JETIR.ORG ISSN: 2349-5162 | ESTD Year : 2014 | Monthly Issue
JOURNAL OF EMERGING TECHNOLOGIES AND INNOVATIVE RESEARCH (JETIR)
An International Scholarly Open Access, Peer-reviewed, Refereed Journal

Deep Study of Vaccine & Sera

Pratiksha Chandrakant Sutar,

Suvarna Bhaurao Jawale,

Yogita Raosaheb Kundhare.

Shivajirao Pawar College of Pharmacy, Pachegaon, Ahmednagar – 413725

Abstract

These are biological product which act by reinforcing the immunological defence of the body against foreign agencies. The agents or product through which immunization is achieved are called immunizing agents. Antisera and immune globulins impart passive immunity readymade antibodies [produce by another person or animal who has been actively immunized] are transferred. Antisera is purified and concentrated preparation of serum of horses/rabbits actively immunized against a specific antigen. Sometimes it shows immediate type of allergic reaction.

Keyword: Vaccination, Antiserum, Immune response, Infections diseases

Introduction

Vaccines impart active immunity – act as antigens which induce production of specific antibodies by the recipients himself. Antisera and immune globulins impart passive immunity – readymade antibodies [produce by another person or animal who has been actively immunized] are transferred.

Active immunization, but the former needs a latent period of one to many weeks, whereas the latter affords immediate protection. Antisera are, therefore, curative also, whereas vaccines are only prophylactic. Acutely ill, debilitated or immmuno compromised individuals may not be able to generate an adequate antibody response and require passive protection.

A vaccine works by training the immune system to recognize and combat pathogens, either viruses or bacteria. To do this, certain molecules from the pathogen must be introduced into the body to trigger and immune response. These molecules are called antigens, and they are present on all viruses and bacteria. By injecting these antigens into the body, the immune system can safely learn to recognize them as hostile invaders, produce antibodies, and remember them for the future. If the the antigens immediately and attack aggressively well before the pathogen can spread and cause sickness.

Vaccines

Vaccines are of 3 types:

1) **Killed [Inactivated] vaccines**: consist of microorganisms killed by heat or chemicals. They generally require to be given by a series of injections for primary immunization. The immunity is relatively shorter – lasting; booster doses are mostly needed at intervals of months or years.

2) **Live attenuated vaccines**: consist of live bacteria or viruses which have been rendered a virulent. They nevertheless grow and multiply in the body of the host to a limited extent. Live vaccines usually produce long – lasting immunity.

Individuals with impaired host defence,

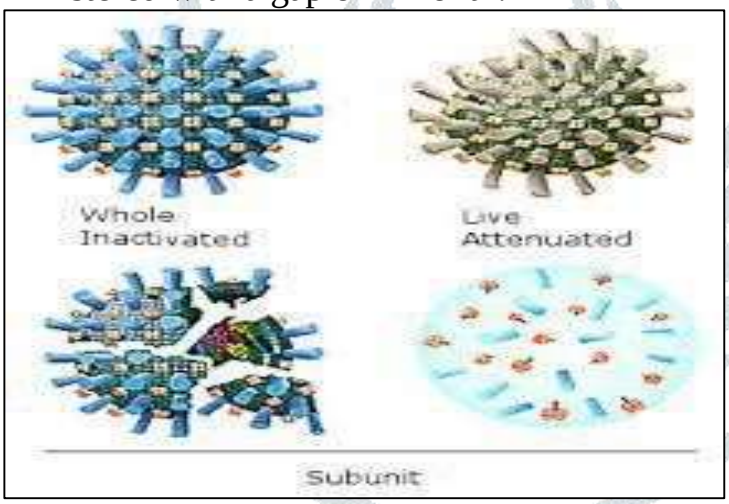
e.g. (a) Leukemia or other malignancies, especially those receiving cytotoxic chemotherapy.

(b) Systemic lupus erythematous.

(c) Corticosteroid recipients.

(d) AIDS and other immune deficiency states.

