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Immunization of Children

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Introduction

Immunization has been one of the great successes of twentieth century medicine for prevention and control of human and animal infectious diseases. The routine immunization programs against childhood diseases have proved to be very successful in both developed and developing countries. The Government of India initiated the Expanded Program on Immunization (EPI) in the year 1978 with the object of providing immunization for all the children against six vaccine preventable diseases i.e. Diphtheria, Tetanus, Pertussis, Tuberculosis, Polio and Measles. The achievements are remarkable and the incidences of these six diseases have been brought down significantly (MHFW, 2000). Tetanus toxoid is administered to the mother either during her pregnancy or prior to pregnancy during the childbearing years to protect new borne against neonatal tetanus. The global Polio eradication initiative began in 1988 (World health Assembly, 1988) through 2001, the number of reported Polio cases in the world has been reduced by more than 99 percent from an estimated 3,50,000 to < 1000 cases and number of countries where Polio is endemic decreased from 125 to 10 (MMWR, 2002). The decrease of the other diseases is remarkable as per the records maintained by centers for Disease Control and Prevention (CDC) and it shows over 99 percent decrease in the case of Diphtheria, Measles, Mumps and rubella and over 97 percent in the case of Whooping cough (MMWR, 1998). As stated by Plotkin and Plotkin, "the impact of vaccination on the health of the world's peoples is hard to exaggerate with the exception of safe water, no other modality, not even antibiotics, has had such a major effect on mortality reduction and population growth" (Plotkin and Plotkin, 1999).

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The breakthroughs in molecular biology, biochemistry, immunology and related fields have resulted in the development of many new vaccines like Hepatitis 'B' as well as in the improvement of several existing ones. The concept of combination of vaccines if developed successfully could help to reduce in the number of injections during the first two years of life. Presently immunization protects the children against Hepatitis B, Measles, Mumps, Rubella (German Measles), Polio, Diphtheria, Tetanus, Pertussis, Haemophilus, Influenza type 'b' and chicken pox. All these immunization need to be given before the children are two years old.

History of Immunization

One of the most important activities in total comprehensive care for children is successful immunization practice. The earliest documented attempts at immunization aimed at preventing small box were reported nearly 1000 years ago. The first milestone in immunization was laid by Edward Jenner in 1796 with a systematic, successful attempt at eradication of small box by vaccination. He actively immunized an eight - year old boy with the fluid from the pustule of a cowpox lesion on the hand of a milkmaid and challenged with small poxvirus. The boy was protected against smallpox virus. The boy was protected against small pox despite exposure to virus and this weakened form of 'Small Pox' was called a vaccine from vacca, the Latin word for cow. During 19th century, the small pox vaccination became very popular and small pox was the first communicable disease to be eradicated globally in the year 1976.

Pasteur in 1885 developed first rabies vaccine successfully proving attenuated germs when injected into the body confers immunity against the disease. Pasteur suggested that all inoculations be called "Vaccinations" to honor Jenner and today the more accurate word "Immunization" is preferred.

The introduction of inactivated vaccines in 1890 heralded a dramatic shift in the methodology used to produce vaccines. The prime reason was safety. The early twentieth century saw the introduction of numerous bacterial and viral vaccine preparations containing either whole-inactivated bacteria or virus or semi purified detoxified bacterial toxins. Some of the important vaccines used in immunization are presented in chronological order in Table 1.

Table 1

Chronology of important human vaccines used

Year of Introduction	Disease	Type of Vaccine
1721	Small pox	'Variolation' with live virus
1798	Small pox	'Naturally attenuated' cow pox virus
1885	Rabies	Attenuated live and inactivated virus
1896	Typhoid fever	Inactivated intact bacteria
1896	Cholera	Inactivated intact bacteria
1897	Plague	Inactivated intact bacteria
1923	Diphtheria	Partially purified formalin toxoid
1926	Pertussis	Inactivated intact bacteria
1927	Tuberculosis	Live attenuated BCG strain
1955	Polio	Inactivated virus
1961	Polio	Live attenuated virus
1963	Measles	Inactivated virus and live attenuated virus
1974	Japanese encephalitis	Inactivated virus
1976	Rabies	Tissue Culture, inactivated virus
1981	Hepatitis B	Inactivated plasma derived
1986	Hepatitis B	Inactivated, Recombinant

