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A SHORT REVIEW ON VACCINE

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ABSTRACT

Due to the current situation, the world vaccine is falling on everyone's ears. So today we will look at what exactly in this vaccine? And how it is made? History of the vaccine, How the vaccine works? Vaccine components, stages of vaccine research, types of vaccine, side effects of vaccines, need of vaccine, Difference between vaccine and medicine etc. In Mythology, gods were cursed by sages, sometimes humans were cursed by gods, sometimes Gandharvas and Apsaras were cursed and then cursed. Let those cursed people be freed because of those curses. Mankind todays is cursed with the corona virus. But the curse on that curse is that the vaccine has not been received yet. Just as in the Mahabharat, Ashwatthama, in spite of being immortal, goes around asking for oil to heal his head, so today all human beings, including doctors, government, researches are looking for the curse on the corona crisis. Any vaccine is a strange chemical. It contains the germs of disease, i.e., bacteria or viruses in one of three ways. Theses bacteria or viruses are either dead, alive or half-dead, or they may be in living form with toxic properties. When such a chemical is injected, the person's body develop immunity to the virus or bacteria and, alternatively, to fight the disease. If the vaccines enter the body, it is like a colorful rehearsal of the disease. Vaccine do not cause disease because they do not have strong germs, but the body experiences fighting those germs. Vaccines are used in three ways to boost immunity. Injections, in the form of drops into the mouth or nasal discharge. Vaccinating someone in this way is called Vaccination. Vaccination reduces the severity of the disease or prevent some diseases.

KEYWORDS: Vaccine, History of vaccine, Need of vaccine, Vaccine effect, & work & content, side effects of vaccine and their cure, Importance of vaccine.

INTRODUCTION

A Vaccine is an antigenic substance the develops immunity against a disease which can be delivered through needle injections or by mouth or by aerosol.

Vaccine	Drug
1)A vaccine is like information / or a drill for the immune system so that it knows whom to attack & How to do it better therefore preventing the potential infection. 2) Vaccine is injected in the body Via antigen. Body built antibodies & Memory cell. & body is now immune.	1) An Drug /Antibiotics is like a weapon used to destroy the enemy, it's not prevention. 2) Drug/Antibiotics have absolutely nothing to do with the immune system. They will simply exercise an action on the bacteria & will cause its death or will stop its.

Vaccine is substance that is introduced into the body to prevent infection or to control disease due to a certain pathogen (a disease-causing organism, such as a virus, bacteria or parasite). The vaccine "teaches" the body how to defend itself against the pathogen by creating an immune response.[1]

1) Unlike traditional pharmaceuticals, vaccines are biological since they are made from living organisms (biological sources).
2) Specifically, vaccines are preparation of components derived from (or related to) a pathogen; they can typically induce a protective effect through one to three very small doses, in the range of micrograms to milligrams.
3) Immunity lasts for an extended period, from one year up to lifetime protection, including prevention of disease and / or related sequalae.

Germs are all around us, both in our environment & in our bodies. When a person is susceptible & they encounter a harmful organism, it can lead to diseases & death. The body has many ways of defending itself against pathogens (disease-causing organism), Skin, Mucus, & cilia (microscopic hairs that move debris away from the lungs) all work as physical barriers to prevent pathogens from entering the body in the first plane.

When a pathogen does infect the body, our body's defenses, called the immune system, are triggered & the pathogen is attacked & destroyed or overcome.[2]

The Body's Natural Response

A pathogen is a bacterium, virus, parasite or fungus that can cause disease within the body. Each pathogen is made up of several subparts, usually unique to that specific pathogen & the disease is causes. The subpart of a pathogen that causes the formation of antibodies is called

ANTIGEN.