The limited virulence of organisms in the live vaccine may be sufficient to cause a disease; live vaccines are contraindicated in them. To live vaccines, if not given together, should preferably be administered with a gap of 1 month.



3) **Toxoids:** are modified bacterial exotoxins so that toxicity is lost but antigenicity is retained. The term 'vaccine' is sometimes restricted to preparations of whole microorganisms and toxoids are enumerated separately.

Actively immunization with vaccines may fail to 'take' during corticosteroid or immunosuppressant medication and should be avoided. Vaccination should be deferred in the presence of any acute (especially respiratory) infection and during pregnancy. Antibiotics added during production of vaccines and present in trace amounts in viral vaccines may cause reaction in individual sensitive to these.

Bacterial vaccines

1. Typhoid – Paratyphoid A, B (TAB vaccine)

It is a steric suspension, 1 ml containing 1 x 10^9 S.typhi and 7.5 x 10^8 each of S. paratyphoid A and B organisms in 5, 10 ml vials. Dose – 0.5 ml, S.C., 2-3 injections at 2-4 weeks intervals. Local tenderness, fever and malaise lasting 1-2 days are common after the first dose. It is

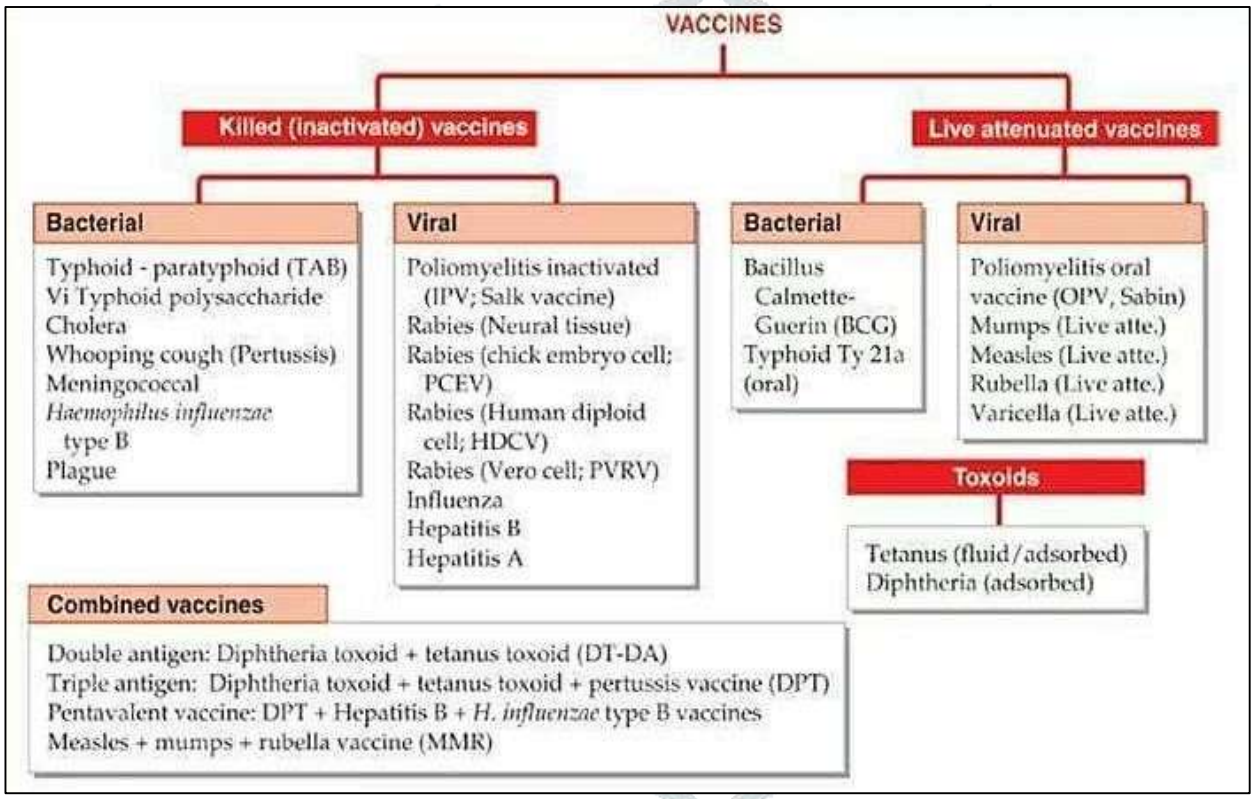
estimated to be 70% effective in preventing enteric fever for 1 year. Booster doses may be given every 2-3 years.