Types of Immunization

Immunization involves the induction or administration of antibodies and other natural defense mechanisms to protect against specific pathogens. There are two types of immunization.

a) Active Immunization

b) Passive immunization

Active Immunization

Active Immunization is achieved by the administration of modified pathogenic agent or a component pathogen, to stimulate the recipient's immune mechanism to produce long lasting protection without causing the clinical manifestation of disease. To produce the active immunity, the preparations can be divided into three broad categories.

a) Live attenuated vaccine:

Live attenuated vaccine is a microorganism that can replicate on its own in the host or infect cells and function as an immunogen without causing its natural disease. Most of these vaccines confer life long immunity but there is a risk of reversion to virulence. The examples include widely used Sabin type of Polio vaccine (OPV) (Sabin & Boulger, 1973), BCG vaccine against tuberculosis (Harboe et al, 1996) the vaccines against Measles, Mumps, Rubella (Gluck & Just, 1991) and Varicella (Takahashi et al., 1974).

b) Inactivated vaccine (Killed or Subunit Vaccine)

Inactivated vaccine is an immunogen that cannot replicate in the host. The immunity conferred is of short duration and requires repeated boosters. The examples includes Salk Poliovirus vaccine (Salk, 1960) commonly called Inactivated Polio Virus Vaccine (IPV), whole cell vaccine against Pertussis and the Influenza vaccine.

c) DNA-based vaccines

DNA- based vaccine, which cannot replicate in humans, is taken up by cells in which it directs the synthesis of vaccine antigens.

Passive Immunization

Passive Immunization is obtained by transferring antibodies against a given disease from an immune person or animal to a non-immune individual by injection of serum (antisera) or some partially serum extract.

Diphtheria antitoxin was the first such product commercially available followed by Tetanus antitoxin which were of equine origin. Their use was associated with untoward side effects such as serum sickness. Presently, human origin sera or globulins are

available but they are very expensive. Because of the cost, the equine globulins being continued to use in all the developing countries. A few immunoglobulins licensed for the preventive or treatment of infectious diseases are listed below:

Immunization Schedule for Children

The principle of any immunization program is, protection must be achieved prior to the time that infants are at high risk from a disease. Infants are highly susceptible for Pertussis soon after birth and it is recommended to start immunization with DPT at 6 weeks of age, with subsequent doses at 10 and 14 weeks.

Neonatal tetanus (NNT) is an important cause of infant mortality in many countries and immunization of women of childbearing age and especially pregnant women is recommended.

The simultaneous administration of several vaccines simplifies routine childhood immunization and reduces the number of contacts or visits. All the EPI vaccines can be administered simultaneously (Galazka, 1991) and it is a common practice to give DTP vaccine and oral Polio Vaccine (OPV) at the same time. BCG vaccine is compatible with OPV, DTP and Measles vaccine (Galazka, 1993). In United States to eliminate the risk of vaccine associated paralytic Polio, routine vaccination of children was recommended with IPV and presently OPV is unavailable for routine use (CDC, 2000). However; OPV remains the vaccine of choice as it induces intestinal immunity and prevents spread among close contacts.

In 1989, the Global Advisory Group (GAG) of EPI officially recommended that Hepatitis–B (HB) vaccination to be administered to all infants as part of EPI in countries where prevalence of chronic carriers of Hepatitis–B virus (HBV) exceed 2% and recommended all the countries to under take universal infant immunization with HB vaccine by 1997 (PATH, 1993). In 1992 world health assembly endorsed these targets and HB vaccine now to be considered the seventh EPI vaccine. The three–dose schedule for primary immunization against HBV should be begun in early infancy. The American Academy of Pediatrics (AAP) recommends giving the first dose before discharge from the hospital after delivery, the second dose should be administered at 12 months of age followed by a third dose at 6 to 18months of age (AAP, 1992).