The antibodies produced in response to the pathogen's antigen are an important part of immune system. You can consider antibodies as the sliders in your body's defense system.[2]

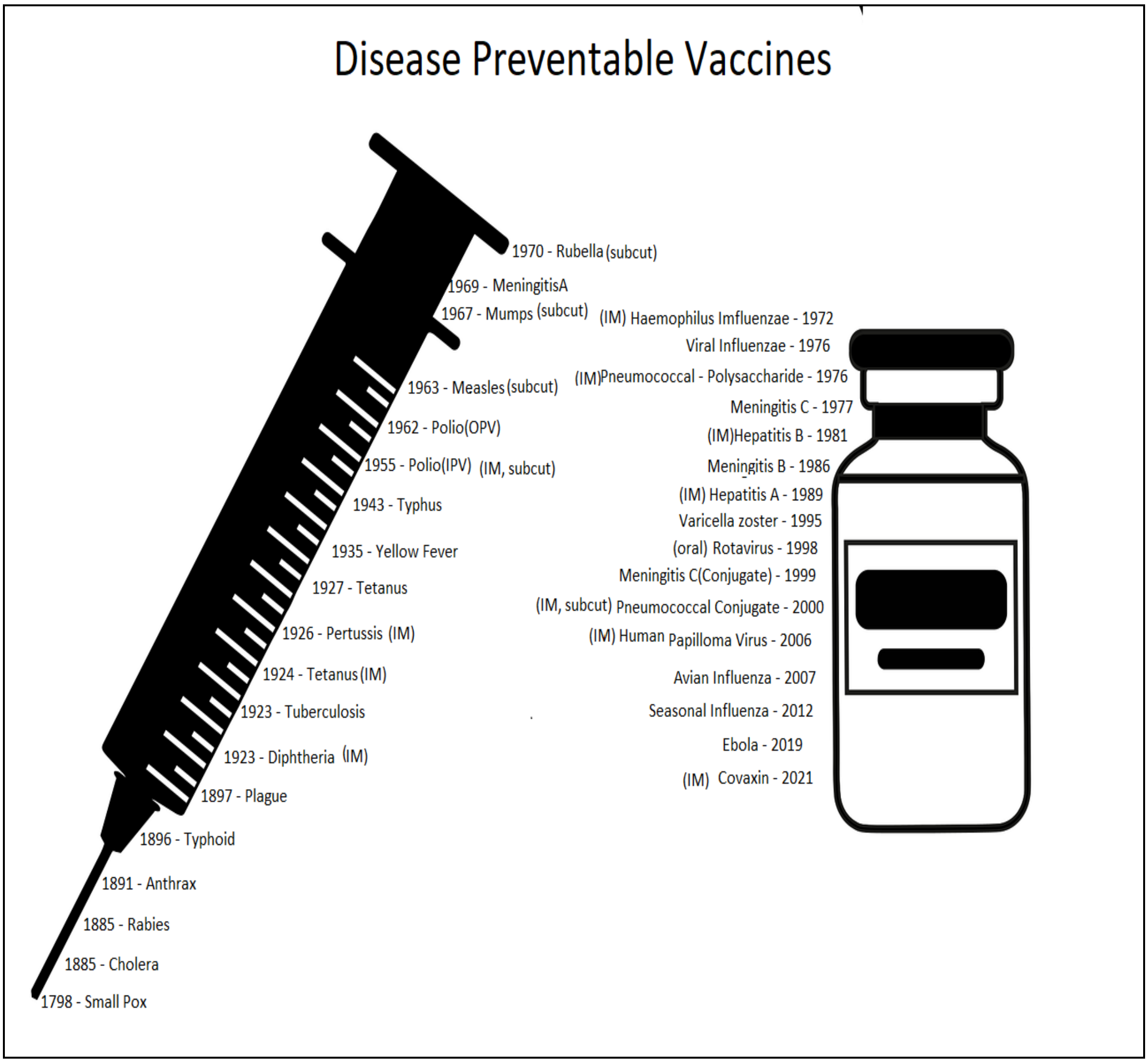
History[15]

Towards the end of the eighteenth century, Edward Jenner, an English physician, decided to investigate the existence of an urban legend. In those days, cow dung was a disease of wounds. It was called 'Cow Pox' or 'Vaccinia'.

People who milked cows also got this disease. But he was healed only by a few wounds on his hands. However, for those who want to have such 'cow pox' on their hands, the disease of the goddess that occurs at the same time does not mean 'small pox'. At that time, many people were suffering from the disease of the goddess. However, these people who get cow pox are completely immune from it.