2. Vi Typhoid polysaccharide vaccine

It contains purified VI capsular antigens en of S. typhi. Single 0.5 ml s.c/i.m dose affords 72% protection at 18 months and 60% protection at 3 years. It produces much less local and systemic side effects than TAB and induces longer lasting immunity, but does not protect against paratyphoid A and B. Thus it is an improvement over the whole cell TAB vaccine. However, it is not approved for use in children below 2 years and in pregnant women

3. Typhoid – Ty21a' oral vaccine

This is a ride and is nonpathogenic. Newer live oral typhoid vaccine prepared from Ty 21a attenuated strain of S. typhi which lacks the VI polysaccharide and nonpathogenic the attenuation is due to absence of the



enzyme uridine diphosphate galactose -4 epimerase which is essential for the production of lipopolysaccharide 'O' antigens.

4. Cholera vaccine

It is a suspension of phenol/formalin killed inaba and ogawa strains of v.cholerae each ml containing 8 X 10^9 organisms in 5, 10, 30 ml vials.

5. Whooping Cough (pertussis) vaccine

It is killed 2 X 10^{10} organisms/ml suspension of Pertussis organisms. Dose 0.25-0.5 ml S.C. or i.m. thrice at 4 week intervals in infants wild children below 5 years (whooping cough in rare after 5 years age).

6. Meningococcal A & C vaccine

It contains purified capsular polysaccharide of N. meningitis group A and C, 50 µg of each per unit in single dose and 10 dose vials.

7. Haemophilus influenza type b (Hib) vaccine

It contains medium oligosaccharide of H. influenzae
Type b (10 µg) of CRM mutant C. diplutheriae toxin along with alum hydrox adjuvant.

8. Antiplaque vaccine formalized

It contains $2X10^2$ Y. pestis organisms per ml.killed by formaline in 10 ml vial.

VIRAL VACCINES

1. Poliomyelitis

The virus (type 1, 2, 3) is grown in monkey kidney cell culture and two vaccines are prepared from it.

a) Oral poliovirus vaccine (OPV; Sabin vaccine)

b) Inactivated poliomyelitis vaccine (IPV, Salk vaccine)

2. Rabies

Four rabies vaccines have been produced

a. Antirabic Vaccine Carbolized [sample vaccine]

Also called 'Neural tissue vaccine' (NTV), it is a 5% suspension of sheep brain substance containing carbolic acid fixed rabies virus.

b. Purified chick embryo cell vaccine [PCEV]

It consist of Flury – LEP strain of rabies virus grown on chick fibroblasts and inactivated by β -Propiolactone; available as 2.5 IU in 1 ml amp (RABIPUR).

c. Human diploid cell vaccine[HDCV]

It is lyophilized in activated rabies virus grown in human diploid cell culture. The vial containing 2.5 IU is freshly suspended in 1 ml of diluents.

3. Influenza virus vaccine

Contain inactivated influenza virus A and B immunization may be done annually or during an epidermis 2 injections of 0.5 1 ml. 1 - 2 months apart Influenza virus undergoes frequent antigenic changes hence the efficacy of the vaccine is inconsistent.

4. Hepatitis B Vaccine

The new hepatitis B vaccine is prepared in yeast cells by recombinant DNA technique and contains aluminum hydroxide adsorbed hepatitis B virus surface antigen 20mg in 1ml suspension. Three 1ml injections in the deltoid muscle given at 0, 1 and 5 months produce protective antibody titers in 99 % subjects.

