Statement of Intent

These guidelines are meant to be a guide for clinical practice, based on the best available evidence at the time of development. Adherence to these guidelines may not necessarily ensure the best outcome in every case. Every health care provider is responsible for the management of his/her unique patient based on the clinical picture presented by the patient and the management options available locally.

Review of the Guidelines

These guidelines were issued in December 2003 and will be reviewed in December 2005 or sooner if new evidence becomes available.

CPG Secretariat
c/o Health Technology Assessment Unit
Medical Development Division
Ministry of Health Malaysia
21st Floor, Bangunan PERKIM
Jalan Ipoh
51200 Kuala Lumpur.

Available on the following website : http://www.moh.gov.my/medical/htm
: http://www.acadmed.org.my
# CLINICAL PRACTICE GUIDELINES ON ADULT VACCINATION

## EXPERT PANEL

<table>
<thead>
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<tr>
<td>Victor Lim (Chairperson)</td>
<td>Rationale for adult vaccination, Anthrax, Cholera, Plague, Travelers Immunocompromised</td>
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<tr>
<td>Chang Kian Meng, Hospital Kuala Lumpur</td>
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<tr>
<td>Cheong Soon Keng, Hospital Universiti Kebanngsaan Malaysia</td>
<td>Immunocompromised</td>
</tr>
<tr>
<td>Gan Gin Gin, University of Malaya Medical Center</td>
<td>Immunocompromised</td>
</tr>
<tr>
<td>Ilina Isahak, Hospital Universiti Kebanngsaan Malaysia</td>
<td>Immunocompromised</td>
</tr>
<tr>
<td>Ismail Merican, Dep Director General, Min of Health</td>
<td>Immunocompromised</td>
</tr>
<tr>
<td>Jayaram Menon, Queen Elizabeth Hosp, Kota Kinabalu</td>
<td>Influnza, Japanese encephalitis, Measles, Rubella, Mumps, Varicella, Hepatitis A, Hepatitis B, Typhoid, Diphtheria, Tetanus, Chronic Illnesses, Adults who have missed or failed to complete childhood vaccinations, Health Care Workers, Immunocompromised</td>
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<tr>
<td>Christopher Lee, Hospital Kuala Lumpur</td>
<td>Immunocompromised</td>
</tr>
<tr>
<td>Leong Chooi Fun, Hospital Universiti Kebanngsaan Malaysia</td>
<td>Meningococcus, Pneumococcus, Tuberculosis, Elderly, Other groups, Passive immunisation, Hepatitis A, Hepatitis B, Veterinarians and Animal Handlers</td>
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<tr>
<td>Nordiah Awang Jalil, Hospital Universiti Kebanngsaan Malaysia</td>
<td>Immunocompromised</td>
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<tr>
<td>Nurliza Ariffin, University of Malaya Medical Centre</td>
<td>Immunocompromised</td>
</tr>
<tr>
<td>Norshahidah Khairullah, Infectious Diseases Research Centre, IMR</td>
<td>Immunocompromised</td>
</tr>
<tr>
<td>Shamshad Begom Mohamed Shafie, Veterinary Research Centre</td>
<td>Immunocompromised</td>
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<td>Yasmin Malik, Hospital Universiti Kebanngsaan Malaysia</td>
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SECTION A - GENERAL

INTRODUCTION

Immunisation against infectious diseases is primarily directed towards infants, children and adolescents and has become a routine practice in paediatrics. However it is not commonplace in adult practice. There is a lack of awareness about the benefits of immunization in adults even though there is considerable morbidity and mortality due to vaccine-preventable diseases. In the United States influenza alone is responsible for 20,000 – 40,000 deaths annually. In epidemic years the mortality rises to 50,000 and this is accompanied by 500,000 excess hospitalizations at a cost of one billion dollars. Pneumococcal disease and hepatitis B infection are other examples of vaccine-preventable diseases that cause significant mortality and morbidity.¹

The primary objective for developing clinical practice guidelines on adult immunisation is to assist doctors and the public in making decisions on the appropriate use of vaccines in the adult population (defined as > 18 years). These recommendations on adult vaccination are evidenced based, appropriate to the Malaysian context and reflect current best practices. Groups of adults who are at a higher risk of contracting specific infections by virtue of their age, underlying diseases or occupation are identified and recommendations made for the appropriate vaccines.

It is hoped that the judicious use of vaccines will provide a cost-effective way of reducing the burden of morbidity and mortality due to infectious diseases among adults in Malaysia.

References.

LEVELS OF EVIDENCE

The scheme for level of evidence adopted in this document is the system devised by the Catalan Agency for Health Technology Assessment (CAHTA), Spain. The system is as follows:

<table>
<thead>
<tr>
<th>Level</th>
<th>Strength of Evidence</th>
<th>Study design</th>
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<tbody>
<tr>
<td>1</td>
<td>Good</td>
<td>Meta-analysis of RCT, Systematic Review</td>
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<tr>
<td>2</td>
<td>Good</td>
<td>Large sample RCT</td>
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<td>3</td>
<td>Good to Fair</td>
<td>Small sample RCT</td>
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<tr>
<td>4</td>
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<td>Non-randomised controlled prospective trial</td>
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<tr>
<td>5</td>
<td>Fair</td>
<td>Non randomized controlled prospective trial with historical controls</td>
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<tr>
<td>6</td>
<td>Fair</td>
<td>Cohort Studies</td>
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<tr>
<td>7</td>
<td>Poor</td>
<td>Case-control studies</td>
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<td>8</td>
<td>Poor</td>
<td>Non-controlled clinical series, descriptive studies multi-centre</td>
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<tr>
<td>9</td>
<td>Poor</td>
<td>Expert Committees, consensus, case-reports, anecdotes</td>
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In the text of this document, the level of evidence is stated in parenthesis and italicized.
GENERAL ADVICE ON VACCINATION

1. Contraindications

1.1. Immunisation should be postponed if the subject is suffering from any acute illness.

1.2. Live vaccines should not be administered to pregnant women because of the theoretical possibility of harm to the fetus.

1.3. Live vaccines should not be given to the following:
   
   1.3.1. patients on high dose corticosteroids or immunosuppressive treatment including irradiation;
   
   1.3.2. those suffering from malignant conditions such as lymphoma, leukaemia, or other tumours of the reticuloendothelial system;
   
   1.3.3. patients with impaired immunological mechanism like hypogammaglobulinemia

1.4. Individuals with immunosuppression from disease or chemotherapy, should not receive live virus vaccines until at least six months after chemotherapy has finished.

1.5. For those on high dose systemic corticosteroids (for adults; daily doses in excess of 20mg for more than two weeks or 60mg of prednisolone), live vaccines should be postponed until at least three months after treatment has stopped.

1.6. Live virus vaccines, with the exception of yellow fever vaccine, should not be given during the three months following injection of immunoglobulin because the immune response may be inhibited.

2. The following are NOT contraindications to vaccinations:

2.1. Minor infections in the absence of fever or systemic upset

2.2. Asthma, eczema, or hay fever

2.3. Treatment with antibiotics or locally-acting (eg topical or inhaled) steroids

2.4. Contact with an infectious disease

2.5. Homeopathy

2.6. History of allergy is NOT a contraindication. Hypersensitivity to eggs contraindicates influenza vaccine; previous anaphylactic reaction to egg contraindicates measles, mumps, rubella, influenza and yellow fever vaccines.
2.7 Siblings and close contacts of the immunosuppressed should be immunised against measles, mumps and rubella. There is no risk of transmission of virus following vaccination.

3. Reconstitution of vaccines
3.1 Freeze dried vaccines must be reconstituted with the diluent supplied and used within the recommended period after reconstitution.
3.2 Before injection, the colour of the product must be checked with that stated by the manufacturer in the package insert. The diluent should be added slowly to avoid frothing. A sterile 1.0-mL syringe with a 21G needle should be used for reconstituting the vaccine, and a small gauge needle for injection (23G for deep subcutaneous or intramuscular; 25G for intradermal injections)

4. Route of administration
4.1 By mouth
   Sugar lumps, if used, should be prepared with oral polio vaccine (OPV) immediately before administration. By allowing them to stand at room temperature for any length of time, it may decrease the potency of the vaccine.
4.2 Subcutaneous and intramuscular injections
   With the exception of BCG, all vaccines should be given by intramuscular or deep subcutaneous injection, preferably on the deltoid muscle.
4.3 Intradermal injections
   BCG vaccine is always given intradermally; rabies vaccine may also be given this way.
   Suitable sites for intradermal injections include:
   • For BCG: left deltoid muscle
   • For Tuberculin test: middle flexor surface of forearm
   • For rabies vaccine: behind posterior border of distal portion of deltoid muscle
5. **Anaphylaxis**

Recipients of vaccine should remain under observation until they have been seen to recover from the procedure.

Any individual carrying out immunization procedures must be able to distinguish between anaphylaxis, convulsions and fainting. The last is relatively common after immunisation of adults.

5.1 Symptoms of anaphylaxis include:

5.1.1 Pallor, limpness and apnoea

5.1.2 Upper airway obstruction: hoarseness and stridor as a result of angioedema

5.1.3 Lower airway obstruction: subjective feelings of retrosternal tightness and dyspnoea with audible expiratory wheeze from bronchospasm

5.1.4 Cardiovascular: sinus tachycardia, profound hypotension in association with tachycardia; severe bradycardia

5.1.5 Skin: rapid development of urticarial lesions – circumscribed, intensely itchy weals with erythematous raised edges and pale blanched centres.

5.2 Management of anaphylaxis

5.2.1 Lie patient in a left lateral position. If unconscious, insert airway

5.2.2 Give 1/1000 adrenaline by deep intramuscular injection **unless there is a strong central pulse and the patient’s condition is good.**

5.2.3 In adults, the dosage is 0.5 to 1.0-mL repeated as necessary up to a maximum of three doses. The lower dose should be used for the elderly or those of slight build.

5.2.4 If oxygen is available, give it by face mask

5.2.5 **Never leave the patient alone**

5.2.6 If appropriate, begin cardio-pulmonary resuscitation (CPR)

5.2.7 Chlorpheniramine maleate (piriton) 2.5 to 5.0-mg may be given **intravenously**. Hydrocortisone 100-mg intravenously may also be given to prevent further deterioration in severely affected cases

5.2.8 If there is no improvement in the patient’s condition in 10 minutes, repeat the dose of adrenaline up to a maximum of three doses

5.2.9 All cases should be admitted to hospital for observation
6. Storage and disposal of vaccines

6.1 On receipt, vaccines are immediately placed under the required storage conditions. Vaccines must not be kept at temperatures below 0°C as freezing can cause the deterioration of the vaccine and breakage of the container.

6.2 A maximum/minimum thermometer should be used in refrigerators where vaccines are stored, irrespective of whether the refrigerator incorporates a temperature indicator dial.

6.3 Special care should be taken when bringing the vaccine to room temperature to ensure that the temperature of the vaccine does not exceed the specified range. An insulated container should be used.

6.4 Reconstituted vaccine must be used within the recommended period, varying from one to four hours, according to the manufacturer’s instructions. Single dose containers are preferable. Once opened, multidose vials must not be kept after the end of the session and any vaccine left unused must be discarded. The reason is that reused vaccines may have reduced potency and there is also the risk of possible contamination. It is thus recommended that multi-dose vials be used for mass vaccination campaigns.

6.5 Unused vaccine, spent or partly spent vials, should be disposed of safely, preferably by heat inactivation or incineration. Contaminated waste and spillage should be dealt with by heat sterilisation, incineration or chemical disinfection as appropriate.

7. Vaccine Combinations

7.1 This is encouraged since it will reduce the number of injections and thus increase compliance.

7.2 Problems of combination:
   7.2.1 Side-effects may be more frequent and worse
   7.2.2 Reduced antibody response due to interference

7.3 Compatible combinations
   7.3.1 BCG + yellow fever
   7.3.2 BCG + DPT + oral polio
   7.3.3 BCG + measles + yellow fever + tetanus
   7.3.4 DPT + hepatitis B
   7.3.5 DPT + yellow fever
7.3.6  DPT + oral polio + yellow fever + measles
7.3.7  DPT + BCG + yellow fever + measles
7.3.8  Measles + mumps + rubella

7.4  Not encouraged :
7.4.1  DT + typhoid + oral polio
7.4.2  Cholera + yellow fever

8. References
1. Immunisation against Infectious Diseases. 1990. Department of Health Welsh Office, Scottish Home and Health Department, UK.
ANTHRAX

Introduction

Anthrax is an infection caused by *Bacillus anthracis*. It is primarily a disease of animals, particularly herbivorous animals, such as cattle, sheep, horses, mules, and goats. Humans become infected incidentally when brought into contact with diseased animals. More recently *Bacillus anthracis* has been used as a bioterrorist weapon. Malaysia is free from anthrax although the disease is endemic in Thailand and Indonesia. No human cases have ever been recorded in Malaysia and the last case in an animal occurred in 1976.

Vaccines available

A non-encapsulated toxigenic strain is used in animals. The Sterne Strain of *Bacillus anthracis* produces sublethal amounts of the toxin that induces formation of protective antibody. The animal vaccine should not be used in man. The anthrax vaccine for humans, which is used in the U.S., is a preparation of the protective antigen from culture filtrate of an avirulent, nonencapsulated strain of *Bacillus anthracis*.\(^1\) This vaccine is manufactured and distributed by BioPort Corporation, Lansing, Michigan for the Department of Defense of the US.

Mode of administration and dosing regimen

Three subcutaneous injections given two weeks apart followed by three additional subcutaneous injections given at 6, 12, and 18 months. Annual booster injections of the vaccine are required to maintain a protective level of immunity.

Contraindications and adverse reactions

The vaccine should only be administered to healthy individuals from 18 to 65 years of age. Pregnant women should not be vaccinated. Mild local reactions occur in 30% of recipients and consist of slight tenderness and redness at the injection site. Severe local reactions are infrequent and consist of extensive swelling of the forearm in addition to the local reaction. Systemic reactions occur in fewer than 0.2% of recipients.

Vaccines available in Malaysia

No anthrax vaccines are currently available in Malaysia.
Target groups in Malaysia

No target groups are identified in Malaysia

Evidence for effectiveness

In a recent metanalysis, two trials involving 16,052 people were included. Compared to placebo, vaccination was associated with a reduced risk of contracting anthrax (relative risk 0.16, 95% confidence interval 0.07 to 0.35). Compared to placebo, the killed vaccine was associated with a higher incidence and severity of adverse effects (odds ratio 5.15, 95% confidence interval 2.28 to 11.61). Just over 5% of participants in the vaccine group reported adverse effects. The effectiveness of the vaccine does not appear to be influenced by the route of inoculation. It was concluded that killed anthrax vaccines appear to be effective in reducing the risk of contracting anthrax with a relatively low rate of adverse effects. (Level 1)

References

b. Jefferson, T; Demicheli, V; Deeks, J; Graves, P; Pratt, M; Rivetti, D. Vaccines for preventing anthrax. Cochrane Database of Systematic Reviews. Issue 2, 2002
CHOLERA

Introduction

Cholera is a disease characterized by severe watery diarrhea and is caused by two serotypes of Vibrio cholerae namely 01 and 0139 (Bengal strain). There is a global resurgence of cholera and it is becoming an increasingly important public health challenge in a number of countries. Cholera is endemic in Malaysia and between 500 to 2000 cases are reported annually.