With this in mind, Edward Jenner conducted an experiment. The experiment was such that neither the FDA in the US nor the ICMR in India would recognize it today. Jenner injected an eight-year-old boy named James Phipps with a solution from a cow's pox cow's ulcer. A month and a half after he fell ill, the boy was given an injection containing the germ of the goddess and a surprise. The boy did not get sick of the goddess. Jenner then tried the experiment on 22 others. They also did not become goddesses. Later, in 1798, Jenner presented his dissertation, Variety Vaccine: Causes and Consequences. Since cow pox was called 'vaccinia', the term 'vaccine' became popular. A doctor who opened the doors of the mind and intellect gave the medical world a unique cure for the vaccine, and the vaccination that came from it further freed mankind from the disease of the goddess forever.[15]

Following Image Shows All Vaccines Invented In India



Vaccine Effect and Work[4,10]

Most of the current vaccines are delivered through intramuscular or subcutaneous injection. Vaccine responses depend on their interaction with immune system.

Five Steps Are Involved

1) Initial events at the site of injection & the draining lymph nodes. (dLNs).
2) Recognition of antigenic specificities at B-& T-CELL level.[11]
3) Cell proliferation, maturation & differentiation.
4) Effector stage with production of antibodies & effector T cells.[11]
5) Building up of immunological memory that allows later responses at the time of exposure to the specific pathogen.

1) When one injects a classical subunit vaccine (e.g., influenza or tetanus toxoid)

intramuscularly, the first reaction is local pain, followed by varying levels of swelling & redness. This reaction reflects an inflammation at the injection site, characterized by increased vascular permeability & local recruitment of inflammatory cells from circulating blood.

2) Vaccine antigen recognition- First vaccine antigens migrate from the injection site to the dLNs through afferent lymphatic channels.

3) GERMINAL ENTER REACTION - The second step of the immune response is essential. It is the GC reaction. Activated antigen T cells (Tfh) are attracted by antigen -bearing follicular dendritic cells (FDCs) & form specialized units, GCs, within lymphoid follicles.

A GC can be considered as a B- cell factory. It is providing an optimal environment where within a few days B -cell clones actively proliferate. Finally, they mature either into antibody producing plasma cells or into memory B cells. Plasma cells become detectable in blood after 10 to 14 days, reaching their peak at 4 weeks after immunization. Most plasma cells die after a few weeks. However, some home to "survival niche "in the bone marrow where they are rescued from apoptosis, become long- lived plasma cells, and are responsible for the prolonged persistence of antibody production. The duration of the antibody response is largely dependent on the number of long -lived plasma cells that have been induced. For example- The persistence of HBsAg vaccine antibodies may be predicted on the basis of initial antibody titers.[5]

BUILDING B-CELL MEMORY-Sustaining protection using a protein vaccine is usually dependent on the administration of a booster dose of the same vaccine several months or years after the priming series. Following a booster dose, antibody levels rise rapidly with a peak around day 7. Antibody titers are higher than after the priming dose and the equality of these antibodies. for example -neutralizing capacity is also better than in the initial stages.[7]

RRSPONSE TO POLYSACCHARIDE VACCINES- Antibody responses to polysaccharides are independent from T -cell help and do not involve a GC reaction. polysaccharides are presented to the immune system during bacterial infections or after vaccination. for example, pneumococcal polysaccharide vaccines.[9,8]

VACCINE – INDUCED T-CELL RESPONCES-- All protein vaccines induce T- cell responses. They are essential to support the induction of antibodies (helper effects). They also participate in effector mechanisms that contribute to reducing the microbial load and clearing pathogens in infections by viruses and intracellular pathogens and they play a major role in controlling immune responses and limiting the risk of concomitant autoimmune manifestation.[6,11]

Innate Immunitybt-Cell Differentiation

Vaccine Induced T-Cell Memory – T-cell memory is a critical component of immune responses to intracellular pathogens. Following the antigen -driven expansion and the death of effector cells after antigen clearance some of the remaining T cells differentiate into memory T cells of two different types.[17,13,14]

1) Central memory T-cell

2) E-ffector memory T-cell[17]

