VIVEKANANDA COLLEGE

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Vaccine and its types

I. Definition of Vaccine:

A product that stimulates a person's immune system to produce immunity to a specific disease, protecting the person from that disease is termed as **vaccines**. Vaccines are usually dispensed through needle injections, but can also be administered by mouth or sprayed into the nose.
Vaccination is a clinical application of immunization conceived to artificially help the body to defend itself.

The body's immune system helps to guard against pathogens that cause infection. Most of the time, it's an efficient system. It either keeps microorganisms at bay or traces them down and gets rid of them.
However, some pathogens can overpower the immune system. When this happens, it can cause serious illness.
The pathogens most likely to cause complications are the ones the body doesn't recognize. Vaccination is a way to "teach" the immune system how to make out and destroy an organism. That way, a person's body is prepared if he/she is ever exposed to infection.
Vaccinations are an essential form of primary prevention. That means they can shield people from getting sick. Vaccinations have allowed human to control diseases that once threatened many lives, such as:

- measles
- polio
- tetanus
- whooping cough

It's imperative that as many people as possible get vaccinated. Vaccinations don't just protect individuals. When enough people are vaccinated, it helps guard the society or a population against an epidemic.
This occurs through **herd immunity**. Widespread vaccinations make it less expected that a predisposed person will come into contact with someone who has a particular disease.
The use of vaccines dates back to 1796 when Edward Jenner revealed that milk maids who had contracted cowpox (vaccinia) were immune to smallpox. He illustrated that inoculating the vesicular fluid from cowpox lesions into the skin of susceptible individuals could shield them against smallpox infection. The term vaccination is derived from this practice. Current vaccine hostile to smallpox, uses the modified cowpox virus (i.e. vaccinia virus).

II. Types of Vaccines:

There are different types of vaccines, table below describes it's types, descriptions, advantages, disadvantages and disease against it is designed.

Table 1. Vaccine and it's types.

Type	Description	Advantages	Disadvantages	Disease	Reference
Live attenuated	Less pathogenic strain of microbe	Induction of long lived responses	Adverse effects in immune-compromised	MMR, Smallpox	World Health Organization, 2017
Inactivated	Pathogens killed through chemical treatment or heat	Cannot replicate	Often induces weaker immune responses than other methods	Cholera	Bi et al., 2017
Subunit	A vaccine designed to induce immune responses to the most dominant epitopes of a pathogen	High level of safety	Multiple doses are usually required	Hepatitis B	Van Den Ende et al., 2017
Toxoid	Induces an immune response to the pathogens toxin	Strong antibody response and long-lasting antigen specific memory	Booster doses are often required	Diphtheria	World Health Organization, 2017
Conjugate	A strong antigen (often a protein) covalently attached to a weak antigen (often a bacterial polysaccharide)	Safe for use in infants. Long lasting immune responses	Expensive to produce	Bacterial Meningitis	Wasserman et al., 2018
DNA	Fragments of DNA encoding antigens for specific pathogens are injected for endogenous production	Non-infectious, no cold chain required	Limited to protein antigen production	Experimental	Vetter et al., 2018
Recombinant	Recombinant DNA delivered through bacterial or viral vaccine vectors	Strong immune responses	Anti-vector immunity can lead to adverse effects	HPV	Sipp et al., 2018

Source: https://www.researchgate.net/figure/Vaccine-types-and-examples_tbl1_3298339

III. How vaccine works ?

Vaccines help in developing immunity by mimicking an infection. This type of infection though, almost never brings about illness, but it does cause the immune system to generate T-lymphocytes and antibodies. Sometimes, after getting a vaccinated, the mimicking infection can create minor symptoms, such as fever. Such minor symptoms are common and should be anticipated as the body builds immunity. Vaccines aid in the development of immunity by imitating an infection. Vaccines are taken up by macrophages, dendritic cells which activate the adaptive immunity. This also occurs in an original infection but vaccine mimicking an infection however, almost never triggers illness, but it does cause the immune system to generate T-lymphocytes, hence induces the **adaptive immunity**. Once the mimicking infection goes away, the body is left with a supply of "memory" T-lymphocytes, as well as B-lymphocytes that will remember how to fight that disease in the future. Still, it usually takes a few weeks for the body to produce T-lymphocytes and B-lymphocytes after vaccination. B-lymphocytes generate antibodies. Hence, both cell mediated and humoral immunity are activated Therefore, it is possible that a person infected with a disease just before or just after vaccination could develop symptoms and get a disease, because the vaccine has not enough time to provide protection. Hence, vaccination can provide immunity if it gets few weeks to trigger the adaptive immunity before any infection has occurred. Please go through Figure 1, for further details.

