-18 days.



Figure 6: Swelling of the right parotid gland caused by mumps

Active Immunisation

Worldwide the Jeryl Lynn strain (or RIT 4385 derived from Jeryl Lynn strain) is the most widely used vaccine strain.

The formerly widely used Urabe strain has been withdrawn from many countries following data concerning vaccine-associated meningitis.

Other vaccine strains have been developed, e.g. in Russia (Leningard-3), Croatia (L-Zagreb), Switzerland (Rubini) and Japan (e.g. Torii).

Most vaccines are produced in chick embryo fibroblast cell cultures.

Mumps vaccine is available in combination with measles and rubella (MMR) or varicella (MMRV) vaccines.

Recommendations

Mumps vaccine is given in a 2-dose schedule in combination with measles and rubella (MMR). The first dose is given at 12-15 months of age and the second dose at 3-4 years of age.

There is no age limit for receiving mumps vaccine and it can be given to adults and adolescents in a 2-dose schedule with an interval of at least 4 weeks between doses. This schedule should provide life-long immunity to 90-97% of recipients.

Long-standing country-wide immunisation programmes have decreased the incidence of mumps dramatically and in some countries mumps has been brought close to elimination.

Note: HNIG is no longer used for post-exposure protection against mumps since there is no evidence that it is effective.

Adverse Reactions

Fever is observed in 5-15% of cases up to 10 days following vaccination.

There has been evidence of a rare association between MMR and febrile convulsions or idiopathic thrombocytopaenic purpura.

Contraindications and Precautions

The vaccine should not be given in cases of:

- ▶ A severe allergic reaction to a vaccine component or following a prior dose
- ▶ Moderate or severe acute illness
- ▶ Pregnancy
- ▶ Immunosuppression

Individuals with HIV-infection should be immunised except if they are severely immunocompromised (low CD4+ T-lymphocyte counts).

Pregnancy should be avoided for at least 4 weeks following any dose of the MMR vaccine.

Rubella

Introduction

Rubella is a viral infection which usually presents as a maculopapular rash beginning on the face, extending from the head to the foot and lasting about 3 days. The prodrome usually includes fever and malaise and enlarged lymph nodes which appear before the rash and last for weeks. The disease is usually mild.

Complications include arthralgia and very rarely thrombocytopaenia, encephalitis and neuritis.

The incubation period is 14 to 21 days and the period of highest infectivity is from one week before until 7 days after the onset of the rash.



Figure 7: Generalised maculopapular rash in rubella

Congenital Rubella Syndrome (CRS)

Rubella can be a most dangerous disease, particularly when rubella occurs in the first trimester of pregnancy. CRS may lead to fetal death, spontaneous abortion and stillbirths and may affect all organs with the most common manifestation being deafness. Other manifestations include cataracts, glaucoma, cardiac defects, microcephaly, learning disability and bone lesions.

Active Immunisation

Most current licensed vaccines are based on the live attenuated RA 27/3 strain of rubella virus propagated in human diploid cells.

Rubella vaccine is available in combination with measles and mumps (MMR) and with varicella (MMRV) vaccines.

Recommendations

Rubella vaccine is given in a 2-dose schedule in combination with measles and mumps (MMR). The first dose is given at 12-15 months of age and the second dose at 3-4 years of age.

There is no age limit for receiving rubella vaccine and it can be given to adults and adolescents in a 2-dose schedule with an interval of at least 4 weeks between doses. Rubella vaccine is compulsory for adolescent females in Malta.

Adverse Reactions

Fever may be observed rarely up to 10 days following vaccination. In very rare cases a mild rash may be observed. This is not contagious.

Contraindications and Precautions

The vaccine should not be given in cases of:

- ▶ A severe allergic reaction to vaccine component or following a prior dose
- ▶ Moderate or severe acute illness
- ▶ Pregnancy
- ▶ Immunosuppression.

Individuals with HIV-infection should be immunised except if they are severely immunocompromised (low CD4+ T-lymphocyte counts).

Pregnancy should be avoided for at least 4 weeks following any dose of the MMR vaccine.

Passive Immunisation

Post-exposure prophylaxis with immunoglobulin does not prevent infection in non-immune contacts and is therefore of little value for the protection of pregnant women exposed to rubella. It may however reduce the likelihood of clinical symptoms which may possibly reduce the risk to the foetus. Rubella immunoglobulin should be given as early as possible after exposure, in a dose of 750mg.

Hepatitis B

Introduction

Hepatitis B is a serious disease that affects the liver. It is caused by hepatitis B virus (HBV) infection. HBV can cause acute or chronic hepatitis. Acute hepatitis is more common among adults and the symptoms include loss of appetite, diarrhoea, vomiting, tiredness, jaundice and myalgia. Children infected with HBV usually remain asymptomatic, but may later develop chronic infection which often leads to cirrhosis, malignancy and death. People who are infected can spread HBV to others, even if they are asymptomatic.

Hepatitis B virus is spread through contact with the blood or other body fluids of an infected person. Transmission of disease can occur from:

- ▶ infected mother to infant during vaginal delivery;
- ▶ contact with infected blood and body fluids through breaks in the skin such as bites, cuts, or sores;
- ▶ having unprotected sex with an infected person;
- ▶ sharing needles when injecting drugs;
- ▶ needle stick injuries;
- ▶ another infected household member, horizontally.

Active Immunisation

The recommended vaccines for immunisation are:

Hepatitis B vaccine (adult or paediatric dose)

Hepatitis B/Hepatitis A combined vaccine (adult or paediatric dose)

Diphtheria/Tetanus/Pertussis/Polio/Hib/Hepatitis B combined vaccine

Hepatitis B vaccine is a recombinant DNA vaccine meaning that through genetic engineering, hepatitis B surface antigen is produced from yeast cells, then harvested and purified. The result is a subunit vaccine which does not contain any human blood products.

Immunisation is by a 3-dose series normally spread over 6 months.