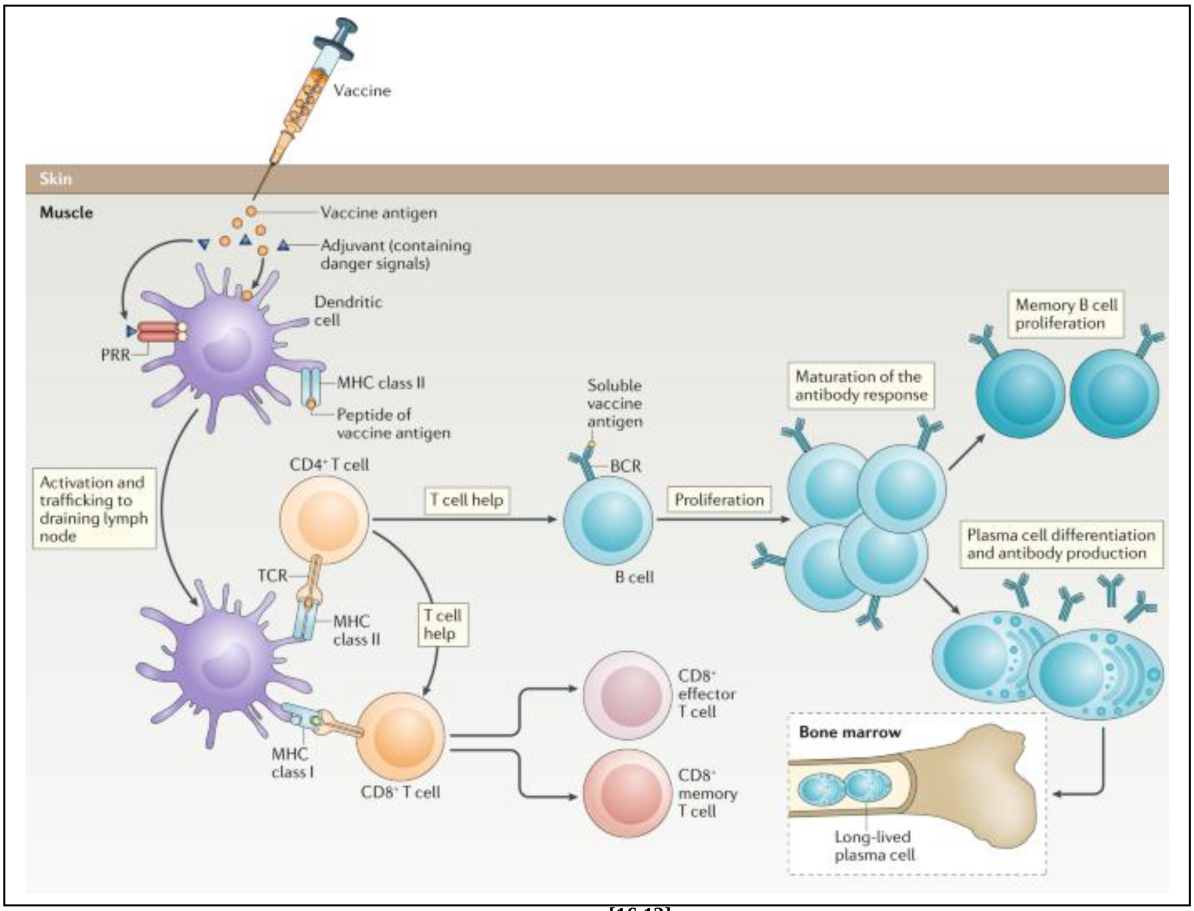


Fig. 3.[16,12]

Vaccine Types and Immune Responces[16]

