

Vaccine Preventable Diseases

A.P. DUBEY, S.B. MUKHERJEE

Department of Pediatrics, Maulana Azad Medical College & Associated Hospital, New Delhi-110002, India

Abstract: Immunizations rank among the greatest public health accomplishments during the twentieth century. Childhood immunization is responsible for a substantial decrease in the morbidity and mortality from certain childhood illnesses globally. Health care providers must remain diligent and aware of the various vaccine preventable diseases and their respective vaccines in order to achieve and sustain the high vaccination levels necessary to prevent transmission of these diseases. It is imperative that no child remains unimmunized due to lack of awareness. Certain vaccines like BCG, DPT, OPV and measles are already included in the Indian National Immunization Schedule. The Indian Academy of Pediatrics has also recommended the inclusion of vaccines for mumps, rubella, hepatitis B (HB), Haemophilus influenzae type b (Hib) infection and Typhoid in the national immunization policy. Additional vaccines like those against hepatitis A and chicken Pox, vaccines have recently been introduced in India and are considered to be highly efficacious and safe. Vaccines against meningococcal infections and Japanese B encephalitis are recommended for use in epidemics. Certain high-risk groups of children need to be vaccinated against pneumococcal infection and Influenza. The anti-Rabies vaccine can be administered both pre-and post exposure. The increase in the number of effective vaccines suitable for use in infancy and early childhood has introduced substantial economic and logistical difficulties. Combination vaccines protect against many pathogens by combining all the antigens recommended for routine immunization into a single multivalent product. Those commonly being used include DT, TB, DPT, IPV, OPV, MR and MMR. The newer vaccines also incorporate conjugate Hib, acellular pertussis, or HB antigens. Advances in genetic engineering and molecular biology have led to more sophistication in vaccine production and administration. Extensive research is being done to develop futuristic vaccines for protection against dreaded diseases like HIV, malaria and tuberculosis.

Introduction

Immunizations rank among the greatest public health accomplishments during the 20th century. Childhood immunization is responsible for more lives saved worldwide, than any other medical innovation. The continued control of vaccine preventable diseases generally will require continued immunizations, at as high a coverage as possible. To make this possible it is essential that one is aware of the various diseases that can be prevented by vaccination. Health care providers must remain diligent and informed in order to achieve and sustain the high vaccination levels necessary to prevent transmission of disease.

Vaccine Preventable Diseases covered under National Immunization Schedule (Table 1)

Tuberculosis :

Tuberculosis (TB) is caused by Mycobacterium tuberculosis. Transmission is by droplet inhalation. The respiratory tract is the commonest portal of entry and the commonest form is pulmonary. Miliary and meningitis presentations are life-threatening. Although commonest in adults, the disease is usually more serious in infants, children and adolescents. TB kills more people worldwide than any other infection. There are 15-20 million cases of infectious TB, worldwide, with 4-5 million new cases and 3 million deaths, annually. In India the number of cases at any one time is estimated to be at least 1.5% of the population suffering from radiological active disease, with about 25% of these being sputum positive¹.

Correspondence: Prof. A.P. Dubey
E-mail : apdubey52@rediffmail.com

Table 1. National Immunization Schedule.

Age	Vaccine
Birth	BCG, OPV 0
6 weeks	DPT1, OPV 1
10 weeks	DPT2, OPV 2
14 weeks	DPT3, OPV 3
9 months	Measles
16-18 months	DPT booster, OPV 4
5 years	DT
10 years	TT
16 years	TT
Pregnancy	TT (2 doses, 4 weeks apart)

BCG vaccine : The BCG (Bacille Calmette-Guerin) vaccine is a live, attenuated vaccine made from Mycobacterium var bovis. The original vaccine has been sub-cultured in different media in variable conditions leading to the production of many BCG vaccines, which differ in morphology, growth characteristics, sensitizing potency and animal potency. The Danish 1331 strain is recommended by the World Health Organization. Although the infection with BCG is localized, it induces cell-mediated immunity and some protection. Numerous, randomized, controlled trials have shown variable (0-80%) protection². Effectiveness rates are highest among those who get the vaccination in early childhood.

A single dose (0.1 mg in 0.1ml) should be given as soon as possible after birth, intra-dermally. The vaccine is a freeze-dried preparation, reconstituted with normal saline. It should be used within 4-6 hours of reconstitution as the organisms are temperature sensitive and bacterial contamination may occur. Bacterial multiplication leads to the development of a papule, which may ulcerate. The complete evolution of this lesion, to healing with

scar formation may take up to 6-12 weeks.

Common reactions to the TB vaccine include local reactions at the injection site. Local ulceration and regional suppurative adenitis occur in 0.1-1% while TB meningitis or disseminated TB may occur in 0.006-1.56 per million vaccinated. It may rarely cause osteitis, but this was apparently due to certain strains which are no longer widely used. Serious or long-term complications after immunization are uncommon. Contraindications are generalized eczema, infective dermatitis, hypogammaglobulinemia and severe immunosuppression³.

Diphtheria

Diphtheria is a bacterial infection caused by *Corynebacterium diphtheriae*, transmitted by droplet infection from carriers. It usually affects the respiratory tract. Diphtheria usually begins with a sore throat, slight fever, and swollen neck. Bacteria multiply in the throat, where a grayish membrane forms. A toxin is released which causes muscle paralysis, myocarditis, renal failure and death. Approximately 5% die from the disease and many more suffer permanent damage.

