Chapter 13
IMMUNOLOGICAL PRODUCTS AND VACCINES

13. IMMUNOLOGICAL PRODUCTS AND VACCINES

Immunity is generally understood to mean protection from infectious diseases.

Immunization may be active or passive. Active immunization involves stimulation with an antigen to develop immunologic defenses against a future exposure. Passive immunization involves administration of preformed antibodies to an individual who is already exposed or is about to be exposed to an antigen.

13.1 IMMUNITY, IMMUNIZATION SCHEDULE AND STORAGE

13.1.1 ACTIVE AND PASSIVE IMMUNITY

ACTIVE IMMUNITY

Vaccines may consist of:

i) a live attenuated form of
   a virus (e.g. measles vaccine) or
   bacteria (e.g. BCG vaccine);

ii) Inactivated preparations of
   the virus (e.g. influenza vaccine) or
   bacteria (e.g. Pertussis, VI Typhoid vaccine) or

iii) extracts of or detoxified exotoxins produced by a micro-organism (e.g. tetanus vaccine, diphtheria vaccine).

They stimulate production of antibodies and other components of the immune mechanism.

For the live attenuated vaccines, immunization is generally achieved with a single dose although multiple doses may also be recommended (e.g. 3 doses are required with oral poliomyelitis and oral typhoid vaccines). Live attenuated vaccines are expected to produce a durable immunity but it is not always as long as that of the natural infection. When two live virus vaccines are required (and are not available as a combined preparation) they should be given either simultaneously at different sites or with an interval of at least 3 weeks. Concomitant vaccination is only carried out after extensive evidence is obtained that the vaccines do not have a negative effect when given together.

Inactivated vaccines may require a primary series of vaccinations to produce adequate antibody response and in most cases reinforcing or 'booster' injections are required; the duration of immunity varies from months to many years depending on the nature of the vaccine components and the route of administration. Oral vaccines require more boosting than parenteral/injectable vaccines.

Extracts of or **detoxified exotoxins** are more immunogenic if adsorbed onto an adjuvant (such as aluminium hydroxide). They require a primary series of vaccination followed by boosting doses.

Side-effects: some vaccines e.g. poliomyelitis produce very few reactions like VAPP or VDPV, while others e.g. measles may produce very mild form of disease. Some vaccines may produce discomfort at the site of injection and mild fever and malaise. Vaccines that have been incorporated into national immunization systems have been well studied and are relatively safe. Although uncommon there can serious untoward reactions related or unrelated to the vaccine and these should always be reported to the proper health authority. Anaphylactic reactions are very rare but can be fatal. For full details of side-effects, the product literature should always be consulted.

Caution: Most of the vaccines are safe to receive. However, vaccination may be postponed if the individual is suffering from an acute illness. It is not necessary to postpone immunisation in patients with minor illnesses without fever or systemic upset. If alcohol or disinfectant is used for cleansing the skin it should be allowed to evaporate before vaccination to prevent possible inactivation of live vaccines.

When 2 or more vaccines are required, they should be given simultaneously at different sites, preferably in a different limb; if more than one injection is to be given in the same limb, they should be administered at least 2.5 cm apart (also see under BCG Vaccines). When 2 live vaccines cannot be given at the same time, they should be separated by an interval of at least 4 weeks.

If *Post-immunisation pyrexia* develops after childhood immunisation, and the infant seems distressed, a dose of paracetamol (infant aged 2–3 months, the dose of paracetamol is 60 mg) can be given and, if necessary, a second dose can be given 4–6 hours later. Ibuprofen (50 mg for 2-3 months aged infants or as per physician's advice) can be used if paracetamol is not suitable, but if a second dose of ibuprofen is required, it is given 6 hours after the first dose. The parent should be warned to seek medical advice if the pyrexia persists.

Predisposition to neurological problems

In children who have had a seizure associated with fever without neurological deterioration, immunisation is ***recommended***; advice on the management of fever (see above) should be given before immunisation. When a child has had a convulsion not associated with fever, and the neurological condition is not deteriorating, immunisation is ***recommended***. Children with stable neurological disorders (e.g. spina bifida, congenital brain abnormality, and perinatal hypoxic-ischaemic encephalopathy) should be immunised according to the recommended schedule. When there is a still evolving neurological problem, including poorly controlled epilepsy, immunization should be deferred and the child referred to a specialist. Immunisation is recommended if a cause for the neurological disorder is identified. If a cause is not identified, immunisation should be deferred until the condition is stable.

See also Cautions under individual vaccines

For individuals with bleeding disorders, see under administration of vaccines, below.

Contraindications: most vaccines have some basic contraindications to their use, and the product literature should always be consulted. In general, vaccination should be postponed if the subject is suffering from an acute illness or if there is a known case of immunodeficiency. Minor infections without fever or systemic upset are not contraindications. A definite severe reaction to a preceding dose is a contraindication to further doses.

Some viral vaccines contain small quantities of antibiotics such as neomycin or polymyxin (or both); such vaccines may need to be withheld from individuals who are *extremely sensitive*

to these antibiotics. *Hypersensitivity to egg* contra-indicates influenza vaccine (residual egg protein present) and, if evidence of previous anaphylactic reactions, also contraindicates immunization with yellow fever vaccine.

Live vaccines should not be routinely administered to *pregnant women* because of possible harm to the fetus but where there is a significant risk of exposure (e.g. to poliomyelitis or yellow fever), the need for vaccination outweighs any possible risk to the fetus. Vaccination is usually not given in the first trimester of pregnancy. In case of Rubella vaccines, it is recommended not to conceive within one month of vaccination.

Live vaccines should not be given to individuals *with impaired immune responses* whether caused by disease (e.g., HIV) or as a result of radiotherapy or other immuno-suppresive drugs or immunodeficiency due to genetic anomolies. These should not be given to those suffering from *malignant conditions* such as leukaemia and tumors of the reticuloendothelial system.

The intramuscular route should not be used in patients with bleeding disorders such as haemophilia or thrombocytopenia.

VACCINES and HIV INFECTION. HIV-positive subjects with or without symptoms can receive the following live vaccines:

Measles, BCG, MMR (but not while severely immunosuppressed), Rubella;

And the following inactivated vaccines:

DPT, HiB, Hepatitis A, Hepatitis B, Inactivated Polio, Meningococcal, Rabies, Tetanus & Typhoid.

HIV positive subjects **should not** be immunized with live vaccines such as BCG and yellow fever vaccines.

Note: Live vaccines should be postponed until at least 3 months after stopping corticosteroids and 6 months after stopping chemotherapy.

False contraindications: It is important to remember that immunization should not be postponed due to conditions wrongly considered to be contraindications for immunization. It is particularly important to immunize children suffering from malnutrition. Low grade fever, mild respiratory infections and other minor illness should not be considered as contraindication. Diarrhoea **should not be considered a contraindication to oral poliomyelitis vaccine (OPV)**. Table below shows the conditions which are NOT contraindications to immunization.

Table 13. A : *Conditions which are NOT contraindications to immunization*

*Minor illness such as upper respiratory infections or diarrhoea with fever < 38.5°C
*Allergy, asthma, or other atopic manifestations, hay fever or "snuffles"
*Pre-maturity, small-for-date infants
*Malnutrition
*Child being breast-fed
*Family history of convulsions
*Treatment with antibiotics, low-dose corticosteroids or locally acting (e.g. topical or inhaled) steroids
*Dermatoses, eczema or localized skin infection
*Chronic diseases of the heart, lung, kidney and liver
*Stable neurological conditions, such as cerebral palsy, spinabifida and Down's syndrome
*History of jaundice after birth

'Vaccination' and 'immunization' are the two terms that are now-a-days being used almost synonymously. But vaccination denotes only the administration of a vaccine, whereas, immunization means the result of vaccination which resulted in providing immunity which is mostly used to indicate active but may also related to passive treatment modules.

PASSIVE IMMUNITY

Immunity with immediate protection against certain infective organisms can be obtained by injecting preparations made from the plasma of immune individuals with adequate levels of

antibody to the disease for which protection is sought. *(See under immunoglobulins, section13.3)*. Passive immunity lasts only for a few weeks. Where necessary, passive immunization can be repeated. Antibodies of human origin are usually termed **immunoglobulins**. The term antiserum is applied to material prepared in animals. Because of serum sickness and other allergic-type reactions that may follow injections of antisera, this therapy has been replaced wherever possible by the use of immunoglobulins. Reactions are theoretically possible after injection of human immunoglobulins but reports of such reactions are very rare.

13.1.2. STORAGE AND USE

Care must be taken to store all vaccines and other immunological products under the conditions recommended in the product literature, otherwise the preparation may become denaturated and totally ineffective. **Refrigerated storage** is usually necessary; many vaccines need to be stored at 2-8 °C and are not allowed to freeze. Vaccines should be protected from light. Opened multi-dose vials that have not been fully used should be disposed of within six hours or at the end of the session whichever come first if no preservative is present. When vaccines containing a preservative WHO multi dose vial policy will be used.

Particular attention must be paid to the instructions on the use of diluents and ampoules of vaccine should always be adequately shaken before use to ensure uniformity of the material to be injected.