5. Hepatitis A vaccine

It is prepared by inactivating with formaldehyde hepatitis A virus grown in human diploid cell culture. A single 0.5ml i.m. injection in deltoid muscle affords protection, but a booster dose after 6 month is recommended.

6. Mumps virus vaccine live attenuated

It is prepared from mumps virus grown in cell culture of chick embryo. A single dose of 5000 $TCID_{50}$ [tissue culture infectious dose50%] affords protection for 10 years; revaccination is not required. Clinical disease may occur if the vaccine is given after exposure to natural pumps.it is generally combined with measles and rubella vaccine [MMR], and is not recommended below 1 year of age. A mild febrile reaction occurs occasionally.

7. Measules vaccine live attenuated

This is also a vaccine grown on chick embryo; available in single dose vials containing 1000 $TCID_{50}$ of Edmonton Schwarz strain

[ROUVAX, RIMEVAX] or Edmonton Zagreb strain [M- VAC] for S.C. injection over right deltoid region. It products a modified infection- fever, rash and coryza may appear after 5-10 days; immunity lasts 8 years and no booster doses are required. It is recommended in children 9 months or older. Ordinarily, adults need not be immunized. Malnourished, chronically ill and tuberculosis children must be protected to minimize the risk of serious complications of natural's measles. Some protection is afforded even if given after exposure.

8. Rubella vaccine

[R-VAC] it contains live attenuated rubella virus wistar RA27\3 strain 1000 $TCID_{50}$ per 0.5 ml inj. for deep s.c. Or i.m. Injection in upper arm. It is used especially in girls from 1 yr age puberty- for immunization against German measules; mostly as combined NMR vaccine. It is contraindicated during pregnancy. Febrile illness and untreated tuberculosis patients. Reaction are fever, malaise, sore throat, joint pain and lymphadenopathy.

9. Measles-Mumps-Rubella [NMR] Vaccine

Two preparations of this combined live vaccine are available: have similar efficacy.

TRIMOVAX lyophilized measles 1000 $TCID_{50}$ Schwarz strain, mumps 5000 TCID50 and rubella 1000 $TCID_{50}$ per unit dose [0.5 ml] vial.

A single dose injected S.C. over right deltoid is indicated in children older than 12 months for protection against these 3 diseases. Mild fever, rash, enlargement of cervical /occipital lymph nodes and parotid glands and local induration may occur after-5 days. It is absolutely contraindicated during pregnancy; adult female vaccines should not concave for at least 2 months.

10. Varicella vaccine

It is lyophilized live attenuated OKa strain of varicella- zoster virus grown in human in human diploid cell culture. Containing 10^{33} PFU [plaque forming units] of the virus.

A single dose induces antibody response in < 98% children and affords protection for 10 years.

Dose: 0.5 ml S.C. single dose for children 1-12 years, and 2 doses 6-10 weeks apart in those > 12 years.

VARILRIX, OKAVAX 0.5 ml inj.

Contraindicated during pregnancy, in those with lymphocytopenia and 1 month of measles vaccination. Mild local reaction, popular eruption and short – lasting fever occurs in 4-5 % children.

TOXOIDS

1. Tetanus toxoid

It is formalin treated exotoxin of tetanus bacilli; indicated for routine immunization in all children and adults. Two types of preparations – fluid and adsorbed are available the adsorbed toxoid is superior – induces higher antibody titers and more prolonged immunity.

Dose: 0.5 ml, preferable route is i.m. can also be given s.c.

Tetanus Toxoid Adsorbed 0.5 ml amp. 5.0 ml vial.

2. Diphtheria toxoid adsorbed

It is modified diphtheria exotoxin adsorbed onto aluminum hydroxide. It is indicated in infants and children below 6 years of age. Older individual seldom require protection against diphtheria. For primary immunization 2-3 injections of 0.5 ml i.m. are given 4-6 weeks apart.

COMBINED ANTIGENS

1. Double antigen (DT-DA)

It consists of alum precipitated toxoids of tetanus and diphtheria available in 0.5 ml ampule and 5 ml vial.