Vaccine Types	Defination	Immune Responses	Examples
Killed, Inactivated	Pathogen is killed, usually through a chemical process such as formalin.	Evokes a robust immune response that mimics most of the responses seen during an infection.	Typhoid vaccine Salk polio vaccine Hepatitis vaccine
Live, attenuated	Pathogen is weakended by genetic manipulatons such that growth in the host is limited and does not cause diseases; other version of live vaccine is using an organism that is related to the pathogen, but grows poorly, naturally, in humans.	Evokes a broad immune response similar to that seen by the host infected with a natural pathogen.	Oral Sabin polio vaccine. Nasal influenza vaccine. Bacilli Calmette-Guerin (BCG) vaccine. Varicella vaccine Rotavirus vaccine.
Subunit ’acellular.	Well defined parts(s) of the organism is purified and used as an antigen (e.g. protein, peptides, polysaccharide, inactivated toxins)	A fragment of the “whole agent “vaccine can create an immune response.	Acellular pertussis vaccine.
Conjugate	Poorer antigen (such as bacterial polysaccharides) are chemically linked to a carrier protein.	Addition of other protein (via conjugation) confers the immunological attributes of the carrier to the antigen, and thus evokes a stronger immune response; effective approach for younger children.	Haemophilus influenza type b (Hib) conjugate vaccine. Pneumococcal conjugate vaccine. Meningococcal C conjugate vaccine. Meningococcal (A,C,Y,W-135) conjugate vaccine.
DNA/RNA	Genetic material from the pathogen enter into human cells and use the cell’s “equipment” to produce some proteins (s) of the pathogen encoded by the gens(s)	Immune system detects protein as a foreign or harmful antigen, produces an immune response against whole pathogen.	AIDS (in development)
Recombinant	Defined genes are incorporated into plasmid vehicle to allow for the production of large quantities of well-defined protiens, which are then used as a vaccine.	Immune response can be modified and targeted by insertion of specific genetic sequences.	Hepatitis B vaccine Human papillomavirus (HPV) vaccine AIDS vaccine (in development)

Side Effects of Vaccine[18] Most vaccine can cause mild side effect. These should be explained to you by your immunization provider. Side Effects after vaccination are usually mild and short lasting and do not need special treatment.

Common reactions: (Side effects)[18]

1) Local reaction (redness and/ or swelling around injection site) what can I do to:

- Place a cold damp cloth (cold compress over the affected area to give relief)
- Paracetamol (not Aspirin) may be used to ease the discomfort.

2) Vomiting and diarrhoea

What can I do

- Continue to breastfeed, giving small frequent feeds.
- Wash hands thoroughly after changing soiled nappies to prevent any spread.

3) A small lump may appear at the injection site.

What can I do

- No treatment is usually required and it will disappear in a few weeks.

4) Fainting (un common, however this may sometimes occur)

What can I do

- Anyone experiencing light- headedness before or after vaccination is advised to lie down until symptoms subside.

5) Mild temperature or fever

What can I do

- Monitor the temperature regularly (a fever is above 38.5) C). Paracetamol (not Aspirin) may be used to help reduce the temperature.
- Extra Fluids are recommended (for example, water, milk)
- Keep cool by not over dressing
- Sponge down with lukewarm water.
- Cold baths or showers are not recommended.

6) irritability decreased appetite, sleepiness

What can I do

- These symptoms are common in children and usually disappear over 24 to 48 hours .it does not usually require any specific treatment.[18]

Some Rere and Serious Side Effects Include The Following

- Thrombosis with thrombocytopenia syndrome- There has been a link between the AstraZeneca covid-19 vaccine and a very rare condition called thrombosis with thrombocytopenia syndrome (TTS) which appears to be more common in younger adults.
- Seizure (also known as convulsion or fit)- some children are more to seizures when experiencing a high fever. The seizure usually lasts approximately 20 seconds and very rarely more than 2 minutes. If you or your child sees a doctor if they have a seizure. There is usually no long-term damage from seizure in young children, but they should be checked by your doctor.
- Intussusception (relates to rotavirus)- this is an uncommon form of bowel obstruction where one segment of the Bowel slides into the next, much like the pieces of a Telescope. There is a very small risk of this occurring in a baby in the first 1 to 7 days after receiving the first dose of rotavirus vaccine, and a smaller risk after the after receiving the first dose of rotavirus vaccine at a smaller risk after the secondary dose of rotavirus vaccine. The baby may have bouts of crying, look pale, get very irritable and pull his or her legs up to the abdomen (stomach) because of pain.
- Anaphylaxis-a severe allergic reaction which occurs suddenly, usually within 15 minutes of vaccination; however, anaphylaxis can occur within hours of vaccine administration. Early signs of anaphylaxis include redness and /or itching of the skin swelling (hives), breathing difficulties a sense of distress. Hence, it is important for you to wait at the place you have received your vaccination so that you can be observed for any reaction.