Administration of Vaccines: Vaccines containing aluminium adjuvants (DPT, DT, Hepatitis B vaccine) should be injected intramuscularly. The preferred site for intramuscular injection in infants and young children is the anterolateral aspect of the upper thigh since it provides the largest muscular mass. In older children the deltoid has achieved sufficient size to offer a convenient site for intramuscular injection. Similarly in adult women, the deltoid is recommended for routine intramuscular administration of TT. Passive immunity is also obtained through fetal transfer of antibodies from vaccinated mothers (e;g with TT vaccine or other vaccines) or via breast milk to infants.

Note: The buttock should not be used routinely as an immunization site for infants, children, or adults because of the risk of injury to the sciatic nerve. Since the depth of gluteal fat in adult women is usually more than 3.5 cm, which is typically the length of the injecting needle, injecting vaccines into the buttock may result in poor absorption of the vaccine from fatty tissues.

If alcohol or other disinfecting agent is used to wipe the injection site, it must be **allowed to evaporate**, otherwise inactivation of a live vaccine may occur.

Age of Vaccination : The age at which vaccines are administered depends on several factors:

- Age-specific risks of disease;
- Age-specific immunological response to vaccines;
- Potential interference with the immune response by passively transferred maternal antibody;
- Age-specific risks of vaccine – associated complications;
- Programmatic feasibility.

In general, vaccines are recommended for the youngest age-group at risk for developing the disease whose members are known to develop an adequate antibody response to immunization without adverse effects from the vaccine. In addition to the need to protect infants before they face the wild disease-causing agents, administering vaccines early in life makes it easier to achieve high immunization coverage. Considering these, the immunization schedule of Bangladesh is planned in such a manner, that soon all children can receive one dose of BCG vaccine, 3 doses of Hib penta (DPT-HepB-HiB), 3 doses of PCV10 and at least 1 dose of IPV during Hib penta3 contact, 4 doses

of OPV, and one dose of measles rubella (MR) vaccine before the first birthday. The second dose of measles vaccine is from 15 months to 18 months child. For child bearing age women (15 years to 49 years TT five dose schedule is recommended.

Interval between Doses: Some vaccines (Hib penta, PCV, OPV, TT etc.) require administration of more than one dose for development of adequate antibody response. Giving dose of a vaccine at less than 4 weeks interval may lessen antibody response and should be avoided. If a vaccine dose is given at less than 4 weeks interval, it should not be counted as part of the primary series. Lengthening the interval between doses of these vaccines leads to higher antibody levels, but it is more important to complete the primary series early and protect the child before the age of high risk of infection than to aim for an optimal immune response.

Simultaneous Administration of Vaccines: To reduce the number of contacts required to complete the immunization series, as many antigens as possible are given at a single visit. Because all the EPI vaccines are safe and effective when administered simultaneously, i.e. during the same immunization session but at different sites. Also, combination vaccines are being made increasingly available which reduces the total number of injections required, improves compliance and reduces drop-outs.

13.1.3 EPI & IMMUNIZATION SCHEDULE

(For immunization schedule see also Appendix-8a, 8b & 8c)

EPI IN BANGLADESH

World Health Organization (WHO) launched a global immunization programme known as Expanded Programme on Immunization (EPI), officially in May 1974, to protect all children of the world against six vaccine preventable diseases. These diseases are Tuberculosis, Diphtheria, Whooping cough, Tetanus, Poliomyelitis and Measles. For developing countries these six killers of children have been the prime focus. EPI was launched in the countries of South-East-Asia Region (SEAR) of WHO in 1977 to cover the above six vaccine preventable diseases. In 1992–93 hepatitis B was added to this list by some countries (Mongolia, Thailand, Indonesia, and Maldives).

In Bangladesh EPI was formally launched on 7th April 1979 and the targeted diseases were Tuberculosis, Diphtheria, Whooping cough, Tetanus, Poliomyelitis and Measles. The country adopted the goal of 'Universal Child Immunization' (UCI) in 1985. In principle UCI is the level of coverage required to stop transmission of EPI targeted diseases. Currently EPI in Bangladesh has set a target at 90% full vaccination coverage at the national level and 85% full vaccination coverage at district level for children. For women of child bearing age, there is 80% coverage at the national level and 75% coverage at district level as per comprehensive multiyear plan for Bangladesh from 2011 to 2016. The country has developed the following national EPI policies:

- Immunize all children under one year of age throughout the country;
- Immunize all women of childbearing age including pregnant women throughout the country;
- Extend service delivery point up to the community to cover all target population;
- Involve community level health and family planning workers as vaccinators.

EPI in Bangladesh committed to achieve the following disease reduction goal:

- Maintain certification of poliomyelitis eradication status;
- Maintain validation of elimination of neonatal tetanus status;

- Achieve measles coverage 95% and reach elimination status by 2016
- Achieve rubella coverage 95% and control rubella and CRS by 2016;
- Achieve 95% measles rubella vaccination coverage among 15 year child bearing age women for prevention of CRS;
- ↓ Prevalence of chr. HBsAg among 3-5 years children by 90% by 2016 compared to 2003 (150,000 in 2003)
- ↓ Mortality of <5 years Children by 90% due to Hib disease by 2016 compared to 2007 (25,000 in 2007)

Some strategies have been adopted to achieve these goals; these are:

- Increase and sustain more than 90% routine immunization coverage of all antigens at all level;
- Implement National Immunization Days (NIDs) if necessary for maintain polio eradication certification status;
- Developing emergency preparedness plan in case of polio virus importation;
- Use of at least one dose of IPV at the time of Hibpenta3 contact for prevention of OPV derived paralytic polio;
- Organize supplementary immunization activities for neonatal tetanus elimination and measles reduction through high risk approach (MNT campaign if necessary);
- Strengthen AFP and EPI disease surveillance activities at all levels.

Immunization Schedule:

WHO Global EPI Advisory Committee recommended a standard schedule, taking into consideration only two small target groups: Infants below one year of age and pregnant women. These are shown below in Table 13B and. 13C respectively. Most developing countries follow these.

Table 13 B : Bangladesh EPI Immunization Schedule for children.

AGE	Vaccine
Birth	BCG and OPV*
6 weeks	Hib penta, PCV and OPV
10 weeks	Hib penta, PCV and OPV
14 weeks	Hib penta, PCV, OPV and IPV
9 months	MR
15 months to 18 months	Measles 2nd dose
9 months to <14 years	Measles, Rubella vaccination

From early 2014, Bangladesh has conducted vaccination of children 9 month to below 15 years aged target population for MR vaccination.
*WHO recommends that a child be given OPV dose soon after birth or along with measles vaccine.

Table 13 C : ***TT immunization schedule for women***

Dose	When to give	Duration of protection
TT-1	At first contact or as early as possible in pregnancy	None
TT-2	At least 4 weeks After TT-1	3 years
TT-3	At least 6 months after TT-2 or during subsequent pregnancy	5 years
TT-4	At least 1 year after TT-3 Or during subsequent pregnancy	10 years
TT-5	At least 1 year after TT-4 Or during subsequent pregnancy	For life*

Note. Minimum time interval between doses must be maintained but no maximum limit is to be considered.

*If these 5 doses are successfully completed in a woman, the immunity lasts during her entire child bearing period.

As it is difficult to ensure clean deliveries in developing countries, immunization of mothers against tetanus by Tetanus Toxoid (TT) has been a more reliable method to prevent neonatal tetanus. Antibodies against tetanus which develop in the mother are passively transferred to her baby via the placenta, thereby conferring immunity against tetanus in the neonate. TT does not confer immunity with the first dose. Protection begins 2 weeks after the second dose, which should be given no earlier than 4 weeks after the first dose. WHO has recommended the above schedule for TT.

In our country, EPI uses a slightly modified version of WHO EPI Immunization Schedule, which is detailed in ***Annex-1*** and recommended for all infants (below one year of age MR 1 dose) and in ***Annex-2*** recommended for all women of child-bearing age (CBA, 15-49 years).

Achievement of EPI in Bangladesh:

Bangladesh is now certified as polio free along with SEAR countries in March 2014, maintaining validation of maternal neonatal elimination status since 2008 and overall success of EPI regarding coverage and diseases reduction is satisfactory.

Booster doses of EPI in Bangladesh:

In Bangladesh, the EPI has not yet addressed the issue of booster doses of EPI vaccines. The first priority is to ensure that infants are completely immunized against target diseases at the youngest age possible. Global immunization policy suggests that where resources are limited, booster doses should not be considered until coverage levels for fully immunized infants are above 80%. Today, many countries have achieved coverage levels above 80% and are administering booster doses of various vaccines. The number and frequency of such booster doses depend on the epidemiological patterns of diseases in a particular country, the level of health services infrastructure, the ability to sustain high coverage of infants, and the availability of resources to buy vaccines. Perhaps the resource constraint to buy vaccine is the main factor for not initiating booster doses in Bangladesh.

Hepatitis B (HB) vaccination within EPI : Hepatitis caused by HB virus is a major cause of morbidity and mortality globally. HB virus is 100 times more infectious than HIV. WHO estimated that, more than 2 billion people have been infected with HBV worldwide and, among them more than 30 crore become chronic carriers. The number of HBV carriers is thought to be increasing at a rate of 2-3% per year and every year more than 2 million deaths occur from chronic complications of HBV infection worldwide.

So considering the alarming situation WHO has suggested to incorporate HB vaccine into EPI. Accordingly some countries of South East Asia Region have incorporated it into their EPI. Bangladesh introduced this vaccine in the year 2003 in a phase wise manner. During 1st phase seven districts and one City Corporation, during 2nd phase 25 districts and 5 City Corporation and during last phase national wide replication by including 32 districts for HepB vaccination. Now this vaccine is a component of Hib penta vaccine (DPT, HepB and Hib) become part of national EPI vaccination program. All cost of the vaccine was covered by GAVI during phasing but now Bangladesh uses this vaccine for maintaining co financing policy developed by GAVI where modest amount payment to UNICEF for Hib penta vaccine since 2009.

