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A REVIEW ON VACCINES AGAINST VARIOUS DISEASES

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ABSTRACT

Vaccines are being used widely against various diseases as it helps in reduction of diseases and death rate. In this article, we have discussed how vaccines generally build our immunity to fight against that specific pathogen and reboot on successive exposure of the same. There are various types of vaccines available and many others are in the trial stage undergoing strict testing. Some commercially available vaccines are live attenuated, killed inactivated, toxoid and subunit type of vaccines. Non-live vaccines contain whole viruses or bacteria which are inactivated and live vaccines contain weakened pathogens, it's a distinctive feature of these two main types of vaccine. Sometimes only a specific part of the virus has been used for vaccine development, like vector vaccines or subunit vaccines. This review is composed of most types of vaccines, explaining their action, being used for which disease, its advantages and disadvantages. To date, various edible vaccines are also in progress but due to various limitations, they are under clinical trials and research to make them effective. These edible vaccines are based on plants, algae, insect cells, lactic acid, whole-cell yeast, etc. as covered in this article. We have provided a short review on vaccines available for various diseases like MMR, DTP, Polio, Cancer, Hepatitis B, TB and included some of the vaccines available for the prevention of the COVID-19.

KEYWORDS: Vaccine, Attenuated, Toxoid, Viral, Vaccination.

INTRODUCTION TO THE VACCINE

Vaccines are among the greatest public health successes of the last century and were estimated to save 2-3 million lives each year. Vaccines have successfully lowered the

increase of diseases and lightened the death rate related to infectious agents such as diphtheria, tetanus, polio, measles, mumps, rubella and hepatitis B. Despite the many successes attained by vaccines, novel technologies and administration routes remain one of the principals focused in the vaccinology field. Although many licensed vaccines are given by injection, in certain cases, this administration route suffers from restrictions.[1,2]

The General Action of Vaccines - Vaccines, like natural infections, act by introducing an innate immune response, which in turn triggers an antigen-specific adaptive immune response. Innate immunity is the first line of defence in contradiction of pathogens that have entered the body. It is recognized within a few hours but is not detailed for a specific pathogen and has no memory. Adaptive immunity provides a second line of defence, generally at an advanced stage of infection, categorized by an extraordinarily diverse set of lymphocytes and antibodies able to identify and eliminate almost all known pathogens. Each vaccine expresses antigens that induce cell-mediated immunity by actuating highly specific subdivisions of T lymphocytes and humoral immunity by motivating B lymphocytes to produce specific antibodies. After the elimination of the pathogen, the adaptive immune system generally produces immunological memory. This immunological memory is characterized by the determination of antibodies and the generation of memory cells that can rapidly reboot upon successive exposure to the same pathogen.

Vaccines have substantially lowered the burden of infectious diseases. In specific, the eradication of smallpox through vaccination in 1980 is one of the crown achievements of medicine. Vaccines prevent diseases affected by a large number of viruses and bacteria, and those against parasites are under development. When live-attenuated vaccines were used, they alone were enough to induce robust long-lasting immunity. Licensed vaccines are now available to prevent over 30 different infectious diseases, various of which can be combined into single vaccines or administered at a single vaccination visit.[3,4]

Administration routes for vaccine

- Oral route: administered by mouth
- Subcutaneous route: injected into the area just under 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

Various Types of Vaccine

Different commercially available vaccines can be classified into one of four types depending on the nature of the vaccine antigens and other various types of vaccine which are under the preclinical or clinical trial of development. Some types are illustrated in Figure 1.