Source: https://www.cdc.gov/vaccines/hcp/conversations/downloads/vacsafe-understand-color-office.pdf

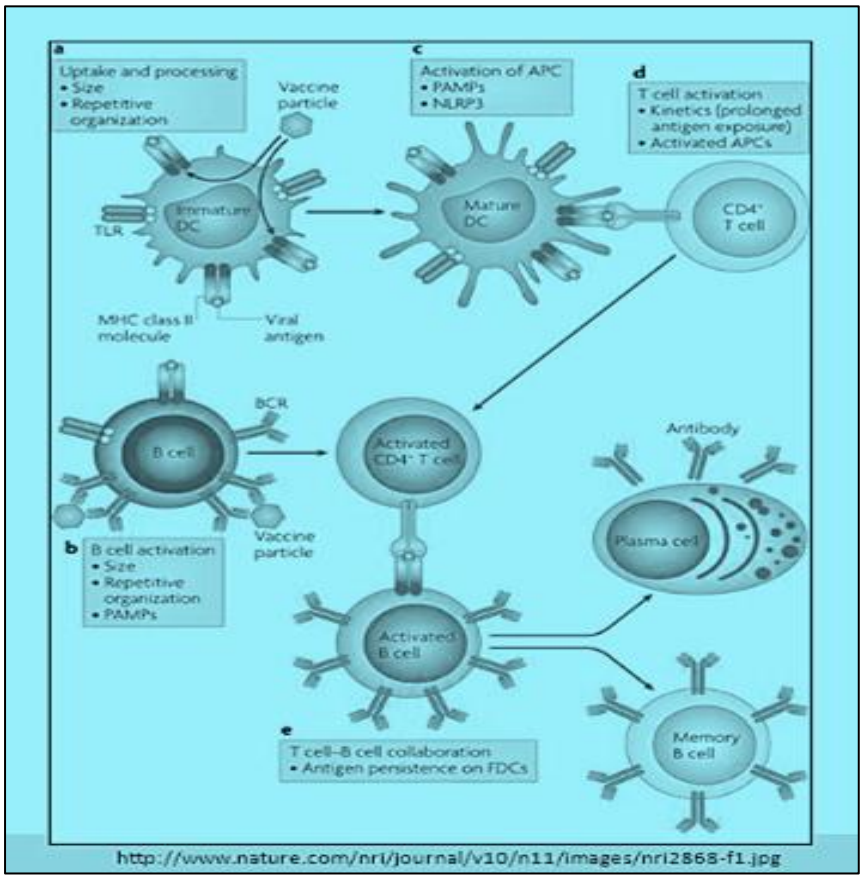


Figure 1. Mechanism of action of a typical vaccine.

IV. Active Immunity and Passive Immunity:

a. Active Immunity:

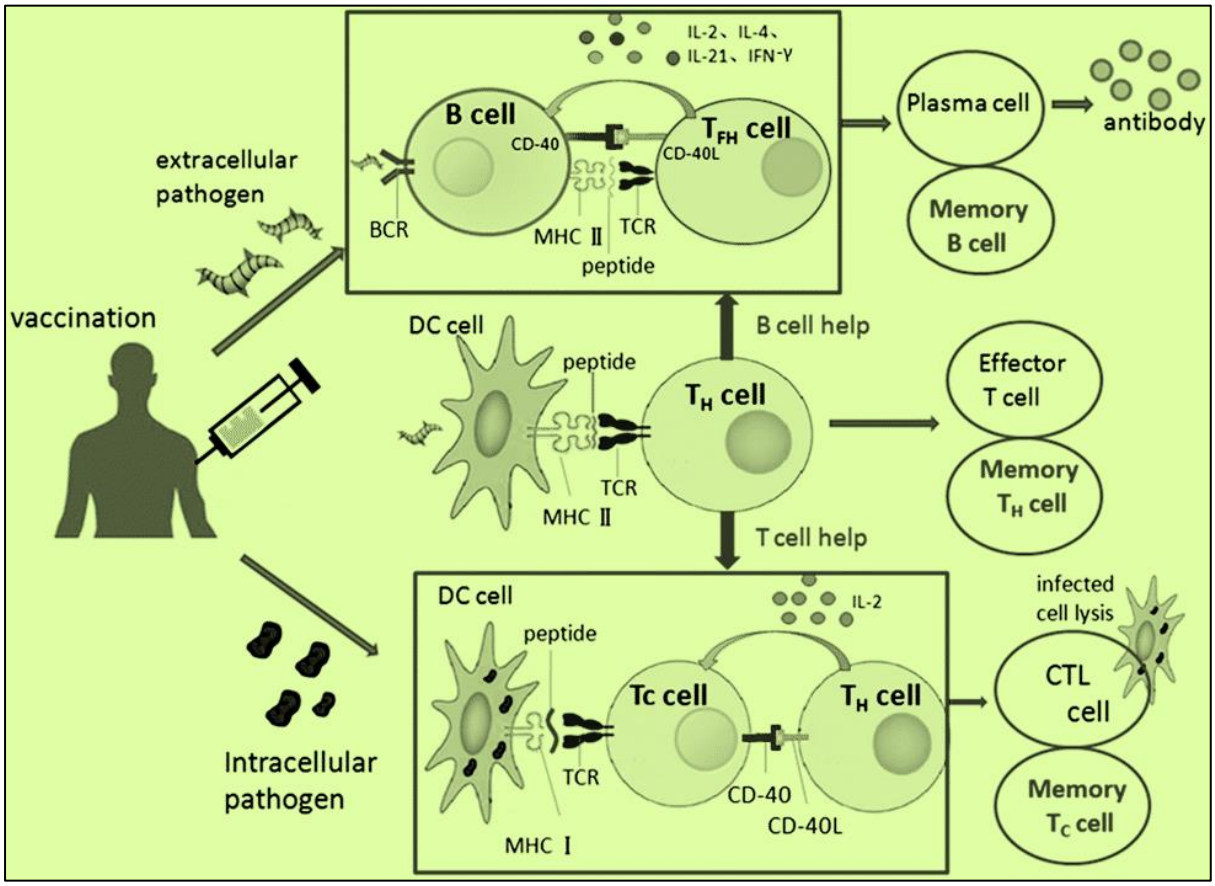
Active immunity triggers when our body is exposure to a pathogen. Surface markers on the pathogen surface perform as antigens, which bear binding sites for antibodies. Antibodies, which can exist free in blood or tissue fluid or can attach to the membrane of special cells. The body doesn't keep a store of antibodies on hand to take down an infection immediately. A process called clonal selection and expansion builds up sufficient antibody pool in the body.

Features of Active Immunity:

- Active immunity requires exposure to a pathogen or to the antigen of a pathogen or vaccine.
- Exposure to the antigen leads to the production of antibodies. These antibodies essentially mark a cell for destruction by special blood cells called lymphocytes.
- Cells involved in active immunity are T cells (cytotoxic T cells, helper T cells, memory T cells, and suppressor T cells), B cells (memory B cells and plasma cells), and antigen-presenting cells (B cells, dendritic cells, and macrophages).
- There is a lag between exposure to the antigen/vaccine and acquiring immunity. The first exposure leads to what is called a primary response. If a person is exposed to the real pathogen again later, the response is much faster and stronger. This is called a secondary response.
- Active immunity lasts a long time. It can endure for years or an entire life.
- There are few side effects of active immunity. It can be implicated in autoimmune diseases and allergies, but generally doesn't cause problems.

There are two types of active immunity, which are **naturally acquired active immunity** and **artificially acquired active immunity.**

- **Naturally acquired active immunity:**
  i. Naturally acquired active immunity occurs when the person is exposed to a live pathogen, develops the disease, and becomes immune to the disease as a result of the primary immune response. Once a microbe penetrates the body's skin, mucous membranes, or other primary defenses, it interacts with the immune system. B-cells in the body generate antibodies that aid to fight against the invading microbes.
  ii. The adaptive immune response generated against the pathogen takes days or weeks to develop but may be long-lasting, or even lifelong i.e. the effect and protection is for whole life.
  iii. Wild infection, viz., with hepatitis A virus (HAV) and ensuing recovery, gives rise to a natural active immune response typically leading to lifelong protection.
- **Artificially acquired active immunity:**
  i. Artificially acquired active immunity is protection generated by planned exposure of a person to antigens in a vaccine, aimed to produce an active and lasting immune response.
  ii. The antigens in the vaccine arouse the immune system to generate antibodies and memory cells which are explicitly directed against the antigens in the vaccine.
  iii. Subsequent to the immunization, if the living infectious agents with the matching antigens that were in the vaccine gain entry to the person's body, the precise antibodies are by now present and they bind to the infectious agents.
  iv. The memory cells generate a quick immune response from the rest of the immune system, and the infectious agents are swiftly take on and destroyed, frequently before symptoms of the disease are expressed.
  v. For example, administration of two doses of hepatitis A vaccine generates an acquired active immune response steering to long-lasting (possibly for whole life) protection.
  vi. Immunization (commonly referred to as vaccination) is the planned induction of an immune response, and characterizes the single most effectual manipulation of the immune system that scientists have developed.