13.1 VACCINES AND ANTISERA

BCG (Bacillus Calmette-Guerin) VACCINE [ED]

BCG vaccine is a dried vaccine prepared from a live attenuated strain known as the Bacillus Calmette-Guerin strain, which is derived from *Mycobacterium bovis.* It contains an amount of viable bacteria such that inoculation, in the recommended dose, of tuberculin negative persons results in an acceptable tuberculin conversion rate. It actually stimulates the development of hypersensitivity to *M. tuberculosis.* It is free from other organisms, and contains a suitable stabilizer. It contains no anti-microbial agent.

BCG vaccine is to be used immediately after its constitution, and any unused portion is to be discarded after 2 hours. It is to be preserved at a temperature between 2° and 8°C. The expiration date is not later than 6 months after date of issue if it is stored between 2° and 8°C. or not later than 1 year after date of issue, if stored at a temperature below 5°C.

BCG vaccine should be given intradermally by operators skilled in the technique. Within 2-6 weeks a small swelling appears at the injection site which progresses to a papule or to a benign ulcer about 10 mm in diameter and heals in 6-12 weeks. A dry dressing may be used if the ulcer discharges, but air should not be excluded.

Serious reactions with BCG are uncommon and most often consist of prolonged ulceration or subcutaneous abscess formation due to faulty injection technique.

BCG vaccine may be given simultaneously with another live vaccine (at 2 different sites), but if they are not given at the same time, an interval of at least 3 weeks should normally be allowed between them. However, when BCG is given to infants, there is no need to delay the primary immunization, including poliomyelitis.

Indication: Prevention or primary TB infection, especially with severe manifestation (miliary TB and TB meningitis)

Special Caution: children born to HIV seropositive mother

Contraindications: congenital or acquired immunosuppression affecting cellular immunity. BCG is also contraindicated in subjects with generalized septic skin conditions (in the case of eczema, a vaccination site free from lesions should be chosen)

Side-effects: adenitis, lymph node suppuration

Dose: ADULT and CHILD ≥ 1 year, 0.1ml; < 1 year 0.05 ml

Route of Administration: *by intradermal injection.*

Proprietary Preparation
BCG vaccine is available in EPI only

DIPHTHERIA VACCINES [ED]

Protection against diphtheria is essentially due to antitoxin, the production of which is stimulated by vaccines prepared from the toxin of *Corynebacterium diphtheriae.* These are more effective and cause fewer reactions if adsorbed onto a mineral carrier. Adsorbed diphtheria vaccines are recommended for the routine immunization of babies and are usually given in the form of a *triple vaccine*, **adsorbed diphtheria, tetanus,** and **pertussis vaccine**. Recently, another *tetravalent vaccine* **adsorbed diptheria, tetanus, pertussis** and **Hepatitis B** has been made available. A dose of poliomyelitis vaccine, live (oral) is generally given at the same time as each of the doses of the triple vaccine *(see Schedule)*. Adsorbed diphtheria and tetanus vaccine is used in place of the triple vaccine when immunization against pertusis is contraindicated.

Diphtheria vaccines for children: (IMPORTANT**: Not** recommended for persons aged 10 years or over).

a) Diphtheria vaccines with pertussis and tetanus (**triple vaccine**) :

ADSORBED DIPHTHERIA, PERTUSSIS AND TETANUS VACCINE (DPT VACCINE) OR DIPHTHERIA-PERTUSSIS-TETANUS COMBINED VACCINE [ED]

Prepared from diphtheria formal toxoid, a suspension of killed *Bordetella pertussis*, and tetanus formal toxoid adsorbed on a mineral carrier.

Indications: protection against Diphtheria, Pertussis and Tetanus

Contraindications: personal history of epilepsy

Side-effects: transient rise in temperature, restlessness, irritability, crying or loss of appetite may sometimes occur a few hours after vaccination. These usually do not call for treatment. Rarely anaphylaxis may occur. Convulsion, infantile spasms and encephalopathy have been reported as rare complication, which are actually due to the pertussis component

Dose: primary immunization of children, 0.5 ml by intramuscular injection at 2 months followed by second dose after 4 weeks and third dose after another 4 weeks *(see Appendix-8a)*

Proprietary Preparations
DPT Vaccine is available from EPI centers only. From 2009 this vaccine is in combination with **Hepatitis B** and **Hib** as **Hib penta** form and using 3 doses in Bangladesh for infant age 6 weeks, 10 weeks and 14 weeks.

b) Diptheria vaccines with pertusis, tetanus and Hepatitis B:

DPT VACCINE WITH HEPATITIS B

Prepared from diptheria and tetanus toxoids, inactivated pertusis bacteria and purified HbsAg. The vaccine is presented as a liquid suspension.

Indications: protection against Diphtheria, Pertusis, Tetanus and Hepatitis B of infants from 6 weeks onwards

Contraindications: as with DPT triple vaccines. It should not be administered intradermally which may result in reduced immune response

Side-effects: as with DPT triple vaccines

Dose: primary immunization of children, 0.5 ml by intramuscular injection at 6 weeks followed by second dose after 4 weeks and third dose after another 4 weeks.

Route of Administration: *by Intramuscular injection* at upper outer quadrant of thigh

Proprietary Preparation
Tritanrix HB[I] (*GSK);* not available in the market.

DIPHTHERIA VACCINE WITH TETANUS

ADSORBED DIPHTHERIA AND TETANUS VACCINE (DT VACCINE)

Prepared from diphtheria formal toxoid and tetanus formal toxoid adsorbed on a mineral carrier.

Contraindications: should not be administered intradermally

Side-effects: *see general discussion*

Dose: primary immunization of children omitting pertussis component, 0.5 ml by intramuscular injection at 2 months, followed by second dose after 4 weeks and third dose after another 4 weeks. Reinforcement at school entry, 0.5 ml

Proprietary Preparation
Td-Pur[I] *(Novertis),* Inj, (P.F syringe) 0.5ml Tk.360.00/Syringe

TYPHOID VACCINE

Typhoid fever is a very common disease in our country that affects adults and children alike. Due to poor nutritional status, and lowered body immunity, majority of our children are especially prone to suffer from the complications of typhoid fever (e.g., gastro-intestinal haemorrhage, intestinal perforation,

bronchitis, septicaemia, cholecystitis, orchitis, meningitis etc.) resulting in an overall child morbidity and mortality rates. So use of typhoid vaccine may be encouraged in our country.

POLYSACCHARIDE TYPHOID VACCINE

This new type of vaccine contains the fraction of capsular polysaccharide of Vi antigen of *Salmonella typhi.* It is given by *intramuscular* or *deep subcutaneous injection*; further doses are needed every 3 years.

Indications: Active immunisation against typhoid fever for adults and children older than two years of age.

Contraindication: intravasular administration may cause anaphylactic reaction, Known allergy to any ingredients of the vaccine

Special Caution: has not been evaluated in children under 2 years of age. pregnant and lactating women : Adequate human data on use during pregnancy or lactation and adequate animal reproduction studies are not available. Postpone vaccination in subjects suffering from acute febrile illness.

Dosage and administration: A single dose of 0.5 ml containing 25 μg of the Vi polysaccharide of *Salmonella typhi* is recommended for both children and adults. Subjects who remain at risk of typhoid fever should be revaccinated using a single dose of vaccine every 3 years.

Consult product literature

This vaccine is not incorporated in EPI program.

Side-effects: *see general discussion*

Storage: *store between 2 to 8℃* (in a refrigerator). *Do not freeze*

Proprietary Preparations

Typherix[(I)] *(GSK),* Inj. (P.Fsyringe) 0.5ml not available in the market

Typhim VI[(I)] **(***Sanofi Pasteur),*Inj.,(P.F Syringe)Tk.672.24/0.5mlsyringe

Vaxphoid *(Incepta*);Inj. Tk 300.00/vial

HAEMOPHILUS INFLUENZAE TYPE B VACCINE

Haemophilus influenzae type b (Hib) has been shown to be an important cause of childhood meningitis and a major cause of bacterial pneumonia in children below 5 years. Currently available conjugate vaccine has shown protective efficacy against Hib bacterial infection in early infancy and can be used safely in EPI.

Indications: prevention of infants from 2 months of age against invasive infections caused by *H. influenzae* type b (meningitis, septicaemia, cellulitis etc.). It does not provide protection against infections due to other types of *H. influenzae* nor against meningitis caused by other microorganisms.

Contraindications: known allergy to one of the ingredients of the vaccine, particularly tetanus protein or allergy appearing after a previous injection of conjugate *H. influenzae* type b vaccine.

Dose :

- Infants between 2-6 months: 3 injections at 1-2 months apart followed by a booster 12 months after 3rd dose.
- If not vaccinated before 6 months:

a) 6-12 months: 2 injections 1-2 months apart followed by a booster 12 months after last injection.
b) 1- 5 years: Only one single injection.