Live attenuated

1. Killed inactivated
2. Toxoid
3. Subunit
4. Other types

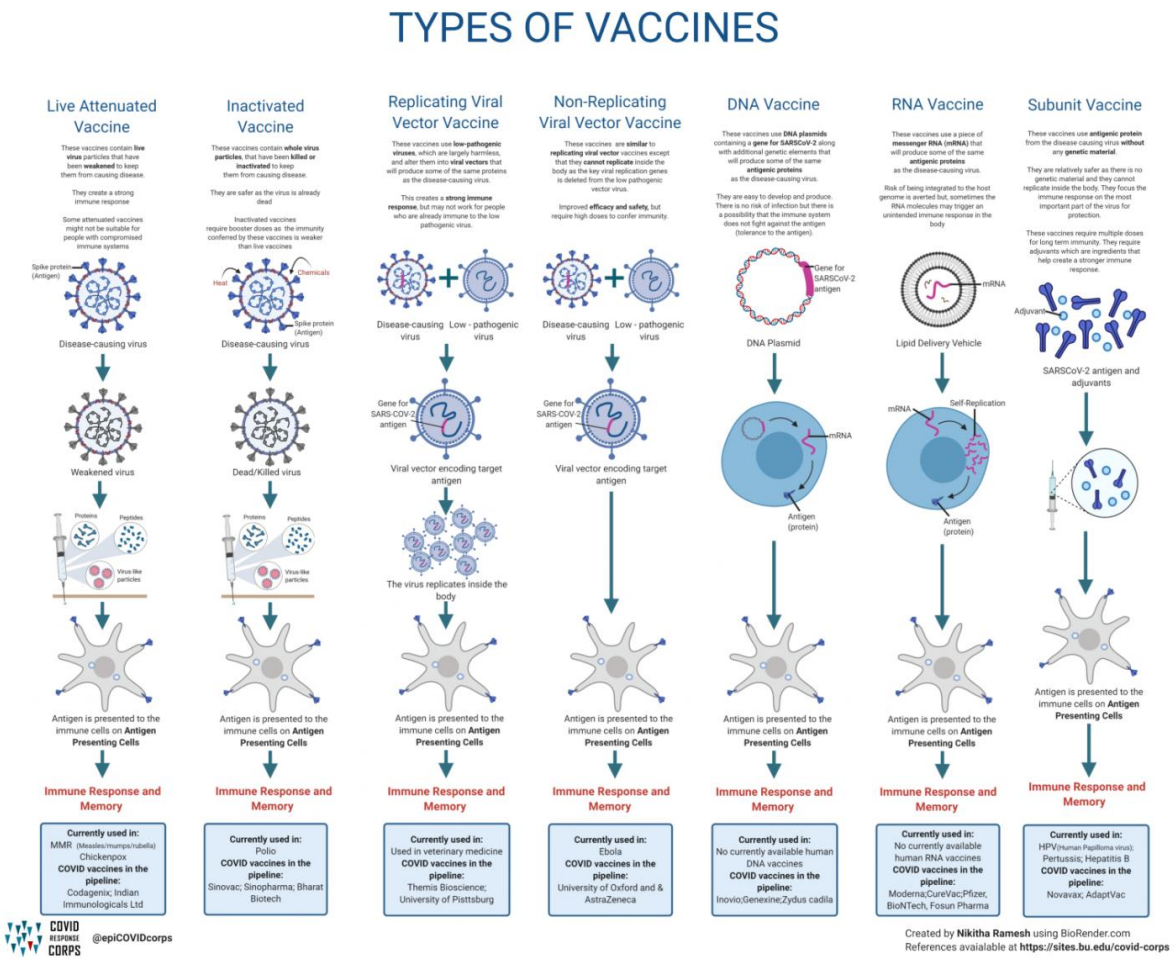

Figure 1: Types of Vaccine.[5]

1. **Non-live vaccines**

- Non- live (Inactivated) vaccines contain whole bacteria or viruses which have been killed or have been altered so that they cannot replicate. Since inactivated vaccines do not

contain any live bacteria or viruses, they cannot cause the diseases against which they protect, even in people with severely weakened immune systems.

- Mechanism- The pathogens maintain some of their integrity to be recognized by the immune system and induce an adaptive immune response.
- A disadvantage of these vaccines is that immunogenicity and time interval of protection tend to be less than for live vaccines, and they may require several doses or adjuvants to improve immunogenicity.
- These vaccines are usually given frequently based on the prime-boost principle to induce long-term immunity. This strategy, used since the beginning of vaccines, aims at boosting antibody and cell-mediated immune responses through multiple primary doses and regular boosters. Impact on asymptomatic nasopharyngeal carriage of the pathogen and, consequently, herd protection by disturbing transmission can be achieved with some non-live vaccines.