2. Triple antigen (DPT)

It is a mixture of toxoids of tetanus and diphtheria with pertussis vaccine.

3. Pentavalent vaccine

It contains toxoids of tetanus and diphtheria along with pertussis vaccine, hepatitis B vaccine and hemophilic influenza type b (Hib) vaccine.

Age	Vaccine
2 months	BCG + DTP + OPV
3 months	DTP + OPV + hepatitis B
4 months	DTP + OPV + hepatitis B
9 months	Measles + hepatitis B
18 months	DTP + OPV (booster)
6 years	DT + OPV + measles + BCG
11 years	DT
14-16 years	TT

BCG, Bacille Calmette-Guérin; DTP, diphtheria, tetanus toxoid and pertussis; OPV, oral polio vaccine; TT, tetanus toxoid.

ANTISERA AND IMMUNE GLOBULINS

Antisera are purified and concentrated preparation of serum of horses actively immunization against a specific antigen.

Immediate type of allergic reactions (urticarial, angioedema, respiratory distress, and anaphylaxis) can occur with any antiserum; adrenaline (1:1000 amp.) should be at hand while injecting them. Prior to each administration, history of reaction to any 'serum' preparation should be elicited and an intracutaneous/scratch test should be performed.

Immune globulins (IGs) are separated human gamma globulins which carry the antibodies. These may be nonspecific (normal) or specific (hyper immune) against a particular antigen. These are more efficacious than the corresponding antisera. Serum sickness does not occur with human IGs.

1] Normal human gamma globulin

It is concentrated IG obtained by fractionation in cold from pooled human plasma. Indications for its use are – viral hepatitis A and B (prophylaxis), measles, mumps, poliomyelitis and chickenpox (prophylaxis and modification of course of illness), and has some beneficial action in burns. It is premature infants and in patients of leukemia or those undergoing immunosuppression.

Dose – 0.02 – 1 ml/kg i.m. for different indications.

GAMMALIN, GLOBUNAL, Sii GAMMA GLOBULIN, GAMAFINE 10%, 16.5% injection in 1, 2 ml amps.

An intravenous preparation (Sii i.V.GG 0.1 – 0.4 G/KG/day) has been made available for conditions requiring high doses which cannot be injected i.m.

2] Anti – D immune globulin 3] Tetanus a. Tetanus immune globulin (human)

It is indicated for prophylaxis in non –immunized persons receiving a contaminated wound who are at high risk of developing tetanus. The $t^{1/2}$ of this antitoxin is 4 weeks and significant blood levels are maintained for up to 14 weeks. It is more efficacious and longer acting than the equine antitoxin (ATS). If tetanus toxoid is given at the same time (but at different site), development of primary immune response to the toxoid is not interfered with.

Dose – Prophylactic 250 – 500 IU, therapeutic 3000 – 6000 IU i.m. and/or 250 – 500 IU intrathecal.

Sii TIG 250 IU (liquid), 500 IU (lyophilized), TETNAL 250 IU/2 inj., TETAGAM 250 IU/ml inj.

b. Tetanus antitoxin (ant tetanic serum, ATS)

It is obtained from horse; is inferior to human antitoxin and should be used for the above indications only when tetanus immunoglobulin is not available.

Dose – prophylactic 1500 – 3000 IU, i.m. or s.c; therapeutic 50000 – 100000 IU part i.v. and rest i.m.

TETANUS ANTITTOXIN 750 IU, 1500 IU, 5000 IU, 10000 IU, 20000 IU, and 50000 IU in 1 – 10 ml ampoules

TETANUS IMMUNE SERUM (enzyme refined, equine) 10000 and 20000 IU vials.

4] Rabies

a. Antirabies serum (ARS) Also called 'equine rabies immune globulin' (ERIG) is refined, concentrated and lyophilized serum from horse's hyper immunized by repeated injections of fixed rabies virus. It is indicated promptly after suspected exposure and is given simultaneously with rabies vaccine to non-immunized individuals.

Dose – 40 IU/kg infiltration round the wound and excess is injected i.m.; single dose at the initiation of anti rabic therapy along with rabies vaccine. It is inferior to HRIG and should be used only when HRIG is not available.