Now this vaccine is a component of Hib penta vaccine become part of national EPI vaccination program.
Cosult product literature

Route of administration: intramuscular

Proprietary Preparations

Combined Vaccine

Diphtheria, Tetanus, Pertussis (Acellular, Component), Poliomyelitis (Inactivated) and Haemophilus Type b Conjugate Vaccine

Pentaxim [I] *(Sanofi Pasteur)*Inj. (P.Fsyringe) Tk 1567.06/ 0.5mlsyringe.
Infarnix Hexa[I] *(GSK)*Inj., (P.Fsyringe) Tk.1737.00/0.5ml syringe.

INACTIVATED INFLUEANZAE VACCINE

The influenza vaccination is an annual vaccination using a vaccine specific for a given year to protect against the highly variable influenza virus. Each seasonal influenza vaccine contains antigens representing three (trivalent vaccine) or four (quadrivalent vaccine) influenza virus strains: one influenza type A subtype H1N1 virus strain, one influenza type A subtype H3N2 virus strain, and either one or two influenza type B virus strains. Influenza vaccines may be administered as an injection, also known as a flu shot, or as a nasal spray.
Indications: Prophylaxis of influenza, especially in those who run an increased risk of associated complications. It is indicated in adults and children from 6 months of age.
Dose: Adults: 0.5 ml. Pediatric population: Children from 36 months onwards: 0.5 ml.Children from 6 months to 35 months: Dosages of 0.25 ml or 0.5 ml may be given.
Contraindications: Hypersensitivity to the active substances, to any of the excipients, to egg, to chicken protein, formaldehyde, gentamicin sulphate or sodium deoxycholate.
Side effects: The most common local adverse reactions and general adverse events were pain and redness at the injection site, muscle aches, fatigue, and headache.

Proprietary Preparations
Fluarix [I] *(GSK*), Inj.(P.F syringe) Tk.364.00/ 0.5ml Syringe.
Agrippal[I] *(Novartis*), Inj. (P.Fsyringe) Tk.650.00/0.5ml Syringe.
Vaxigrip Enfant[I]*(Sanofi Pasteur)* Inj., ((P.Fsyringe) Tk456.62/syringe
Vaxigrip [I] *(Sanofi Pasteur),* Inj. P.Fsyringe) Tk. 406.40/ syringe.

MENINGOCOCCAL VACCINE

Meningococcal Meningitis and septicaemia are caused by various serogroups of *Neisseria meningitidis*. Endemic disease occurs worldwide and is mostly caused by meningococci of serogroups A, B, or C, although group Y is gaining importance. In recent years, also group W135 meningococci have caused an outbreak in the “African meningitis belt” as well as in Saudi Arabia. Current internationally marketed meningococcal vaccines are either bivalent (groups A and C) or tetravalent (groups A, C, Y and W135). The vaccines are purified, heat-stable, lyophilized capsular polysaccharides from meningococci of the respective serogroups. These vaccines are very safe, and significant systemic reactions have been extremely rare.

Travellers to areas affected by meningococcal outbreaks are advised to be vaccinated. For **pilgrims to the Hajj and Ramadan Omrah, Saudi Arabia requires visitors obtain a tetravalent vaccine (A, C, Y and W135)** at least ten days prior to their arrival in the country.

MENINGOCOCCAL A, C, W, Y VACCINE

Indications: indicated for the active immunisation of children from 2 years of age, adolescents and adults against meningococcal disease caused by meningococci of serogroups A, C, W-135 and Y. The vaccine is particularly recommended for subjects at risk, for example those living in or visiting areas where the disease is epidemic or highly endemic. It is also recommended for subjects living in closed communities and close contacts of patients with disease caused by *meningococci* of serogroups A, C, W-135 and Y.
Caution: seroconversion rate of Children below 2 years is lower for the serogroup C and to a lesser extent for A, W_{135} and Y. However, seroconversion for the serogroup A is acceptable in children from age 6months onward.

Side-effects: erythema, slight induration and tenderness hyperthermia and mild erythema at the site of injection.

This vaccine is not incorporated in EPI program as yet.

Proprietary Preparation
Mencevax ACWY [I] *(GSK)*, Inj.0.5ml, Tk.600/vial

Dose: *by the subcutaneous route* ADULT and CHILD over 2 years 0.5ml

Menveo[I]*(Novertis),* Inj.Tk.2945.00/vial
Dose*: by intramuscular injection ,*
ADULT and CHILD over 1 year 0.5mL as a singledose; CHILD 3 months–1 year 2 doses of 0.5mL separated by an interval of 1 month

MENINGOCOCCAL A, C VACCINE

Indications: Protection against mening-ococci belonging to serogroups A and C for children from 2 years and adults.

Caution: Children<18 months not recommended.

Side-effects: Temporary hyperthermia and mild erythema at the site of injection.

Dose: See under preparation

This vaccine is not incorporated in EPI program.

Proprietary Preparations
Meningococcal A+C Vaccines[I]*(Aventis),* Inj .,(P.F syringe) Tk.489.54/ 0.5ml Syringe
Dose : *by intramuscular injection*, ADULT and CHILD over 18 months 0.5ml
Consult product literature

HUMAN PAPILLOMA VIRUS VACCINES

Human papilloma virus vaccine is used in females for the prevention of cervical cancer and other pre-cancerous lesions caused by human papillomavirus. This vaccine is available as a bivalent vaccine or quadrivalent. Quadrivalent is licensed for use in females for the prevention of cervical cancer, genital warts and pre-cancerous lesions caused by human papillomavirus types 6, 11, 16, and 18. Bivalent vaccine is licensed for use in females for the prevention of cervical cancer and other pre-cancerous lesions caused by human papillomavirus types 16 and 18.
The vaccines may also provide limited protection against disease caused by other types of human papillomavirus. The two vaccines are not interchangeable and one vaccine product should be used for an entire course.
Human papillomavirus vaccine will be most effective if given before sexual activity starts. From October 2013, a 2-dose schedule is recommended, as long as the first dose is received before the age of 15 years. The first dose is given to girls aged 9 years onwards and the second dose is given 5-13 months after the first dose. Females older than 15 years require 3 dose schedule with the second dose given between 1-2.5 months and the third dose between 5-13 months after the first dose. Consult product literature.

HUMAN PAPILLOMA VIRUS VACCINES

Indications: *see notes above*
Caution: see section 13.1.1
Contraindications: *see section 13.1.1*
Side-effects: *see section 13.1.1*
Dose: *see notes above* and under the preparation

Proprietary Preparations
Cervarix *(GSK)* suspension of virus-like particles of human papillomavirus type 16 (40 micrograms/mL), type,18 (40 micrograms/mL Prefilled syringe 0.5ml. Tk1903.69/0.5ml
Dose: prevention of premalignant genital lisions and cervical cancer, by intramuscular injection into deltoid region, for females aged 9 years onwards. For girls aged 9-14 years, 2 dose of vaccine is recommended at 0, 6 months schedule. For women aged 15 years above, 3 dose of vaccine is recommended at 0, 1 & 6 months schedule.
Gardasil[I] *(MSD),* suspension of virus-like particles of human papillomavirus type, 6(40micrograms/mL), type 11 (80 micrograms/mL), type 16 (80 micrograms/mL),

type 18 (40 micrograms/mL).0.5ml vial,Tk.4254.15/vial
Dose: prevention of premalignant genital lesions, cervical cancer and genital warts, by intramuscular injection preferably into deltoid region or higher anterolateral thigh, ADULT and CHILD over 9 years, 3 doses of 0.5 mL, the second 2 months and the third 6 months after the first dose

POLIOMYELITIS VACCINES [ED]

There are 2 types of vaccines against poliomyelitis : poliomyelitis vaccine, live (oral) (Sabin) and poliomyelitis vaccine, inactivated (injectable) (Salk).

Oral poliomyelitis vaccine (OPV) is composed of the three types of attenuated strains of poliovirus types 1, 2, and 3. Because of its low cost, ease of administration, superiority in conferring intestinal immunity, and the potential to infect household contacts secondarily, it is used in the EPI, as the vaccine of choice for eradication of poliomyelitis.

Dose: 2-3 drops (as guided by the manufacturer) from a multi-dose container constitute a single dose. Usually 3 such doses are given at intervals of 4 weeks on 3 occasions at the same time as routine immunization against diphtheria, tetanus and pertussis. A fourth dose is also advocated during immunization against measles at the age of 9 months.

Note: Once the container has been opened the poliomyelitis vaccine loses potency, therefore any vaccine remaining at the end of an immunization session should be discarded.

Contraindications: *see general discussion*. The efficacy of the vaccine may be impaired if given in subjects having diarrhoea or vomiting.

Side-effects: vaccine related paralysis might occur on very rare occasions.

Proprietary Preparations
Oral polio vaccine is available from EPI centers only. The SEAR countries including Bangladesh certified as polio free from March 2014, as per WHO recommendation to eradicating polio from the world all OPV using countries like Bangladesh need to incorporate at least one dose of IPV in routine EPI during DPT3 contact. Bangladesh decided to incorporate one dose of IPV with OPV3/Hibpenta3 dose from the month of October 2014. The IPV vaccine cost is covered by GAVI due to global unique need to eradicate polio.

MEASLES VACCINE[ED]

Measles is an acute viral infection transmitted by close respiratory contact. In some countries (such as under EPI in Bangladesh), routine immunization of children against measles is given as one dose of single component vaccine; in other areas, a two-dose schedule has been found to be more applicable.