Vaccines available

Two types of vaccines are available. The parenteral killed whole cell vaccines have been used widely since the 1960s when large scale trials were conducted in Bangladesh, India and the Philippines. These vaccines are killed whole cell preparations of V.cholerae 01 cells containing a mixture of biotypes and serotypes. In the 1980s research into oral vaccines was started. There are two main types of oral vaccines. The first comprised oral killed whole cell vaccines containing a mixture of biotypes and serotypes, with or without added B subunit of cholera toxin. The second are live recombinant vaccines consisting of live attenuated strains of V.cholerae.

Mode of administration and dosing regimen

The parenteral vaccines are normally administered intramuscularly or subcutaneously in two doses given 7 to 28 days apart. The oral killed whole cell vaccine requires 2 or 3 doses given at 6 weeks interval. The oral live vaccine is administered as a single dose.

Contraindications and adverse reactions

Vaccination should be avoided during episodes of high fever, intercurrent illnesses and in pregnancy. The vaccine is also contraindicated in individuals with a known allergic reaction to a previous dose. Tenderness and induration may occur at the injection site. Fever and malaise following vaccination are infrequent and serious reactions are rare.

Vaccines available in Malaysia

- Berna Swiss Serum killed whole cell parenteral vaccine
**Target groups**

No target group is identified. WHO has deleted from the International Health Regulations the requirement for presentation of a cholera vaccination certificate and no country today requires proof of cholera vaccination as a condition for entry. Generally WHO also does not recommend the use of vaccines to prevent or control cholera outbreaks because it may give a false sense of security to vaccinated subjects and to health authorities, who may then neglect more effective measures.

**Evidence for effectiveness**

A recent systematic review of the efficacy and safety of cholera vaccines was undertaken by Graves et al.\(^1\) A total of thirty-two trials were included; seventeen efficacy trials involving over 2.6 million subjects and nineteen safety trials which involved 11,459 people. For all types of vaccines an efficacy rate of 51% was obtained. The authors concluded that cholera killed whole cell vaccines appear to be relatively effective and safe. Live oral recombinant vaccines appear to be safe, but efficacy data are not yet available. Protection against cholera appears to persist for up to two years following a single dose of vaccine, and for three to four years with an annual booster. *(Level 1)*

**References**

DIPHTHERIA

Introduction

Diphtheria is an acute, communicable, respiratory infection caused by *Corynebacterium diphtheriae*. The causative organism produces a toxin which results in local tissue destruction and membrane formation. The toxin may then undergo haematogenous dissemination resulting in myocarditis, neuritis, thrombocytopenia and proteinuria. Humans are the only known reservoir of *C. diphtheriae*. Carriers are important in disease transmission as natural or vaccine-induced immunity does not prevent carriage. Diphtheria occurs primarily among unvaccinated or inadequately vaccinated individuals. In Malaysia, the incidence of the disease has declined dramatically with the introduction of routine childhood immunisation and improved living standards. Small outbreaks may still occur in unimmunised communities. In 1995 only 1 case of diphtheria was reported while in 2001, 3 cases with 2 deaths were reported. Limited serosurveys done in the USA since 1977 indicate that 22%-62% of adults 18-39 years of age and 41%-84% of those greater than or equal to 60 years of age lack protective levels of circulating antitoxin against diphtheria.

Vaccines available

The vaccine is a toxoid derived from the toxin by treatment with formaldehyde. It is then adsorbed onto an aluminium salt, usually aluminium phosphate, and preserved with thimerosal. The combined preparation Td is recommended for use among adults because a large proportion of them lack protective levels of circulating antibody against tetanus. Furthermore, Td contains much less diphtheria toxoid than other diphtheria toxoid-containing products, and, as a result, reactions to the diphtheria component are less likely. Vaccination with any diphtheria toxoid does not, however, prevent or eliminate carriage of *Corynebacterium diphtheriae*.

Mode of administration and dosing regimen

The dose is 0.5ml given by deep intramuscular route. A primary series for adults is three doses of preparations containing diphtheria and tetanus toxoids, with the first two doses given at least 4 weeks apart and the third dose given 6-12 months after the second.

Contraindications and adverse effects

Neurologic or anaphylactic sensitivity to a previous dose of tetanus-diphtheria vaccine is the only contraindication. Pain, tenderness, localised erythema and oedema at the injection site have been reported. Fever and other systemic symptoms such as headache or malaise are rare.

Vaccines available in Malaysia and local sources

At time of printing Td is not yet available in Malaysia.
Target groups

- All adults lacking a completed primary series of diphtheria and tetanus toxoids should complete the series with Td.
- All adults for whom greater than or equal to 10 years have elapsed since completion of their primary series or since their last booster dose should receive a dose of Td. Thereafter, a booster dose of Td should be administered every 10 years. There is no need to repeat doses if the schedule for the primary series or booster doses is delayed.
- Patients who have recovered from diphtheria should complete the full immunisation schedule as the disease does not confer immunity.
- All household and other close contacts who have received less than three doses of diphtheria toxoid or whose vaccination status is unknown should receive an immediate dose of a diphtheria toxoid-containing preparation and should complete the primary series according to schedule. Close contacts who have completed a primary series of greater than or equal to three doses and who have not been vaccinated with diphtheria toxoid within the previous 5 years should receive a booster dose of a diphtheria toxoid-containing preparation appropriate for their age.

Evidence for effectiveness

Complete and appropriately timed vaccination is at least 85% effective in preventing diphtheria. Long-term efficacy rates of over 90% after 10 years have also been shown.

References

HEPATITIS A

Introduction

The term infectious hepatitis was coined in 1912 to describe outbreaks of jaundice, which have been reported over many centuries. In 1973, WHO adopted the term ‘hepatitis type A’ to describe this type of hepatitis the same year. Hepatitis A virus (HAV) is classified in the genus enterovirus of the family picornaviridae based on its biophysical and biochemical characteristics. HAV is transmitted by faecal-oral route. Person-person spread is the most common method of transmission in developed countries. Infections occur readily under conditions of poor sanitation, hygiene and overcrowding. Subclinical infection is common in children and severity tends to increase with age. Occasional cases of fulminant hepatitis may occur but there is no chronicity and little likelihood of liver disease. Hepatitis A occurs endemically in all parts of the world with frequent reports of minor and major outbreaks. The exact incidence is difficult to estimate because of the high proportions of subclinical infection and infections without jaundice, difference in surveillance and differing patterns of disease. The degree of underreporting is very high.

Hepatitis A has been a reportable disease in Malaysia since 1988. The overall incidence of hepatitis A has decreased tremendously from 11.65 in 1988 to 9.16 in 1991, 4.72 in 1997 per 100,000 populations. On the other hand, the seroprevalance rate has also decreased from 67% in 1986 to 54.9% in 1993 and 48.4% in 2000. In terms of age related seroprevalence of HAV infection, Malaysia portrays a pattern typical of declining endemcity i.e. from intermediate to low endemcity. The proportion of seroconverted children and adolescents have decreased in line with socioeconomic development. However, a relatively high seroprevalence still occurs in older adults (age group 41-60 years; 76.1 %) although this is expected to decline as younger adults replace the current cohort.

There is an obvious shifts of the seroprevalence curve in Malaysia, to the right and downwards from 1986 to year 2000 similar to the one shown by developed countries like Singapore and the United States.

Vaccines available

Hepatitis A vaccine is a formaldehyde-inactivated vaccine prepared from either the GBM or the HM 175 strain or CR326F strain of HAV grown in human diploid cells. It is supplied as a suspension in prefilled syringes.

Mode of administration and dosing regimen

The vaccine should be given intramuscularly in the deltoid region. It should not be given into the gluteal region because vaccine efficacy may be reduced, nor should it be administered intravenously, or intradermally and should not be

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routinely given subcutaneously unless for hemophiliacs. The dose in adults is 1440 ELISA units (1ml) of the HM 175 strain or 160 Antigen units (0.5ml) of the GBM strain or 50 units (0.5ml) of the CR326 F strain. The dose in children or adolescents (1-15 years), in a separate presentation of 720 Elisa units (0.5ml) of the HM175 strain, 25 units of the CR326 strain.

Contraindications and adverse reactions

Immunization should be postponed in individuals suffering from severe febrile illness. The effect of HAV development has not been assessed. Since it is an inactivated vaccine, the risks of the fetus are likely to be negligible but it should be given in pregnancy unless there is a definite risk of infection.

Adverse reactions are usually mild and confined to the first few days after immunization. The most common reactions are mild transient soreness, erythema and induration at the injection site. General symptoms such as fever, malaise, fatigue, headache, nausea and loss of appetite are also reported though less frequently.

Vaccines available in Malaysia

Havrix monodose (adults) and Havrix monodose junior (children and adolescents up to 15 years)

Avaxim (all preparation) GBM strains

Vaqta monodose (adults) and Vaqta monodose (2-18 years)

Target groups

Travelers to countries where Hepatitis A endemicity is high
Patients with chronic liver disease
Hemophiliacs
Occupational exposure: healthcare workers, food handlers and laboratory personnel
Homosexuals
Individuals at risk during outbreaks

Evidence for effectiveness

Immunogenicity studies show that levels of antibodies produced after a primary course of vaccine administered intramuscularly are well in excess of those found after the administration of human normal immunoglobulin (HNIG). The primary course produced anti-HAV, which persists for at least one year. Antibody persistence can be prolonged for up to 10 years with administration of a booster dose of vaccine 6-12 months after the initial dose.1-4 (Level 2-4)
References


HEPATITIS B

Introduction

Hepatitis B was referred to originally as ‘serum hepatitis. It is the most common cause form of the parenterally transmitted viral hepatitis, and an important cause of acute and chronic infection of the liver. More than a third of the world’s population has been infected with the hepatitis B virus (HBV), and WHO estimates that it results in 1-2 million deaths annually. The clinical features of acute infection resemble those of the other viral hepatitides. The virus persists in 5-10% of immunocompetent adults and in as many as 90% of infants infected perinatally. Persistent carriage of HBV is defined by the presence of hepatitis B surface antigen (HBsAg) in the serum and occurs in more than 350 million individuals worldwide, although not all these individuals are infectious. Long term continuing virus replication may lead to chronic liver disease, cirrhosis and hepatocellular carcinoma. Primary liver cancer is one of the 10 most common cancer worldwide and about 80% of these are ascribed to persistent infection with HBV.

About 1.1 million Malaysians are thought to be chronically infected with HBV. This data is based on the seroprevalence data obtained from voluntary testing which indicated that about 5.24% of 17,048 sera screened were positive for HBsAg (Malaysian Liver Foundation 1998 ). Another study conducted by the same group on 2115 convenience samples from all over Malaysia reported the prevalence of HBsAg and hepatitis B s antibody (HBsAb) of 6.5% and 51% respectively (Malaysian Liver Foundation). Taking into consideration that the documented seropositivity among blood donors is about 2.5%, the estimated prevalence in Malaysia of HBsAg and most likely the rate of chronically infected individuals is approximately 4.7% of the population.

Vaccines available

Hepatitis B vaccine contains HBsAg adsorbed on aluminum hydroxide adjuvant. It is currently prepared from yeast cells using recombinant DNA technology. The plasma derived vaccine is no longer marketed in Malaysia.

Mode of adminstration and dosing regimen

The basic immunization regime consists of 3 doses of vaccine, with the first dose at the elected date, the second dose one month later and the third dose at six months after the first dose.

An accelerated schedule has also been used where more rapid immunization is required, for example for travelers or following exposure to the virus, when the third dose may be given at two months after the dose with a booster at 12
months. This dosage schedule for the rapid acquisition of immunity can be used to prevent perinatal transmission if given to neonates born to HBsAg mothers. The vaccine should be given intramuscularly. The injection should be given in the deltoid region, though anterolateral thigh is preferred site for infants. The buttock must never be used as it may cause reduced vaccine efficacy.

The subcutaneous or intradermal route may be used for haemophiliacs. The response may be poor in those who are immunosuppressed and further doses may be required.

An antibody level of 10mlu/ml is classified as non-response to the vaccine whilst an antibody level of 100mlu/ml is considered to be protective. Antibody levels>100mlu/ml persist in some individuals much longer than 5 years. There is some evidence that protective immunity is still present even though levels have fallen below 100mlu/ml. Those with antibodies below 10mlu/ml 2-4 months after completing the primary course will require hepatitis B immunoglobulin (HBIG) for protection if exposed. Poor responders (antiHBs of 10-100mlu/ml) should receive a booster dose. Non-responders should be considered for a repeat course.

Contraindications and adverse reactions

Immunization should be postponed in individuals suffering severe febrile illness. Hepatitis B infection in pregnant women may result in severe disease for the mother and chronic infection of the newborn. Immunization should never be withheld from a pregnant woman if she is in the high-risk category. Information available on the outcome in those in those immunized during pregnancy does not reveal any cause for concern.

Hepatitis B vaccine is generally well tolerated. The most common adverse reactions are soreness at the injection site. Injection intradermally may produce a persisting nodule at the site of the injection, sometimes with local pigmentation. Other reactions include fever, rash malaise and influenza-like syndrome, arthritis, arthralgia , myalgia.

Vaccines available in Malaysia

Energix-B (Hepatitis B)
HB Vax 11
Euvax-B
Korea Green Cross Hepatitis B vaccine
Target groups

Parenteral drug abusers
Close family contact of a case or those chronically infected
Hemophiliacs
Patients with chronic renal failure
Health care workers
Staff and residents of residential accommodation for mentally handicapped
Travelers to areas of high endemicity

Evidence for effectiveness

Overall about 80-90% of individuals mount a response to the vaccine with anti HBs levels of > 10mlu/ml. Those over the age of 40 are less likely to respond. Patients who are immunodeficient or on immunosuppressive therapy may respond less well than healthy individuals and may require larger doses of vaccine or additional dose. The duration of antibody persistence is not known precisely. On present evidence, it is felt that a single booster 5 years after completion of a primary course is sufficient to retain memory in those who continue to be at risk of infection (Level 2-4)

References


Combination vaccine for hepatitis A and B (Twinrix)

This is a combined vaccine formulated by pooling bulk preparations of purified inactivated hepatitis A (HA) and purified hepatitis B surface antigen (HBsAg), separately adsorbed onto aluminium hydroxide and aluminium phosphate. The HA virus is propagated in MRC5 human diploid cells. HBsAg is produced by culture in a selective medium, of genetically engineered yeast cells.

The standard primary course consists of three doses, the first administered at the elected date, the second one month later and the third six months after the first dose. In exceptional circumstances in adults when travel is anticipated within one month or more after initiating the course but insufficient time is available to follow the standard 0,1,6 months schedule, a schedule of three intramuscular injections given at 0,7 and 21 days may be used with a fourth dose recommended 12 months after the first.