Source: https://pubs.rsc.org/en/content/articlelanding/2016/bm/c5bm00507h/unauth#!divAbstract

Figure 2. Immune activation due to vaccination

b. Passive Immunity:

Passive immunity can be defined as immunity, which builds up when any person is having components of the immune system from the other person. This kind of immunity can happen naturally, for instance when a new born baby is receiving the antibodies from his or her mother by breast milk or placenta; or it could even happen artificially, such as when any specific person is receiving these antibodies within the form of an injection like gamma globulin injections.

Passive immunity doesn't need the body to make antibodies to antigens. The antibodies are brought in from outside the organism.

Features of Passive Immunity

- Passive immunity is conferred from outside the body, so it doesn't need contact to an infectious agent or its antigen.
- There is no lag in the action of passive immunity. Its response to an infectious agent is instantaneous.
- Passive immunity is not as enduring as active immunity. It is typically only effectual for a few days.
- A condition called **serum sickness** can result from exposure to antisera.

There are two types of passive immunity, which are **naturally acquired passive immunity** and **artificially acquired passive immunity**.

➢ **Naturally acquired passive immunity:**

i. The maternal passive immunity can be denoted to the kind of **naturally acquired passive immunity**, which consequently refers to an antibody-mediated immunity conveyed to the foetus by the respective mother.

ii. This type of naturally acquired passive based immunity could be appropriately produced while the mother is expecting and also by breastfeeding. For human beings, maternal antibody (MatAb) is being transferred on through placenta to infant or foetus through the receptor of FcRn over the cells of placenta. It occurs predominantly within the first three months of pregnancy.

iii. Hence, it is being often diminished in infants, who have a premature birth. IgG or immunoglobulin G is considered as the only antibody 'isotype', which could simply pass through placenta of human beings.
iv. IgG majorly secures against any type of viral or bacterial infection within the foetus.
v. Secretory immunoglobulin A (sIgA) is a special immunoglobulin. It's the main antibody found in your breast milk. IgA is considered the most important immunoglobulin in breast milk.
vi. The IgA antibodies can protect your child from a variety of illnesses including those caused by bacteria, viruses, fungi, and parasites.

- **Artificially acquired passive immunity:**

i. Artificially acquired passive immunity is referred to as a short term immunization that is being accomplished by efficacious transference of the antibodies that could be administered within some of the most typical forms such as in serum or animal blood plasma and even in the human beings as being pooled within the IG or intramuscular utilization.
ii. The reason for such distinctiveness is that the high titre of human antibodies is required for recuperating from diseases. The passive transferring could be employed for thwarting the diseases or could even be employed prophylactically for a small number of immune deficiency diseases, viz., of hypogammaglobulinemia.
iii. The artificially acquired passive immunity is even being employed during the therapy of various acute infections as well as treating effects of poison.
iv. The immunity that is being resulting from the passive immunization at most lasts for only a few weeks to almost 3 to 4 months. The human body never build up memory so the patient may again get infected in future.
v. Such passive immunization may lead to hypersensitivity reactions such as gamma reactions.

- **Agents of Passive immunization:**

1. Antitoxins: Antiserum comprising toxin, neutralizing antibodies specific for a toxin is given. (a) Diphtheria antitoxin is prepared in horse by injecting toxoid of *C. diphtheria*, used in the treatment and prophylaxis, (b) Tetanus antitoxin. One prepared in horse is not recommended. Used in prophylaxis and treatment, and (c) Botulism antitoxin is prepared in horse.
2. Immunoglobulin: Gamma-globulin is made from pooled normal adult human plasma/ serum. It contains IgM antibodies. Utilised against hepatitis A and measles.
3. Particular immunoglobulin: It is gamma-globulin acquired either from recuperating patients (people who have recently recovered from the disease), or from people who have been hyper-immunized against a specific infectious disease. Example: (i) Hepatitis B immunoglobulin, (ii) Rabies immunoglobulin, (iii) Tetanus immunoglobulin.