Measles vaccine is administered in some countries as part of a combined preparation with mumps vaccine and rubella vaccine (MMR vaccine); a single dose primary immunization is followed by a reinforcing dose 2-5 years later. (MMR vaccines are available in the private market in Bangladesh)

MEASLES VACCINE, LIVE

Measles Vaccine, Live is a preparation containing a suitable modified strain of live measles virus grown in cultures of chick embryo cells or in other suitable approved cell cultures. It is prepared immediately before use by reconstitution from the dried vaccine with the liquid stated on the label to give a suspension. The vaccine does not contain any added antimicrobial preservative.

Dose: a single dose of 0.5 ml reconstituted vaccine is administered subcutaneously (SC) at the anterolateral part of mid-thigh at the age of 9 months. Currently available measles vaccine is not given before the age of 9 months because it interferes with the maternal antibodies passively transmitted to a child.

Note: Administration of measles vaccine (measles containing vaccine) to children may be associated with a mild measles-like syndrome with a measles-like rash and pyrexia about a week after injection. Much less commonly, convulsions and, very rarely, encephalitis have been reported. Convulsions in infants are much less frequently associated with measles vaccines than with other conditions leading to febrile episodes. **Contraindications:** *see general discussion*

Proprietary Preparations
Single component measles vaccine is available in EPI centers only.

MEASLES, MUMPS AND RUBELLA (MMR) VACCINE

A combined measles/mumps/rubella (MMR) vaccine aims to eliminate rubella (and congenital rubella syndrome), measles, and mumps. Ideally, every child should receive two doses of MMR vaccine by entry to primary school.

Infants between 9 and 12 months of age: The first dose of MMR vaccine may be given to infants from 9 months of age. Infants in their first year of life may not respond sufficiently to the components of the vaccines. In case an epidemiological situation requires infants in their first year of life, a second dose of prior should be given in the second year of life, preferably within three months after the first dose. Under no circumstances the interval between doses should not be less than four weeks.

Individuals 12 months of age or older: The dose is 0.5 ml. A second dose should be given according to official recommendation.

In some countries, the policy of protecting women of childbearing age against rubella has been replaced by a policy of eliminating rubella in children through MMR vaccination. MMR vaccine may be administered to women of child bearing age in substitution of rubella vaccine.

In Bangladesh from 2012 MR vaccine is used for infants from nine months of age and measles 2nd dose for 15 to 18 months of age children. The spared MR vaccine for children is now offered to 15 year child bearing age women for prevention of rubella and congenital rubella syndrome (CRS).

Contraindications: *see general discussion;* hypersensitivity to neomycin or to any other component and egg, children who have received another live vaccine by injection within 3 weeks, if given to women, pregnancy should be avoided for 3 months after vaccination

Side-effects: malaise, fever or rash may occur following the first dose of MMR vaccine, most commonly about a week after immunization and lasting about 2-3 days. Paracetamol can be given to reduce the fever followed if necessary by a second dose 4-6 hours later. After a second dose of MMR vaccine, adverse reactions are considerably less common than after the first dose.

Post-vaccination meningo encephalitis was reported (rarely and with complete recovery) following immunization with MMR vaccine containing Urabe mumps vaccine. This strain has been discontinued in most developed countries including UK. No cases have been confirmed in association with the Jeryl Lynn mumps vaccine.

Dose: 0.5 ml by deep subcutaneous or intramuscular injection *(consult manufacturer's literature)*

Proprietary Preparations
Priorix[I] (GSK), Inj.,Tk. 529.00/0.5ml vial
Trimovax[I]*(SanofiPasteur)*,Inj., Tk.412.70/0.5ml vial

TETANUS VACCINE (TETANUS TOXOID) [ED]

Tetanus toxoid (TT) is prepared from tetanus toxin produced by the growth of *Clostridium tetani*. The toxin is converted to tetanus toxoid by treatment with formaldehyde solution and adsorbed on

to aluminium salts to increase its antigenicity.

Note: An advantage of the adsorbed preparation is that antitoxins (immunoglobulins) do not neutralize them. So they can be given concurrently unlike the plain tetanus toxoid (where a *6 weeks wait is necessary* to allow the antitoxin levels to fall). TT is stable and can withstand exposure to room temperature for months and to 37°C for a few weeks without significant loss of potency. But usually it is preserved at a temperature between 2° and 8°C. In that condition the expiration date is not later than 2 years after date of issue from manufacturer's cold storage. TT is a highly effective vaccine and induces the formation of specific antitoxins, which neutralize the toxin. Antitoxin, which passes to the foetus across the placenta following active immunization of the mother, prevents neonatal tetanus. In EPI TT is used to prevent neonatal tetanus by immunizing women.

Dose: When most women of child-bearing age have not previously immunized with TT in their infancy or adolescent or when there is little or no documentation of past immunization, implementation of a TT five dose schedule for women of childbearing age is of the utmost importance *(Appendix-8b).*

This TT immunization schedule should include a first dose given at the first contact, a second dose at least 4 weeks after the first dose, and a third dose given 6-12 months after the second dose (or next pregnancy). Protective antibody levels are attained in 80-90% of women after the second dose and in 95-98% of women after the 3rd dose. This basic course will provide protection for at least 5 years. Fourth and fifth dose of TT given later will prolong the duration of immunity for 10 and 20 years (or life long) respectively. Since women who received only three doses of DPT in infancy may not respond well to one booster dose of TT, it is prudent to give them two doses of TT (during pregnancy) with an interval of 1 month, and complete the full immunization with one dose of TT one year later (or in a subsequent pregnancy).

In Bangladesh from 1993 for child bearing age women (15 to 49 years) TT-five doses schedule recommended which are as follows: The TT1 is at 15 years, TT2 four weeks after TT1, TT3 six months after TT2, TT4 one year after TT3 and TT5 one year after TT4. If an infant received three doses of Hib penta in that case when she reaches 15 years of age will receive only three doses of TT instead of five doses if there is valid document for vaccination. Here at 15 years she will receive TT3, after one year TT4 and TT5 one year after TT5.

Contraindications: *see general discussion* and individuals who had developed transient thrombocytopenia or neurological complications previously after administering any dose of tetanus toxoid

Side-effects: local reactions such as tenderness, erythema, induration oedema and nodule at the injection site. Headache, circulatory reactions, sweating, chills, fever, dyspnoea, muscle and joint complaints. GI discomfort, exanthema, blood disorders

Interactions: immunosuppressive therapy, s*ee also Appendix-2*

Proprietary Preparations

Tetavax(I) *(Aventis)* Inj.. Tk.179.84/0.5ml vial; P.F syringe 0.5mlTk. 240.00/0.5 ml Syringe
Tetanol-pur *(Novertis***),** Tk. 280.00/0.5ml Prefilled Syringe

Vaxitet *(Incepta*), Inj.,Tk.60/0.5ml amp; TK 80/vial
T. VaccinumTetani (I) *(Biomed),* Inj., Tk.64.73/0.5ml amp
TT Vax (*Popular*), Inj. TK. 80.00/0.5ml Vial

HEPATITIS B VACCINE [ED]

Hepatitis B vaccine contains inactivated hepatitis B virus surface antigen (HbsAg) adsorbed on aluminium hydroxide adjuvant. It is made biosynthetically using recombinant DNA technology. The vaccine is safe and immunogenic even when administered at birth (Maternal anti-HbsAg antibody does not interfere

with the response to the vaccine), and highly efficacious. Over 90% of susceptible children develop a protective antibody response (over 10 IU/ml) following three doses of vaccine. Infants of HbsAg–positive carrier mothers respond less well to the vaccine since it is delivered after infection has occurred.

A combined DTP and Hepatitis B vaccine is also available for infants.

Immunization schedule

Primary immunization : A series of three intramuscular injections is required to achieve optimal protection.

Two primary immunization schedules can be recommended :

- A rapid schedule, with immunization at 0, 1 and 2 months, will confer protection more quickly and is expected to provide better patient compliance.
- Schedules which have more time between second and third doses, such as immunization at 0, 1 and 6 months, may take longer to confer protection, but will produce higher anti-HBs antibody titres.

The rapid schedule is more appropriate for Bangladesh.

Booster dose : It would seem advisable to recommend a booster dose when the anti-HBs antibody titre falls below 10 IU/L, particularly for all people at risk.

From available data, a general recommendation for booster dose can be made as follows :

- After the 0, 1, and 2 months primary immunization schedule a booster dose is recommended 12 months after the 1st dose. The next booster dose will not probably be required for another 8 years.
- After the 0, 1, and 6 months primary immunization schedule a booster dose will probably not be required earlier than 5 years after the primary course.

Special Dosage Recommendations :

*** Dosage recommendation for neonates born of mothers who are HBV carriers :**

The 0, 1, and 2 months immunization schedule is recommended, and should start at birth. Concomitant administration of HBIg is not necessary, but when HBIg is given simultaneously with Hepatitis B vaccine, a separate injection site must be chosen.

*** Dosage recommendation for known or presumed exposure to HBV :**

In circumstances where exposure to HBV has recently occurred (e.g. Needle stick with contaminated needle) the first dose can be administered simultaneously with HBIg which however must be given at a separate injection site. The rapid immunization schedule should be advised.

*** Dosage recommendation for immunocompromised persons :**

The primary immunization schedule for chronic haemodialysis patients or persons who have an impaired immune system is four doses of 40 mcg at elected date, 1 month, 2 months and 6 months from the date of the 1st dose. The immunization schedule should be adapted in order to ensure that the anti-HBs antibody titre remains above the accepted protective level of 10 IU/L.