Recommendations

The Hepatitis B vaccine should be given to all children from 12 months of age, except in high risk infants where vaccination is carried out at birth. If the hepatitis B vaccine is given as part of a six-antigen combination vaccine (DTaP/IPV/Hib/HepB), the course may be started at 6 weeks of age, but in this case a fourth dose in the second year of life is recommended.

Furthermore, all unvaccinated adults at risk of HBV infection should be vaccinated. These include:

- ▶ sex partners of people infected with HBV,
- ▶ men who have sex with men,
- ▶ people who inject street drugs,
- ▶ people with more than one sexual partner,
- ▶ people with chronic liver or kidney disease,
- ▶ people with jobs that expose them to human blood,
- ▶ household contacts of people infected with HBV,
- ▶ residents and staff in institutions for the developmentally disabled,
- ▶ renal dialysis patients,
- ▶ people who travel to countries where hepatitis B is common,
- ▶ people with HIV infection.

The following schedule is normally used when administering the monovalent *Hepatitis B vaccine*:

Children from birth up to 16 years of age:

Dose 1	0.5ml i.m.
Dose 2	0.5ml i.m. one month after 1 st dose
Dose 3	0.5ml i.m. five months after 2 nd dose

Adults and children over 16 years of age:

Dose 1	1ml i.m.
Dose 2	1ml i.m. one month after 1 st dose
Dose 3	1ml i.m. 5 months after 2 nd dose

No further booster doses are normally required.

Dialysis patients and other immunocompromised persons:

Under 16 years of age: 0.5ml i.m. in 3 doses at 0, 1 and 6 months.

Over 16 years of age: 2ml (double vaccine dose administered at the same site) i.m. in 4 doses at 0, 1, 2 and 6 months.

Accelerated schedule:

Under 16 years of age: 0.5ml i.m. at 0, 1, 2 and 12 months.

Over 16 years of age: 1ml i.m. at 0, 1, 2 and 12 months.

This schedule is designed for certain populations (e.g. neonates born to hepatitis B infected mothers, others who have or might have been recently exposed to the virus, certain travellers to high-risk areas). If this alternate schedule is used, a fourth dose given 12 months after the first dose is recommended for prolonged maintenance of protective titres.

When Hepatitis B is given as part of the *Diphtheria, Tetanus, Polio, Pertussis, Hib* combined vaccine the following schedule is used:

1 st Dose	0.5ml i.m. at 6 weeks to 2 months of age
2 nd Dose	0.5ml i.m. at 3 months of age
3 rd Dose	0.5ml i.m. at 4 months of age
Booster dose	0.5ml i.m. at 12 to 18 months of age.

When Hepatitis B is given as a combined vaccine with Hepatitis A, the following schedule is used:

Children from 1 to 15 years of age:	1 st dose	0.5ml i.m
	2 nd dose	0.5ml i.m. after 1 month
	3 rd dose	0.5ml i.m. 5 months after 2 nd dose

Adults 16 years and over:	1 st dose	1ml i.m.
	2 nd dose	1ml i.m. after 1 month
	3 rd dose	1ml i.m. 5 months after 2 nd dose

An accelerated schedule for this combination also exists where 3 doses are given at 0, 7 and 21 days with a booster dose after 12 months to obtain lasting immunity.

Adverse Reactions

The Hepatitis B vaccine is generally well tolerated. The most frequently reported systemic adverse reactions in decreasing order of frequency are irritability, fever, diarrhoea, fatigue/weakness, diminished appetite, and rhinitis. The Hepatitis B vaccine is not associated with increased incidence or exacerbations of multiple sclerosis. Of those children experiencing a side effect, most will have only a very mild reaction, such as soreness at the injection site (fewer than one out of three children) or low-grade fever. Adults are slightly more likely to experience such mild symptoms. Serious allergic reactions following hepatitis B vaccination are rare.

Contraindications

1. Persons who had a serious allergic reaction to one dose of the hepatitis B vaccine should not have another dose of the hepatitis B vaccine.
2. Persons with a history of hypersensitivity to yeast should not receive this vaccine.
3. Persons with a moderate or severe acute illness should postpone receiving the vaccine until their condition has improved.

Immunological Testing Following Vaccination

Testing after vaccination is not recommended routinely. Testing after vaccination is recommended only for people whose medical care is affected by knowledge of their response to the vaccine. This includes infants born to HBV infected mothers; healthcare and public safety workers at risk of continued exposure to blood and body fluids; immunocompromised people (e.g. people with AIDS or on haemodialysis); and sex and needle-sharing partners of people with chronic HBV infection. Testing should be performed 1-2 months after the last dose of the vaccine.

Protocol for Non-responders

If anti-HBs antibody titre is less than 10 mIU/ml when taken 1-2 months after the last dose of the primary course of vaccination, a further dose should be given and testing for anti-HBs should again be carried out 1-2 months later. If the result is still negative, a second vaccine series may be given. If testing after this series is still negative, then the person is considered a non-responder to hepatitis B vaccination. These persons should be counselled about precautions to prevent HBV infection and the need to obtain hepatitis B immune globulin (HBIG) prophylaxis for any known or likely exposure to HBsAg-positive blood.

Storage

The vaccine should be stored at +2°C to +8°C.

Hepatitis A

Introduction

Hepatitis A is an acute, usually self-limiting disease of the liver caused by the hepatitis A virus (HAV). HAV is transmitted from person to person, primarily by the faecal-oral route. In young children HAV infection is usually asymptomatic whereas symptomatic disease occurs more commonly among adults. Infection with HAV induces lifelong immunity. The clinical course of acute hepatitis A is indistinguishable from other types of acute viral hepatitis. Symptoms typically include fever, malaise, anorexia, nausea and abdominal discomfort, followed by dark urine and jaundice. The severity of disease and mortality increases in older age groups. The convalescence following hepatitis A infection may be slow, and is characterised by fatigue, nausea and lack of appetite. Complications of hepatitis A include relapsing hepatitis, cholestatic hepatitis and fulminant hepatitis. Fulminant hepatitis occurs in approximately 0.01% of clinical infections and is characterised by rapid deterioration in liver function and a very high fatality rate. Chronic infection with HAV does not occur. No specific antiviral therapy is currently available.