This vaccine is targeted primarily for travelers.

Evidence for effectiveness

In a pivotal study of an accelerated schedule, two groups with comparable demographic data were recruited from travel clinics in Germany and the United Kingdom and given Twinrix and monovalent Hepatitis A or Hepatitis B respectively, It was found that one week after the third dose, 100% of subjects in the Twinrix group were seropositive for hepatitis A virus antibodies compared to 99% in the group given monovalent hepatitis A or Hepatitis B vaccine (Nortdruft HD, Dietrich M, Zuckerman JN et al. Vaccine 2002;20: 1157-62) (Level 2)
INFLUENZA

Introduction

Influenza in the tropics occurs all year round; sometimes with two peaks. Influenza viruses can cause pandemics, during which rates of illness and death from influenza related complications can increase dramatically worldwide.

Uncomplicated influenza is characterized by abrupt onset of constitutional and respiratory signs and symptoms (fever, myalgia, headache, severe malaise, nonproductive cough, sore throat and rhinitis). Influenza can exacerbate underlying medical conditions (e.g. pulmonary or cardiac disease), lead to secondary bacterial pneumonia or primary influenza viral pneumonia, or occur as part of a co-infection with other viral or bacterial pathogens. Influenza has also been associated with encephalopathy, transverse myelitis, Reye’s syndrome, myositis, myocarditis, pericarditis, secondary meningococcal infection.1

The risks for complications, hospitalization and deaths from influenza are higher among persons aged >65 years, very young children, and persons of any age with certain underlying disease conditions.

Nature of vaccine

Influenza vaccine contains three strains (two type A and one type B), representing the influenza viruses likely to circulate. The vaccine is made from highly purified, egg-grown viruses that have been made noninfectious (inactivated). Subvirion and purified surface–antigen preparations are available. Because the vaccine viruses are initially grown in embryonated hens’ egg, the vaccine might contain small amount of residual egg protein.

Two formulations are available: Northern and Southern Formulations. The Northern formulations vaccines are made available in October and the Southern formulation in April of each year. The public is advised to take the newest available vaccine.

Mode of administration and dosing regimen

The intramuscular route is recommended for influenza vaccine. Adults and older children should be vaccinated in the deltoid muscle. A single dose (0.5 ml) of inactivated vaccine should be given annually. Annual immunization is recommended because influenza vaccines have been shown to decline in efficacy against subsequent circulating strains.
Contraindications and adverse reactions

Inactivated influenza vaccine should not be given to persons known to have anaphylactic hypersensitivity to eggs or to other components of the influenza vaccine. Persons who have documented immunoglobulin E (IgE)-mediated hypersensitivity to eggs including those who have occupational asthma or other allergic response to egg protein might also be at risk for allergic reaction to influenza vaccine. Persons with acute febrile illness usually should not be vaccinated until their symptoms have abated.²

Soreness at the vaccination site is the most frequent side effect. Systemic reactions include fever, malaise, myalgia. These reactions begin 6-12 hours after vaccination and can persist for 1-2 days. Immediate, presumably allergic reactions, rarely occur after influenza vaccination.

Vaccines available in Malaysia

Vaxigrip

Target groups

- Residents of institutions for the elderly or the disabled
- Elderly non-institutionalized individuals with ≥1 more of the following chronic conditions: chronic cardiovascular, pulmonary, metabolic or renal disease, or who are immunocompromised
- Other individuals in the community who have chronic cardiovascular, pulmonary, metabolic or renal disease, or who are immunocompromised
- Those with regular, frequent contact with high-risk persons such as healthcare workers and household contacts.
- Large groups of pilgrims gathering in the same area for several weeks

Evidence for effectiveness

A meta-analysis by Gross³ based on 20 cohort studies gave the following pooled estimates of vaccine efficacy: 56% for preventing respiratory illness, 53% for preventing pneumonia, 48% for preventing hospitalization and 68% for preventing mortality. In the case-control studies, vaccine efficacy ranged from: 32-45% for preventing hospitalization, 31-65% for preventing mortality from pneumonia and influenza, 43-50% for preventing hospital deaths from all respiratory illness and 27-30% for preventing deaths from all cases. In the randomized double-blind placebo controlled trials the vaccine was found to result in 50% or greater reduction in influenza-like illness. In conclusion, annual vaccination of elderly persons >65% is an indispensable part of their care. (Level 1)
Hak et al. assessed the clinical effectiveness of influenza vaccination program in preventing complications in 1696 adult patients with chronic pulmonary disease. The results showed that the overall attack rate of any complication, including all cause death, lower respiratory tract infection, and acute cardiac disease was 15%. Exacerbations of lung disease were most frequent (13%). Death, pneumonia and acute cardiac disease were mainly limited to patients > 65 years (n=630), the occurrence of any complication was reduced by 50% (95% CI 17, 70%). The economic benefit was estimated at 50.00 pound sterling per elderly vaccine. The study suggests that in the Netherlands immunization of elderly patients with chronic lung disease against influenza is effective and cost saving, hence these patients should be given high priority (Level 6).

References
2. MMWR. Prevention and control of influenza April 20, 2001/50 (RR04):1-46
JAPANESE ENCEPHALITIS

Introduction

Japanese encephalitis is one of the most common causes of viral encephalitis worldwide, with estimated 50,000 cases and 15,000 deaths annually. About one third of patients die, and half of the survivors have severe neuropsychiatric sequelae. Most of China, Southeast Asia and the Indian subcontinent are affected by the virus. Japanese encephalitis virus is transmitted by Culex mosquitoes.

The true incidence of JE in Malaysia is not known but the virus has been isolated from mosquitoes. Antibodies to the virus has been detected in swine and other animals and confirmed clinical cases have been reported.

Nature of vaccine

The Biken vaccine is a freeze–dried preparation of formaldehyde inactivated JE virus derived from infected mouse brain. Reconstituted vaccine should be stored at 35-46 F and used within 8 hours. Reconstituted vaccine is a clear, colourless liquid. Do not administer if discoloured or contains particulate matter.

Mode of administration and dosage regimen

Initially 2 subcutaneous injections of 1 ml each at 1-2 weeks interval & additional 1 ml after 1 year. After receiving the 3 doses, another 1 ml is given every 3-4 years to maintain immunity. For adults >60 years or those going to highly endemic areas for the first time, 1 more injection of 1 ml is recommended 1 month after the initial 2 doses.

Precautions

Vaccinated persons should be monitored for 30 minutes and have ready access to medical care for 10 days after vaccination. Injectable epinephrine should be immediately available in the event of anaphylactic reactions (severe allergic reaction with shock)

Contraindications and adverse reactions

Fever, severe malnutrition, cardiovascular, renal or hepatic diseases in acute, exacerbation or active phases, a history of abnormal adverse reaction caused by this vaccine and a history of spasmodic symptoms within 1 year are contraindications.

Local reactions include redness, swelling, tenderness at the injection site. Fever, chills, headache and lassitude can also occur. In Caucasians itching, urticaria, and occasional angioedema of the face can occur several days after vaccination.
Vaccines available in Malaysia
Japanese encephalitis vaccine lyophilized BIKEN.
Japanese encephalitis vaccine GCVC, Green Cross Vaccine

Target groups

- Native or expatriate residents of endemic areas
- Laboratory workers exposed to the virus
- Travelers spending more than 30 days or more in endemic areas.

Evidence for effectiveness

A large randomized placebo controlled trial in Thailand involving over 60,000 subjects showed an efficacy of 91% (95 percent confidence interval, 70 to 97 percent).\(^5\) (Level 2)

References

MEASLES

Introduction
Measles is a systemic viral infection whose main features are respiratory disease and rash. It is highly infectious among susceptible individuals and almost always produces clinical disease in those affected. The important impact of measles is threefold (i) It can be severe and debilitating illness (ii) Secondary bacterial respiratory disease is common and may be severe (iii) Post–measles encephalitis is life-threatening and can leave severe sequelae. The most common complications are otitis media, diarrhea, pneumonia and encephalitis. Pneumonia is more common in young children and encephalitis is more common in adolescents and adults.

Nature of vaccine
Measles vaccine contains the live attenuated Schwarz strain. The Schwarz strain was derived from the Edmonston strain. Schwarz strain vaccine was first licensed in 1965 in United States and serves today as the standard measles vaccine in much of the world. The closely related Moraten strain was licensed in 1968 and has replaced the Schwarz strain in the United States.

Measles vaccine is available in a monovalent formulation and in combination with live attenuated rubella and mumps vaccines (MMR).

Mode of administration and dosing regimen.
The live attenuated measles vaccine is administered in 0.5 ml subcutaneously. The standard dose of live attenuated measles vaccine contains between $10^3$ and $10^4$ TCID$_{50}$ of infectious measles virus, usually in 0.5 ml.

Contraindications and adverse reactions
Pregnancy, anaphylactic allergy to eggs or neomycin, compromised immunity, except HIV infection and certain hematological malignancies that are in remission and for which immunosuppression therapy has been stopped for at least 3 months, and recent administration of immunoglobulin, IGIV, or other immunoglobulin containing products are all contraindications.

Like measles virus, measles vaccine is associated with transient immunosuppression that resolves within 4 weeks after vaccination. Tuberculin skin test may be abrogated for 4-6 weeks after immunization, but, unlike wild-type measles vaccine does not exacerbate tuberculosis.
Vaccines available in Malaysia

- M-M-R II
- Priorix [Live attenuated Schwarz measles RT 4385 mumps (derived from Jeryl Lynn strain) and Wistar RA27/3 rubella strains of viruses.]
- Rimevax [highly attenuated Schwarz strain of measles virus 1 000 TCID50]

Target groups

Adults who have no history of measles or previous measles immunization should receive the immunization. Because the same epidemiologic characteristics pertain to mumps and rubella, MMR rather than the monovalent measles vaccine is the vaccine of choice. There is no evidence to suggest that adverse consequences will occur from giving MMR to a person who is already immune to one or more of its components.

Evidence for effectiveness.

A meta-analysis based on 12 studies (10 cohort and 2 case control) done in children from developing countries showed estimates of vaccine efficacy against death were heterogenous (X^2=26.3; df=9; P=0.002). Standard measles immunization had a large effect on mortality (30-80% reduction on mortality). The studies comparing children from the same community show a reduction in mortality in the range of 38-86%. In studies comparing immunized and unimmunized children from different communities, estimates of efficacy against death were in the range of 30-67%.

References

MENINGOCOCCAL DISEASE

Introduction

Meningococcal disease most commonly is manifested as meningitis or septicaemia, but can present as septic arthritis or pneumonia. The case fatality of meningococcal disease is 10% and substantial morbidity. Between 11-19% of survivors have sequelae e.g. neurological deficit or hearing loss. Septicaemia without meningitis may be fulminant with hypotension, extensive purpura resulting from disseminated intravascular coagulopathy with high mortality. Preventing and controlling meningococcal disease remains a public health challenge because of the multiple serogroups and limitation of available vaccines. On the basis of surface polysaccharide, Neisseria meningitides, the causative organism, is divided into 13 serogroups of which serogroups A, B, C, X, Y, Z, W-135 and L, have been associated with invasive disease. Serogroup A and C are the main cause of epidemic meningococcal meningitis. Serogroup B is generally associated with sporadic disease but may cause some upsurges or outbreaks. In 1987, a meningococcal serogroup A epidemic occurred among the Hajj pilgrims and an epidemic of W-135 meningococcal disease was reported among the Hajj pilgrims in year 2000

Vaccine available

Bivalent capsular polysaccharide vaccine of serogroups A and C confers protective immunity to the 2 serogroups only. A quadrivalent polysaccharide vaccine comprising serogroups A, C, Y and W-135 is now available. A conjugate meningococcal serogroup A and C vaccine; and a conjugate meningococcal serogroup B vaccine; which will induce T-cell memory response and provide long term protection for all ages are under active development at present.

Mode of administration and dose regimen

A single dose of 0.5 ml vaccine is given subcutaneously or intramuscularly. Revaccination after 2-3 years is required if the subject remains in a high risk area.

Contraindication and adverse reactions

Vaccination should be avoided during acute febrile illnesses. It is contraindicated in persons with previous serious reactions to the vaccine or its components. The adverse reaction is generally mild with pain and redness at the injection site lasting for 1-2 days. Transient fever occurs in up to 5% of vaccinees. Systemic allergic reaction and anaphylaxis has
been reported but are extremely rare.

Vaccine available in Malaysia

a. Meningococcal A & C
b. Meningococcal A & C
c. Menomune A, C, Y, W-135
d. Mencevax A, C, Y, W-135

Each dose contains 50 ìg each of purified bacterial capsular antigen of the respective serotypes

Target groups

Meningococcal vaccine is not routinely recommended, but it is compulsory for the Hajj pilgrims and Umrah following the 1987 serogroup A meningococcal disease outbreak. Since 1988, Malaysian Hajj pilgrims had received the bivalent A and C vaccine. Beginning from the 2002 Hajj, Saudi health officials require certification of quadrivalent meningococcal vaccination covering serogroups A, C, Y, and W-135 for all entering pilgrims.

Travelers to Kenya, India, and the sub-Saharan African meningitis belt, are recommended to receive the meningococcal vaccine. Persons who have certain medical conditions are at high risk for developing meningococcal disease particularly persons who have deficiency in the terminal common complement pathway (C3, C5-9), is another target group. Vaccine is recommended to control meningococcal outbreak by that specific serotype. In United Kingdom, students entering higher education or college are recommended to receive meningococcal vaccine².

Evidence of effectiveness

The serogroups A and C vaccines have demonstrated estimated clinical efficacies of 85% in school-age children and adults and are useful in controlling outbreaks³.⁴. Serogroups Y and W-135 are safe and immunogenic in adults and children aged >2 years⁵. (Level 7)

References


MUMPS

Introduction

Mumps is a systemic viral infection commonly regarded as epidemic parotitis. Orchitis is common in adult men (affects up to 38%) but rare before puberty. Mumps orchitis is a rare cause of infertility. Meningitis and meningoencephalitis affect around 15% of cases, but are often so mild as to be overlooked. Rare manifestations of mumps include mastitis, cochlear infection with hearing impairment, oophoritis in women and arthritis. Myocarditis can occur and may be involved in rare fatalities in adult cases.\(^1\) Although mumps in pregnant women does not produce congenital malformations, infection during the first trimester increases the risk of fetal death.\(^3\)

Nature of vaccine

Mumps vaccine is a live, attenuated preparation, usually administered as part of combined MMR vaccine. The vaccine currently used in Malaysia contains the Jeryl Lynn strain of live mumps virus. Mumps vaccines containing Urabe Am9 and Leningrad 3 have been withdrawn due to increased frequency of vaccine-related mumps meningitis.

Mode of administration and dosing regimen

Mumps vaccine is given in 0.5 ml by the subcutaneous route.

Contraindications and adverse reactions

Administration of MMR is contraindicated in pregnant women, in persons who have received immunoglobulin therapy within the preceding 3 months or in persons who are significantly immunocompromised.