Diphtheria was a cyclical epidemic disease, but with increasing DPT immunization, it now occurs as sporadic cases and intermittent outbreaks of low intensity. However, in areas where the immunization rate has fallen, resurgence has been seen. Recent outbreaks have also demonstrated a shift in the age distribution to older children and adults⁴.

Pertussis

Pertussis (whooping cough) is caused by *Bordetella pertussis*. The infection is transmitted by droplet infection. Although it may occur at any age, maximum morbidity and mortality are observed in early infancy. The incidence of pertussis in older individuals varies with the frequency of exposure to *B. pertussis* and the vaccination coverage. Virulence factors include pertussis toxin, filamentous haemagglutinin, fimbriae and pertactin. Following an incubation period of 7-10 days, susceptible individuals develop catarrhal symptoms, which gradually develop into whooping paroxysms. Pneumonia is a common complication; seizures and encephalopathy occur more rarely. In its early stage pertussis is highly communicable, with a secondary attack rate of up to 90% among non-immune household contacts. Pertussis occurs endemically and epidemically. Worldwide, it causes 20-40 million cases of pertussis and 200,000-400,000 fatalities annually. Mortality rates in developing countries range from 4-15% in infants¹.

Pertussis vaccine : Pertussis results in long-lasting but not necessarily lifelong immunity. Currently, approximately 80% of the world's children are vaccinated with inactivated whole cell vaccines (wP). However due to serious adverse effects, the acellular pertussis (aP) vaccine was developed. This contains different components of *B. pertussis* and shows similar efficacies with wP vaccines (70%-90%). The duration of immunity after wP wanes over time, therefore young adults even if vaccinated in childhood can still develop pertussis. The duration of immunity after aP is still unknown. WHO endorses the use of aP vaccines in countries where wP vaccination is not widely accepted because of its reactogenicity. The main impediment to their wider use is their high cost- and concern about the duration of protection. A

number of aP vaccines are now available, either as individual vaccines or DTaP combinations, with or without the addition of hepatitis B, Hib, or inactivated polio vaccine⁵.

Immunization with wP vaccines is frequently associated with local reactions, fever and agitation. Prolonged crying and seizures are less common (<1%) whereas hypotonic-hyporesponsive episodes (HHE) are rare (<1 in 2000). Acute encephalopathy can also occur in temporal association with wP immunization, but very rarely (<1 in 10.5 million). In large multicentre studies, aP proved to be significantly less reactogenic than the wP vaccines in terms of high fever, seizures and HHE's. No causal link has been identified between either vaccine and permanent neurological damage or death³. Absolute contraindications to pertussis vaccine administration are anaphylaxis to previous vaccination and encephalopathy within 7 days of vaccination. Relative contraindications are seizures within 3 days, persistent, inconsolable crying for more than 3 hours within 48 hours, HHE occurring within 48 hours, temperature of more than 104°F, unexplained by any other cause within 48 hours and progressive neurological disorders⁶.

Tetanus

Tetanus is acquired through environmental exposure to the spores of *Clostridium tetani*. The disease is caused by the action of a potent neurotoxin. Tetanus results in severe, paroxysmal, muscle spasms. Tetanus may be post-traumatic, post-puerperal, otogenic, neonatal or idiopathic. Infection does not stimulate immunity. Tetanus is now a comparatively rare disease in the developed countries. However in developing countries neonatal tetanus is still a major health problem. Neonatal tetanus continues to be seriously underreported, since the populations at highest risk tend to live in rural areas and have the poorest access to health care and birth registration. The WHO and UNICEF have set a target of elimination of maternal and neonatal tetanus by 2005, where elimination is defined as a rate of neonatal tetanus below 1 per 1000 live births, per year, at the district level.

Tetanus toxoid : Protection is acquired through tetanus toxoid-containing vaccines (TT, DTP, DT, Td), which can be given before birth, continued during infancy, and be sustained by reinforcing doses in older individuals⁷. Doses given at the time of school entry should be Td (or TT if Td is not available). The IAP recommends TT at 10 and 16 years and then every 10 years⁸. The total number of doses is 7 by the age of 16 years. Each dose (0.5ml) is given intra-muscularly (IM). Protection against *neonatal tetanus* is determined by the maternal immunization status. Previously unimmunized women should receive two doses of TT or Td during their first pregnancy. Both doses should be at least four weeks apart, and the final dose should be given at least two weeks before delivery. Single dose, during each subsequent pregnancy up to a maximum of five doses should be continued. Supplementary immunization should be conducted in order to vaccinate at least 90% of women of childbearing age with three properly spaced doses of tetanus toxoid in high-risk areas where women have not been sufficiently immunized. This provides protection for at least five years. Women who have received a full course of 7 doses do not require immunization during pregnancy for another 10 years. Subsequently boosters should be continued as the norm. Immunization in addition to the use of clean practices during delivery, improved access to health care, and umbilical cord care should be successful in eliminating neonatal tetanus.

Elimination is maintained in former high-risk districts by strengthening routine antenatal vaccination and school-based immunization.