Components of Vaccine- Vaccines include a variety of ingredients including antigens, stabilizers, adjuvants, antibiotics, and preservatives. They may also contain residual by-products from the production process. Knowing precisely what is in each vaccine can be helpful when investigating adverse events following immunization (AEFIs) and for choosing alternative products for those who have allergies or have had an adverse event known or suspected to be related to a vaccine component.[19,20]

Antigen- Antigens are the components derived from the structure of disease-causing organisms, which are recognized as 'foreign' by the immune system and trigger a protective immune response to the vaccine.[19]

Stabilizer- Stabilizers are used to help the vaccine maintain its effectiveness during storage. Vaccine stability is essential, particularly where the cold chain is unreliable. Instability can cause loss of antigenicity and decreased infectivity of LAV. Factors affecting stability are temperature and acidity or alkalinity of the vaccine (pH). Bacterial vaccines can become unstable due to hydrolysis and aggregation of protein and carbohydrate molecules. Stabilizing agents include MgCl2 (for OPV), MgSO4 (for measles), lactose-sorbitol and sorbitol-gelatine.[19]

Adjuvants- Adjuvants are added to vaccines to stimulate the production of antibodies against the vaccine to make it more effective. Adjuvants have been used for decades to improve the immune response to vaccine antigens, most often in inactivated (killed) vaccines. In conventional vaccines, adding adjuvants into vaccine formulations is aimed at enhancing, accelerating and prolonging the specific immune response to vaccine antigens. Newly developed purified subunit or synthetic vaccines using biosynthetic, recombinant, and other modern technology are poor vaccine antigens and require adjuvants to provoke the desired immune response. [3]Chemically, adjuvants are a highly heterogeneous group of compounds with only one thing in common: their ability to enhance the immune response. They are highly variable in terms of how they affect the immune system and how serious their adverse reactions are, due to the resulting hyperactivation of the immune system Today there are several hundred different types of adjuvants that are being used or studied in vaccine technology.[19,3]

Antibiotiscs- Antibiotics (in trace amounts) are used during the manufacturing phase to prevent bacterial contamination of the tissue culture cells in which the viruses are grown. Usually only trace amounts appear in vaccines, for example, MMR vaccine and IPV each contain less than 25 micrograms of neomycin per dose (less than 0.000025 g). Persons who are known to be allergic to neomycin should be closely observed after vaccination so that any allergic reaction can treated at once.[19]

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Preservatives- Preservatives are added to multidose vaccines to prevent bacterial and fungal growth. They include a variety of substances, for example Thiomersal, Formaldehyde, or Phenol derivatives.[20]

Thiomersal- Very commonly used preservative. Thiomersal is an ethyl mercury-containing compound,[20]

- It has been in use since the 1930ies and no harmful effects have been reported for doses used in vaccination except for minor reactions (e.g., redness, swelling at injection site),
- It is used in multidose vials and for single dose vials in many countries as it helps reduce storage requirements/costs,
- Thiomersal has been subjected to intense scrutiny, as it contains ethyl mercury. The Global Advisory Committee on Vaccine Safety continuously review the safety aspects of Thiomersal. So far, there is no evidence of toxicity when exposed to Thiomersal in vaccines. Even trace amounts of thiomersal seem to have no impact on the neurological development of infants.[19,20]

Formaldehyde- Used to inactivate (e.g.IPV) and to detoxify bacterial toxins, such as the toxins used to make diphtheria and tetanus vaccines. During production, a purification process removes almost all formaldehyde in vaccines. The amount of formaldehyde in vaccines is several hundred times lower than the amount known to do harm to humans, even infants. E.g., DTP-HepB+Hib*5-in-1*vaccine contains less than 0.02% formaldehyde per dose, or less than 200 parts per million.[20]

Need of Vaccine[21]

1. Vaccine-preventable diseases have the viruses and bacteria that cause illness and death still exist and can be passed on to those who are not protected by vaccines. While many diseases are not common in the US, global travel makes it easy for diseases to spread.

2.Vaccines will help keep you healthy The Centers for Disease Control and Prevention (CDC) recommends vaccinations throughout your life to protect against many infections. When you skip vaccines, you leave yourself vulnerable to illnesses such as shingles, pneumococcal disease, flu, and HPV and hepatitis B, both leading causes of cancer.