In regions of low disease endemicity, vaccination against hepatitis A is indicated for individuals with increased risk of contracting the infection, such as:

- a)** Laboratory workers
- b)** Travellers to areas of intermediate or high endemicity
- c)** Contacts of persons with Hepatitis A infection
- d)** Intravenous drug users

Active Immunisation

Hepatitis A vaccine contains Hepatitis A virus grown on human diploid cells and which is harvested, purified and inactivated. The recommended vaccines for immunisation are

Hepatitis A Vaccine Adult

Hepatitis A Vaccine Paediatric

Hepatitis A and Hepatitis B combined Vaccine Adult

Hepatitis A and Hepatitis B combined Vaccine Paediatric

Immunisation is by a 2-dose series in the case of the monovalent preparation and a 3-dose series if the combination preparation is used. The vaccine should only be given to children over 1 year of age.

Recommendations

The following schedule is normally used when administering the monovalent Hepatitis A vaccine:

Children over 1 year of age:

Dose 1 0.5ml i.m.

Booster 0.5ml i.m. six to twelve months after 1st dose

Adults and children over 15 years of age:

Dose 1 1ml i.m.

Booster 1ml i.m. six to twelve months after 1st dose

If the combination preparation with Hepatitis B is used, the following schedule should be adopted:

Children over 1 year of age

Dose 1 0.5ml i.m.

Dose 2 0.5ml i.m. one month after 1st dose

Dose 3 0.5ml i.m. five months after 2nd dose

Adults and children over 15 years of age:

Dose 1	1ml i.m.
Dose 2	1ml i.m. one month after 1 st dose
Dose 3	1ml i.m. 5 months after 2 nd dose

In the case of travellers, the vaccine should be given at least 2 weeks before travel to the high risk area.

Adverse Reactions

The most commonly reported adverse reactions are soreness at the injection site and headaches. Both reactions are self-limiting.

Contraindications

History of a severe allergic reaction to a previous Hepatitis A-containing vaccine, or to any of the components of the vaccine.
Febrile illness at the time of vaccination.

Storage

The vaccine should be stored at +2°C and +8°C.

Bacillus Calmette-Guérin (BCG) (Tuberculosis)

The BCG vaccine is a live-attenuated strain derived from *Mycobacterium bovis*. It offers documented protection mostly against the most severe forms of the disease, namely meningeal and miliary tuberculosis in children. This vaccine is only available from the Immunisation Section in the Department of Primary Health Care.

Recommendations

The following groups are recommended for immunisation with the BCG vaccine:

- ▶ School children between the ages of 12-14 years
- ▶ Healthcare workers who may have contact with infectious patients or their specimens
- ▶ Veterinary and other staff who handle animal species known to be susceptible to tuberculosis
- ▶ Contacts of patients suffering from active pulmonary TB
- ▶ Newborn infants of parent/s coming from countries with high incidence rates of TB.

The BCG vaccine is also recommended for the following two groups of travellers:

- ▶ Previously unvaccinated tuberculin-negative travellers under 16 years of age, going to live or work with local populations for three or more months in a country where the annual incidence is $\geq 40/100,000$ persons
- ▶ Individuals at occupational risk including healthcare workers aged less than 35 years, irrespective of the duration of stay.

Recommendations

The vaccine should be administered intradermally, at the site of the deltoid insertion on the left arm. Infants below 12 months of age should receive half the dose given to older children.

Adverse Reactions

Correct intradermal BCG vaccination usually results in minor local reactions: erythema, induration and tenderness. This is often followed by a small ulceration at the site of injection. Within a few months the local reaction is followed by a small scar.

Severe injection site reactions, large ulcers and abscesses are most commonly caused by a faulty injection technique where the dose is administered too deeply (subcutaneously instead of intradermally). To avoid this, health professionals who administer BCG vaccine should be trained in the technique of intradermal injection.

General reactions are rare and mostly consist of lymph adenitis with or without suppuration and discharge. Very rarely a lupoid type of local lesion has been reported.



Figure 8: Intradermal administration of the BCG vaccine

Source: Expert Rev Vaccines © 2008 Expert Reviews Ltd

Contraindications

- ▶ Those on corticosteroids or other immunosuppressive treatment including radiotherapy
- ▶ Patients suffering from a malignant condition such as lymphoma, leukaemia, Hodgkin's disease or other tumour of the reticulo-endothelial system
- ▶ Persons having impaired immunological function, as in hypogammaglobulinaemia and neutrophil disorders
- ▶ HIV-positive individuals and infants born to HIV-positive mothers
- ▶ Pregnancy. It is wise to avoid immunisation in the early stages and if possible to delay it until after delivery
- ▶ Positive tuberculin skin test result : Mantoux reading ≥ 6 mm induration
- ▶ Pyrexia
- ▶ Generalised septic skin conditions. If the patient is suffering from eczema, an immunisation site that is free from skin lesions should be chosen
- ▶ The BCG vaccine may be given concurrently with another live vaccine either at the same time or at an interval of at least 4 weeks between such vaccines. No further immunisations should be given for at least 3 months in the arm used for BCG immunisation because of the risk of regional lymphadenitis.
- ▶ When BCG is given to infants, there is no need to delay the primary immunisations, including oral polio vaccination.

Storage

The freeze dried vaccine should be protected from light, stored between $+2^{\circ}\text{C}$ and $+8^{\circ}\text{C}$ and never frozen. It has a shelf life of 12 to 18 months and should not be used after the expiry date.