Killed, subunit and toxoid are some examples of non-live vaccines.

2. Subunit Vaccines

- These vaccines typically contain one or more specific antigens from the surface of the pathogen. The immune response can emphasize recognising a small number of antigen targets.
- Subunit vaccines do not always produce such a strong or long-lasting immune response as live attenuated vaccines. They frequently require repeated doses primarily and subsequent booster doses in subsequent years.
- Adjuvants are often added to subunit vaccines. These are substances that help to toughen and extend the immune response to the vaccine. As a result, common local reactions may be more noticeable and frequent with these types of vaccines.
- Recombinant Protein Vaccines - These are made using bacterial or yeast cells to the production of the vaccine. A small piece of DNA is taken from the virus or bacterium against which we want to protect and introduced into the manufacturing cells.

e.g Hepatitis B Vaccine.

3. Toxoid Vaccines[6,7]

- Some bacteria liberate toxins when they attack the body, and it is the toxins before the bacteria itself that we want to be protected against. The immune system identifies these toxins on the surface of the bacteria, and can mount an immune response to them. Some

vaccines are made with inactivated forms of these toxins. They are called 'toxoids' because they appear like toxins but are not poisonous. They activate a strong immune response.

e.g DPT Vaccine

There are three main advantages of toxoid vaccines

- Safe because they cannot cause the disease they prevent and there is no possibility of degeneration to virulence.
- Vaccine antigens are not energetically multiplying, they cannot spread to unimmunized individuals.
- Usually constant and long-lasting as they are less susceptible to changes in temperature, humidity and light which can result when vaccines are used out in the community.

Toxoid vaccines have two disadvantages -

- Frequently need an adjuvant and require several doses.
- Local reactions at the vaccine spot are more common, this may be due to the adjuvant or a type III (Arthus) reaction.

4. Live attenuated vaccine[8]

- Live attenuated vaccines contain pathogens that have been weakened, transformed or selected to be less virulent than their wild-type counterparts. In their transformed form, they cannot cause the actual disease or only mimic the disease in a very mild way.
- Live attenuated vaccines are generally formed from viruses rather than bacteria because viruses contain rarer genes and attenuation can be obtained and controlled more reliably.
- Live attenuated vaccines act by producing a very limited type of infection. Healthy individuals develop immune responses comparable to those encouraged by natural infection.
- These vaccines bring robust cell-mediated and antibody responses and often discuss long-term immunity after only one or two doses. Another advantage of live viral vaccines, and risk also, is that they can encourage herd immunity through excretion of viral particles (i.e. viral shedding), which may indirectly "vaccinate" individuals living in the atmosphere of the vaccine.
- Live attenuated vaccines have some restrictions. Although rare, the clinical disease can occur after vaccination, but vaccine-induced symptoms are typically much lighter than after natural infection.

- Live attenuated vaccines are contraindicated during pregnancy due to the theoretical risk of foetal infection that results in congenital disease.
- Mechanism - Vaccine functions by encouraging the creation of cells, such as CD8+ and CD4+ T lymphocytes, or molecules, such as antibodies, that are precise to the pathogen. The cells and molecules can moreover prevent or reduce infection by killing infected cells or by producing interleukins. Live attenuated vaccines can bring long-term, possibly lifelong, immunity without requiring multiple vaccine doses.

5. Viral Vectored Vaccines

- Viral vectored vaccines are a fresher technology, using inoffensive viruses to deliver the genetic code of target vaccine antigens to cells of the body so that they can produce protein antigens to excite an immune response.
- Viral vectored vaccines are grown in cell lines and can be established quickly and easily on a large scale.
- Replicating - Replicating viral vectors maintain the ability to make a new viral particle together with delivering the vaccine antigen when used as a vaccine delivery platform. Replicating viruses can provide a continuous source of vaccine antigen over a longer period compared to non-replicating vaccines, and so is likely to produce a stronger immune response. E.g rVSV-ZEBOV vaccine against Ebola.
- Non-replicating - Non-replicating viral vectors do not maintain the ability to make new viral particles during the process of delivering the vaccine antigen to the cell. This has the advantage that the vaccine cannot cause disease and adverse events related to viral vector replication are reduced. There are some types of non-replicating vaccines, including live-attenuated vaccines, inactivated vaccines, subunit, and conjugated vaccines, and RNA vaccines.