V. Adjuvants and types:

The quality and level of the vaccine-induced immune response or titre of antibody production will be subject to several factors including, the route of vaccination, number and timing of administrations of a vaccine (if booster is used), the nature of the antigen and also the quality of antigen presentation. This whole process is smoothed by the **adjuvants**. Undeniably, adjuvants aids in overcoming the weakly immunogenic properties of most protein, peptide and DNA vaccines (deficient of natural immune triggers) or the induction of inappropriate immune responses. Thus adjuvants can be used to

(1) Augment the immune response,

(2) Accommodate the immune response through modulation of the Th1/Th2 balance and

(3) Cut the amount of antigen needed and the number of injections required to induce protection (termed as 'antigen-dose sparing').Table below elucidates different categories of adjuvants, its description in brief and representative examples.

Table 2. Different categories of adjuvants with examples.

Adjuvant category	Representative examples	Brief description
Mineral salts	Aluminum and calcium salts	Licensed for human use Many bacterial and viral antigens have been adsorbed onto alum and Ca salts
Emulsions and surfactant-based formulations	MF59, AS02, montanide ISA-51 and ISA-720, QS21	Micro-fluidized detergent-stabilized emulsions Surfactants derived from natural sources
Particulate delivery vehicles	Microparticles, immuno-stimulatory complexes; liposomes, virosomes, virus-like particles	Antigens and adjuvants can be trapped inside or coated onto the surface of particles
Microbial deriva-tives	Monophosphoryl lipid A, CpG oligonucleotides, cholera toxin and heat labile toxin from *Escherichia coli*, lipoproteins	Bacterial products or synthetic mimics are potent stimulators of the innate immune system Most of these agents signal through TLRs
Cells and cytokines	Dendritic cells; IL-12 and GM-CSF	Cytokines stimulate cells of the immune system Autologous dendritic cells pulsed with tumor-derived pep-tides efficiently present antigenic epitopes

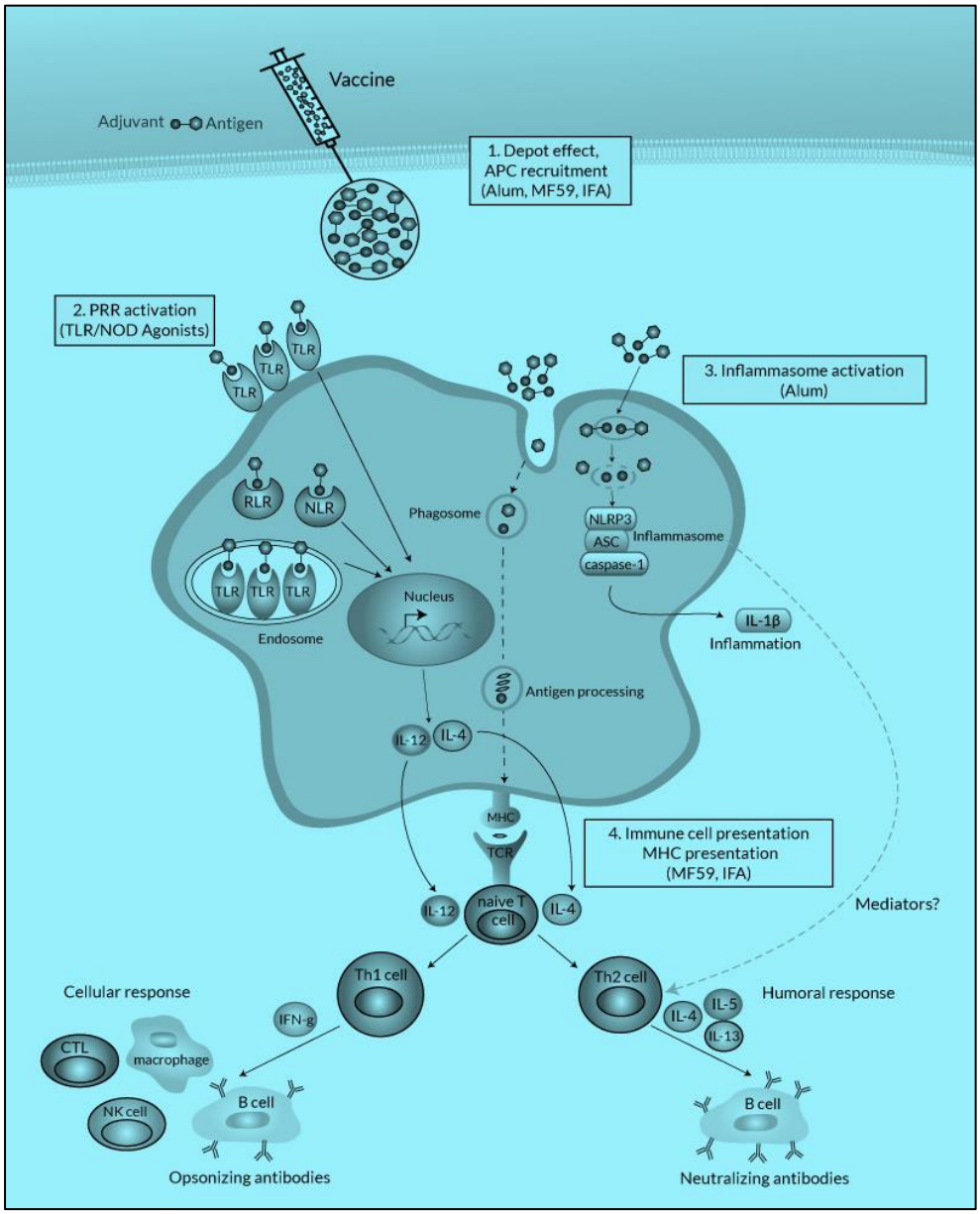
Source: https://www.researchgate.net/publication/7924908_Targeting_the_innate_immune_response_with_improved_vaccine_adjuvant