Pneumococcal Disease

Introduction

Pneumococcal disease is an infection caused by a bacterium called *Streptococcus pneumoniae* (pneumococcus). *S. pneumoniae* is an encapsulated Gram positive bacterium which is a common commensal of the nasopharynx in humans, especially in children. Although >90 pneumococcal serotypes have been described (differentiated by chemical differences in the polysaccharide capsule), globally only 12-14 serotypes are frequently associated with disease. Worldwide, morbidity and mortality from pneumococcal infections are high. Acute otitis media and pneumonia are responsible for the majority of the disease burden of pneumococcal infections, with bacteraemia and meningitis being serious manifestations of invasive disease. Invasive pneumococcal disease occurs more frequently in children <5 years of age (especially those <2 years old), smokers, the elderly aged >65 years and in individuals with certain immune defects, such as splenic dysfunction. Rates of antibiotic resistance in the pneumococci are increasing, making management more difficult. Pneumococcal disease can take the form of: (symptoms in brackets)

- ▶ pneumococcal pneumonia (fever, cough, shortness of breath, and chest pain)
- ▶ meningitis (stiff neck, fever, mental confusion and disorientation, and visual sensitivity to light - photophobia)
- ▶ middle ear infection - otitis media (painful ear, a red or swollen eardrum, and sometimes sleeplessness, fever and irritability)
- ▶ bacteraemia - (similar to some of the manifestations of pneumonia and meningitis. Symptoms are joint pains, chills and possibly a rash).

Pneumococcal disease can be severe and fatal, in some cases resulting in long-term problems, like neurological damage, hearing loss, and limb loss.

S. pneumoniae is an obligate human pathogen. Close contact is necessary for transmission which occurs through aerosol, droplets or direct contact with infected respiratory secretions from a carrier or an individual with pneumococcal disease.

Active Immunisation

The following at risk individuals should be immunised with the pneumococcal vaccine:

- ▶ children <5 years of age
- ▶ children with respiratory disease secondary to aspiration, or a neuromuscular disease (e.g. cerebral palsy) who are at risk of aspiration
- ▶ the elderly
- ▶ smokers
- ▶ patients with
 - ▶ chronic bronchitis and emphysema
 - ▶ bronchial asthma
 - ▶ bronchiectasis or cystic fibrosis
 - ▶ interstitial lung fibrosis
 - ▶ pneumoconiosis
 - ▶ bronchopulmonary dysplasia (BPD)
 - ▶ absent or non-functioning spleen
 - ▶ HIV infection at all stages
- ▶ other causes of impaired immunity like patients undergoing chemotherapy, individuals on or likely to be on systemic steroids for more than a month at a dose equivalent to prednisolone at 20mg or more per day (any age), or for children under 20kg, a dose of 1mg or more per kg per day
- ▶ skull defects, cerebrospinal fluid (CSF) leaks, cochlear implants or fractures of the skull
- ▶ ischaemic heart disease
- ▶ congenital heart disease
- ▶ hypertension with cardiac complications
- ▶ chronic heart failure

- ▶ chronic renal disease like nephrotic syndrome, chronic renal failure and renal transplantation
- ▶ liver conditions like cirrhosis, biliary atresia and chronic hepatitis
- ▶ diabetes mellitus requiring insulin or oral hypoglycaemic drugs.

There are two types of the pneumococcal vaccine:

Pneumococcal polysaccharide vaccine (PPV) (Pneumo 23[®], Pneumovax II[®])

- ▶ contains purified capsular polysaccharides from each of 23 capsular types* of the pneumococcus
*1, 2, 3, 4, 5, 6B, 7F, 8, 9N, 9V, 10A, 11A, 12F, 14, 15B, 17F, 18C, 19F, 19A, 20, 22F, 23F, 33F
- ▶ there is a poorer response in those with immunological impairment (e.g. multiple myeloma, Hodgkin's and non-Hodgkin's lymphoma and chronic alcoholism) and those with an absent or dysfunctional spleen
- ▶ it is 50 to 70% effective in preventing pneumococcal bacteraemia
- ▶ not effective in protecting against non-bacteraemic pneumococcal pneumonia
- ▶ does not prevent otitis media or exacerbations of chronic bronchitis
- ▶ antibody levels usually begin to wane five years post-immunisation, but may decline more rapidly in asplenic patients and in children with nephrotic syndrome.

Pneumococcal conjugate vaccine (PCV)

PCV contains polysaccharide chains conjugated to a protein. Conjugation improves the antibody response in young children from 2 months of age. It protects against specific types of pneumococcal meningitis, bacteraemia, pneumonia and otitis media. There are 2 formulations of PCV:

- A.** one that contains polysaccharides from ten[†] common capsular types (Synflorix[®]) and which incorporates the protein D of non-typeable *Haemophilus influenzae* (NTHi)
[†]1, 4, 5, 6B, 7F, 9V, 14, 18C, 19F, 23F.
▶ indicated in children from 6 weeks to 2 years of age
- B.** one contains polysaccharides from thirteen^{††} common capsular types (Prevenar 13[®]) and which utilises CRM 197 as a carrier protein.
^{††}1, 3, 4, 5, 6A, 6B, 7F, 9V, 14, 18C, 19A, 19F, 23F.
▶ indicated in children from 6 weeks to 5 years of age

Recommendations

PPV

Adults over 65 years and at-risk groups aged two years or over:
A single dose of 0.5ml of PPV.

Booster doses should be administered at 5 year intervals in patients with asplenia, splenic dysfunction or chronic renal disease.

In patients with HIV, an additional dose may need to be given if they do not mount an adequate antibody response.

PCV

Children aged 6 weeks to 6 months:

2 or 3 doses (0.5ml) starting at 6-8 weeks of age, with at least a one month interval between doses. A booster dose is recommended at 11-15 months of age.

If forming part of a routine immunisation programme, 2 doses (0.5ml) starting at 6-8 weeks, with at least a 2 month interval between each dose. A 3rd dose is recommended at 11-15 months of age.