Method of administration :

The vaccine should be injected intramuscularly in the deltoid region in adults, anterolateral thigh is the preferred site in infants and children. It should not be injected into the buttock (vaccine efficacy reduced); subcutaneous route used for patients with haemophilia.

Contraindications : The Hepatitis B Vaccine should not be administered to subjects with known hypersensitivity to any component of the vaccine, or to subjects having shown signs of hypersensitivity after previous administration.

Special warnings and cautions for use :

Because of the long incubation period of Hepatitis B it is possible for unrecognized infections to be present at the time of immunization. The vaccine may not prevent Hepatitis B infection in such cases.

Dose: 3 doses of 1 ml (20 mcg) *by intramuscular injection* **for adults and children over 15 years**. 0.5 ml (10 mcg) **for children under 15 years**.

The immune response to Hepatitis B vaccine is related to age. In general, people over 40 years of age respond less well.
Now this vaccine is a component of Hib penta vaccine become part of national EPI vaccination program.

Proprietary Preparations
Engerix B[(I)] *(GSK);* Inj. 0.5 ml vial. Tk298.81/vial; 1ml vial TK 531.22/vial; Prefilled syringe 1ml TK 608.00/syringe; Prefilled syringe 0.5ml.TK 386.40/syringe
Hepa-B*(Incepta),*Inj. Tk.400.00/0.5ml vial;Tk.500.00 /1mlvial.
Hepavax *(Popular)*Inj.,Tk.400.00/0.5ml vial;vial.Tk500.00/1mlvial

With DPT vaccine
Tritanrix HB[(I)] *(GSK);* See DPT Vaccine with Hepatitis B

With DPT and influenza vaccine
Essyfive *(Popular)* Inj., Tk.1000/0.5 ml vial

HEPATITIS A VACCINE

Hepatitis A vaccine is prepared from formaldehyde-inactivated & purified hepatitis A virus (HAV) grown in human diploid cells.

Indication: This is effective for prevention of HAV in adults and children. In view of the endemicity and an increasing risk of morbidity and mortality, the use of the vaccine may be of significant value in our community. Immunisation against HAV is especially recommended for:

- Occupationally exposed persons (especially fecal materials) such as healthcare professionals, laboratory personnel, laundry & cleaning staff in hospitals & staff at day-care centers.
- Travellers/armed forces/aid workers
- Food-handlers.
- Injectable drug users/ haemophiliacs as well as subjects with chronic liver conditions due to Hepatitis B, D.C or E viruses or alcohol.

Dosage and administration: The vaccine is available in 1ml dose for adults and 0.5 ml dose for children. **Child dose** is 0.5 ml at a given date followed by a booster dose 6-12 months later *by intramuscular administration* into the anterolateral part of thigh in young children and deltoid region in older children. **Adult dose** is 1 ml at a given date followed by a booster dose 6-12 months later administered *by intramuscular injection* into the deltoid region.

Consult product literature

This vaccine is not incorporated in EPI program.

Contraindications: *see general contraindications*

Side-effects: usually mild including transient soreness, erythema and induration at the injection site.

Proprietary Preparations
Havrix [(I)] *(GSK),* Inj., Tk.755.60/0.5ml Prefilled Syringe; Tk.1189.90/ 1ml Prefilled Syringe
Avaxim 160[(I)] *(Sanofi),* Inj. .(P.F syringe) Tk.1524.00/0.5ml syringe
Avaxim 80[(I)] ***(****Sanofi****),*** Inj., .(P.F syringe) Tk.1110.00/0.5ml Syringe

PNEUMOCOCCAL VACCINES

Pneumococcal vaccines protect against infection with *Streptococcus pneumoniae* (pneumococcus). These vaccines contain polysaccharide from capsular pneumococci. Pneumococcal polysaccharide vaccine contains purified

polysaccharide from 23 capsular types of pneumococci, whereas pneumococcal polysaccharide conjugate vaccine (adsorbed) contains polysaccharide from either 10 capsular types or 13 capsular types and the polysaccharide is conjugated to protein

Pneumococcal vaccination is recommended for individuals at increased risk of pneumococcal infection as follows:
age over 65 years; asplenia or splenic dysfunction asthma treated with continuous or frequent use of a systemic corticosteroid;chronic heart , renal diseaseand liver disease;diabetes mellitus requiring insulin or oral hypoglycemic drugs; HIV infection, prolonged systemic corticosteroid treatment for over 1 month at dose equivalents of prednisolone. ADULT and CHILD over 20 kg, 20mg or more daily; child under 20 kg, 1 mg/kg or more daily); presence of cochlear implant; conditions where leakage of cerebrospinal fluid may occur; CHILD under 5 years with a history of invasive pneumococcal disease; at risk of occupational exposure to metal fume (e.g. welders).
Where possible, the vaccine should be given at least 2 weeks before splenectomy, cochlear implant surgery, chemotherapy, or radiotherapy; patients should be given advice about increased risk of pneumococcal infection. If it is not practical to vaccinate at least 2 weeks before splenectomy, chemotherapy, or radiotherapy, the vaccine should be given at least 2 weeks after the splenectomy or, where possible, at least 3 months after completion of chemotherapy or radiotherapy. Prophylactic antibacterial therapy against pneumococcal infection should not be stopped after immunization
Selection of vaccine Children under 2 years at increased risk of pneumococcal infection should receive the 13-valent pneumococcal polysaccharide conjugate vaccine (adsorbed) at the recommended ages, followed by a single dose of the 23-valent pneumococcal polysaccharide vaccine after their second birthday. Children at increased risk of pneumococcal infection presenting late for vaccination should receive 2 doses (separated by at least 1 month) of the 13-valent pneumococcal polysaccharide conjugate vaccine (adsorbed) before the age of 12 months, and a third dose at 12–13 months.
Children over 12 months and under 5 years (who have not been vaccinated or not completed the primary course) should receive a single dose of the 13-valent pneumococcal polysaccharide conjugate vaccine (adsorbed) (2 doses separated by an interval of 2 months in the immunocompromised or those with asplenia or splenic dysfunction). All children under 5 years at increased risk of pneumococcal infection should receive a single dose of the 23-valent pneumococcal polysaccharide vaccine after their second birthday and at least 2 months after the final dose of the 13-valent pneumococcal polysaccharide conjugate vaccine (adsorbed). Children over 5 years and adults who are at increased risk of pneumococcal disease should receive a single dose of the 23-valent unconjugated pneumococcal polysaccharide vaccine.

PNEUMOCOCCAL VACCINE

Indications: immunisation against pneumococcal infection and *see also notes above*
Cautions: *see also section 13.1and note above*
Contra-indications: *see section 13.1*
Pregnancy and Breast-feeding
Side-effects: *see section 13.1*
Revaccination: In individuals with higher concentrations of antibodies to pneumococcal polysaccharides, revaccination with the 23-valent pneumococcal polysaccharide vaccine more commonly produces adverse reactions. Revaccination is therefore not recommended,
except every 5 years in individuals in whom the antibody concentration is likely to decline rapidly (e.g. asplenia, splenic

dysfunction and nephrotic syndrome). If there is doubt, the need for revaccination should be discussed with a haematologist, immunologist, ormicrobiologist.
Dose: *See under preparations*

Proprietary Preparations
Pneumococcal polysaccharide vaccine
Pneumo 23(I) *(Sanofi Pasteur)*, Inj. Tk.982.76/ 0.5ml Prefilled Syringe
Dose by intramuscular or subcutaneous injection, ADULT and CHILD over 2 years, 0.5 mL; revaccination, see notes above consult product literature

Pneumococcal polysaccharide conjugate vaccine (adsorbed)
Synflorix(I) *(GSK*), Inj. .(P.F syringe) Tk.1936.49/0.5ml Syringe;
Dose: *by intramuscular injection,*
CHILD 6 weeks–5 years, consult product literature
Note. Deltoid muscle is preferred site of injection in young children; anterolateral thigh is preferred site in infants

RABIES VACCINE [ED]

Rabies is an under-reported, neglected deadly disease that causes more than 50,000 human deaths annually, most of which occur in the poorest regions of the world (WHO position paper). Rabies, also known as hydrophobia is caused by Lyssavirus type 1. Although some countries have achieved Rabies free status, it is still Endemic in Bangladesh. Bites from rabies-infected dogs, cats, monkeys and foxes are common in Bangladesh and most cases occur during the months of August and September, the mating season of the dogs.

One of the most important elements in the effective control of human rabies is the use of efficacious vaccines. Vaccines produced in neural tissues have been in existence for over 100 years. However, it is the availability and use of cell culture and purified embryonated egg rabies vaccines that has dramatically decreased the number of human deaths throughout the world, most notably in countries where canine rabies is endemic.

Rabies vaccine is a fluid or dried preparation of rabies “fixed” virus grown in the neural tissues of rabbits, sheep goats, mice or rats or in embryonated duck eggs, or in tissue cultures, and inactivated by a suitable method.

Rabies vaccines produced in mammalian neural tissues (brain of adult animals such as sheep and goat; brain of suckling animals such as mouse, rat and rabbit) have been in worldwide use for many years. It is well known that their use has led to adverse reactions following immunization, such as encephalomyelitis and polyneuritis. Although the risk of such adverse reactions is reduced when the virus is grown in the brains of newborn animals, such as rats and mice, before the development of myelin in the brain, the safety profile of these vaccines is still unacceptable. Moreover, there is evidence for a lack of potency of these neural tissue vaccines, leading to inadequate protection in humans, making a strong argument for the discontinuation of their production and use.
Nerve tissue Rabies Vaccines are still used commonly in Bangladesh. However Government has already started taking necessary steps to shift from nerve tissue rabies vaccines to tissue culture purified embryonated egg rabies vaccines.