VI. Mechanism of adjuvant's action:

Adjuvants may exert their effects through diverse mechanisms. Some adjuvants, such as alum and emulsions (e.g. MF59®), work as delivery systems by creating depots that entrap antigens at the injection site, offering slow release in order to maintain the stimulation of the immune system. These adjuvants augment the antigen maintenance at the injection site and surge recruitment and activation of antigen presenting cells (APCs). Particulate adjuvants (e.g. alum) have the capacity to truss antigens to form multi-molecular aggregates which will assist uptake by APCs.

Some adjuvants are also adept of directing antigen presentation by the major histocompatibility complexes (MHC).

Other adjuvants, basically ligands for pattern recognition receptors (PRR), act by rousing the innate immunity, largely targeting the APCs and therefore inducing the adaptative immune response. Members of nearly all of the PRR families are possible targets for adjuvants. These comprise Toll-like receptors (TLRs), NOD-like receptors (NLRs), RIG-I-like receptors (RLRs) and C-type lectin receptors (CLRs). They signal through pathways that take in distinct adaptor molecules steering to the activation of different transcription factors. These transcription factors (such as NF-κB, IRF3) induce the synthesis of cytokines and chemokines that play a significant role in the priming, expansion and polarization of the immune responses. Activation of certain members of the NLR family, such as NLRP3 and NLRC4, triggers the development of a protein complex, called **inflammasome**, involved in the induction of the pro-inflammatory cytokines IL-1β and IL-18. The NLRP3 and NLRC4 inflammasomes have been concerned in the innate immunity (Figure 2) stimulated by certain adjuvants but their mechanism of action remains indeterminate.



Source: https://www.invivogen.com/review-vaccine-adjuvants

Figure 3. Mechanism of adjuvant action.

VII. Benefits of Immunizations

Immunizations tender a number of benefits,that includes the following:

i. Cost-effective – Preventing diseases is much less costly than treating them; immunizations save money by checking diseases.
ii. Safe – Immunizations are designed to safeguard children, and receive all-encompassing testing and monitoring to make sure they are safe for humans.
iii. Effective – Most vaccinations are 90 to 95% efficacious at preventing the diseases they target.
iv. Protect those around you – Not one and all are able to get immunized. By making sure one and his/her children are vaccinated, one can help stop the spread of diseases and protect those who can't get immunized.
v. Simple and mostly painless – Immunizations are generally fast and easy to administer, and usually leave the patient with little or no pain from the injection.
vi. Protection for travel – Traveling can put any body at risk for diseases that are uncommon in their own country. Immunizations help protects one from diseases that one may encounter in other countries.

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