Diphtheria-Pertussis-Tetanus (DPT) vaccine : In the mid-1940s, the diphtheria toxoid was combined with tetanus toxoid and wP vaccine to formulate DPT. According to WHO. According to WHO, the priority for every country is to reach at least 90% coverage with three primary doses of DTP, however since 1990 the global coverage has only been around 80%. Other combinations available are DTaP, DTaP in combination with Haemophilus influenzae type b (Hib) vaccine, hepatitis B or inactivated polio vaccines⁷. DTaP is now recommended because the rate of serious reactions is lower. It is also about 95% effective in preventing diphtheria, while the protection rates are lower for pertussis and higher for tetanus. Diphtheria and tetanus toxoids do not produce lifelong immunity. Hence a booster dose of Td (tetanus-diphtheria) vaccine is needed every 10 years to maintain immunity. Each dose of DPT (0.5ml) should be given IM. The immunization schedule includes 3 primary doses during the first year of life; a booster dose in the second year and another booster at the age of 4-6 years. From seven years onwards, the adult form (Td) is used which contains approximately one-tenth of the amount of diphtheria toxoid in the paediatric form. It is used because prior subclinical infection by C. diphtheriae, or vaccination, may cause increasing sensitivity to the diphtheria component. Fifty percent of DTP vaccinees will experience no side effects. The others will experience mild reactions such as local soreness, fever, reduced appetite, tiredness, or vomiting. Some children may experience a temporary swelling at the site where DTaP was given (commoner after the fifth dose). Rarely, serious reactions (usually due to the pertussis component) may occur. Children who experience adverse reactions to DTwP or DTaP should receive DT for each of the remaining doses in the primary series.

Poliomyelitis

Polio is an intestinal viral infection caused by picornaviruses, that spread mainly via the faeco-oral route and rarely by droplet infection. There are 3 serotypes (1,2 and 3). Main is the only known reservoir of infection. Cases are most infectious 7-10 days before and after the onset of symptoms. Most people infected (approximately 95%) are asymptomatic. Abortive polio with minor symptoms (sore throat, low-grade fever, nausea, and vomiting) occurs in 4-8%. One to two percent will have non-paralytic polio while less than 1% develop paralysis. The most vulnerable age group is between 6 months to 3 years⁹.

In the pre-vaccination era, polio was found worldwide. Following the Salk (inactivated) polio vaccination from 1955 onwards, the incidence fell dramatically. It was further reduced by the advent of the Sabin (oral) polio vaccine in 1961. Currently widespread vaccination has virtually eliminated it from the developed countries. However, as long as small pockets of unimmunized persons exist, even in these areas there is a risk of sudden outbreaks. Polio still remains a major threat in developing countries. In India the last epidemic occurred in 1987.

Oral polio vaccine (OPV) and Inactivated polio vaccine (IPV): OPV is a trivalent, live attenuated vaccine while IPV is a formalin-inactivated, vaccine, containing 20, 2 and 4D antigen units of serotypes 1,2 and 3 respectively. A modified and improved IPV, which is more potent and has better antigen stabilization, is available

containing 40, 8 and 32D antigen units (1). Both OPV and IPV are highly immunogenic and protective. OPV remains the vaccine of choice for global eradication as it helps to increase herd immunity, and replaces the wild polio strains by vaccine strains (10). Multiple doses are necessary to ensure antibody response to all 3 serotypes. The IPV vaccine is 90% effective after two doses and 99% effective after three doses. Duration of immunity is unknown. IPV is also available in combination with DTaP and hepatitis B vaccines. The primary three doses of OPV (3 drops each) and booster coincide with DPT vaccination. The IAP has recommended an additional dose at birth (or as early as possible-zero dose) and 2 doses as community campaigns each year (pulse polio), till the age of 5 years¹¹. IPV is given at 2 and 4 months followed by the third dose between 8 to 18 months.

Most people have no side effects to OPV. However it may cause vaccine associated paralytic polio (VAPP) in a very small percentage (about 1 out of 6.2 million doses), due to mutation of serotype 3. This is more likely to occur in those with weakened immunity. IPV does not cause any serious side effects. Some people have local soreness. However allergic reactions to certain trace constituents of IPV (streptomycin, neomycin and polymyxin B) may occur in hypersensitive individuals. Contraindications for OPV administration are HIV infection immunosuppressive states, contact with such people or pregnancy. Contraindications to IPV are anaphylaxis to the aforementioned trace constituents are pregnancy.

Measles (Rubeola)

Measles is caused by the Morbillivirus of the paramyxoviridae family, which spreads by droplet infection. The period of greatest contagiousness is at the end of the prodromal phase. The secondary attack rate is 90% in susceptible household contacts. Measles begins with a prodromal phase followed by a typical erythematous, maculopapular rash. Otitis media, pneumonia, croup, and diarrhea are common complications. Measles encephalitis and Subacute sclerosing panencephalitis (SSPE) occurs in 1 per 1,000 and 7 out of a million cases of natural measles, respectively. Death is more common in infants, malnourished children and immunocompromised persons. Measles is endemic worldwide. Epidemics tend to occur when the proportion of susceptible children reaches 40%. In India, with an increase in vaccination, the inter-cyclical intervals of measles have increased, while the intensity of each cycle has decreased¹.

Measles vaccine : Measles vaccine is a live, attenuated virus derived from the attenuated Edmonston strain. The measles vaccine does not contain any antibacterial preservative, hence the vial should be discarded within 4-6 hours of opening. Since the vaccine became available, there has been a 99% reduction in the incidence of measles. Immunity is life long. The vaccine is available as a monovalent form or as a combination vaccine-MR (Measles-Rubella) or MMR (Measles-Mumps-Rubella). The reconstituted vaccine is given as 0.5 ml, subcutaneously, at 9 months age (270 days). Infants less than 9 months old should receive the monovalent vaccine if there is a measles outbreak. In these children, a repeat dose should be given after 3 months. A mild 'measles like' illness may occur 5-10 days after immunization in 15-29% vaccinees. Contraindications to vaccine administration include people with allergies to gelatin or any other vaccine component, immunocompromised persons and pregnancy¹².