Mumps vaccine is produced in chick embryo cell culture and may contain minute amounts of neomycin, so immunization is not recommended for persons with a history of severe allergic reaction to those substances.

Target groups

All susceptible adults should receive the vaccine.

Evidence for effectiveness

More than 97% of persons who are susceptible to mumps develop measurable antibody following vaccination and, in controlled clinical trials,
one dose of vaccine was approximately 95% efficacious in preventing mumps disease. However, field studies have documented lower estimates of vaccine efficacy, ranging from 75% to 95%.\textsuperscript{1-4} The 2-dose MMR vaccination schedule was adopted in response to increase rate of measles, but it effectively addressed the problem of primary mumps vaccine failure. (Level 2-3)

Vaccines available in Malaysia

- M-M-R II
- Priorix [Live attenuated Schwarz measles RT 4385 mumps(derived from Jeryl Lynn strain) and Wistar RA27/3 rubella strains of viruses.]

References

PLAGUE

Introduction

Plague is a zoonotic infection caused by *Yersinia pestis*. It occurs in many parts of the world. Sporadic cases occur when humans are exposed to infected wild rodents or their fleas. Epidemic plague may result when domestic rat populations and their fleas become infected. Plague is not endemic in Malaysia and no human cases have so far been reported. *Yersinia pestis* has been identified as a potential bioterrorist weapon.

Vaccines available

A parenteral killed whole cell vaccine is prepared from *Y. pestis* organisms grown in artificial media, inactivated with formaldehyde, and preserved in 0.5% phenol.\(^1\) A live attenuated vaccine, EV76 has been produced in the former USSR.

Mode of administration and dosing regimen

The killed whole cell vaccine is administered intramuscularly. Primary vaccination comprises 3 doses. The first dose, 1.0 ml, is followed by the second dose, 0.2 ml, 4 weeks later. The third dose, 0.2 ml, is administered 6 months after the first dose. 3 booster doses should be given at approximately 6-month intervals. Thereafter, antibody levels decline slowly and booster doses at 1- to 2-year intervals are given if required. The live attenuated vaccine can be administered as an aerosol or subcutaneously.

Contraindications and adverse reactions

Plague vaccine should not be administered to anyone with a known hypersensitivity to any of the constituents, such as beef protein, soya, casein, and phenol. Patients who have had previous severe local or systemic reactions to plague vaccine should not be revaccinated. Vaccination during pregnancy should be avoided. Primary vaccination may result in general malaise, headache, fever, mild lymphadenopathy, and erythema and induration at the injection site. These reactions occur more commonly with repeated injections. Rarely sterile abscesses and sensitivity reactions can occur.

Vaccines available in Malaysia

No plague vaccine is currently available in Malaysia.

Target groups

No target grouping Malaysia is identified.
Evidence for effectiveness

A recent systematic review\(^2\) concluded that there is not enough evidence to evaluate the effectiveness of any plague vaccine, or the relative effectiveness between vaccines and their tolerability. (\emph{Level 1}) Circumstantial data from observational studies suggest that killed types may be more effective and have fewer adverse effects than attenuated types of vaccine. No evidence appears to exist on the long-term effects of any plague vaccine.

References

POLIOMYELITIS

Introduction

Poliomyelitis is an acute gastrointestinal illness with affinity for the nervous tissue and is caused by one of the three types of poliovirus (I,II,III) from the Picornaviridae family. The infection is often clinically inapparent, with a very small percentage presenting with symptoms ranging from non-paralytic fever to aseptic meningitis to paralysis. However, while the proportion of inapparent to paralytic infections may be as high as 1000 to one in children, it is 75 to one in adults, depending on the poliovirus type and the social conditions.

The last reported case of wild poliovirus poliomyelitis in Malaysia was in 1990. Since 2000, the World Health Organisation has included Malaysia among the countries which have eliminated indigenous poliomyelitis and is certified polio-free.

Nature of vaccine

Inactivated poliomyelitis vaccine (Salk) was introduced in 1956 for routine vaccination, and was replaced by attenuated live oral vaccine (Sabin) in 1962. Two types of poliovirus vaccines are currently available: oral poliovirus vaccine (OPV) and enhanced potency inactivated poliovirus vaccine (eIPV). A primary vaccination series with either vaccine produces immunity to all three types of poliovirus in more than 95% of recipients. While the oral poliovirus vaccine will provide lifelong immunity, the duration of immunity provided by IPV still remains uncertain.

Mode of administration and dosing regimen

Primary vaccination for oral poliovirus vaccine is given in 3 doses. Two doses are given 6-8 weeks apart, and the third dose 6 weeks – 12 months after second dose.

Inactivated poliovirus vaccine is given intramuscularly over the deltoid muscle. For primary vaccination 3 doses are required; two doses are given 4-8 weeks apart, and a third dose 6–12 months after second dose.

For those exposed to a continuing risk of infection, a single reinforcing dose is desirable every 10 years.

Contraindications and adverse reactions

Oral poliovirus vaccine (OPV) should not be given to persons and household contacts of the immunocompromised and immunosuppressed. OPV should be given either three weeks before or three months after an injection of normal immunoglobulin – for instance for hepatitis A.
In general vaccination of pregnant women and immunocompromised persons should be avoided. However, if immediate protection is needed eIPV is recommended.

Oral poliovirus vaccine (OPV) has, in rare instances, been associated with paralysis among healthy recipients and their contacts. The risk however is very low. No serious side effects have been documented with eIPV but as the vaccine contains trace amounts of streptomycin and neomycin, hypersensitivity to these antibiotics may occur.

Vaccines available in Malaysia

1. Oral poliovirus vaccine (OPV)
2. Inactivated poliovirus vaccine (eIPV)

Target groups

- Travelers to areas where wild poliovirus is epidemic or endemic.
  - If never vaccinated, the traveler would need two doses of eIPV one month apart. If travel plans do not permit this interval, a single dose of either OPV or eIPV is recommended.
  - If previously incompletely vaccinated with OPV or IPV, give the remaining dose of either vaccine for completion, regardless of interval since the last dose or the type of vaccine previously received.
  - If have previously completed a primary series of OPV, give a single supplementary dose of OPV.
  - If have previously completed a primary series of IPV, give a single supplementary dose of OPV or eIPV

- Health-care personnel in close contact with patients who may be excreting wild poliovirus will need to be vaccinated. In the case of a health care worker without proof of having completed a primary series, completion with eIPV is recommended because adults have a slightly increase risk of vaccine-associated paralysis after receiving OPV. In addition, vaccine poliovirus may be excreted by OPV recipients for up to or more than 30 days thus increasing the risk of vaccine-associated paralytic poliomyelitis among the susceptible immunocompromised patients

- Laboratory personnel handling specimens that may contain wild poliovirus

Evidence for effectiveness and cost effectiveness

Tested in both industrialised and developing countries, the enhanced-potency IPV appears to be effective. In one randomized control trial the third dose of inactivated polio vaccine produced significant increases in the reciprocal geometric mean titers against each of the three poliovirus types and resulted in significantly higher reciprocal geometric mean titers after three doses of vaccine
for recipients of inactivated polio vaccine than for recipients of oral polio vaccine.\(^3\) (Level 2)

Even so, almost all developed and developing countries have chosen OPV for routine immunization, based on cost consideration and, in some cases, on the predicament that despite incomplete induction of immunity with OPV, the degree of ‘free vaccination’ of the community by the introduction of OPV circulation will compensate. It appears that eIPV may just have a complementary role in adults and immunocompromised persons, and perhaps in normal children in selected situations as well.

References

PNEUMOCOCCUS

Introduction

Streptococcus pneumoniae (pneumococcus) is a leading cause of illness in young children and causes illness and deaths among the elderly and persons who have certain underlying medical conditions. Pneumococcal diseases include pneumonia, bacteremia, meningitis, otitis media and sinusitis There are more than 90 serotypes identified, based on the antigenicity and chemical composition of pneumococcal capsular polysaccharide. The capsular polysaccharide also acts as the virulence factor, inhibiting phagocytosis and interfering with intracellular killing of phagocytosed bacteria.

Vaccines available

Pneumococcal polysaccharide vaccine

The 14-valent pneumococcal vaccine was first licensed in 1977 which was later replaced by the 23-valent vaccine in 1983. The composition of the pneumococcal vaccine was determined by the observed frequency of individual serotypes that caused invasive diseases. The 23-valent vaccine represents at least 85-90% of the serotypes that cause invasive pneumococcal infections. Drug-resistant pneumococcal serotypes causing invasive infection are also represented in the 23-valent vaccine. One dose (0.5 ml) of the 23-valent vaccine contains 25 µg of each capsular polysaccharide antigen (serotypes 1, 2, 3, 4, 5, 6B, 7F, 8, 9N, 9V, 10A, 11A, 12F,14, 15B, 17F, 18C, 19A, 19F,20, 22F, 23F and 33F)

Pneumococcal conjugate vaccine

Pneumococcal polysaccharide antigens are covalently coupled to carrier proteins to induce immunological response in children under 2 years of age. Current conjugate vaccine development has focused on the serotypes most commonly causing infections in childhood. The 7-component conjugate pneumococcal vaccine efficacy study is ongoing.

Mode of administration and dosing regimen

One dose of 0.5 ml 23-valent vaccine is administered by intramuscular or subcutaneous route. Routine revaccination of immunocompetent persons previously vaccinated is not recommended. However, a single revaccination is recommended for persons aged 2 years who are at highest risk for serious pneumococcal infection and those who are likely to have a rapid decline in pneumococcal antibody levels, provided 5 years have elapsed since receipt of the first dose of pneumococcal vaccine.
Contraindications and adverse reactions

Children under 2 years of age do not respond satisfactorily to the 23-valent polysaccharide vaccine. In these children the pneumococcal conjugate vaccine is a promising vaccine candidate. Immunization should be deferred during pregnancy.

Local reactions include pain, redness and induration which usually last less than 48 hours. Systemic reactions such as fever, rash, myalgia, headache are uncommon. Severe reactions such as serum sickness and anaphylaxis are extremely rare.

Vaccination is not recommended for subjects who have been vaccinated within the previous 3 years unless indicated otherwise.

Vaccines available in Malaysia

1. Pneumovax 23
2. Pneumo 23

At present, the conjugate pneumococcal vaccine is not yet available.

Target groups

Pneumococcal vaccine is recommended for the following 1:

1. Persons aged 65 years. A second dose of vaccine is recommended if patient received vaccine 5 years previously and were aged <65 years at the time of primary vaccination.
2. Persons aged 2-64 years with chronic cardiovascular disease, chronic pulmonary disease (COPD or emphysema, but not asthma), or diabetes mellitus, alcoholism, chronic liver disease, or cerebrospinal fluid leaks.
3. Persons aged 2-64 years with functional or anatomical splenia. Revaccination is recommended if 5 years have elapsed after previous dose in patients aged >10 years. If patient is aged 10 years, consider revaccination 3 years after previous dose.
4. Persons aged 2-64 years living in special environment or social settings
5. Immunocompromised persons aged 2 years, including those with HIV infection, leukemia, lymphoma, Hodgkins disease, multiple myeloma, generalized malignancy, chronic renal failure or nephrotic syndrome; those receiving immunosuppressive chemotherapy (including corticosteroids); and those who have received an organ or bone marrow transplant. Single revaccination is indicated if 5 years have elapsed since receipt of first dose. If patient is aged 10 years,
consider revaccination 3 years after previous dose.

Evidence of effectiveness

A meta-analysis by Cornus et al.\(^2\) based on 14 randomised trials confirms unambiguously the high efficacy of pneumococcal polysaccharide vaccine in reducing definite (bacteremic) pneumococcal pneumonia by 71% and presumptive pneumococcal pneumonia by 40% with a possible 32% reduction in mortality due to pneumonia. (*Level 1*)

References

Rabies Vaccine

Introduction

Rabies is due to the rabies virus and is transmitted to man by contact, (generally as the result of a bite) with animals carrying the virus. The incubation period is generally two to eight weeks, but may range from nine days to two years. It manifests itself in the form of acute encephalomyelitis, the development of which is always fatal resulting from respiratory paralysis.

Rabies is widespread throughout the world. In Asia domestic animals like dogs and cats are predominantly infected. Indigenous human rabies is rarely seen in Malaysia because of the strict preventive measures as well as control of imported animals. The small number of cases that are reported appear to occur along the borders of Thailand, a country where rabies is endemic. The last reported case was in 1999 in Terengganu, following the bite of an infected dog.

Nature of vaccine

Rabies vaccine is used for pre-exposure protection, whilst both vaccine and rabies specific immunoglobulin may be needed for rabies post-exposure treatment.

The vaccine currently available is a human diploid cell vaccine (HDCV) which was first introduced in 1978. It is a killed virus human virus, grown in WI-38 (US) or MRC-5 (Europe) cells and is inactivated by tri-n-butyl phosphate (WI-38 strain) or beta propiolactone (MRC-5 strain).

The human rabies immunoglobulin (HRIG) is prepared by cold ethanol fractionation of plasma to obtain a concentrated gamma globulin fraction from hyperimmunized human donors. (Further details may be obtained from the section on “Passive Immunisation”)

Mode of administration

Two forms of human diploid cell vaccine (HDCV)

- Intramuscular – lyophilized vaccine reconstituted to 1.0-mL before administration
- Intradermal – reconstituted to 0.1-mL before administration

Dosing regimen

1. Pre exposure prophylaxis
   - Intramuscular injection: Three 1.0-mL injections of HDCV on days 0, 7 and 28
   - Intradermal injection: Three 0.1-mL injections of HDCV on days 0, 7 and 21 or 28
• Booster for those at continued risk every two years

2. Post exposure prophylaxis with HDCV
   • Intramuscular injection of HDCV is the only form indicated.
   • If the following criteria are met, two 1.0-mL doses of HDCV are to be given on days 0 and 3 (HRIG need not be given):
     - have previously received post exposure prophylaxis with HDCV; or
     - have received a three-dose pre exposure regimen of HDCV
   • If the above criteria are not met, give:
     - A single 20.00-IU/kg dose of HRIG, and
     - Six 1.0-mL doses of HDCV on days 0, 3, 7, 14, 21 and 28.

3. Post exposure treatment with HRIG
   • This should be given at the beginning of HDCV post exposure prophylaxis but, it can be delayed up to the 8th day after the first dose of HDCV.
   • A single 20.00-IU/kg dose is required
     - Half should be infiltrated into the area of the wound after thorough cleansing by scrubbing with soap and water under a running tap for five minutes;
     - The rest is to be administered intramuscularly, but never in the same site or in the same syringe as HDCV

Contraindications and adverse reactions

It is contraindicated in patients on steroids and other immunosuppressives. If the vaccinee experiences a possible anaphylactic reaction after receiving HDCV, no further preexposure doses of HDCV should be given. Pre exposure vaccines should only be given to pregnant women if the risk of exposure to rabies is high.