Infants aged 7-11 months:

2 doses (0.5ml), with at least 1 month interval between each dose. A booster dose is recommended in the 2nd year of life.

Children aged 12-23 months:

2 doses (0.5ml), with at least a 2 month interval between each dose.

Children aged 2-5 years:

Prevenar 13[®]: 1 dose of 0.5ml

Pre-term infants:

3 doses of 0.5ml each starting at 2 months of age with an interval of at least 1 month between doses. A booster dose is recommended at least 6 months after the last primary dose.

Children and adults requiring splenectomy or who are commencing immunosuppressive treatment (if previously unvaccinated):

- ▶ immunise according to the schedule for this specific risk group
- ▶ children under five years of age who have been fully immunised with PCV as part of the routine programme and who then develop splenic dysfunction more than one year after completing immunisation should be offered an additional dose of PCV
- ▶ ideally, immunise four to six weeks before elective splenectomy or initiation of treatment such as chemotherapy or radiotherapy. If this is not possible, it can be given up to two weeks before
- ▶ if splenectomy is performed urgently, immunisation should be delayed until at least two weeks after the operation
- ▶ immunisation should also be delayed until at least three months after completion of chemotherapy if it is not possible to do this before (as above). This will maximise the antibody response.

Adverse Reactions

PCV

- ▶ Swelling and redness at the injection site
- ▶ Low grade fever

PPV

- ▶ Mild soreness and induration at the site of injection lasting one to three days
- ▶ low grade fever (less common)

Contraindications

The vaccines should not be given to those who have had:

- ▶ a confirmed anaphylactic reaction to a previous dose
- ▶ a confirmed anaphylactic reaction to any component of the vaccines

If an individual is acutely unwell, immunisation should be postponed until full recovery. Immunisation should not be postponed in those with minor illnesses without fever or systemic upset.

Pregnancy and breast-feeding

Pneumococcal vaccines may be given to pregnant women when the need for protection is required without delay. There is no evidence of any risk from these vaccines in pregnant women or those who are breast-feeding. However, the SPCs of the individual vaccines advise caution in these situations (see also Cautionary note below).

Storage

Vaccines should be stored in the original packaging at +2°C to +8°C and protected from light.

Cautionary note

Since more than one vaccine has been described above, it is always advisable to check the SPCs of the individual vaccines for full details and updated information.

Serogroup C Meningococcal Disease

Introduction

Neisseria meningitidis, also known as the meningococcus, is a Gram negative encapsulated bacterium that is a strict human pathogen. Serogroup classification of the meningococcus is based on the biochemical composition of the polysaccharide capsule with six serogroups, namely A, B, C, W-135, Y and more recently X, being responsible for most cases of invasive meningococcal disease worldwide. *N. meningitidis* serogroups B and C are the most prevalent circulating serogroups in Europe. Although all age groups may be affected, the majority of the disease burden of meningococcal meningitis or septicaemia occurs disproportionately in infants, followed by 1-4 year old children and adolescents. Despite major advances in intensive care and the prompt initiation of appropriate antibiotics, the overall mortality rate from meningococcal disease reaches 8-14%. Permanent long-term disabilities such as hearing loss, neuro-developmental impairment, seizures and amputations are seen in 11-19% of survivors.

About 10% of adults are colonised with *N. meningitidis* during non-epidemic settings. Transmission occurs through mucosal exposure to infected respiratory droplets or secretions from a carrier or an individual with meningococcal disease. Progression from colonisation to infection is incompletely understood but certain risk factors, such as age (as described above), overcrowding, intimate contact and immunodeficiency, for example terminal complement deficiency and splenic dysfunction, are associated with a higher risk of meningococcal disease. Invasive meningococcal disease may occur within 1-14 days of exposure.

Active Immunisation

Vaccination is the most rational approach to prevent invasive meningococcal disease. A comprehensive serogroup B vaccine is currently unavailable. A polysaccharide vaccine against serogroups A, C, W-135 and Y is available for individuals over 2 years of age. For infants from the age of 2 months a polysaccharide-protein conjugate meningococcal serogroup C vaccine is able to induce protection against *N. meningitidis* serogroup C. This is administered intramuscularly. A 2 dose primary vaccination schedule, followed by a booster dose in the second year of life, induce robust immunity against serogroup C disease, although another boost at around 12 years of age might be necessary to sustain immunity through adolescence. Children from 1 year of age and adults require one dose of the meningococcal C conjugate vaccine.

Adverse reactions

- ▶ Swelling and redness at the injection site
- ▶ Low grade fever

Storage

Vaccines should be stored in the original packaging at +2°C to +8°C and protected from light.

Varicella-zoster Virus

Introduction

The varicella-zoster virus (VZV) is a herpes DNA virus which is a strict human pathogen. Primary infection, which manifests as varicella (chickenpox), may occur at any age but is more common in 1-9 year old children in temperate climates. Characteristically, VZV establishes latency and, following re-activation, may manifest as herpes zoster. Similar to the presentation of primary infection, reactivation may occur in all ages but is more prevalent in the elderly who have an increased risk of post-herpetic neuralgia. In healthy children varicella is usually a self-resolving disease but may rarely result in serious complications such as bacterial superinfection of the skin lesions that may progress to necrotising fasciitis, thrombocytopenia, pneumonitis, hepatitis, arthritis, osteomyelitis, and central nervous system manifestations including cerebellar ataxia, meningoencephalitis and intracranial vasculitis. Adults and pregnant mothers are more prone to get severe chickenpox complicated by pneumonitis. In addition, varicella during the first 20 weeks of pregnancy may result in congenital varicella syndrome in 2% of infants. Varicella infection in newborns and in the immunocompromised often disseminates to involve multiple organs and may be fatal. Approximately 1/4000 children with VZV infection will develop encephalitis.

Varicella is extremely contagious with an attack rate reaching >85% following exposure. In healthy individuals the contagious period starts 1-2 days before the appearance of the rash and lasts until all the lesions have crusted, usually within 5-7 days. Transmission occurs by respiratory droplets or through aerosols from the skin lesions. The incubation period varies from 10-21 days with an average of 14-16 days.