VPDs other than those covered under UIP

Mumps : Mumps is a viral infection, caused by Myxovirus parotiditis, which spreads by droplet infection. The secondary attack rate is 86%. It is largely an endemic disease and is prevalent worldwide. It usually begins with swelling and tenderness for one or more of the salivary glands. The disease is more severe in adults. Complications include orchitis (20-50% post-pubertal males), encephalitis and aseptic meningitis (15%), pancreatitis (2-5%), ovarian inflammation (5% post-pubertal females) and deafness (1/2,000). Higher rates of fetal death have been reported in the first trimester.

Mumps vaccine : It is a live attenuated vaccine made from the Jeryl Lynn strain. Post-widespread vaccination, the incidence of mumps and reported mortality has decreased substantially. The duration of long-term immunity is not known. It is available as a monovalent or a combination vaccine (MMR). Indications for the monovalent vaccine are people who cannot receive either or both of the other component vaccines in MMR and people who are immune to either or both measles and rubella. A single dose (0.5ml) given IM produces detectable antibodies in 95% of vaccinees. It is usually given at 12-15 months of age and older. Adverse reactions are rare.

Rubella (German Measles)

An RNA virus belonging to the togavirus family, which is transmitted by droplets, causes rubella. Infectivity is greatest when the rash erupts. It mainly affects children between 3 to 10 years. A single attack results in life long immunity. Rubella is usually a mild illness. Symptoms include low-grade fever, cervical lymphadenitis and a generalized rash. Complications include joint pain, encephalitis and thrombocytopenia. Transient arthritis may occur (in adolescents and women). Rubella in pregnancy often leads to congenital rubella syndrome (CRS), which is characterized by deafness, microcephaly, mental retardation, cataracts, heart defects, thrombocytopenia and diseases of the liver and spleen. The incidence and severity of congenital defects are greater if infection occurs during the first trimester.

Rubella vaccine : It is a live, attenuated vaccine, which was developed in 1962. The current vaccine available is derived from RA 27/3 strains. The rubella vaccine is highly immunogenic, promoting an antibody response in 95% of vaccinees. It probably provides life long protection. It is available as a monovalent or as MMR. Those who cannot receive other components of MMR or those who are immune to measles or mumps or both may receive the monovalent rubella vaccine, though MMR is usually recommended. The vaccine is given as a single dose (0.5ml), subcutaneously after the age of 1 year.

The primary goal for rubella vaccination is to prevent cases of CRS¹³. It is particularly important for post-pubertal women. Susceptible people working in childcare centers and institutions should be immunized to prevent transmission to pregnant women, as well as for self-protection. Susceptible women should be vaccinated at least 28 days before conception. About 0.5% of infants and 15% of post-pubertal females vaccinees may develop acute arthritis. It usually begins 1-3 weeks after vaccination. Occasionally lymphadenopathy may also occur. Contraindications are the same as for measles vaccine.

MMR vaccine : IN 1971, measles and rubella vaccines were

combined with the live attenuated mumps vaccine as the trivalent MMR. The respective strains used are Edmonston Zagreb (measles), L-Zagreb (mumps), and Plotkins RA 27/3 (Rubella). Both measles and rubella strains are produced using human diploid cells while the mumps strain is produced from chick embryo cells. The individual harvests are then pooled and blended to yield a virus concentration of more than 1000 TCID₅₀ for measles, more than 5000 TCID₅₀ for mumps and more than 1000 TCID₅₀ for rubella. The combined vaccine yields results similar to administering individual vaccines at different sites¹⁴. MMR has high levels of immunogenicity and low levels of reactogenicity. It causes adequate seroconversion and a significant reduction in the incidence of the three target diseases. Studies in Indian children using indigenously produced vaccine have shown almost total seroconversion against measles and rubella and 90% seroconversion against mumps¹⁵. Immunity is life long.

All infants, 12 months or older should receive MMR. Susceptible adults who do not have evidence of measles immunity (diagnosed case of measles, measles antibodies or proof of receiving the vaccine) may also receive the vaccine. The reconstituted vaccine (0.5ml) is given subcutaneously. IAP recommends a single dose at 12-15 months, if measles vaccine has been given at 9 months. If measles vaccine was missed, MMR can replace it after 12 months. In 1989, the American Academy of Family Physicians, the American Academy of Pediatrics, and the Centers for Disease Control recommended administration of two doses of MMR. This was done in order to immunize the small percentage of people who had primary vaccine failure. The first dose is generally given at 12 to 15 months, and the second dose at four to six years of age³. More than 80% vaccinees will have no side effects. The side effects are mainly due to the measles component. Most children will have mild local reactions, mild rash, low-grade fever, lymphadenitis and transient arthralgia or arthritis. In about 5-15% of children, high-grade fever and rarely (0.03%) febrile seizure may occur. In extremely rare cases (<1/10,000), serious reactions like coma, anaphylaxis or shock may occur. One per 22,000 vaccinations may cause idiopathic thrombocytopenic purpura (ITP). There are allegations that MMR causes autism or inflammatory bowel disease, which have not been proved. Contraindications for administration are similar to that for measles vaccine.