Local reactions occur in up to 74% of vaccinees who report pain, erythema, swelling or itching at injection site within 24-48 hours of administration. Systemic reactions are mild in 5-40% of recipients and include fever, headache, nausea, vomiting, abdominal pain, muscle aches, and dizziness. An allergic reaction occurs in 11 of 10,000 vaccinees and range from hives to anaphylaxis.

Reactions with HRIG include local pain and low grade fever may follow the injection. No serious adverse reactions have been reported

Vaccines available in Malaysia

1. Human diploid cell vaccine (HDCV)
2. Human Rabies Immunoglobulin (HRIG)

Target groups

1. Persons whose vocations bring them into contact with potentially rabid animals. They include those working
• at animal quarantine premises for imported animals and zoological establishments
• as carrying agents authorised to carry imported animals
• at national ports of entry where contact with imported animals is likely (e.g. Customs and Excise Officers)
• as veterinary and technical staff of the Ministry of Agriculture and Fisheries
• at approved research centres where primates and other imported animals are housed
• in laboratories handling rabies virus

2. Travelers planning to spend more than one month in areas of countries where rabies is a constant threat

Evidence for effectiveness

Studies demonstrate remarkably good immunogenicity in both preexposure and post exposure prophylaxis using HDCV.\(^1,2,3,4\) (Level 2). The use of human rabies immunoglutulin (HRIG) in conjunction with vaccination has clearly reduced human rabies mortality.\(^5\) (Level 4)

References

RUBELLA

Introduction
Rubella is a systemic viral infection with many features, including a rash. Although highly infectious, it often produces subclinical or trivial disease. It is important because even subclinical viraemia can infect the developing fetus, causing severe tissue damage and progressive developmental defects. The primary objective of vaccination is to prevent congenital rubella syndrome. Complications of rubella include thrombocytopenia purpura, and encephalitis (1 in 5000 cases) occurring soon after the rash.

Although Malaysia had adopted a selective immunization rubella vaccination program in 1988 for female school children age 11-14 years, congenital rubella syndrome continues to occur because transmission continues among adults.\(^1\) A recent study in 2002 showed that 92.7% of women age 15-26 years are immune to rubella, 92.9% in the 27-34 years age group and only 88.9% were immune in the 35-45 years age group.\(^2\)

Nature of vaccine
Live attenuated rubella vaccine containing RA27/3 strain.

Mode of administration and dosing regimen
Rubella vaccine is administered 0.5 ml dose subcutaneously
Susceptible women should receive rubella vaccine in the immediate postpartum period prior to discharge

Contraindications and adverse reactions
Rubella vaccine is contraindicated in pregnancy. Persons with anaphylactic allergy to eggs or neomycin, compromised immunity, except HIV infection and certain hematological malignancies that are in remission and for which immunosuppression therapy has been stopped for at least 3 months, and recent administration of immunoglobulin, IGIV, or other immunoglobulin containing products

Swelling of cervical & occipital lymph nodes, rash, fever. 25% of susceptible post pubertal female vaccines develop arthralgia or arthritis beginning 7-21 days after vaccination.

Recommendations for laboratory tests
Premarital serologic screening for rubella immunity will booster attempts at identifying susceptible women of childbearing age. Prenatal and antenatal serologic screening for rubella immunity should be routinely performed..
Vaccines available in Malaysia

- M-M-R II
- Priorix [Mumps, measles and rubella vaccine]
- Gunevax (monovalent rubella vaccine)
- Ervevax [monovalent rubella vaccine]

Target groups

- All susceptible adults, particularly females.
- All susceptible healthcare workers.

Evidence for effectiveness

In clinical trials, greater than or equal to 95% of susceptible persons aged greater than or equal to 12 months who received a single dose of strain RA 27/3 rubella vaccine developed serologic evidence of immunity. Clinical efficacy and challenge studies indicate that greater than 90% of vaccinated persons have protection against both clinical rubella and viremia for at least 15 years\(^3-6\). (Level 2-3)

References

3. Tischer A, Gerike E Immune response after primary and re-vaccination with different combined vaccines against measles, mumps, rubella. Vaccine. 18(14):1382-92, 2000
SMALLPOX VACCINE

Introduction

Smallpox or variola major was a specifically human disease caused by the smallpox virus of the Orthopoxvirus genus. The incubation period was characteristically 12 days. It was manifested by the presence of generalised vesicular rash with complications that included osteomyelitis, arthritis and conjunctivitis. The patients transmitted the infection most commonly four to six days after the illness started. Mortality depends on the virus strain and immunity, thus it ranged from 1-40%. Nothing was available that would successfully treat smallpox once the disease was clinically obvious.

Nature of vaccine

The vaccine used was a live unattenuated preparation of vaccinia virus that induces protection against smallpox virus in 95% or more of recipients. It is also highly effective in providing protection against vaccinia and other orthopox viruses.

In December 1979 the Global Commission for the Certification of Smallpox Eradication declared the world free of smallpox and this declaration was ratified by the World Health Assembly in May 1980.

This virus however is still considered a potentially biohazard weapon. Currently an attenuated vaccine (CV1-78) is available for those at risk.

Mode of administration

Scarification using a bifucated needle is required.

Dosing regimen

One dose was required with a booster to be given at least every 10 years

Contraindications & Adverse reactions

Mild satellite lesions or non-descript rashes may occur in 8% of primary vaccinees. Systemic adverse events are very rare and include disseminated vaccinia, vaccinia necrosum and encephalitis.

Vaccines available in Malaysia

It is currently no longer in general distribution. Only two reference laboratories retain smallpox virus and the Global Commission has recommended that 200 million doses of vaccine should be stockpiled to cover possible emergencies.
Should an outbreak of smallpox be detected, this is considered an international emergency. WHO will help to pool available resources so as to contain the disease as rapidly and effectively as possible.\(^4\)

**Target groups**

In October 2001, the World Health Organisation further reiterated that pre-exposure vaccination of entire populations is not recommended. The reason is that there is a risk of severe reactions to the vaccine, including death. In any case, postexposure vaccination can prevent the onset of clinical smallpox.\(^2\) The vaccine would thus only be given to those who are at risk of exposure, namely:

- Laboratory workers in research centres involved with orthopox viruses,
- Health care workers involved in clinical trials of vaccinia recombinant vaccines, and
- Health care workers involved in search and containment exercise should an outbreak occur

Currently there are no identified target groups in Malaysia.

**References**

TETANUS:

Introduction:

Tetanus is a disease caused by exotoxins produced by Clostridium tetani. The sites of entry for these organisms are through open wounds and lacerations, penetrating injuries, animal bites and needle puncture sites. Clostridium tetani produces two toxins, tetanolysin and tetanospsasmin. Tetanospsasmin, a powerful neurotoxin, is responsible for the features of tetanus. It disseminates through the blood stream into peripheral nerve endings where it is transported to the spinal cord and brain where it irreversibly binds to the gangliosides and blocks the inhibitory neurotransmitters glycine and gamma-aminobutyric acid. This results in unopposed muscle contractions.

There has been a steady decline in the number of cases of adult tetanus in Malaysia. In 1995 there were 12 cases with 2 deaths reported while in 2001 only 4 cases (with no mortality) were reported.

Nature of vaccines:

Tetanus vaccine is a toxoid prepared by extraction of the toxin from culture of C. tetani. The cell-free product is detoxified after treatment with formaldehyde. The toxoid is adsorbed on to an aluminium phosphate adjuvant and thimerosal is used as a preservative. The antigenic potency is expressed as international immunising units (iu or iu) by WHO. Each toxoid dose should contain no less than 40iu. Tetanus Immune Globulin is derived by cold-ethanol fractionation of the plasma of hyperimmune adults. It has a half-life of 28 days with a shelf-life of 36 months.

Mode of administration and dosing regimen

Td(Tetanus toxoid+Adult Diphtheria toxoid) is administered by giving 0.5ml by deep intramuscular injection. It can be administered with other vaccines as long as different syringes and different anatomic sites are used. A primary series for adults is three doses of preparations containing tetanus and diphtheria toxoids, with the first two doses given at least 4 weeks apart and the third dose given 6-12 months after the second.

For post-exposure prophylaxis please see below.

Contraindications and adverse reactions

Although no evidence suggests that diphtheria and tetanus toxoids are teratogenic, waiting until the second trimester of pregnancy to administer Td is a reasonable precaution. A history of a neurologic reaction or a severe
hypersensitivity reaction after a previous dose and severe febrile illness contraindications.

Local reactions (usually erythema and induration, with or without tenderness) can occur after Td is administered. Fever and other systemic symptoms are less common. Arthus-type hypersensitivity reactions, characterized by severe local reactions starting 2-8 hours after an injection and often associated with fever and malaise, may occur, particularly among persons who have received multiple boosters of tetanus toxoid, adsorbed. Rarely, severe systemic reactions, such as generalized urticaria, anaphylaxis, or neurologic complications, have been reported.

### Availability in Malaysia

In Malaysia tetanus toxoid is available as follows:

- **Tetanus toxoid**
  - Tetavax (Aventis Pasteur)
  - Te Anatoxal Berna (Swiss Serum)
  - TT Vaccine (BioFarma, Indonesia)

- **Tetanus Immune Globulin (TIG)** is available as follows:
  - Tetuman Berna (Swiss Serum)
  - Serotet (Green Cross, Korea)

At the time of printing, Td is not yet available in Malaysia.

### Target groups (Toxoid indications):

- All adults lacking a complete primary series of diphtheria and tetanus toxoids should complete the series with Td.
- All adults for whom greater than or equal to 10 years have elapsed since completion of their primary series, or since their last booster dose, should receive a booster dose of Td. Thereafter, a booster dose of Td should be administered every 10 years.
- Pregnant women not vaccinated previously against tetanus and diphtheria should receive two doses of Td, properly spaced. Those who have previously received one or two doses of tetanus or diphtheria toxoid should complete their primary series during pregnancy. Pregnant women who have completed a primary series should receive a booster dose of Td if greater than or equal to 10 years have elapsed since their last dose.
- Patients who have recovered from tetanus should complete the full immunisation schedule as the disease does not confer immunity.
- Patients with traumatic wounds (See post-exposure prophylaxis and treatment below).
Post-exposure prophylaxis and treatment

For wound management, the need for active immunization, with or without passive immunization, depends on the condition of the wound and the patient's vaccination history (Table 1). Only rarely have cases of tetanus occurred among persons with a documented primary series of toxoid injections.

Table 1. Summary guide to tetanus prophylaxis in routine wound management

<table>
<thead>
<tr>
<th>Immunisation status</th>
<th>Clean, minor wounds</th>
<th>All other wounds*</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Td</td>
<td>TIG</td>
</tr>
<tr>
<td>Uncertain or &lt;3 doses</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>&gt;3 doses</td>
<td>No**</td>
<td>No</td>
</tr>
</tbody>
</table>

Td = Tetanus and diphtheria toxoids, adsorbed (for adult use).
TIG = Tetanus immune globulin

* Such as, but not limited to: wounds contaminated with dirt, feces, and saliva; puncture wounds; avulsions; and wounds resulting from missiles, crushing, burns, and frostbite.

** Yes, >10 years since last dose

*** Yes, >5 years since last dose. (More frequent boosters are not needed and can accentuate side effects.)

Persons who have not completed a full primary series of injections or whose vaccination status is unknown or uncertain may require tetanus toxoid and passive immunization at the time of wound cleaning and debridement. Ascertaining the interval since the most recent toxoid dose is not sufficient. A careful attempt should be made to determine whether a patient has previously completed primary vaccination and, if not, how many doses have been given. **Persons with unknown or uncertain previous vaccination histories should be considered to have had no previous tetanus toxoid doses.**

In managing the wounds of adults, Td is the preferred preparation for active tetanus immunization. This toxoid preparation is also used to enhance protection against diphtheria, because a large proportion of adults are susceptible. Primary vaccination should ultimately be completed for persons documented to have received fewer than the recommended number of doses, including doses given as part of wound management.

If passive immunization is needed, human tetanus immune globulin (TIG) is the product of choice. The currently recommended prophylactic dose of TIG for wounds of average severity is 250 units IM. When T or Td and TIG are given...
concurrently, separate syringes and separate sites should be used. Most experts consider the use of adsorbed toxoid mandatory in this situation.

**Evidence for effectiveness**

Essentially all adult vaccinees achieve and maintain protective antitoxin levels for years. A Swedish study showed that the vaccine had a long-term efficacy rate of 94% after 10 years. Studies done in Denmark show efficacy rates of 96% after 13 to 14 years and 72% after 25 years. In one study, however, only 77% of elderly subjects had protective antitoxin levels 8 years after receiving a primary 3-dose series. Therefore, booster doses are recommended every 10 years\(^3,4\).

**References:**

TUBERCULOSIS

Introduction

Tuberculosis is caused by mycobacterium infection, mainly by *Mycobacterium tuberculosis* and more rarely *M. bovis* or *M. africanum*. *M. tuberculosis* is transmitted via respiratory droplets. Primary infection occurs in the lung which can lead to active or latent infection. Reactivation of pulmonary tuberculosis occurs mostly in adolescents and adults. Extra pulmonary TB include TB meningitis and military TB. There is a resurgence of TB globally in tandem with HIV/AIDS epidemic. It is a leading public health problem worldwide particularly in the developing countries. WHO estimated there are currently 16-20 million cases worldwide with 8 million new cases every year. Two million people die every year. These constitute 26% of eminently avoidable adult deaths worldwide. In Malaysia, there are 14,500-15000 new cases detected each year with an average of 41 cases per day and 2 deaths per day.

Vaccine available

The Bacillus Calmette and Guérin (BCG) vaccines are live vaccine derived from a strain of *M. bovis* that was attenuated by Calmette and Guérin at the Pasteur Institute. BCG was first administered to humans in 1921. Many different BCG vaccines are available worldwide. Although all currently used vaccines were derived from the original *M. bovis* strain, they differ in their characteristics when grown in culture and in their ability to induce an immune response to tuberculin. These variations may be caused by genetic changes that occurred in the bacterial strains over time and by differences in production techniques. However, the superiority of any one particular vaccine strain has not been demonstrated. Whereas, it is known that cell mediated immunity plays a major role in protection against TB, it is uncertain which particular vaccine antigen determines the immunity. Currently, there are no immunological markers that correlate with vaccine efficacy. Neither the presence nor the size of post-vaccination Mantoux test reactions predict the protection conferred by vaccination.

Mode of administration

Adults and children over 1 year of age: 0.1 ml strictly by intradermal injection in the upper arm, over the insertion of the deltoid muscle. Infants under 1 year of age: 0.05 ml strictly by intradermal injection.
Contraindications and adverse reactions

Until the risks and benefits of BCG vaccination in immunocompromised host are clearly defined, BCG vaccination should not be administered to persons (a) whose immunologic response are impaired because of HIV infection, congenital immunodeficiency, leukemia, lymphoma or generalized malignancy. (b) whose immunologic response have been suppressed by steroids, alkylating agents, anti-metabolites or radiation.

Its use in pregnancy should be avoided, though no harmful effects to the fetus have been associated with BCG vaccine.