Available rabies vaccines are mainly of 3 types :

1. Nervous tissue vaccines (NTV) :
   a) derived from adult animal nervous tissue (e.g. Sheep);
   b) derived from suckling mouse brain;
2. Duck embryo vaccine (DEV);
3. Tissue-culture vaccine :
   a) Human diploid cell vaccine;
   b) “Second generation” tissue culture (animal cell) vaccine.

Duck embryo vaccines are now rarely available in the world but not available in Bangladesh. At present available vaccines against rabies in our country are Anti-Rabies Vaccine (ARV) manufactured at the Institute of Public Health (IPH), Mohakhali, Dhaka, and Tissue Culture (Chick Embryo/Vero Cells) Rabies Vaccine imported by some pharmaceutical companies.

NERVOUS TISSUE VACCINE

This vaccine is prepared at the Institute of Public Health (IPH), Mohakhali, Dhaka, from sheep's brain infected with a strain of attenuated rabies virus. The vaccine contains inactivated virus treated with1% phenol.

Indications: Active immunization against rabies of person bitten by known or suspected rabid dog (or other animals)

Dosage and administration: On suspicion of infection one ampoule (5 ml) subcutaneously under the abdominal skin daily for 10-14 days, depending upon severity of the injury.

For class III bites (severe bites, multiple bites, bite on neck or above), Rabies immunoglobin (RIg) is also recommended at the start.

Warnings: Due to its side-effects like allergy, encephalomyelitis, peripheral neuritis, and some local reaction this vaccine should only be used when there will be no other alternative to face the situation (suspicion of rabies).

TISSUE CULTURE VACCINE

These are inactivated cell culture rabies vaccine used for protection against rabies both in pre-exposure and post-exposure cases.

Dose and administration : The dose is same for all age groups and should be administered *by deep subcutaneous* or *by intramuscular injection*.

a) **Post Exposure Treatment**: Begin vaccination as soon as possible. A complete course of vaccination for adults and children consists of a total of 6 injection; one injection on each of days 0, 3, 7, 14, and (28 or 30). In case of severe bites (bites on the head, face, neck, hands or groin, and after contact of the mucous membrane with saliva from wild animals or from definitely or suspected rabid animals), a supplementary passive immuni-zation with rabies immunoglobulin is indicated.

   Passive Immunization: Rabies immunoglobulin (human) 20 IU/kg or rabies immunoserum (animal) 40 IU/kg; Half of total dose is infiltrated in the wound area and the other half is given intramuscularly in the gluteal region.

b) **Pre-exposure Prophylaxis**: The protective pre-exposure vaccination against rabies consists of one injection on days 0, 7, and 28. Booster dose after 1 year and then after 2-5 years

Contraindications: in the case of exposure, none. In view of the fatal outcome of the clinically manifest rabies every suspicion of exposure to infection must lead to treatment by vaccination. Pre-exposure immunization is recommended for all persons at high risk, such as medical practitioners, veterinarians, nursing staff etc. Pre-exposure vaccination is to be postponed in case of sick and convalescent persons, and those considered being in the incubation stage of disease. Where there is known allergy to neomycin, chlortetracycline, amphotericin B or chicken protein a prophylactic vaccination should not be undertaken.

Side-effects : mild, local in less than 5% of the patients**.** Headache; lethargy, mild allergic skin reactions and slight elevation in temperature may be seen in some sensitive patients.

Cautions: immunosuppressive therapy and excessive alcohol should be avoided during immunization.

Presentation: presented as 1 dose vial

This vaccine is not incorporated in EPI program.

Proprietary Preparations
Rabipur[I]*(Chiron),*Inj.2.5 I.U.; Tk.680.00/vial
Rabix-VC (*Incepta),* Inj. Tk. 500.00/vial
Verorab[I] *(Sanofi),* Inj. 0.5ml.(P.F syringe)Tk. 604.94/0.5ml syringe

VARICELLA VACCINE

Varicella (Chicken Pox) vaccine is a lyophylised preparation of the live-attenuated OKA strain of varicella-zoster virus.

Indication: effective for prevention of chicken pox in healthy infants (from the age of 9 months onwards), children, adolescents and adults.

Dosage and administration: 0.5 ml of the reconstituted vaccine contains one immunising dose. CHILD dose from the age of 9 months up to 12 years of age, 1 single dose. ADULT dose from 13 years of age and up, 2 doses with an interval of 6-8 weeks; The vaccine should be given *by subcutaneous injection*. The upper arm (deltoid region) is the preferred site of injection.

Contraindication: pregnancy (avoid pregnancy for 3 months after vaccination) and during breast feeding.

This vaccine is not incorporated in EPI program.

Proprietary Preparations
Varilrix[I] *(GSK),* Inj. 0.5ml, Tk.1487.39/vial

ROTAVIRUS VACCINE

Rotavirus vaccine is a live, oral vaccine that protects young children against gastro-enteritis caused by rotavirus infection.
The recommended schedule consists of 2 doses, the first at 2 months of age, and the second at 3 months of age. The first dose of rotavirus vaccine must be given between 6–15 weeks of age and the second dose should be given after an interval of at least 4 weeks; the vaccine should not be started in children 15 weeks of age or older.
Indications: protection against gastro-enteritis caused by rotavirus.
Cautions: vaccination should be postponed in subjects suffering from diarrhea or vomiting; immunosuppressed close contacts.
Contra-indications: see section (13.1.1); also predisposition to, or history of, intussusception
Side-effects: see section (13.1.1)
Dose: By mouth, CHILD over 6 weeks, 2 doses of 1.5 ml, separated by an interval of at least 4 weeks; first dose must be given between 6–15 weeks of age; course should be completed before 24 weeks of age (preferably before 16 weeks)

Proprietary Preparations
Rotarix[I] (*Glaxo),* Oral susp. Tk.1548/1.5 ml oral Prefilled Syringe
Rotateq[I] (*MSD),* Oral susp, Tk.1490.35/Tube

YELLOW FEVER VACCINE

Live yellow fever vaccine is indicated for those travelling to, passing through or living in an endemic area and for laboratory staff who handle the virus or who handle clinical material from suspected cases. The immunity which probably lasts for life is officially accepted for 10 years starting from 10 days after primary immunization and for a further 10 years immediately after revaccination.
Pregnancy : Live yellow fever vaccine should not be given during pregnancy because there is a theoretical risk of fetal infection. If exposure cannot be avoided during pregnancy, then the vaccine should be given if the risk from disease in the mother outweighs the risk to the fetus from vaccination
Breast-feeding : Should not be given to nursing mothers, seek specialist advice if exposure to virus cannot be avoided.

YELLOW FEVER VACCINE, LIVE

Indications: Immunization against yellow fever
Contra-indications: see section (13.1.1) also children under 6 months; history of thymus dysfunction.
Pregnancy : see notes above.
Breast-feeding: see notes above.
Side-effects: see section (13.1.1); also associated viscerotropic disease and neurotropic disease
Dose: ADULT and CHILD over 9 months,0.5ml (see also notes above) Consult product literature.
Route of administration: subcutaneous

Proprietary Preparations
Stamaril[(I)] (*Sanofi Pasteur),* Inj. prefilled syringe. 0.5ml. Tk.1000.63/syringe

ANTITOXINS OR ANTISERA

Antitoxins or antisera are prepared in animals such as horses. Originally these were used for passive immunization. Administration of antiserum frequently gives rise to serum sickness and anaphylactic shock. These are gradually being replaced by human immuno-globulin preparations that are much safer.

DIPHTHERIA ANTITOXIN (ADS) [ED]

Diphtheria antitoxin is used for passive immunization. It is prepared in horses. Therefore reactions are common after administration.

It is now only used in suspected cases of diphtheria (without waiting for bacterio-logical confirmation). Before adminis-tration, test for hypersensitivity should be carried out. When the serum is injected into a patient suffering from diphtheria the anti-bodies combine with the diphtheria toxin, thereby neutralizing the symptoms of the disease. Protection lasts for 3 weeks. It cannot neutralize toxins already attached to organs.

Dosage and administration: prophylactic dose : 500 to 2000 units SC or IM; For attacks of diphtheria : mild cases - 30,000-40,000 units; moderate cases - 50,000-80,000 units and severe cases - 80,000-100,000 units;Doses up to 30,000 units are given IM; larger amounts, half IM, the rest IV 30 minutes later. All IM injections are to be given on the lateral aspect of the thigh.

Contents: purified serum obtained from horses, which have been hyper-immunized with diphtheria toxoid and toxin

Indications: prophylaxis and therapy of diphtheria

Dose: Prophylaxis 1,000-2,500 IU SC. IM Inj. 500-2000 units

Therapy 5,000-40,000 IU, if possible, administer in hospital by infusion.

Side-effects: anaphylaxis with cardiovascular and respiratory complication; serum sickness, nephritis, myocarditis, polyarthritis, neuritis and uveitis.

Proprietary Preparation
Not available commercially

TETANUS ANTITOXIN (ATS)

Tetanus Antitoxin is prepared from serum of horses that have been immunized against the toxins of the tetanus bacilli. It is used to confer passive immunity against tetanus.