Haemophilus influenzae B infection

Haemophilus influenzae type b (Hib) is an important cause of meningitis and pneumonia in children less than 2-3 years old. It is transmitted through droplet infection. The secondary attack rate in household contacts is highest in children less than 2 years (3.2%) and rare in those older than 47 months (<0.1%). Invasive disease occurs most often at three months to three years of age, peaking at six to seven months of age. Hib can cause a wide spectrum of diseases: meningitis, pneumonia, cellulitis, epiglottitis, septicemia, osteomyelitis, otitis media, arthritis and pericarditis. Complications include blindness, deafness, mental retardation, learning disabilities, and death. About 5% of children with Hib meningitis die despite antibiotic treatment. Prior to universal Hib immunization, it was the most common cause of bacterial meningitis in preschool-age children. Mortality and morbidity still remains a problem worldwide, primarily in unvaccinated children.

Haemophilus influenzae B (Hib) vaccine : The first generation unconjugated Hib vaccine licensed in 1985 was made from the Hib capsular polysaccharide (PRP). Presently available vaccines

are conjugated to protein antigens to improve immunogenicity, by promoting a T-cell immune response. These include TT (PRP-T), DT (PRP-D), meningococcal outer membrane protein (PRP-OMP), or CRM 197, a nontoxic mutant diphtheria toxin (HbOC). Hib vaccine is more effective at providing immunity than natural infection. Hib vaccine is available as a monovalent form, or in combination with DTaP, DTaP or recombinant hepatitis B vaccine.

Due to the high risk of disease, all children younger than five years should receive the Hib vaccine, beginning at two months of age. High-risk groups are unimmunized children who are daycare attendees, household contacts, belong to a low socioeconomic status, or are immunocompromised (sickle-cell disease, leukemia, HIV infected or post-splenectomy). Children over five years do not need Hib vaccine unless they have specific immunosuppressive conditions. These children may not develop protective antibodies from a single dose and may require additional doses. As Hib is age dependent, immunization involves boosting of natural infection. When initiated below 6 months of age, 3 doses should be given (1-2 months apart), 2 doses between 6-12 months and a single dose, between 12-15 months. A booster is recommended at 15 to 18 months. Beyond 18 months a single dose is recommended up to 5 years of age. Approximately 25% of children who receive the Hib vaccine experience mild side effects such as local reactions. Serious reactions are infrequent. No scientific association between diabetes and Hib vaccination has been found till now, as some authors claim¹⁶. Contra-indications to vaccine administration include children younger than six weeks and people who have had previous anaphylaxis to the vaccine.

Hepatitis B : Hepatitis B virus (HBV) is transmitted through the parenteral route, perinatal transmission, sexual contact, and rarely by surface contact. It is most commonly spread to infants by vertical transmission. Approximately 30% have no known risk factors.

HBV primarily affects the liver. Symptoms of infection include loss of appetite, fatigue, nausea, jaundice, joint pain, and skin rashes. More than 50% show no signs or symptoms, although they may become chronic carriers and develop chronic liver disease or cancer later on. Approximately 90% who are infected by vertical transmission, and 3-50% of those infected before five years, become chronic HBV carriers. People who are infected as adults have only a 6-10% risk of chronic infection. Worldwide, over 350 million people have chronic HBV infection, and approximately 1 million HBV patients die annually. Hepatitis B is a major health problem in India. About 30-40% of deaths due to viral hepatitis were due to HBV (1). In India, 3-7% of individuals are chronic carriers¹⁷. Hence, hepatitis B immunization is recommended for routine administration in countries with a high prevalence rate of HBV infection. The WHO recommends universal HB vaccination. Unfortunately the high cost has been a major deterrent for inclusion in national immunization programmes in many countries. Delhi State Government has included HB vaccination in the immunization schedule, free of cost since 1996. Govt. of India has also initiated this as a pilot project in some states/cities since 2002. However, it is yet to be included throughout the country.

Hepatitis B vaccine : HB vaccines are highly purified preparations of HbsAg. These are available as plasma derived vaccines, or recombinant vaccines (the viral genes are incorporated into yeast or mammalian cells). These vaccines are safe and immunogenic. The recombinant hepatitis B vaccines are 95% protective after a

3 dose course. Immunity is probably life long. Hepatitis B vaccine is available as a monovalent form, or in combination with Hib vaccine, DTaP, IPV or Hepatitis A vaccine¹⁸.

Everyone 18 years and younger should receive the HBV vaccine. High-risk adults (promiscuous individuals, health care workers, homosexuals, or drug addicts) should also receive the vaccine. The vaccine is given IM as a dose of 10 microgram in children. For infants the recommended schedules are 3 doses at birth, 6 and 14 weeks or at 6, 10 and 14 weeks of age. An infant whose mother is HBV infected should receive the first dose of monovalent HBV vaccine within 12 hours of birth along with hepatitis B immunoglobulin. For older children the schedule is the elected date (0), 1 and 6 months. Boosters are not routinely recommended. Infants born to HbsAg positive mothers, dialysis patients and immunocompromised patients may require additional doses if appropriate seroconversion does not occur (antibody titres less than 10 mIU/ml), 1 to 2 months after the third dose. Majority of the people (65%) do not experience any reactions. About 3% develop local reactions, low-grade fever (about 1-6%), while anaphylaxis occurs in less than 0.001%. There is substantial evidence against any causal relationship between the vaccine and Guillain-Barre Syndrome, multiple sclerosis and chronic fatigue syndrome¹⁹.