Recommendations

Live attenuated varicella-zoster vaccines may be given as from the age of 12 months and are administered subcutaneously. Two doses are now recommended for all age groups, separated by an interval of at least 4-8 weeks (an interval of 3 months is ideal for children <12 years of age). When given within 96 hours of exposure the VZV vaccine is 80-90% effective in preventing moderate to severe disease in varicella susceptible individuals. The VZV vaccine should not be given to infants, during pregnancy and to most immunocompromised individuals.

A combination vaccine containing Measles, Mumps, Rubella and Varicella-zoster (MMRV) is available and can be given between the ages of 12 months and 12 years in 2 doses with an interval of 6 weeks to 3 months between doses.

Passive immunisation

Following exposure to VZV, human varicella-zoster immunoglobulin (VZIG) is used to protect susceptible high risk individuals, including newborns exposed to maternal varicella, non-immune pregnant mothers and the immunocompromised. VZIG is only available from hospital.

Seasonal Influenza

Introduction

Influenza is an acute viral disease of the respiratory tract affecting all age groups and typically prevalent during the winter months. It is characterised by the abrupt onset of fever, chills, cough, headache, myalgia and prostration. Children may present with fever, vomiting and diarrhoea. It is usually a self-limiting disease with recovery in two to seven days, but it can be a serious illness especially in those with underlying chronic medical conditions, the elderly and women in the last trimester of pregnancy. In these cases, complications are common and hospitalisation rates are high. The main causes of increased mortality are secondary bacterial pneumonia and complications of the underlying disease.

Influenza is highly infectious and rapid spread by droplet infection and hand to mouth transmission is common and can lead to epidemics. The incubation period is 24 to 72 hours and shedding of the virus can occur up to 7 days after the start of infection and even longer in children. The highest rates of infection are often in school age children since they are usually in close contact with each other in class and during play. Institutions are also susceptible to rapid spread of the disease.

Influenza may be of three major types A, B or C. Most outbreaks of influenza are caused by type A viruses. Influenza virus is antigenically labile due to the tendency for change in the main surface antigens, haemagglutinin and neuraminidase. Minor changes known as “antigenic drift” are seen progressively from season to season, necessitating the annual change in the composition of the seasonal flu vaccine. Sometimes, mixing of the virus with non-human influenza virus can lead to the acquisition of a completely different haemagglutinin or neuraminidase. This is known as “antigenic shift” and results in the formation of a new subtype of influenza virus for which populations have little or no immunity.

Emergence of new influenza virus subtypes may lead to pandemics. This is typically exemplified by the 2009 - 2010 A(H1N1) influenza pandemic.

Active Immunisation

The influenza vaccine is prepared each year using virus strains similar to those considered most likely to be circulating in the forthcoming season. Current vaccines are trivalent containing two type A and one type B virus strains. Monovalent vaccines are produced against one particular virus strain in the case of new strains which may cause pandemics. Annual immunisation against seasonal influenza is necessary with a vaccine containing the most recent strains as declared by the World Health Organization prior to production of the annual vaccine. Patients should be warned that many other organisms cause respiratory infections during the influenza season and that influenza vaccine will not prevent these infections. It will also not protect against the common cold.

Recommendations

Yearly flu vaccination should begin in September, or as soon as the vaccine is available, and continue throughout the influenza season into December, January, and beyond. This is because the timing and duration of influenza seasons vary. While influenza outbreaks can happen as early as October, most of the time influenza activity peaks from mid-December to January.

In February 2010, in the wake of the influenza pandemic, vaccine experts worldwide recommended that everyone aged 6 months and older should get a flu vaccine each year starting with the 2010-2011 influenza season. While everyone should get a flu vaccine each flu season, it is especially important that the following groups get vaccinated either because they are at high risk of having serious flu-related complications or because they live with or

care for people at high risk for developing flu-related complications:

1. Health Care workers
2. Pregnant women
3. Children younger than 5, but especially children younger than 2 years of age
4. People 50 years of age and older
5. People of any age with certain chronic medical conditions
6. People who live in nursing homes and other long-term care facilities.

Doses:

- ▶ Adults and children over 8 years - a single injection of 0.5ml i.m.
- ▶ Children aged 3-8 years - 0.5 ml i.m. repeated after 4 weeks if receiving the influenza vaccine for the first time.
- ▶ Children aged 6 months to 35 months - 0.25ml i.m. repeated after 4 weeks if receiving the influenza vaccine for the first time.

Adverse Reactions

Different side effects can be associated with the influenza vaccine. The viruses in the vaccine are inactivated and cannot cause influenza. Some minor side effects that could occur are:

- ▶ Soreness, redness, or swelling at the site of vaccine administration
- ▶ Fever (low grade)
- ▶ Aches and pains.

If these problems occur, they begin soon after vaccination and usually last 1 to 2 days. Almost all people who receive the influenza vaccine have no serious problems from it. However, on rare occasions, vaccination can cause serious problems, such as severe allergic reactions. This may be caused by residual egg proteins in the vaccine or by one of its excipients.

Contraindications

There are some people who should not get the flu vaccine without first consulting a physician. These include:

- ▶ People who have a severe allergy to chicken eggs
- ▶ People who have had a severe reaction to an influenza vaccination
- ▶ Children less than 6 months of age (influenza vaccine is not approved for this age group), and
- ▶ People who have a moderate-to-severe illness with fever (they should wait until they recover to get vaccinated)

Storage

The vaccine should be stored at +2°C to +8°C and protected from light.

Human Papilloma Virus (HPV)

Introduction

The first link with cervical neoplasia was first established in 1983. There are over 100 different types of HPV; 99.7% of cases establish the presence of HPV in cervical carcinoma. HPV types may be subdivided into two:

High risk: associated with cervical cancer and precancerous lesions

Low risk: not associated with cervical cancer but can cause genital warts.