A local reaction is common with a papule forming in 1-2 weeks. An ulcer forms in 2-6 weeks and healing occurs in about 12 weeks. Permanent scarring at the injection site occurs and keloids may form. Serious local reaction with ulceration and regional suppurative lymphadenitis with draining sinuses rarely occur. Rarely, osteitis affecting the long bones can occur several years later. Disseminated, fatal disease is extremely rare and occurs in those with impaired immunity.

Vaccines available in Malaysia

1. BCG vaccine (Merieux derived-Glaxo1077 strain)
2. Glutamate BCG vaccine (Tokyo 172 strain)
3. BCG Evans (English derived-Glaxo 1077 strain)

The BCG vaccine is available both as a multi-dose vial and a single dose vial.

Storage and handling

BCG vaccine should be stored and transported at +2 °C to +8 °C. The multi-dose vial contains a white freeze-dried plug, which disperses easily to form an opalescent liquid on reconstitution. It should be protected from exposure to light, refrigerated when not in use, and used within 8 hours of reconstitution. The diluent should not be frozen but kept cold.

Target groups

The national immunization programme recommends BCG vaccination to all newborn babies.

The efficacy of BCG vaccine in health care workers and HIV infected patients has not been well determined.
Evidence of effectiveness

New information about the protective efficacy of BCG has become available. Two recent meta-analyses of the published results of BCG vaccine of 24 clinical trials and 20 case-control studies confirmed that the protective efficacy of BCG for preventing serious forms of TB in children is high (i.e., >80%)\(^1\,^2\). (Level 1) These analyses, however, did not clarify the protective efficacy of BCG for preventing pulmonary TB in adolescents and adults; this protective efficacy is variable and equivocal. These studies also were not useful in determining the efficacy of BCG vaccine in health care workers, thus comprehensive infection control practices remain the fundamental strategy to protect HCWs from infection with *M. tuberculosis*. The protective efficacy of BCG vaccine in children and adults who are infected with HIV also has not been determined.

References

TYPHOID

Introduction

Typhoid fever is an acute invasive septicaemic illness caused by Salmonella typhi (current taxonomical designation S.enterica serovar Typhi). This organism consists of 3 different antigenic structures viz. the somatic (O) antigen, the flagellar (H) antigen and the capsular (Vi) antigen. The Vi antigen is the polysaccharide responsible for virulence. Typhoid fever may be preceded by a diarrhoeal illness. It is usually associated with constitutional symptoms. Untreated it may result in perforation, gastrointestinal haemorrhage, peritonitis and death.

In Malaysia, the incidence of enteric fever (typhoid and paratyphoid fever) ranged from 906 cases with 8 deaths in 1995 to 695 cases with 1 death in 2001. Another major concern is the emergence of multidrug resistant S.typhi especially from the Indian subcontinent, Asia and the Middle East.

Nature of vaccine

There are two types of typhoid vaccine. A parenteral vaccine based on the Vi polysaccharide antigen as well as an oral vaccine containing a live attenuated Ty 21a strain of S.typhi are available.

Mode of administration and dosing regimen

The Vi vaccine is administered as a single 0.5ml dose intramuscularly with boosters at 3 yearly intervals. The oral Ty 21a vaccine is administered by giving one capsule on days 1, 3 and 5, one hour before a meal. Boosters are required every 3 years to maintain immunity.

Contraindications and adverse reactions

The live oral (Ty21a) vaccine is contraindicated in immunocompromised patients and should not be administered to anyone on antimicrobial therapy. It should be administered >24 hours after an antimicrobial dose. In addition, it should be delayed for 3 days if malaria prophylaxis is administered. The only contraindication to vaccination with the parenteral (Vi) vaccine is a history of severe local or systemic reactions following a previous dose. Typhoid vaccines are generally safe. Local reactions at the injection site consisting of pain, redness and swelling can occur with the parenteral vaccines. Fever and headache can occur but are uncommon.

Availability in Malaysia
- Vi capsular polysaccharide vaccine
  Typhim Vi (Aventis Pasteur)
  Typhovax (Propharm)

- Live attenuated oral vaccine (Vivotif Berna, Swiss Serum).

**Target groups**

- Food handlers and vendors
- Travelers to areas in which there is a recognized risk of exposure to *S. typhi*. Risk is greatest for travelers to developing countries (e.g., countries in Latin America, Asia, and Africa). However, travelers should be cautioned that typhoid vaccination is not a substitute for careful selection of food and drink.
- Persons with intimate exposure (e.g., household contact) to a documented *S. typhi* carrier.
- Microbiology laboratory personnel who work frequently with *S. typhi*.

**Evidence for effectiveness**

In controlled field trials conducted among schoolchildren in Chile, three doses of the Ty21a vaccine in enteric-coated capsules administered on alternate days reduced laboratory-confirmed infection by 66% over a period of 5 years (95% confidence interval [CI]=50%–77%). *(Level 2)*

Two field trials in disease-endemic areas have demonstrated the efficacy of ViCPS in preventing typhoid fever. In a trial in Nepal, in which vaccine recipients were observed for 20 months, one dose of ViCPS among persons 5–44 years of age resulted in 74% (95% CI=49%–87%) fewer cases of typhoid fever confirmed by blood culture than occurred with controls. In a trial involving schoolchildren in South Africa who were 5–15 years of age, one dose of ViCPS resulted in 55% (95% CI=30%–71%) fewer cases of blood-culture-confirmed typhoid fever over a period of 3 years than occurred with controls. *(Level 2)*

A metanalysis comprising seventeen studies and nearly two million people showed that for the whole cell vaccines single dose regimens provide significant protection for the first two years. Two dose regimens provided significant protection for five years. For the Ty 21a vaccine, both the two and three dose regimens provided statistically significant protection for two years. The three dose regimen provided protection in the third and fourth years, but protection was not statistically significant in the fifth year. The Vi vaccine provided protection for two years, but the protection in the third year was not significant. *(4)*
References


VARICELLA

Introduction

Varicella (chickenpox) is a systemic viral infection with a characteristic vesicular-papular rash and is highly contagious. It is caused by varicella zoster virus or herpes zoster virus. In children, the illness is usually self-limiting but at least 1% of children under 15 years of age experience a complication. Rare cases of fetal injury have occurred after infection in pregnancy. Adults experience more severe disease (hospitalization 18 per 1000) and death (50 per 100 000)\textsuperscript{1,2}

Complications of varicella include intravascular coagulation, renal damage, disturbed renal function, haemorrhagic rash and secondary bacterial infections. Post-chickenpox encephalitis is common but usually mild and self-limiting. Cerebellar disturbance is rare with ataxia and nystagmus.

In temperate countries, 95% of varicella cases occur among persons less than 20 years of age. Seropositivity is lower in adults from tropical and subtropical countries. A seroprevalence study in Malaysia (1991-1993) by Malik et al showed that only 70% of persons below 20 years of age had been infected. However by 40 years of age, 91.3% had acquired the infection. This data implies that a substantial proportion of Malaysian young adults including females of child-bearing age are at risk of varicella

Nature of vaccines

1. Live-attenuated vaccine.
2. Varicella zoster immunoglobulin (VZIG) prepared from plasma containing high titres of specific antibody. VZIG is not available in Malaysia

Mode of administration

The live-attenuated vaccine is administered subcutaneously.

Dose regimen

Two doses with 4-8 weeks interval for persons more than 13 years of age.

Contraindications and adverse reactions

The vaccine is contraindicated in patients undergoing reinforcement therapy for leukemia or extensive therapy using strong immunosuppressives and in patients with acute myeloid leukemia, T-cell leukemia or malignant lymphoma. Adverse reactions include fever,
rashes, injection site reaction, herpes zoster, pharyngitis, cellulitis, hepatitis, pneumonia, erythema multiforme and Stevens-Johnson syndrome, arthropathy, thrombocytopenia, anaphylaxis, vasculitis, aplastic anemia, neuropathies.

**Vaccines available in Malaysia**

Varirix  
Varivax  
Okavax

**Target groups**

All susceptible individuals, regardless of age, who are at risk for varicella exposure.

**Evidence for effectiveness**

Pre-licensure, controlled, clinical trials demonstrated varicella vaccine to be 70-91% effective for preventing varicella and >95% effective for preventing severe varicella. In adults, effectiveness is shown by one nonrandomized controlled trial and two prospective cohort studies with maximum duration of follow up of six years. Further evidence is provided by one RCT providing combined data from both arms of a two dose adult trial. All but one adult study calculated effectiveness based on self reporting of disease. Adult and child vaccinees experiencing close contact with varicella are also protected.  

**Special storage procedures**

Varivax requires special storage issues because of its sensitivity to temperature. Shipment and storage in a **frozen** state is essential to maintain potency.

**References**

YELLOW FEVER VACCINE

Introduction

Yellow fever is an anthropozoonosis caused by the yellow fever virus of the Flavivirus genus. The virus is transmitted from monkey to monkey, from monkey to man, and from man to man predominantly by the *Aedes aegypti* mosquito. It occurs in the tropical and subtropical regions of Africa and South America but has never been seen in Asia. There is however, a risk of transmission from imported cases since the mosquito vector, *Aedes aegypti*, occurs in Malaysia.

The incubation period is two to five days. The acute form of the disease is viral haemorrhagic fever which can lead to death within ten days in 50% of cases in non-indigenous individuals (namely travelers) and during epidemics. Among the indigenous populations in endemic areas fatality is around 5%. There is no specific curative treatment, and symptomatic treatment is of unproven value. Fortunately, targeted vaccination of at risk populations provides efficient protection and help reduce the risk of epidemics.

Nature of vaccine

Yellow fever vaccine ia a live attenuated freeze-dried preparation of the 17D strain of yellow fever virus. It is propagated in leucosis-free chick embryos. A single dose correctly given confers immunity in nearly 100% of recipients lasting at least ten years and may be for life.

Mode of administration and dosing regimen

The vaccine should be given by subcutaneous injection as a single 0.5 mL dose irrespective of age. The International Certificate is valid for ten years from the tenth day after primary vaccination and immediately after revaccination.

Contraindications and adverse reactions

The usual contraindications to live virus vaccine should be observed. Some vaccinees (2-5%) may present with mild headache, myalgia, low grade fever, or other mild symptoms 5-10 days after vaccination. Immediate hypersensitivity reactions are extremely uncommon and are characterised by rash, urticaria, and/or asthma. It occurs principally among those with history of egg allergy

Vaccines available in Malaysia

- Live attenuated parenteral vaccine
- Certification of Vaccination can be obtained from the Virology Division, Infectious Diseases Research Centre, Institute for Medical Research,
Kuala Lumpur, and seven other designated government centres in the country (details to obtained from IMR Tel: 03 2698 6033).

**Special storage precautions**

The vaccine should be stored at 2-8°C and protected from light. The diluent supplied for use with the vaccine should be stored below 15°C but not frozen. The vaccine should be given within one hour of reconstitution.

**Target groups**

- Persons traveling or living in areas in which yellow fever infections occur. Vaccination is mandatory for all persons travelling from or to countries endemic for yellow fever
- Laboratory personnel who may be exposed to the virulent virus.

**Evidence for effectiveness**

Close to 100% seroconversion rates have been shown with yellow fever vaccines.\(^1\) Studies reported indicate that the thermostable 17-D yellow fever vaccine is comparable in immunogenicity and reactogenicity to its thermolabile counterpart.\(^2\) *(Level 3)*

**References**

PASSIVE IMMUNISATION

Passive immunisation means the provision of temporary immunity by the administration of preformed antibodies. This can prevent or attenuate the expression of the disease. The protective effect of immunoglobulins is immediate upon administration but the protection may be incomplete and is short-lived.

The preformed antibodies that will be emphasized in these guidelines are
- standard immune globulin (IG) of human origin / gamma globulin
- specific immunoglobulins

Immune Globulin (Human)

Human immune globulin (IG) is a sterile, concentrated solution containing between 100g/L and 180g/L (10%-18%) of protein and the preservative thimerosal. It is obtained from pooled human plasma and contains mainly IgG with small amounts of IgA and IgM. IG is stable for prolonged periods when stored at 2°C to 8°C. Maximum plasma levels are reached about 2 days after intramuscular injection, and the half life in the recipient’s circulation is 21 to 27 days.

Human IG which is available in Malaysia is
- Globuman Berna (Diethlem, Tel : 03 7966 0288)

Recommended usage
Prophylactic use of IG has been shown to be effective in a limited number of clinical situations.

1. Measles prophylaxis
   IG can be given to prevent or modify measles in susceptible persons within 6 days after exposure, preferably within 3 days. The duration of protection is estimated to be between 3-6 weeks.
   Prophylaxis dose: 0.2ml/kg
   Therapy: 1.0 – 2.0ml/kg

2. Hepatitis A prophylaxis
   IG is recommended for non-immune persons who are in close contact with a hepatitis A patient. Post exposure prophylaxis should be given as soon as possible and is effective up to 14 days after exposure.
   Prophylaxis dose: 0.1ml/kg; maybe repeated after 4 to 5 months.

Contraindications and adverse reactions

Persons with thrombocytopenia or coagulation disorders that contraindicate intramuscular injection should not be given intramuscular IG.
IG administration may interfere transiently with the subsequent immune response to MMR vaccines. Please refer to the table below for recommended interval between the administration of IG and these vaccines. IG should not be given to persons with isolated IgA deficiency or with a known allergy to the preservative thimerosal, a mercury derivative. Pregnancy is not a contraindication to the use of IG or other immune globulin.

Reactions at site of injection include tenderness, erythema and stiffness of local muscles. Mild fever or malaise may occasionally occur. Less common side effects include flushing, headache and atheralga.

**Intravenous Immune globulin (IVIG)**

Intravenous immune globulin (IGIV) is a preparation that contains 50g/L (5%) protein with maltose, sucrose or glycine as a stabilizing agent. It is used for replacement therapy in patients with congenital agammaglobulinaemia, treatment of idiopathic thrombocytopenic purpura and Kawasaki syndrome, and for the prophylaxis of infection following bone marrow transplantation. The details of IVIG usage is beyond the scope of these guidelines.

**Hyperimmune Globulin (specific)**

These are special preparations obtained from blood plasma from donor pools pre-selected for a high antibody content against a specific antigen. Examples of specific immune globulin are hepatitis B immune globulin, varicella-zoster immune globulin, rabies immune globulin, tetanus immune globulin, cytomegalovirus immune globulin, respiratory syncytial virus immune globulin and botulism immune globulin.

Specific immune globulin which are available in Malaysia are:

1. Hepatitis B immune globulin
2. Tetanus immune globulin
3. Rabies immune globulin

- **Hepatitis B immune globulin**
  The indications for use are for percutaneous or mucosal exposure to blood containing hepatitis B virus or sexual contact with an acute case of hepatitis B. It should be given within 7 days after exposure (preferably within 72 hours)
  - Hepuman Bema Injection (1ml vial)
    Dose: 4ml (IM)
  - Hepabig Injection (1ml vial)
    Dose:1000-2000 IU (IM)
2. Tetanus immune globulin (*Please see section on tetanus*)

3. Rabies immune globulin (*Please see section on Rabies*)

Suggested interval between administration of immune globulin preparation for various indications and vaccine containing live measles virus.