Typhoid : Typhoid fever is caused by *Salmonella typhi*. Transmission occurs via the faeco-oral route. Man is the only reservoir. Typhoid is closely associated with poor food hygiene and inadequate sanitation. The highest incidence of disease occurs in the 5-19 years age group. It is characterized by a typical, continuous fever and constitutional symptoms. Typhoid may occur sporadically, endemically or epidemically. Asymptomatic intestinal carriers are common in endemic areas. Treatment of the disease and the carrier state has become complicated by the emergence of multidrug-resistant strains of *S. typhi* (20). WHO estimates the annual global incidence of typhoid fever at 0.3% (16 million) with about 600,000 deaths. Typhoid remains a serious public health problem in several parts of Russia, SouthEast Asia, Africa and South America. It is endemic in India.

Typhoid vaccines : Vaccination of high-risk populations of recommended. The previous heat-inactivated whole-cell vaccine showed protective efficacy rates ranging between 57-75%, but was associated with frequent adverse reactions. Two newer typhoid vaccines confer comparable protective efficacy rates without significant side-effects. Both vaccines induce protective immunity for 3-5 years, after which repeat doses are required.

The first, Ty21a, is a live, attenuated, lyophilized vaccine that is administered orally. It is genetically stable. There is limited gut multiplication and a very large number of bacteria (at least 10^9) are required to induce sufficient degree of local immunity. Since the bacteria are acid labile these vaccines are available as enteric-coated capsules. The course consists of 3 separate doses on alternate days, one hour before meals. It is recommended for children above 6 years because the capsules are large and not well tolerated in younger children. The vaccine is contraindicated in acute intestinal infection, acute febrile illnesses and immunosuppressive states. The second, a parenteral vaccine is a purified and adjuvanted form of Vi polysaccharide of *S. typhi*. It is administered IM as 0.5ml dose. Since these antigens are T cell independent the vaccine is non-immunogenic below 2 years of age. Also since it induces an IgM response without an IgG response, it does not have any immunological memory.

Hepatitis A

Hepatitis A virus (HAV) is a type 72 enterovirus of the picornaviridae family. It most commonly spreads via the faecal-oral route; however rarely it can also spread through infected blood or due to sexual contact in homosexuals. Infected people are most likely to spread HAV during the two-week period before they are symptomatic.

It is a relatively benign infection in children. When infected by HAV, adults and adolescents are more likely to develop signs and symptoms than young children, and are more likely to experience severe disease. Symptoms usually last less than two months, but 10-15% will have prolonged or relapsing disease lasting up to six months. A chronic state does not occur. High risk groups are people of low socio-economic strata, people working in endemic areas, laboratory workers dealing with the virus or HAV-infected primates, homosexuals, drug addicts, chronic liver disease patients non-immune to HAV and liver transplant recipients. The exact incidence of the disease is difficult to estimate due to the large number of asymptomatic cases. However according to the WHO, 10-50 person per lakh are affected annually.

Hepatitis A vaccine : The vaccine is an inactivated form of the HM 175 strain. The vaccine efficacy is 94-100% and the duration of protection is long lasting. Immunity develops within four weeks after the initial dose. It is recommended for those who live in HAV endemic areas. Food handlers should also consider vaccination²¹. It is recommended after two years of age, when maternal antibody levels decline. A 0.5ml dose is given IM, at 0 and 6 months in children between 2-18 years. After that it is given at double the dose at 0 and 6-12 months. About 50% will have no side effects. Others may have only mild local reactions (56%), headache (14%), or temporary weakness (7%). In very rare cases a person may be allergic to some vaccine component (i.e. the preservative). The vaccine is available as a monovalent form and in combination with HBV vaccine. The hepatitis A and B combination vaccine is as safe and effective as both vaccines given separately¹⁸. Contraindications are any previous serious adverse reaction to the vaccine.

Chickenpox

Varicella (chickenpox) is caused by the varicella-zoster virus (VZV), and is characterized by a vesicular, pleomorphic, centripetal rash accompanied by fever and malaise. The virus spreads by droplet infection or drop let nuclei. It is highly communicable with a secondary attack rate of 90%. The period of communicability is 1-2 days before the onset of rash and lasts till 4-5 days after. It is generally a mild disease, but can be severe and even fatal in otherwise healthy children (<1/10,000). It can cause pneumonia and put the child at risk for invasive Group A streptococcal disease. Complications include arthritis, hepatitis, thrombocytopenia and encephalitis (1/10,000) commonly seen among adolescents, adults, and immuno-compromised persons. If infected in early pregnancy, the fetus may develop congenital abnormalities (scarring of the skin, limb deformities, eye damage, low birth weight, cerebral atrophy, and mental retardation) in 2% of cases, or it may cause spontaneous abortion or neonatal mortality. While only 5% of cases are in adults, they account for 35% of the mortality. Chickenpox is worldwide in distribution, occurring as both epidemics and endemics.