The schedules of childhood immunization vary slightly from country to country and the immunization schedules recommended by EPI (Galazka, 1993) and our country (NIM) are presented in the Table 3 & 4. In addition to these, United States recommends the following vaccines for childhood immunization.

Table 2

Immunoglobulins available for Treatment of Infectious Diseases

Viral Diseases	Bacterial Disease
Rabies	Tetanus
Measles	Diphtheria
Chicken Pox	Pertussis
Hepatitis B	

1. Haemophilus influenza type b (Hib) conjugate Vaccine: three doses are given at the age of 2,4 and 6 months. (The bacteria cause meningitis, pneumonia and throat infection).

2. Measles, Mumps and Rubella Vaccine (MMR): two doses are recommended and the 1st dose to be given at the age of 12 months or after 12 months. Second dose is recommended at age 4-6 years. (Viral infection is characterized by rashes, fever and potentially serious side effects such as heart damage and pneumonia).

3. Varicella Vaccine: recommends at or after 12 months of age for all susceptible children. (Protects against chicken pox).

4. Pneumococcal Vaccine: Recommended for all children aged 2-23 months.

5. Hepatitis–A Vaccine: Recommended in high-risk groups between 2-18 years.

6. Influenza Vaccine: Recommended annually for children age of more than 6 months with certain risk factors.

Table 3

The Immunization Schedule Recommended By The EPI

AGE	VACCINES	HEPATITIS B (HB) VACCINE	
		Scheme A	Scheme B
Birth	BCG, OPVO*	HB1	
6 weeks	DTP1, OPV1	HB2	HB1
10 weeks	DTP2, OPV2		HB2

14 weeks	DTP3, OPV3	HB3
9 months	Measles, Yellow fever**	HB3
Women of childbearing age, and especially pregnant women		TT1 - as soon as possible in pregnancy or as early as possible in the childbearing years
		TT2 - at least 4 weeks after TT1
		TT3 – at least 6 months after TT2 TT4 and TT5- at least one year after the previous TT dose

* OPV at birth (OPVO) is recommended in countries where poliomyelitis has not been controlled.

** Yellow fever vaccine is recommended in countries at high risk

Progress of Immunization Programmes in India

The EPI programme was introduced in 1978 with Diphtheria Pertussis, Tetanus vaccine (DPT), Diphtheria, Tetanus vaccine (DT), Tetanus Toxoid (TT) and BCG vaccines followed by Polio and Typhoid vaccines in the 1979. Measles immunization programme was included in EPI during 1985-86. The Government of India launched 'Universal Immunization Programme' (UIP) in 1985-86 and implemented in phased manner. The programme was given the status of a National Technology Mission in 1986 and became operational in all districts of the country during 1989-90. UIP became a part of Child Survival and Safe Motherhood (CSSM) programme in 1992 and Reproductive and Child Health (RCH) programme in 1997 (MHFW, 2000). Remarkable progress has been made under this programme on vaccine coverage levels and also significant decline in the incidence of EPI diseases (Table 5&6). At the beginning of programme in

1985-86, vaccine coverage level ranged between 29 percent for BCG and 41 percent for DPT. By the end of March 1999, coverage levels have improved significantly and ranged between 80 percent for TT for pregnant women to 90 percent for BCG.

Table 4:
Ideal Immunization Schedule for children

Vaccine	At 1½ months	At 2½ months	At 3½ months	At 9 months	At 16 – 24 months	At 5 years	At 10 – 16 years
B.C.G*	One injection						
DPT	First injection	Second injection	Third injection		Booster injection		
O.P.V.	1st dose	2nd dose	3rd dose		Booster dose		
Measles				One injection			
D.T.						One injection	
T.T.							One injection

* If the infant has been delivered in a hospital/clinic, she should be given the B.C.G. injection at birth.