<table>
<thead>
<tr>
<th>Immune globulin</th>
<th>Suggested interval before measles vaccination</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tetanus (TIG)</td>
<td>3 months</td>
</tr>
<tr>
<td>Hepatitis A (IG)</td>
<td>3 months</td>
</tr>
<tr>
<td>Hepatitis B (HBIG)</td>
<td>3 months</td>
</tr>
<tr>
<td>Rabies (HRIG)</td>
<td>4 months</td>
</tr>
<tr>
<td>Measles (IG)</td>
<td>5-6 months</td>
</tr>
</tbody>
</table>
# RISK GROUPS

## ADULTS WHO HAVE MISSED CHILDHOOD VACCINATION

All adults should complete a primary series of the following vaccines & toxoids if they have not done so during childhood.

<table>
<thead>
<tr>
<th>Adults: Age group</th>
<th>Vaccine recommended</th>
<th>Schedule: 1st vaccination &amp; boosters</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>All Adults:</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>▪ 18-24 years</td>
<td>Tetanus, Diptheria</td>
<td>Combined tetanus &amp; diptheria toxoids (Td): 1st. 2 doses given 4 weeks apart &amp; 3rd. dose 6-12 months after 2nd dose. Booster: every 10 years</td>
<td>Doses need not be repeated when vaccine schedule delayed. Persons with uncertain histories of receiving diphtheria or tetanus toxoids should receive a full three-dose primary series of Td.</td>
</tr>
<tr>
<td>▪ 25-64 years</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>▪ &gt; 65 years</td>
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<thead>
<tr>
<th>Adults in the following age groups:</th>
<th>Vaccine recommended</th>
<th>Schedule: 2 doses of measles-mumps-rubella (MMR) live vaccine; given at least 1 month apart</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>▪ 18-24 years</td>
<td>Measles, Mumps, Rubella</td>
<td></td>
<td>Recommended if no history of physician-documented infection, laboratory evidence of immunity</td>
</tr>
<tr>
<td>▪ 25-64 years</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Vaccines and toxoids recommended for adults, by age groups.

Summary:

<table>
<thead>
<tr>
<th>Age group (years)</th>
<th>Td +</th>
<th>Measles</th>
<th>Mumps</th>
<th>Rubella</th>
<th>Influenza</th>
<th>Pneumococcal Polysaccharide</th>
</tr>
</thead>
<tbody>
<tr>
<td>18-24</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td></td>
</tr>
<tr>
<td>25-64</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td></td>
</tr>
<tr>
<td>&gt;=65</td>
<td>X</td>
<td></td>
<td></td>
<td></td>
<td>X</td>
<td>X</td>
</tr>
</tbody>
</table>
**ELDERLY (>65 YEAR OLD) AND PATIENTS WITH CHRONIC DISEASES**

<table>
<thead>
<tr>
<th>Category</th>
<th>Vaccines recommended</th>
<th>Timing</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Elderly (&gt;65 year old) including residents of nursing homes and other</td>
<td>Influenza(^1) (Level 1)</td>
<td>Annual vaccination</td>
<td>Vaccination can be given throughout the year.</td>
</tr>
<tr>
<td>chronic care facilities</td>
<td></td>
<td>No optimal time in Malaysia</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Pneumococcal(^1) (Level 4)</td>
<td>To be given if not vaccinated before or unknown vaccination status</td>
<td>Person who have not received vaccination within the last 5 years and &lt;65 years of age at time of vaccination should be vaccinated.</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Patients with chronic illnesses eg chronic pulmonary, cardiac and</td>
<td>Pneumococcal(^3) (Level 9)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>liver disease, diabetes mellitus, anatomic or functional asplenia and</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>cerebrospinal fluid leaks</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**References:**
HEALTH CARE WORKERS (HCW) *

* The category of healthcare workers (HCWs) include persons who provide healthcare to patients or work in institutions that provide patient care eg. doctors, nurses, emergency medical personnel, dental professionals and students, medical and nursing students, laboratory technicians, hospital volunteers and support staff providing patient care in healthcare institutions.

On the basis of documented nosocomial transmission, HCWs are considered to be at significant risk for acquiring and transmitting the following vaccine-preventable infections. The following vaccinations (listed in the table) are **strongly recommended among HCWs:**

<table>
<thead>
<tr>
<th>Category of HCW</th>
<th>Vaccines recommended</th>
<th>Timing</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>All health care workers</td>
<td>• Hepatitis B (1)</td>
<td>1&lt;sup&gt;st&lt;/sup&gt; vaccination should be given at onset of career.</td>
<td>Prevacervation serologic screening recommended before vaccination.</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Booster doses not necessary. (2,3,4)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Post vaccination serologic testing for antibodies recommended. (1)</td>
</tr>
<tr>
<td></td>
<td>• Measles, mumps and rubella (5-10)</td>
<td>1&lt;sup&gt;st&lt;/sup&gt; vaccination (2 doses) before onset of career</td>
<td>Indicated for HCWs who do not have documented vaccination, physician-diagnosed infection or serologic evidence of immunity</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>MMR vaccine preferred.</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Booster doses not necessary (8,9)</td>
</tr>
<tr>
<td>Healthcare workers who have contact with patients at high-risk of influenza or its complications; HCWs who work in chronic care facilities.</td>
<td>• Influenza (12-14)</td>
<td>Annual vaccination (IM)</td>
<td></td>
</tr>
</tbody>
</table>
All healthcare workers but especially those in close contact with immunocompromised patients, special care nurseries and pregnant mothers.

| **Varicella (15-21)** | Vaccination (Two 0.5 ml S/C doses 4-8 weeks apart) should be given before posting to unit. Booster doses not necessary. | Prevaccination serologic testing is cost-effective in those who do not have a reliable history of varicella infection or serologic evidence of immunity

| **Level 4** |

The following vaccines are **not routinely recommended for HCWs (exceptions listed in parenthesis)**

- **BCG** (only considered for HCWs in areas where Multidrug resistant tuberculosis is prevalent, where there is strong likelihood of infection & when comprehensive infection control measures have failed to prevent transmission to HCWs.)
- **Hepatitis A**
- **Typhoid** (considered in workers in microbiology laboratories who frequently work with *Salmonella typhi*.)
- **Meningococcal polysaccharide vaccine** (indicated for laboratory personnel working frequently with *N. meningitides*)
- **Vaccinia** (indicated only for laboratory workers involved with orthopox viruses and certain health-care workers involved in clinical trials of vaccinia recombinant vaccines)
- **Anthrax** (indicated for laboratory personnel working with Bacillus anthracis)
- **Rabies** (pre-exposure vaccination only indicated for laboratory workers directly involved with testing or isolating rabies virus)
- **Pertussis**
The following vaccines are **recommended as for the general adult population**:  

- Tetanus
- Diptheria
- Pneumococcal polysaccharide vaccine

**References:**

IMMUNOCOMPROMISED PATIENTS

VACCINATION FOR INDIVIDUALS WITH SPLENECTOMY OR FUNCTIONAL/ANATOMICAL ASPLENIA

<table>
<thead>
<tr>
<th>Vaccines</th>
<th>Recommendation</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Recommended: Polyvalent pneumococcus, Meningococcus, Hib</td>
<td>To be given at least 2 weeks before splenectomy or soon after surgery</td>
<td>Booster doses recommended every 5 years for pneumococcus and 3 years for meningococcus</td>
</tr>
<tr>
<td>Use if indicated: BCG, Hepatitis A, Influenza, MMR, Inactivated polio vaccine, Rabies, Td, Typhoid, Varicella and Vaccinia</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

VACCINATION FOR INDIVIDUALS WITH SUPPRESSED IMMUNITY DUE TO DISEASE OR TREATMENT

<table>
<thead>
<tr>
<th>Vaccine</th>
<th>HIV</th>
<th>Immunosuppression</th>
<th>Renal failure</th>
<th>Diabetes</th>
<th>Alcoholism</th>
</tr>
</thead>
<tbody>
<tr>
<td>BCG</td>
<td>C</td>
<td>C</td>
<td>UI</td>
<td>UI</td>
<td>UI</td>
</tr>
<tr>
<td>Hep A</td>
<td>UI</td>
<td>UI</td>
<td>UI</td>
<td>UI</td>
<td>UI</td>
</tr>
<tr>
<td>Hep B (Double dose)</td>
<td>UI</td>
<td>UI</td>
<td>R</td>
<td>UI</td>
<td>UI</td>
</tr>
<tr>
<td>Hib</td>
<td>UI</td>
<td>R</td>
<td>UI</td>
<td>UI</td>
<td>UI</td>
</tr>
<tr>
<td>Influenza</td>
<td>R</td>
<td>R</td>
<td>R</td>
<td>R</td>
<td>R</td>
</tr>
<tr>
<td>MMR</td>
<td>R</td>
<td>C</td>
<td>UI</td>
<td>UI</td>
<td>UI</td>
</tr>
<tr>
<td>Meningococcus</td>
<td>UI</td>
<td>UI</td>
<td>UI</td>
<td>UI</td>
<td>UI</td>
</tr>
<tr>
<td>IPV polio</td>
<td>UI</td>
<td>UI</td>
<td>UI</td>
<td>UI</td>
<td>UI</td>
</tr>
<tr>
<td>OPV polio, live</td>
<td>C</td>
<td>C</td>
<td>UI</td>
<td>UI</td>
<td>UI</td>
</tr>
<tr>
<td>Pneumococcus</td>
<td>R</td>
<td>R</td>
<td>R</td>
<td>UI</td>
<td>UI</td>
</tr>
<tr>
<td>Rabies</td>
<td>UI</td>
<td>UI</td>
<td>UI</td>
<td>UI</td>
<td>UI</td>
</tr>
<tr>
<td>Td</td>
<td>UI</td>
<td>UI</td>
<td>UI</td>
<td>UI</td>
<td>UI</td>
</tr>
<tr>
<td>Typhoid, inactivated &amp; Vi</td>
<td>UI</td>
<td>UI</td>
<td>UI</td>
<td>UI</td>
<td>UI</td>
</tr>
<tr>
<td>Varicella</td>
<td>C</td>
<td>C</td>
<td>UI</td>
<td>UI</td>
<td>UI</td>
</tr>
<tr>
<td>Vaccinia</td>
<td>C</td>
<td>C</td>
<td>UI</td>
<td>UI</td>
<td>UI</td>
</tr>
</tbody>
</table>

C – contraindicated  R – recommended  UI – use if indicated
Note 1: Immunisation for individuals with suppressed immunity due to disease or treatment (Level 9).

The following groups of individuals should not receive live vaccines:

1. patients receiving high dose oral or intravenous steroids or other immunosuppressive treatment including total body or lymphoid irradiation. Daily doses of corticosteroids in excess of 20mg of prednisolone or equivalent for >14 days are associated with significant immunosuppression. Lower doses may also be associated with an impaired immune response. For patients receiving the above high dose steroids or who have received prolonged or extensive therapy topically, orally or by inhalation, live vaccines should be postponed until 3 months after cessation of therapy.
2. patients with lymphoma, leukaemia or other malignancies of the reticuloendothelial system. These includes patient in remission who have received chemotherapy within the last 3 months or those whose remission status may not be clear.
3. patients who impaired immunity including severe combined immunodeficiency syndrome and HIV.

Inactivated vaccines (such as pertussis and hepatitis A), modified vaccines (such as diphtheria and tetanus vaccines) and subunit vaccines (such as Hib and hepatitis B) may not be harmful to the above recipients and can be safely given but may be of doubtful efficacy.

Note 2: Vaccination of HIV-infected individuals (Level 9).

Vaccination of HIV-infected individuals poses different problems. The immune status of the individual can range from minimal to profound deficiency. There is a risk that live vaccines may cause progressive infection. The immune response to vaccines may be inadequate and higher or more frequent doses may be required. It is highly likely that individuals with good CD34 counts or who are well controlled will respond well to vaccines.

1. Pneumococcal infection is a frequent cause of morbidity. Pneumococcal polysaccharide vaccine may be given although there may be limited efficacy.
2. Influenza vaccine may also be given to individuals at risk as the benefit outweighs the risk.
3. Recombinant Hepatitis B vaccines are safe to use but the normal dosage should be doubled and given on 3 occasions. It is recommended that the antibody response be monitored. (>10mIU/L)
4. Hepatitis A vaccine has not been evaluated in this population but may be given if indicated.
5. BCG vaccine should NOT be given.
6. For travel – live attenuated typhoid or yellow fever vaccines should NOT be given. Meningococcal, typhoid, cholera and rabies vaccines are safe with the usual indications.
Note 3: Vaccination for haemodialysis and chronic renal failure patients (*Level 9*).

The above persons are at high risk of infection with HBV and routine serologic screening is advised. Susceptible patients should receive three doses of HB vaccine of double strength. Postvaccination antibody screening is recommended. Revaccination is considered for non-responders and if anti-HBs levels remain < 10mIU/mL. As these patients are at increased risk of lower respiratory infections, pneumococcal and influenza vaccination are also recommended.