Presentation: solution of enzyme refined globulin is available in ampoules of 1,500 IU and 10,000 IU

Uses: immediate protection is its advantage and short-lived immunity is its disadvantage. They are used for emergency prophylaxis and treatment of tetanus.

Doses and administration: for prophylaxis : 1,500 IU intramuscularly (or subcutaneously) as soon a possible after injury; routine use of tetanus antitoxin after an injury has been discarded because of the very short-lived immunity it offers and the possible anaphylaxis

reactions following its administration. For treatment previously a large dose 1,00,000 IU intravenously at the start and a repetition of the same dose in one or two days and is followed by a further 15,000 IU weekly (until symptoms abate) was used. But now a small dose of only 3,000 IU is given intravenously for patients of all ages soon after diagnosis without any repetition

Side-effects: frequent hypersensitivity reactions

Cautions: patients should be asked about previous history of serum reaction, history of asthma, urticaria, allergy or eczema. An intradermal test dose of 0.1 ml of a 1 in 10 dilution may be given to elicit sensitivity. Preparation is to be kept ready to face the reaction after injection. These are Adrenaline, antihistamine and hydrocortisone injection ampoules, disposable syringe and airway tube etc

Proprietary Preparation
Vaxitet-IG *(Incepta)*, Inj.TK 408.00/Vial

13.2 IMMUNOGLOBULINS

Human immunoglobulins have replaced immunoglobulins of animal origin (antisera) which were frequently associated with hypersensitivity. Injection of immunoglobulins produces immediate protection lasting for several weeks. Human immunoglobulins are of two types: Normal Human Immunoglobulin (NHIg) and Specific Immunoglobulin.

NORMAL HUMAN IMMUNOGLOBULIN [ED] (GAMMA GLOBULIN)

Normal Human Immunoglobulin is prepared from a pool of at least 1000 donations of human plasma. It contains antibody to measles, mumps, varicella, hepatitis A and other viruses that are currently prevalent in the general population. It is used to prevent measles in highly susceptible individuals and to provide temporary protection (up to 12 weeks) against hepatitis A infection for travellers to endemic areas and to control institutional and household outbreaks of hepatitis A infection.

Live vaccines should not normally be given for 12 weeks after an injection of NHIg and if a live vaccine has already been given NHIg injection should be deferred for 2 weeks.

Proprietary Preparations
Human gama globulin(I) (*Chiron),* Inj.16%. Tk.133.82/2ml amp
Octagam(I) *(Octapharma),* Inj. 2.5gm/50ml. Tk.6157.88/50ml
Pentaglobin(I) (*Biotest))* Inj. 50mg/ml,10ml vial; Tk.4478.28/vial
Humaglobin(I) **(***Bioplazma),*Inj.100ml Tk.31386.48/vial
Rhophlac(I) *(Lilly)* Inj.(prefilled pen)Tk.3050.00/2 ml pen

SPECIFIC IMMUNOGLOBULINS

Specific human immunoglobulins or hyperimmune immunoglobulins are prepared from the plasma of selected donors who have recently recovered from an infection or who have been immunized against a specific infection. That is why they have high levels of the specific antibody required, e.g,Hepatitis-B Immunoglobulin (HBIg), Rabies Immunoglobulin (RIg) *(See under Rabies vaccine)*, Tetanus Immunoglo-bulin (TIg).

ANTITETANUS IMMUNOGLOBULIN (TIG) [ED]

Presentation : Purified immunoglobulin obtained from the sera of healthy human donors known to have high levels of tetanus antitoxin following active immunization with tetanus vaccine. Each vial contains 250 IU of tetanus antitoxin in 1.0 ml solution.

Uses : For passive immunization against tetanus, in conjunction with adsorbed tetanus vaccine as soon as practicable after a tetanus susceptible person has sustained wound. Also for the treatment of tetanus

Doses and administration :

a) Prevention of tetanus following injury :

ADULTS : TIG should be administered by IM injection usually in a dose of 250 IU. Persons not immunized or inadequately immunized with tetanus vaccine are susceptible to tetanus and all wounds are prone to tetanus infection. In cases of doubt a person should be regarded as inadequately immunized. Administration of immunoglobulin does not obviate the need for debridement of and wound cleansing, nor does it contraindicate the use of antibiotics. The prophylactic immunization schedule against tetanus should be carried out as soon as possible after a person has sustained a

wound. Passive immunization with immunoglobulin should be accompanied by simultaneous active immunization with adsorbed tetanus toxoid. If more than 24 hours have elapsed since the wound was sustained or if there is a risk of heavy contamination with *Clostridium tetani* 2 ml (500 IU) should be given irrespective of immunization history. TIg and adsorbed tetanus toxoid should be administered with separate syringes and into separate sites. Tetanus toxoid in single solution is unsuitable for administration concurrently with TIg. A single dose of TIg usually provides a protective level of tetanus antitoxin over 0.01 IU per ml serum, for a period of 4 weeks. Long-term immunity against tetanus is conferred by giving further doses.

CHILDREN : As for adults

b) Treatment of tetanus :

ADULTS : 30-300 IU /Kg given IM

CHILDREN : As for adults

Contraindications : TIG should not be given intravenously. The administration of immunoglobulin may be contra-indicated by a history of anaphylaxis resulting from administration of a previous dose of human gamma globulin.

Cautions: TIG should not be given concurrently with tetanus toxoid in single solution. Although anaphylaxis is rare, facilities for its management should always be available during vaccination.

Side-effects: local reaction, consisting of a small area of inflammation and tenderness, may occur after administration of the immunoglobulin, but this rarely constitutes more than temporary inconvenience. Constitutional upsets, and particularly anaphylactic reactions are uncommon. Patients with antibody deficiency syndromes may be liable to have local reactions after administration of the immunoglobulin. USE IN PREGNANCY AND LACTATION *:* Accurate information is not available on the safety of TIG in pregnancy and lactation

Proprietary Preparations

Tetuman Berna[(I)] *(Swiss Serum)*. Inj. 250IU/ml; Tk.541.73/vial

ANTIRABIES IMMUNOGLOBULIN (RIG)[ED]

Indications : Rabies Immunoglobulin provides passive immunization against rabies for prevention of rabies in patients after contact with a rabid animal or an animal presumed to be rabid. Anti rabies serum itself does not constitute an anti rabies treatment and should always be used in conjunction with rabies vaccine.

Dosage and administration: The recommended dose for both ADULTS and CHILD is 40 IU/kg of body weight. If anatomically feasible, as much as possible of the dose should be infiltrated around and into the wound(s). The remainder should be *administered intramuscularly* (into the gluteal region) in a single injection.

However, for children, particularly in the case of multiple wounds, it has been proposed to dilute the dose 2-3 times in a 0.9% sodium chloride solution to obtain a sufficient quantity of equine rabies immunoglobulin to infiltrate the wound(s) correctly.

Contra-indications: Known history of allergic symptoms to horse proteins. Nevertheless, the lethal risk associated

with rabies overcomes any potential contraindication.

Drug interactions: For treatment associating rabies immunoglobulin and rabies vaccine, the rabies vaccine should be injected in a contra lateral anatomic site (i.e., on opposite side) using a different syringe. As a general rule, corticosteroids, liable to attenuate the immune response, should be avoided.

Pregnancy and Lactation: The safety of rabies immunoglobulin when used during pregnancy has not been established in clinical trials in human beings. Considering the lethal risk associated with rabies, pregnancy may not be a contraindication to the administration of rabies immunoglobulin subsequent to exposure.

Side effects: Immediate or delayed hypersensitive type reactions may be developed on administration of rabies immunoglobulin. The observed immediate reactions are hypotension, dyspnoea, and urticaria. Delayed reactions consist of inflammatory reaction, fever, pruritis, rash or urticaria, adenopathy and arthralgia.

***Proprietary preparation**:*

Rabix-IG *(Incepta)*, 1000 IU/5ml, Tk 1000/Vial

13.4 INTERNATIONAL TRAVEL

A vaccination plan should be established, taking into account the traveler's destination, overall state of health and current immune status, the duration and type of travel.

Smallpox: No country any longer requires a certificate of vaccination against smallpox.

Cholera: Cholera Vaccine is no longer recommended for international travel due to low risk of cholera in travelers and the limited benefit of available vaccines. In rare circumstances when an unofficial demand may be anticipated, confirmation of non-requirement of cholera vaccine may be given on official notepaper signed and stamped by the medical practitioner.

No particular immunization is required for travelers to the United States, Europe, Australia, or New Zealand although all travelers should have immunity to tetanus and poliomyelitis and childhood immunization should be up to date. In Non-European areas surrounding the Mediterranean, in Africa, the Middle East, Asia and South America, certain special precautions are required *(see also Appendix-8C)*

Poliomyelitis: On 5 May 2014, the Director–General of WHO declared the international spread of wild polio virus a Public Health Emergency of International Concern. The declaration followed advice given by an Emergency Committee under the International Health Regulations (IHR) that was convened to assess whether the international spread of polio in 2014, As per declaration by DG WHO the temporary recommendation for states currently exporting wild polio virus and states infected with wild poliovirus but not currently exporting: *To ensure all* residents and long-term visitors (i.e. within four weeks), who have not received a dose of OPV or IPV in the previous four weeks to 12 months, receive a dose of oral polio vaccine at least by the time of departure as this will still provide benefit, particularly for frequent travelers.