Varicella vaccine : The varicella vaccine was developed from the Oka strain. It is a live attenuated, lyophilized vaccine, containing traces of neomycin and gelatin. Both humoral and cell-mediated immunity develop in more than 95% cases after a single dose in children between 1-12 years and 99% after 2 doses in children 13 years and above. Varicella vaccine is 85% to 90% effective. The older the child when vaccinated, the better the vaccine protection²². The duration of immunity is variable. In USA, protection has been observed for 11 years, whereas in Japan it was demonstrated for at least 20 years. Breakthrough infection can occur (<1-4%) in immunized persons, as compared to annual rates of 7-8% in unvaccinated children. However the disease is milder, with fewer skin lesions, of shorter duration and there is no or low fever. It has been seen in preschoolers that even when low percentages of children were immunized, the incidence of varicella in unimmunized children decreased substantially. It has been hypothesized however, that even though this herd immunity helps protect unimmunized people during childhood, it increases the risk later on by causing infection in adulthood, when serious illness and complications are more common²³.

The vaccine is recommended for all children aged 12-18 months, and all older individuals who have not had chickenpox and are not vaccinated. However opinion is divided about the need for varicella vaccination. A mild illness in childhood, chickenpox may become more severe if it is postponed to adulthood. The chickenpox vaccine virus also may establish a latent disease and produce zoster later on, which is more severe and frequent than the natural disease. The recommended dose is 0.5ml, given subcutaneously. It is given as a single dose in children between 12 months to 12 years. In older children 2 doses are administered, 4-8 weeks apart. No booster is recommended. The majority of recipients have no side effects. Local soreness and swelling and a mild rash may occur. Very rarely (less than 0.02%), seizures caused by high fever may occur. Contraindications include a previous life-threatening allergic reaction, pregnancy, T-lymphocyte immunodeficiency states and recipients of antibody-containing products.

Meningococcal infections

The meningococcus causes septicaemia, meningitis or both. It is found in the nasopharynx of cases and carriers and spreads by droplet infection. The disease is usually caused by the serogroups, A,B,C,Y, and W-135. Most epidemics are caused by serogroup C. Death occurs in 10% to 15% and is highest in infants and adolescents. Risk factors include close living conditions and close contacts of an infected person.

Meningococcal Vaccine : The first vaccines were effective against only two groups of meningococcus. The quadrivalent vaccine is protective against groups A,C,Y and W-135. Currently available vaccines provide some protection against all groups except B. Children are not routinely vaccinated because their infection rate is low and immunity short-lived. Also if they receive the vaccine early, subsequent doses may not be protective. In older children, and adults, it is 85-100% effective and protection lasts for at least three years²⁴. Indications for vaccine administration include susceptible people during epidemics, travelers, immunosuppressed patients, people living in dormitories and laboratory personnel. A single dose (0.5ml) is given subcutaneously or by IM. Children may be revaccinated in 2-3 years if initial vaccination was before

four years. Older individuals need to be revaccinated in 3-5 years for continuous protection. The majority of vaccinees experience no adverse reactions. Local reactions are seen in 40%. Rarely (<1/10,000), an allergic response can occur. Contraindications to vaccination are people who had an allergic reaction to a previous dose, or during acute infectious diseases.

Japanese B Encephalitis

Japanese B encephalitis (JE) is a culicine mosquito-borne, flavivirus zoonotic disease. Maximum cases occur in children less than 15 years and those above 60 years. JE is endemic in parts of Eastern and South-Eastern Asia. In 2002, the WHO reported a 5-35% case fatality rate and a 75% disability rate(1).

Japanese B encephalitis vaccine : This is a formalin-inactivated vaccine, recommended for the high-risk groups and is best used in the inter-epidemic interval. However high costs, limited production, short-term protection and neurological side effects hamper its widespread use. Two doses of 1ml each should be given subcutaneously at an interval of 1-2 weeks. Revaccination can be given after 3 years. Other vaccinees currently under development are a live-attenuated vaccine, a vero cell-derived inactivated vaccine, recombinant vaccinees using pox vectors and a chimeric, live-attenuated, vaccine using the 17D yellow fever strain.

Rabies

Rabies is caused by a rhabdovirus, which is most often spread by the saliva from an infected animal. Rarely cases due to infection by airborne virus in laboratory workers and cave explorers have been reported. Virtually 100% of those infected and who do not receive the vaccine die.

Rabies vaccine : The first rabies vaccinees developed were made from nerve tissue. Currently tissue culture vaccinees are in use, which include human diploid cell (HDCV), purified chick embryo cell culture (PCEC) and Vero cell vaccinees. Indications for pre-exposure vaccination are for high-risk groups who may be exposed to the rabies virus. It is given as 3 doses of 1ml each, IM, on days 0, 7 and 28. Booster doses of vaccine are recommended every two years for those who continue to be at increased risk. Antibody levels should be tested six monthly and boosters should be given as necessary. The schedule of post-exposure vaccination depends upon the previous immunization status. Unvaccinated people should receive the vaccine at 0, 3, 7, 14 and 28 days with rabies immune globulin (RIG) with the first dose. Previously vaccinated people (within 5 years) should receive two doses of the vaccine on days 0 and 7 and RIG should not be given (25). Mild local reactions at the injection site are reported among 30-74%, while headache, nausea, abdominal pain, muscle aches, and dizziness are reported in 5-40%.