References:


## PASSIVE IMMUNIZATION FOR IMMUNOCOMPROMISED PERSON

<table>
<thead>
<tr>
<th>Subgroup at risk</th>
<th>Immune globulin</th>
<th>Timing / recommendation</th>
<th>Comment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients with primary hypogammaglobulinemia (IgG &lt; 400mg/dl)</td>
<td>Immune Globulin (IVIG)</td>
<td>IV 0.4 – 0.6 gm / kg every 4 weeks&lt;sup&gt;1&lt;/sup&gt; (Level 3)</td>
<td></td>
</tr>
<tr>
<td>Secondary hypogammaglobulinemia (IgG &lt; 400mg/dl) with recurrent severe infections. (&lt; 2 episodes / year)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Secondary hypogammaglobulinemia (IgG &lt; 400mg/dl) with recurrent severe infections. (&lt; 2 episodes / year)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Immunocompromised persons :</td>
<td>Immune Globulin (IMIG)</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Specific conditions :</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Measles</td>
<td>Postexposure :</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Measles</td>
<td>IM 0.25ml / kg (max 15ml) administered as soon as possible (within 6 days after exposure) regardless of the previous vaccination status.&lt;sup&gt;2&lt;/sup&gt; (Level 9)</td>
<td>IM IG may not be necessary for HIV-infected patients who are receiving IV IG 0.1 – 0.4 gm / kg at regular intervals and the last dose was administrated within 3 weeks of exposure to measles.</td>
<td></td>
</tr>
<tr>
<td>Hepatitis A</td>
<td>Postexposure :</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hepatitis A</td>
<td>IM 0.02ml / kg (max 15ml) administered as soon as possible (within 2 weeks) after exposure.&lt;sup&gt;2&lt;/sup&gt; (Level 9)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Subgroup at risk</td>
<td>Immune globulin</td>
<td>Recommendation</td>
<td>Comment</td>
</tr>
<tr>
<td>------------------------------------------------------</td>
<td>--------------------------------------</td>
<td>-----------------------------------------------------</td>
<td>-------------------------------------------------------------------------</td>
</tr>
</tbody>
</table>
| Susceptible, severely immunocompromised persons after significant exposure to chickenpox or zoster. | Varicella-Zoster Immune Globulin (VZIG) | IM 125 Units / 10 kg. (maximum : 625 Units) administered as soon as possible or within 72 hours after known contact.³ (Level 8) | Definition of significant exposure to a person with varicella:
  • Household contact, close contact indoors of > 1 hour.
  • Sharing the same 2 to 4 bed hospital room
  Prolonged direct, face-to-face contact e.g occurs with nurses or doctors who care for patient. |
| Susceptible, severely immunocompromised persons after significant exposure to needlestick, sexual exposure to person positive for hepatitis B surface antigen. | Hepatitis B Immune Globulin (HBIG) | IM 0.06ml / kg as soon as possible after exposure.⁴ (Level 3) If the Hepatitis B vaccine series has not been started.
  - 2nd dose of HBIG should be administered 1 month later (for percutaneous / mucous membrane exposure) or 3 months later (sexual exposure) | Hepatitis B vaccine should be given at a different site simultaneously or within 1 week of exposure, and the vaccination should be repeated at 1 month and 6 months after the 1st dose.⁴ |
<table>
<thead>
<tr>
<th>Subgroup at risk</th>
<th>Immune globulin</th>
<th>Recommendation</th>
<th>Comment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Immunocompromised persons (Ig G &lt; 400 mg/dl), with non-clean, non-minor wound in a persons with unknown tetanus toxoid status or inadequate tetanus vaccination.</td>
<td>Tetanus Immune Globulin (TIG)</td>
<td><strong>Tetanus</strong> &lt;br&gt;For wound &lt; 24 hours &lt;br&gt;- IM 250 Units (^3) <em>(Level 9)</em> &lt;br&gt;For wound &gt; 24 hours or risk of heavy contamination &lt;br&gt;- IM 500 Units</td>
<td>Inadequate tetanus vaccination is defined as less than 2 previous doses of Tetanus vaccines</td>
</tr>
<tr>
<td>Immunocompromised persons (Ig G &lt; 400 mg/dl), exposure to rabies, with no history of recommended pre-exposure or post-exposure prophylaxis with Human Diploid Cell Vaccine (HDCV).</td>
<td>Rabies Immune Globulin, human (RIG)</td>
<td><strong>Rabies</strong> &lt;br&gt;20 IU/kg, up to half infiltrated around wound, remainder IM. (^6) <em>(Level 9)</em></td>
<td>For not-previously vaccinated persons: IM HDCV 1.0 ml injection (deltoid area), one each on day 0, 3, 14, and 28. &lt;br&gt;For previously vaccinated persons: IM HDCV 1.0 ml injection (deltoid area), one each on day 0 &amp; 3.</td>
</tr>
</tbody>
</table>

**REFERENCES**


5. CDC. Varicella zoster immune globulin for the prevention of chickenpox. MMWR 1984;33:84-90,95-100.


### VACCINATION SCHEDULE FOR BLOOD AND MARROW TRANSPLANTATION (ALLOGENEIC AND AUTOLOGOUS)*1,2,3,4*(Level 9)

<table>
<thead>
<tr>
<th>Vaccine or toxoid</th>
<th>Time after Transplantation</th>
<th>Chronic GVHD</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Inactivated vaccine or toxoid</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Diphtheria, tetanus, Pertussis</td>
<td>12 months</td>
<td>14 months</td>
<td>24 months</td>
</tr>
<tr>
<td>Children aged &lt; 7 yrs</td>
<td>Diphtheria toxoid-tetanus toxoid-pertussis vaccine (DTP) or diphtheria toxoid-tetanus toxoid (DT)</td>
<td>DTP or DT</td>
<td>DTP or DT</td>
</tr>
<tr>
<td>Children aged &gt; 7 yrs</td>
<td>Tetanus-diphteria toxoid (TD)</td>
<td>TD</td>
<td>TD</td>
</tr>
<tr>
<td>Adults</td>
<td>TD</td>
<td>TD</td>
<td>TD</td>
</tr>
<tr>
<td>Hemophilus influenzae type b</td>
<td>Hib conjugate</td>
<td>Hib conjugate</td>
<td>Hib conjugate</td>
</tr>
<tr>
<td>Pneumococcus* (level 5)</td>
<td>PPV23</td>
<td>---</td>
<td>PPV23</td>
</tr>
<tr>
<td>Influenza</td>
<td>Use if indicated</td>
<td></td>
<td>yes</td>
</tr>
<tr>
<td>Hepatitis B (Hep B)</td>
<td>Hep B</td>
<td>Hep B</td>
<td>Hep B</td>
</tr>
<tr>
<td>Inactivated polio (IPV)</td>
<td>IPV</td>
<td>IPV</td>
<td>IPV</td>
</tr>
<tr>
<td>Meningocccocal</td>
<td>Use if indicated</td>
<td></td>
<td>---</td>
</tr>
</tbody>
</table>
### Live-attenuated Vaccine

<table>
<thead>
<tr>
<th>Vaccine</th>
<th>Measles-mumps-rubella (MMR)</th>
<th>BCG</th>
<th>Varicella Vaccine</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>-----</td>
<td>Not recommended</td>
<td>Not recommended (Insufficient data)</td>
</tr>
<tr>
<td>MMR</td>
<td></td>
<td>---</td>
<td>---</td>
</tr>
<tr>
<td>No</td>
<td></td>
<td>---</td>
<td>---</td>
</tr>
</tbody>
</table>

# Whether to vaccinate if the patient has chronic graft versus host disease.

Notes on Foreign Travel\(^4\) (level 9):

For transplant patients who wish to travel abroad, additional advice and extra immunisation may be necessary. Patients should seek advice from their respective transplantation teams.

Vaccines which should be safe for blood and marrow transplant patients intending to travel include:

- Typhoid – Not the oral form which is live
- Cholera – not recommended because of low protective efficacy
- Hepatitis A – both active and passive are safe

The following vaccines are contraindicated:

- Yellow Fever
- Japanese B encephalitis
- Oral active Polio vaccine

References:

2. Guidelines for preventing opportunistic infection among hematopoietic stem cell transplant recipients. Recommendations of CDC, the Infectious Diseases Society of America, and the America Society of blood and marrow transplantation. ASBMT 2000;6(6a) :705-6
3. Singhal S, Mehta J. Reimmunisation after blood or marrow stem cell transplantation. Bone Marrow Transplant 1999;23(7): 637-646

VACCINATION SCHEDULE FOR ADULTS AWAITING SOLID ORGAN TRANSPLANTATION AND SOLID ORGAN TRANSPLANT RECIPIENTS

<table>
<thead>
<tr>
<th>Vaccine</th>
<th>Timing</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Inactivated Vaccine</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Diptheria, tetanus</td>
<td>3 doses, last within 10 years</td>
<td>Td-1</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Td-2</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Td-3</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Td every 10 years</td>
</tr>
<tr>
<td>Haemophilus Influenza Type B conjugate</td>
<td>Not routinely recommended</td>
<td></td>
</tr>
<tr>
<td>Hepatitis B⁺</td>
<td>3 doses</td>
<td>HepB-1</td>
</tr>
<tr>
<td>(level 8)</td>
<td></td>
<td>Hep B-2</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Hep B-3</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Booster if titer &lt;10mIU/ml</td>
</tr>
<tr>
<td>Pneumococcal</td>
<td>2 doses of PPV23</td>
<td>PPV23-1</td>
</tr>
<tr>
<td></td>
<td></td>
<td>-----</td>
</tr>
<tr>
<td></td>
<td></td>
<td>-----</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Complete 2 doses, second dose 5 years after first dose</td>
</tr>
<tr>
<td>Hepatitis A⁺</td>
<td>2 doses, at risk patients only</td>
<td>Hep A-1</td>
</tr>
<tr>
<td>(level 9)</td>
<td></td>
<td>-----</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Hep A-2</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Recommended for patients at risk, complete 2 doses</td>
</tr>
<tr>
<td></td>
<td></td>
<td>At risk includes those waiting for liver transplant, all with chronic liver disease and those with risk of exposure to hepatitis A</td>
</tr>
<tr>
<td>Influenza</td>
<td>Use if Indicated</td>
<td></td>
</tr>
<tr>
<td>Inactivated polio vaccine</td>
<td>3 doses + 1 booster, at risk patients only</td>
<td>IPV-1</td>
</tr>
<tr>
<td></td>
<td></td>
<td>IPV-2</td>
</tr>
<tr>
<td></td>
<td></td>
<td>IPV-3</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Recommended for patients at risk</td>
</tr>
<tr>
<td>Meningococcal Vaccine</td>
<td>1-2 doses, at-risk patients only</td>
<td>Mening-1</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Recommended for patients at risk, complete 1-2 doses, 2nd dose</td>
</tr>
<tr>
<td></td>
<td></td>
<td>At risk includes those with asplenia, travel exposure and</td>
</tr>
<tr>
<td>Vaccine</td>
<td>dose 5 years after</td>
<td>college students</td>
</tr>
<tr>
<td>-------------------------------------</td>
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<td>------------------</td>
</tr>
<tr>
<td><strong>Live vaccine</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Measles-mumps-rubella</td>
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<td></td>
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<tr>
<td>Live vaccine</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Measles-mumps-rubella</td>
<td>Fully Immunised</td>
<td>Defined</td>
</tr>
<tr>
<td>Varicella</td>
<td>Fully Immunised</td>
<td>Defined</td>
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<td>Varicella</td>
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<tr>
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<td>REFERENCES:</td>
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</tbody>
</table>
## TRAVELLERS

<table>
<thead>
<tr>
<th>Category</th>
<th>Vaccine</th>
<th>Comments</th>
</tr>
</thead>
</table>
| Mandatory vaccination       | Yellow fever for all travelers traveling to or from yellow-fever endemic countries  
Meningococcal vaccine (tetavalent) for all Haj and Umrah pilgrims | These vaccines are legal requirements for travel. Failure to obtain vaccines could result in non-entry/quarantine in destination as well as home country                                                                 |
| Routine vaccination         | Diphtheria/tetanus/pertussis        | Although not mandatory all travelers are generally advised to ensure that they have these necessary vaccination and boosters (*Level 9*)                                                                 |
|                             | Hepatitis B                        |                                                                                                                                                                                                          |
|                             | Measles-Rubella-Mumps              |                                                                                                                                                                                                          |
|                             | Poliomyelitis                      |                                                                                                                                                                                                          |
| Selective use for travelers | Cholera                             | Recommendations for these vaccines depend on the countries of destination, the current outbreak situation at the time of travel, the purpose for travel, the intended length of stay and the health status of the traveler.  
As recommendations will change from time to time, it is prudent to access the latest advisories from the following sites maintained by the CDC and WHO  
1. [www.cdc.gov.travel](http://www.cdc.gov.travel)  
2. [www.who.int/ith](http://www.who.int/ith) |
|                             | Influenza                           |                                                                                                                                                                                                          |
|                             | Hepatitis A                        |                                                                                                                                                                                                          |
|                             | Japanese encephalitis              |                                                                                                                                                                                                          |
|                             | Lyme disease                       |                                                                                                                                                                                                          |
|                             | Meningococcal                      |                                                                                                                                                                                                          |
|                             | Pneumococcal                       |                                                                                                                                                                                                          |
|                             | Rabies                              |                                                                                                                                                                                                          |
|                             | Tick-borne encephalitis            |                                                                                                                                                                                                          |
|                             | BCG                                 |                                                                                                                                                                                                          |
|                             | Typhoid                             |                                                                                                                                                                                                          |

### References

1. WHO. International travel and health. (Website: [www.who.int/ith](http://www.who.int/ith))  
2. Centers for Disease Control (Website: [www.cdc.gov.travel](http://www.cdc.gov.travel))
<table>
<thead>
<tr>
<th>Category</th>
<th>Vaccines recommended</th>
<th>Timing</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Personnel working exclusively with non-feral rodents and rabbits from approved sources and cold blooded vertebrates</td>
<td>BCG if Mantoux negative <em>(Level 9)</em></td>
<td>At time of employment</td>
<td>Health check-up at time of employment.</td>
</tr>
<tr>
<td></td>
<td>Tetanus toxoid <em>(Level 9)</em></td>
<td>At time of employment</td>
<td></td>
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<tr>
<td></td>
<td></td>
<td>At time of employment and boosters every 10 years</td>
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<tr>
<td>Personnel working or exposed to feral animals and purpose bred laboratory animals from non-approved sources and farm animals</td>
<td>BCG if Mantoux negative <em>(Level 9)</em></td>
<td>At time of employment</td>
<td>Health check-up at time of employment 6 ml of serum to be taken at initial examination and stored at -20 C. Additional samples to be taken after a bite or scratch at the discretion of the physician when animal-related illness suspected</td>
</tr>
<tr>
<td></td>
<td>Tetanus toxoid <em>(Level 9)</em></td>
<td>At time of employment</td>
<td></td>
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<tr>
<td></td>
<td></td>
<td>At time of employment and boosters every 10 years</td>
<td></td>
</tr>
<tr>
<td>Personnel exposed to cats, dogs, feral animals from populations known to be potential carriers of rabies</td>
<td>BCG, Tetanus plus rabies immunization <em>(Level 9)</em></td>
<td>At time of employment pre-exposure primary series and boosters every two years</td>
<td></td>
</tr>
<tr>
<td>Personnel working with non-human primates</td>
<td>BCG, Tetanus plus Measles <em>(Level 9)</em></td>
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<td></td>
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<tr>
<td></td>
<td>Hepatitis B <em>(Level 9)</em></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Personnel involved in animal care whether laboratory animals or primates</td>
<td>BCG, Tetanus, Rabies, Measles, Hepatitis B <em>(Level 9)</em></td>
<td></td>
<td>6 ml of serum to be taken annually and stored at -20 C.</td>
</tr>
</tbody>
</table>
## OTHER GROUPS

<table>
<thead>
<tr>
<th>Category</th>
<th>Vaccines Recommended</th>
<th>Timing</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prisoners</td>
<td>Hepatitis B</td>
<td>Vaccine dose and schedule should follow the recommendation for normal adults</td>
<td></td>
</tr>
<tr>
<td>Inmates of correctional facilities</td>
<td>Hepatitis B</td>
<td></td>
<td></td>
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<tr>
<td>Homosexuals/Heterosexuals with multiple partners</td>
<td>Hepatitis A and B</td>
<td></td>
<td>Pre-vaccination screening for HAV and HBV is recommended.</td>
</tr>
<tr>
<td>Intravenous drug users</td>
<td>Hepatitis A and B</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Institutionalized mentally dysfunctional persons</td>
<td>Hepatitis A and B</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>(Level 9)</td>
<td></td>
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</tbody>
</table>

**References:**