IMORAB 1000 IU/5 ml inj.

b. Rabies immune globulin human (HRIG)

It is used in the same manner as ARS and is superior to it with longer $t^{1/2}$. Dose – 20 IU/kg, on day 0 only, infiltrated round the bite; excess may be injected i.m. elsewhere. Passive protection with HRIG or ARS is needed because active immunity takes 2 or more weeks to develop.

BERIRAB – P 300 IU/2 ml and 750 IU/5 ml inj. RABGLOB 300 IU/2 ml inj.

5] Hepatitis B immune globulin

It is 10-18% solution of human IG containing a high titer of antibody to hepatitis B surface antigen. It is better prophylactic than normal human gamma globulin. Indicated in individuals acutely exposed to HBsAg positive blood or blood products. Hepatitis B vaccine should be given concurrently.

Dose: 100 IU [0.5ml], 200 IU [1ml] per vial for i.m. inj.

6] Diphtheria antitoxin [Antidiphtheritic serum ADS]

It is obtained from horse and is used therapeutically in clinical diphtheria without waiting for bacteriological report. Because each hour's delay increases the dose requirement and decreases beneficial effects: damage already caused by the toxin is not reversed. The antitoxin neutralizes the exotoxin released at the site of infection and that circulating in blood but not that fixed to tissues.

Dose: 20,000-10,000 IU i.m. or i.v. for pharyngeal/ laryngeal disease of upto 48 hour duration. Higher dose [upto 100,000 IU may be needed.

DIPHTHERIA ANTITOXIN 10,000 IU 10 ml amp.

7] Gas gangrene antitoxin [Anti gas gangrene serum, AGS]

It is enzymes refined equine antitoxin against Cl. Edematiens.Cl.perfringens and Cl. Septicum.

Dose: Prophylactic 10,000 IU; therapeutic 30,000-75,000 IU s.c/ i.m/i.v.

AGGS 10, OOO IU amp.

8] Antisnake venom [ASV] serum polyvalent

It is available as purified. Enzyme refined and concentrated equine globulins in lyophilized vials with 10 ml ampule of distilled water. After reconstitution, each ml neutralizes:

0.6 mg of standard cobra [Naja naja] venom.

0.6 mg of standard Russell's viper [vipera Russell] venom.

0.45 mg of standard sawscaled viper [Echis carminative] venom.

0.45 mg of standard krait [bungarus caeruleus] venom.

ANTISNAKE VENOM SERUM POLYVALENT ASVS

Dose – 20 ml i.v. (1ml/min injection) repeated at 1 – 6 hourly intervals till symptoms of envenomation disappear; upto 300 ml may be required in viper bites, while still larger amounts (upto 900 ml) have been used in cobra bites, but it is important to continue ASV treatment till evidence of envenomation persists. In case of viper bite some serum should also be infiltrated around the site to prevent venom induced gangrene.

Allergic reactions, including anaphylactic shock, to the serum are possible. When time permits, sensitivity test should be done; otherwise adrenaline may be injected S.C. concurrently. An antihistaminic and a glucocorticoid may also be given prophylactically.

Reference

1. Ko K., Tekoah Y., Rudd P.M., Harvey D.J., Dwek R.A., Spitisin S. Function and glycosylation of plant – derived antiviral monoclonal antibody. PNAS (USA) 20003; 100:8013-8018.
2. Janes Kuby, 2007, Vacines, immunology, W.H. Freeman and Company, Newyork, sixth Edition, Pg. 413-428.
3. Satynarayana U., 2010, Vaccines, Biotechnology, BOOK'S AND ALLIEDD (P) Ltd, Kolkata, sixth edition, Pg. 211-212.
4. K.D.Tripathi Essentials of Medical Pharmacology 2013 edition.
5. https://en.wikipedia.org/wiki/Vaccine
6. https://en.wikipedia.org/wiki/Antiserrum
7. www.niaid.nih.gov
8. www.pathmicro.med.in