Table 3: HPV vaccines

Vaccine/Manufacturer	HPV types	Oncogenic	Non-oncogenic
Silgard®/MSD	6/11/16/18	Types 16/18	Types 6/11
Cervarix®/GSK	16/18	Types 16/18	0

Documented evidence shows that in Malta the average annual number of new cases of cervical carcinoma is approximately 11 cases per annum and the average annual number of attributable deaths is 5.

The virus is introduced into the cervix through a foreign body or a microabrasion. The main mode of transmission for HPV is the sexual route. When the virus replicates, there is the production of late HPV proteins (L1 & L2) as well as early HPV proteins (E1, E2, E5, E6 & E7). Initial HPV infection may lead to persistent infection (Cervical Intraepithelial Neoplasia CIN 1) within a period of 3–6 months. The immune system may clear the initial HPV infection or alternatively the persistent infection may progress to CIN 2 or 3 within a period of 4-5 years. CIN 2/3 may persist for 9-15 years which together with co-factors (viral, host, environmental) may lead to cervical cancer. Persistent infection is critical for development of neoplastic change. HPV may also lead to vaginal/vulvar, penile,

anal, oro-pharyngeal, laryngeal and aerodigestive tract carcinoma besides cervical carcinoma.

The neoplasia related HPV types include HPV 16 (53%), HPV 18 (13%), HPV 45 (5%), HPV 31 (4%) and HPV 33 (3%). Infection with oncogenic HPV types is the most significant risk factor in cervical cancer aetiology. Established co-factors involved in HPV carcinogenesis include high parity, oral contraceptive use, smoking and HIV infection. Potential co-factors include co-infection with other sexually transmitted infections, diet, endogenous hormones and genetic factors. HPV is transmitted mainly through sexual intercourse but can also be transmitted by orogenital or hand-genital routes. Proper condom use may help to reduce the risk but is not fully protective against infection. Nonsexual routes include vertical transmission from mother to infant as well as transmission via fomites which has been hypothesised but not well documented. The HPV can also cause genital warts. Most individuals are unaware that they are infected by the virus and may unknowingly spread HPV.

Active Immunisation

There are two types of prophylactic HPV vaccines on the market. The Silgard[®] vaccine by MSD contains HPV types 6, 11, 16 and 18 L1 proteins. It is a recombinant vaccine and contains an aluminium adjuvant of 225mcg per dose. It is given intramuscularly and each 0.5 ml injection volume contains HPV types 6/11/16/18 (20/40/40/20 mcg, respectively).

The Cervarix[®] vaccine by GSK consists of recombinant L1 proteins which self assemble into Virus like Particles (VLP). It is composed of 20mcg L1 HPV-16 & 20 mcg HPV-18. The innovative adjuvant AS04 is composed of 500mcg Al(OH)₃ and 50mcg MPL.

Recommendations

The dosing regimen for Silgard[®] is 0, 2 and 6 months. However, the 2nd dose may be administered 1 month after the 1st dose and the 3rd dose may be given at least 3 months after the 2nd dose. All 3 doses should be given within a 1-year period.

The dosing for Cervarix[®] is 0, 1 and 6 months. There is an option to give the 2nd dose up to 2.5 months after the first dose and the 3rd dose can be given from 5 months up to 12 months after the 2nd dose.

Adverse reactions

The vaccine is generally well tolerated. The most common adverse event is local discomfort at the injection site.

Note: These vaccines offer an excellent protective effect and there are various studies confirming this which will be extended over a number of years in order to confirm long term protection. Since both vaccines contain antigens from HPV 16 and 18 these are expected to protect against at least 70% of cervical carcinoma. The vaccine that also contains HPV 6 and 11 antigens protects against at least 90% of genital warts. The vaccines should be stored at +2°C to +8°C and protected from light. They are supplied as suspensions of VLPs in pre-filled syringes. The vaccines are given intramuscularly. The HPV vaccines may be given at the same time as other vaccines but should be given at a separate site.

The aim of HPV vaccination is to protect females before sexual debut. Cervarix[®] is licensed for use in females from 10-25 years of age and Silgard[®] for females from the age of 9 years. There is no known risk of using the vaccine during pregnancy or whilst breastfeeding, however it is not recommended to immunise against HPV during pregnancy. It would be advisable to vaccinate individuals with HIV infection or individuals who are immunosuppressed even though the expected antibody response may not be induced.

Rotavirus

Introduction

Rotavirus (RV) is a *Reoviridae* virus of which many strains exist worldwide. All produce gastroenteritis (GE), which may manifest with profuse watery diarrhoea and vomiting, sometimes with fever and abdominal pain. These symptoms are caused by the rotaviruses sticking to and damaging the small bowel lining, resulting in malabsorption with significant water and salt loss from the bowel. The incubation period lasts from 0.5 to 4 days, followed by symptoms for 4-8 days. The disease is generally self-limiting in healthy well-nourished children. Natural immunity develops after 2-3 bouts of rotavirus gastroenteritis, with the first attack generally being the most severe. Complications result from subsequent dehydration due to excessive fluid losses from the bowel and this, together with concomitant electrolyte imbalance and occasionally secondary bacterial overgrowth, may lead to death.

Rotavirus is ubiquitous worldwide with very high levels of infection especially in young children, 95% of who are usually infected by 3-5 years of age. Indeed, it is the commonest cause of GE in the world, accounting for almost 50% of all cases of GE in both developed as well as in developing countries. Outbreaks of rotavirus GE occur throughout the year and are more likely to occur where many children are confined in cramped conditions with poor sanitation. Per annum, it accounts for >125 million cases of GE, with 2 million hospitalisations and 440,000 deaths worldwide. In Europe, rotavirus causes 2.8 million GE cases, 87,000 admissions to hospital and 230 deaths per year.