Indications for Immunization

1. The immunization schedule mentioned in table 4 till 9 months of age is the most important part of immunization.

2. Even if the mother is late in bringing the infant for the D.P.T. and O.P.V. injections/ doses, all the three injections/doses must still be given, keeping a difference of 1 month between them, before the infant is one year old.

3. The infant must be given the measles injection at 9 months of age. Even if the mother is late in bringing the infant, the infant must still be given the injection before she is 1 year old because without measles injection, the infant is not fully immunized.

4. Ensure that the infant is given 1 B.C.G. injection, 3 D.P.T. injections, 3 O.P.V. doses and 1 measles injection before she is 1 year old.

5. Children, especially girls, should be given one injection of T.T. at 10 years and one at 16 years of age.

TABLE 5

Yearwise And Antigenwise Achievement as Percentage of Annual Target

Year	DPT	OPV	BCG	MEASLES	TT (PW)
1995-96	91.03	91.61	97.07	82.64	80.33
1996-97	89.32	90.75	97.10	82.01	78.70
1997-98	88.70	89.20	94.80	30.00	78.50
1998-1999	92.80	94.30	97.00	87.30	82.90

Precautions for Immunization

1. The infant should be immunized even if she is suffering from diarrhoea, fever and malnutrition.

2. After the B.C.G. injection, a small blister will appear at the site of injection after 1 to 1 A months. This is normal and is indicative of the fact that the vaccine is working.

3. Abscess should not form after DPT injection and if any abscess develops, the parents are advised to consult the doctor.

4. Immunization process should not be stopped unless the child is very sick and needs hospitalization.

Safety of Vaccines

Modern vaccines are safe and effective, however no biological or drug is completely safe and 100 percent effective. A few adverse events have been reported after administration of vaccines. With in the first 24 hours of vaccination, reactions include erythema and swelling at the site of injection, fever, prolonged crying, syncope, seizures and rarely hypo tonic, hypo responsive episodes or anaphylaxis

TABLE 6
Reported Incidence of Diseases

Disease	1987	1999	% Decline
Polio	28,257	4,320	84.70
Diphtheria	12,952	2,725	79.00
Pertussis	1,63,786	36,716	77.60
NNT	11,849	4,488	62.10
Measles	2,47,519	38,950	84.30

(Ada G, 2001). Late reactions, which occur within a few weeks after vaccination, include encephalitis and encephalopathy and some times to brain damage. But overall there is no clinical or scientific evidence that inoculation of any vaccine causes a specific allergy, asthma, autism, multiple sclerosis or sudden infant death syndrome (Ada G, 2001).

A few major reasons for low rates of immunization among children have been identified by the National Vaccine Advisory Committee (NVAC, 1991). First, many opportunities to vaccinate children are missed because of failure to administer recommended immunizations during health care visits, due to wrong information on contraindications or they are unwilling to give more than two vaccines in the same visit. In most cases, multiple vaccines can be given with out increased risk of adverse effects and impairment of immunological response (Eskola et al., 1987&

Deforest et al., 1988). Second reason is deficiencies in the health care delivery system in the public sector, which includes insufficient staff and polices that serve as barriers. The other reasons are inadequate access to medical care and lack of public awareness in some communities.

Conclusions

The first vaccine was developed 200 years back and millions of lives have been saved from infectious diseases. In the past 50 years the incidence of vaccine preventable diseases were reduced by nearly 90 percent from their peak levels. A better understanding of immune system and its process has driven the explosion of interest in vaccines by both private and public sectors. Presently we are probing into even greater depths into the mechanisms of pathogens use to infect us and cause disease. Genomic research has sequenced genes of many organisms and sequencing is currently in progress for more number of organisms and vaccine research is benefited to develop safe and effective vaccines. New generation technologies like DNA vaccines and edible vaccines emerged from the recent research are in progress to develop vaccines which are more effective longer periods in less frequent doses, quality vaccines at lower price, more stability in wide range of environmental conditions, easy to administer and finally safe and effective. Immunization remains on of the most powerful tools in control and prevention of infectious diseases.

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