References

1. Park K. Epidemiology of communicable diseases. In: Park's textbook of preventive and social medicine. 15th ed. Jabalpur, Banarsidas Bhanot; 1997:pp115-268.
2. Starke JR, Munoz F. Tuberculosis. In: Behrman RE, Kliegman RM, Jenson HB (eds), Nelson textbook of pediatrics. 16th ed. Philadelphia, WB Saunders; 2000:pp885-897.
3. CDC. General recommendations on immunization: Recommendations of the Advisory Committee on Immunization Practices (ACIP) and the American Academy of Family Physicians (AAFP). *Morb Mortal Wkly Rep* 2002;51(RR-02):1-35.
4. CDC. Diphtheria. In: Atkinson W, Wolfe C, Humiston S, Nelson R (eds), *Epidemiology and prevention of vaccine-preventable disease*. (The Pink Book). 6th ed. Atlanta, CDC; 2000:pp308-323.
5. Halperin S, Smith B, Russell M. Adult formulation of a five component acellular pertussis vaccine combined with diphtheria and tetanus toxoids and inactivated poliovirus vaccine is safe and immunogenic in adolescents and adults. *Ped Inf Dis J* 2000;19:276-83.
6. Woods CR, Abramson JS. Immunization practices. In: Burg FD, Ingelfinger JR, Polin RA, Gershon AA (eds). *Gellis & Kagan's current pediatric therapy*. 17th ed. Philadelphia, WB Saunders; 2002:pp 190-211.
7. ACIP, AAP, AAFP. Combination Vaccines for Childhood Immunization: Recommendations of the Advisory Committee on Immunization Practices (ACIP), The American Academy of Pediatrics (AAP), and the American Academy of Family Physicians (AAFP). *Pediatrics* 1999;103(5):332-324.
8. IAP committee on immunization. Tetanus toxoid. In: Parthasarathy A, Dutta Ak, Bhavne SY (eds). *IAP guidebook on immunization*, 2nd ed, Mumbai, 2001;23.
9. AAP, Committee on Infectious Diseases. Polio virus infections. In Pickering LK (ed). *Red Book: Report of the Committee on Infectious Diseases*, 25th ed. Elk Grove Village, Illinois, AAP; 2000:pp 465-470.
10. Aylward RB, Hull HF, Cochi SL, Sutter RW, Olive J-M, Melgaard B. Disease eradication as a public health strategy: a case study of poliomyelitis eradication. *Bull WHO* 2001;78(3):285-297.
11. IAP committee on immunization. Polio vaccine. In: Parthasarathy A, Dutta Ak, Bhavne SY (eds). *IAP guidebook on immunization*, 2nd, Mumbai, 2001;18-21.
12. Duclos P, Ward BJ. Measles vaccinees: A review of adverse events. *Drug Safety* 1998;19(6):435-454.
13. Cuttrts FT, Robertson SE, Diaz-Ortega J-L, Samuel R. Control of rubella and congenital rubella syndrome (CRS) in developing countries, part 1: burden of disease from CRS. *Bull WHO* 1997;75:55-68.
14. Dubey AP, Banerjee S. Measles, Mumps, Rubella (MMR) Vaccine. *Ind J Ped* 2003;70:579-584.
15. Bhargava I, Chhapparwal BC, Phadke MA, Irani SF, Chhapparwal D, Dhorje S, et al. A study of immunogenicity and reactogenicity of indigenously produced MMR vaccine. *Indian pediatrics* 1995;32:983-988.
16. Karnoven M, Cepaitis Z, Tuomilehto J. Association between type 1 diabetes and Haemophilus influenzae type b vaccination: Birth cohort study. *Br Med J* 1999;318(7192):1169-1172.
17. IAP committee on immunization. Hepatitis B vaccine. In: Parthasarathy A, Dutta AK, Bhavne SY (eds). *IAP guidebook on immunization*, 2nd ed, Mumbai, 2001:pp28-30.
18. Joines RW, Blatter M, Abraham B, Xie F, De Clercq N, Baine Y, et al. A prospective, randomized, comparative U.S. trial of a combination hepatitis A and B vaccine (Twinrix) with corresponding monovalent vaccinees (Havrix and Engerix-B) in adults. *Vaccine* 2001;19(32):4709-4710.
19. Azcherio A, Szhang SM, Hernan MA, Olek MJ, Coplan PM, Brodovicz K, et al. Hepatitis B vaccination and the risk of multiple sclerosis. *N Eng J Med* 2001;344(5):327-332.
20. Ivanoff BN, Levine MM. Typhoid Fever: continuing challenge from a resilient foe. *Bulletin Institute Pasteur* 1997;95:129-142.
21. Centers for Disease Control and Prevention. Prevention of hepatitis A through active or passive immunization. Recommendation of the Advisory Committee on Immunization Practices (ACIP). *Morb Mortal Wkly Rep*, 1999, 48(RR-12):1-37.
22. Vasquez M, LaRussa PS, Gershon AA, Steinberg SP, Freudigman K, Shapiro E. The effectiveness of the varicella vaccine in clinical practice. *N Eng J Med* 2001;344(13):955-960.
23. Taylor JA. Herd immunity and the varicella vaccine: Is it a good thing? *Arch Ped Adol Med* 2001;155(4):455-461.
24. Centers for Disease Control and Prevention. Prevention and control of meningococcal disease. *Morb Mortal Wkly Rep*, 2000, 49(RR-7):1-10.
25. American Academy of Pediatrics, Committee on Infectious Diseases. Rabies. In *Red Book: Report of the Committee on Infectious Diseases*, 25th ed. Elk Grove Village, Illinois; 2000:pp.475-482.