All children are at risk of rotavirus GE but especially those between 6-24 months of age, with younger infants being more vulnerable and at risk of severe disease and death in low income countries. Those requiring hospitalisation are generally admitted for a mean of three days, creating an additional socioeconomic burden as parents take time off work to attend to their sick children, productive workdays are lost and insurance claims escalate.

Rotavirus is predominantly spread by the faeco-oral route, but respiratory droplets also provide an important portal for infection. Viral particles abound in the faeces of infected individuals, may be shed before the diarrhoea sets in and continues after this has subsided. Rotavirus is particularly resistant to disinfectants and can contaminate inert objects for several days.

Diagnosis and Management

The diagnosis can be confirmed by identifying viral antigens in stool, enzyme immunoassay (ELISA) identification of RV proteins, and observation of rotavirus on electron microscopy of stool samples. The clinical picture, particularly during established outbreaks, is usually highly suggestive.

Management is aimed at preventing and treating dehydration. Hence, control of diarrhoea, prevention of vomiting and treating other symptoms such as fever is indicated and this could entail the use of probiotics and antipyretics, as required. Correction of fluid and electrolyte imbalance is paramount, and is often achieved with simple oral rehydration therapy (ORT). Hospitalisation with intravenous fluid replacement is required in those with or at risk of severe illness and, therefore, is far more likely in the less than one year olds.

Active Immunisation

Breastfeeding is the only effective, natural method that offers significant protection against rotavirus GE. When dealing with infected or suspected cases, rigorous disinfection, scrupulous hand washing and, in hospital, strict hygiene are required in order to prevent spread of the virus. Moreover, vaccination is available and effective in providing immunity against rotavirus on a large, population-based scale. Indeed, only vaccination can provide a significant impact on the burden of disease, worldwide.

Two vaccines have been produced that provide effective cover against the four most common (and fifth emerging) serotypes of rotavirus, including G1P1[8] that accounts for 65% of all cases, G2P[4], G3P1[8], G4P1[8] and G9P1[8] strain. A Human-Bovine pentavalent re-assorted live vaccine (Rotateq[®]) includes all these serotypes, thus offering homotypic protection against all 5 main serotypes. A monovalent Human live attenuated vaccine (Rotarix[®]) contains G1P1[8] antigen and offers heterotypic cross-protection against all 5 main serotypes.

Recommendations

As shown in Table 4, the human-bovine pentavalent live vaccine can be administered from 6 weeks of age and requires three doses of 2ml each given orally, at a minimum of 4-week intervals, which preferably has to be completed by 26 weeks of age. The Human monovalent live attenuated vaccine requires two 1.5ml doses, also taken orally from 6 weeks of age with a minimum 4-week interval between doses and which have to be completed by 24 weeks of age. Efficacy has been shown to cover up to 96% of RV gastroenteritis and adequate immunity is generally achieved 2 weeks after completion of the course.

Early protection against Rotavirus GE is crucial since young infants are most at risk.

Table 4: Rotavirus vaccine schedules

Dose: by mouth	Rotarix [®] (1.5ml)	Rotateq [®] (2ml)
1	6-10 weeks	6-12 weeks
2	10-24 weeks	10-22 weeks
3	-	14-26 weeks

Rotavirus vaccines can be safely given with other monovalent or combination vaccines.

Adverse Reactions

These are generally absent but mild to moderate diarrhoea, vomiting and fever may be observed in around 10% of vaccinees. Serious events are extremely rare.

Contraindications and Precautions

As with other vaccines, rotavirus vaccines should not be administered to children who are unwell (particularly febrile, have diarrhoea or vomiting). They must be avoided in those with previous serious adverse events, known hypersensitivities to any of the vaccine components and in those with any risk for developing intussusception. Their use in immunocompromised patients has not been studied but they should be avoided in severe immunodeficiency states and HIV. Live viral shedding in recipient stools may persist for some days after vaccination and carers and immunocompromised contacts should ensure careful hygiene.

Storage

Dry, dark refrigeration at +2°C to +8°C and not frozen.

Other Vaccines

The National Immunisation Service offers a number of other vaccines which are directed at selected groups considered at high risk of becoming infected through their particular occupation, or for individuals wishing to travel overseas for pleasure or business.

These vaccines include:

- Cholera
- Quadrivalent pure polysaccharide meningococcal ACW-135Y
- Rabies
- Typhoid
- Yellow Fever.

Doctors are urged to contact, or ask prospective travellers to contact the Immunisation Section at the Floriana Health Centre for advice on the vaccination requirements/recommendations as early as possible before the proposed travel date.

Further information on travel vaccinations may be obtained from the following websites:

www.who.int/ith/en/index.html

wwwnc.cdc.gov/travel/destinations/list.aspx

The National Immunisation Service also carries out specific ad hoc programmes of immunisation against particular diseases as part of a strategy for the prevention and/or control of epidemics. Specific guidelines for vaccination, other than those contained in this booklet, are issued in such situations.

The National Immunisation Schedule

Age	Vaccine
From 6 weeks	DTaP/IPV/Hib
3 months	DTaP/IPV/Hib
4 months	DTaP/IPV/Hib
12 months	Hep B
13 months	Hep B + MMR
18 months	Hep B + DTaP/IPV/Hib
3-4 years	MMR
12 years	BCG
16 years	Td/IPV

- ▶ In case of additions or alterations to the schedule mentioned above, further guidelines will be issued accordingly by the Superintendent of Health.
- ▶ In case of any difficulties or for further information, please contact:

National Immunisation Service

Floriana Health Centre

Tel: 2568 0222/3

Primary Health Directorate

7, Harper Lane, Floriana

Tel: 2557 6306, 2557 6120

Notes

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ADVISORY COMMITTEE ON IMMUNISATION POLICY MALTA



5B, The Emporium, C. De Brocktorff Str., Msida MSD 1421 Malta.
Tel: 2326 6000, Fax: 2326 6104, www.ehealth.gov.mt



**Ministry for Health, the Elderly
and Community Care**