3. Vaccines are as important to your overall health as diet and exercise Like eating healthy foods, exercising, and getting regular check-ups, vaccines play a vital role in keeping you healthy. Vaccines are one of the most convenient and safest preventive care measures available.

4. Vaccination can mean the difference between life and death Vaccine-preventable infections can be deadly. Every year in the US, prior to the COVID-19 pandemic, approximately 50,000 adults died from vaccine-preventable diseases.
5. Vaccines are safe The US has a robust approval process to ensure that all licensed vaccines are safe. Potential side effects associated with vaccines are uncommon and much less severe than the diseases they prevent.
6. Vaccines will not cause the diseases they are designed to prevent Vaccines contain either killed or weakened viruses, making it impossible to get the disease from the vaccine.
7. Young and healthy people can get very sick, too Infants and older adults are at increased risk for serious infections and complications, but vaccine-preventable diseases can strike anyone. If you are young and healthy, getting vaccinated can help you stay that way.
8. Vaccine-preventable diseases are expensive Diseases not only have a direct impact on individuals and their families, but also carry a high price tag for society as a whole, exceeding $10 billion per year. An average flu illness can last up to 15 days, typically with five or six missed work or school days. Adults who get hepatitis A lose an average of one month of work.
9. When you get sick, your children, grandchildren, and parents may be at risk, too Adults are the most common source of pertussis (whooping cough) infection in infants which can be deadly for babies. When you get vaccinated, you are protecting yourself and your family as well as those in your community who may not be able to be vaccinated.
10. Your family and co-workers need you In the US each year, millions of adults get sick from vaccine-preventable diseases, causing them to miss work and leaving them unable to care for those who depend on them, including their children and/or aging parents.[21]

Storing of Vaccine

- Place a thermometer in the vaccine fridge and check and record temperature on a regular basis.
- Check expiration dates on vaccine and discard expired products.
- Store vaccine closest to expiration date in the front so it gets used first.
- Don't overstock vaccine because it was a “good deal”

The vast majority of vaccines should be stored at between 2-8^{0}C in a refrigerator, with a preferred average of 5^{0}C, though some should remain frozen in a range between -15 to -50^{0}C.

Additionally, many should be protected from light and are packaged appropriately, as UV-light can damage them.

Sufficient space is to be provided within the fridge for vaccines to allow for air to circulate freely. The fridge should be no more than 50% full. Vaccines should be stored on the shelves but not in the compartments on the door or on the floor of the main unit.

Vaccine refrigerators are designed to store vaccines and other medical products at a stable temperature to ensure they do not degrade. In developing countries with a sunny climate, solar-powered vaccine refrigerators are common.[20,21]

Vaccine A Complex Manufacturing Process[21]

1) Bacterial virus or cell culture-The antigen are developed using raw material.
2) Harvesting-The antigens produced from microorganisms are extracted.
3) Purification-Impurities are removed and concentrated through physical and chemical processes.
4) Inactivation- Pathogenicity is suppressed while retaining immunological properties.
5) Valence assembly- The active antigenic substances are combined in a single Component.
6) Formulation-All the ingredients are melt together.
7) Filling-The vaccine is filled into a vial or a syringe
8) Freeze drying- These steps make it possible to remove the water in a product by transforming it into powder, which ensures a better stability and there for a better conservation
9) Packaging- The vaccine is a labelled in accordance with regulatory requirements and packed ready for shipping
10) Batch release- Quality assurance confirms the product has been manufactured and tested in accordance with the correct procedures. The national regulatory authority gives the final authorization to release the product for distribution.
11) Transport- Our vaccines are distributed all around the world. Respecting the cold chain and a temperature between 2 and 8 degree Celsius.

Vaccine administration routes include[22]

- Oral route: administered by mouth.
- Subcutaneous route: injected into the area just beneath the skin into the fatty, connective tissue.

- Intramuscular route: injected into muscle tissue.
- Intradermal route: injected into layers of the skin.
- Intranasal route: administered into the nose.

For both children and adults, the best position and type of comforting technique should be determined by considering the patient's age, activity level, safety, comfort, and administration route and site. Parents play an important role when infants and children receive vaccine.

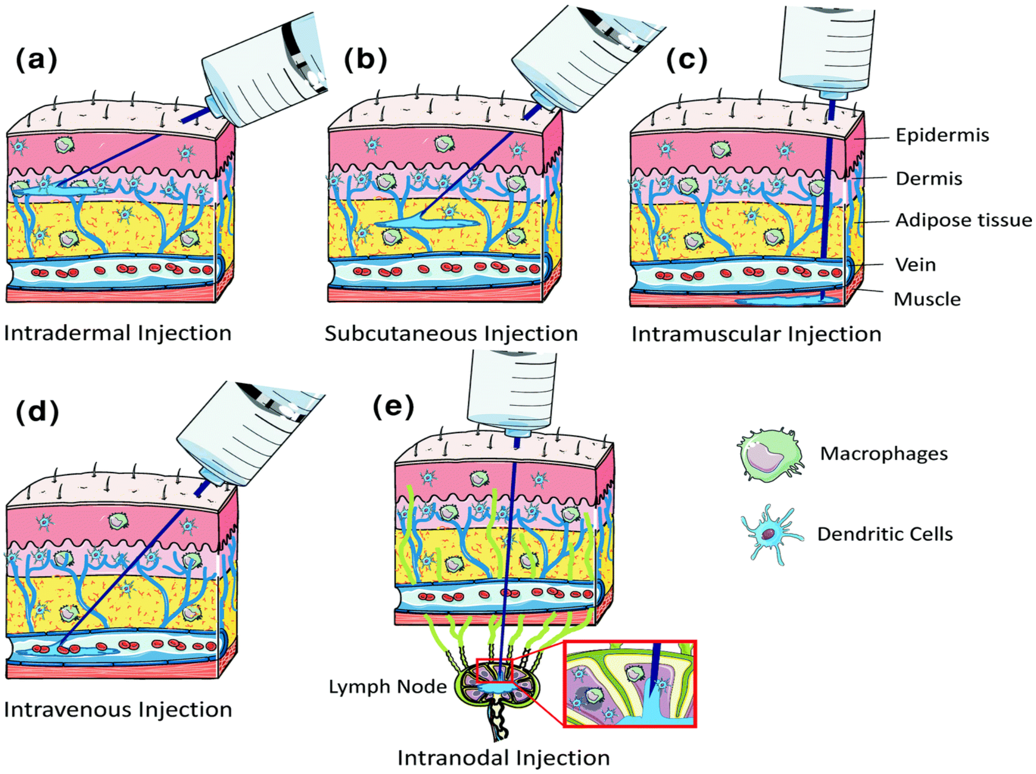

Fig 5[22]

CLINICAL TRIALS AND ASSESSMENT OF VACCINE[23]

Clinical trial phase1

- Activity – Test the safety and immunogenicity of a vaccine candidate in a few low-risk individuals (usually healthy adults) to determine tolerability.
- Sample (estimates)-10-100
- Detection of adverse events - Common = + /-, Rare = -

Clinical trial phase2

- Activity- Monitor safety, potential side effects, immune response, and determine optimum dosage and schedule.

- Sample size (estimates)- 100-1,000
- Detection of adverse events – Common = +, Rare = -

Clinical trial phase3

- Activity- Address clinical efficacy in disease prevention and provide further safety information from more more heterogeneous populations and longer times of observation.
- Sample size (estimates) – 1,000-10,000
- Detection of adverse events- Common- +, Rare- -

Submission- The vaccine application is submitted to regulatory authorities for approval to market.

CONCLUSION

Finally, we must not forget that the 21st century must deal with 3 major social issues in vaccinology: safety and the rise of antivaccinationism, cost for developing countries, and adequacy of supply. These issues could be the subject of a separate article. Although solutions have been proposed, considerable wisdom will have to be exercised to put those solutions into place. Despite these many problems, vaccinology continues to advance through its peculiar combination of fundamental research and empiricism. As W. H. Auden remarked in a wider context, “We may not know very much, but we do know something.” Vaccination has come a long way since Jenner, and we can be confident that vaccinologists will continue to extract beautiful melodies from the orchestra of the immune system.

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