6. Nucleic acid vaccines

- Nucleic acid vaccines work differently from other vaccines in that they do not impart the protein antigen to the body.
- They provide the genetic instructions of the antigen to cells in the body and in turn the cells produce the antigen, which excites an immune response.
- Nucleic acid vaccines are quick and easy to develop and provide important promise for the development of vaccines in the future.

- RNA vaccines - RNA vaccine uses mRNA inside a lipid membrane. This fatty cover protects the mRNA when it enters the body, and also helps it to get inside cells by combining with the cell membrane. This mRNA usually lasts for a few days, but in that time adequate antigen is made to excite an immune response. It is then naturally broken down and detached by the body. RNA vaccines are not capable of merging with the human genetic code (DNA).
- DNA vaccines - DNA is more stable than mRNA so doesn't need the same initial protection. DNA vaccines are usually administered along with a technique called electroporation. This uses low-level electronic waves to permit the body cells to take up the DNA vaccine. DNA must be decoded to mRNA within the cell nucleus before it can be translated to protein antigens which stimulate an immune response.

7. Edible Vaccines[9]

- Edible vaccines are genetically modified crops that contain immunity for specific diseases. Edible vaccines are also considered a pharmafood. Oral vaccines stimulate the group of immunity in gut-associated lymphoid tissue (GALT), which comprises lymph nodes, Peyer's patches and isolated lymphoid follicles in the gastrointestinal tract (GIT).
- Edible vaccines are subunit vaccines. They aimed at producing pathogen-specific responses, it is necessary to conquer mucosal tolerance. Briefly, mucosal tolerance is attained against certain foreign antigens, such as those contained in our food, and serves to stop unnecessary and potentially detrimental immune responses in the gut mucosa.
- For edible-based vaccine immunizations, it is important to consider the characteristics of the GIT, in which some factors, including proteolytic enzymes, acidic pH, bile salts, and limited permeability, may delay the induction of a protective immune response.

Different Types of Edible Vaccines

a) Plant-Based Vaccines
b) Algae-Based Vaccines
c) Insect Cell-Based Vaccines
d) Lactic Acid Bacteria-Based Vaccines
e) Whole-Cell Yeast-Based Vaccines

Some of the examples of edible vaccines are listed in table 1.

Table 1: Examples of Edible Vaccines.[10]

S. No.	Vaccines	Vector used	Diseases/Condition it is used for
1.	Hepatitis B virus	Tobacco Potato Lettuce	Hepatitis B
2.	Norwalk virus	Tobacco Potato	Diarrhoea Nausea Stomach cramps
3.	Rabies virus	Tobacco	Rabies
4.	Transmissible gastroenteritis Corona virus	Tobacco Maize	Gastroenteritis
5.	Rabbit hemorrhagic diseases virus	Potato	Hemorrhage
6.	HIV virus	Tomato	AIDS
7.	*Vibrio cholerae*	Potato	Cholera

VACCINES AGAINST VARIOUS DISEASES

1. MMR - Measles, Mumps and Rubella Vaccine

- Measles is a highly contagious viral infectious disease. Rubella is an infection caused by the rubella virus. A rash due to rubella or the area affected is similar to that of measles but the rash is less intensely red. Mumps is another viral disease that was common, especially during childhood and painful swelling of the parotid glands was seen as a major symptom. The MMR vaccine is a vaccine for prevention of measles, mumps, and rubella.
- Trade Names - M-M-R II, Priorix, Tresivac, etc.
- Combination MMR vaccines are live virus vaccines designated for the prohibition of measles, mumps, and rubella. The MMR vaccine is administered by a subcutaneous injection. It is suggested as a two-dose series with the first dose at 12–15 months of age and the second dose at 4–6 years of age. The route of administration of a dose is subcutaneous.
- MMR vaccine is well accepted. Common disadvantages include injection site reactions, fever and mild rash. MMR vaccine is related to febrile seizures, Thrombocytopenia, Arthralgia.
- Global measles vaccination, in the form of MMR vaccine or combination measles-rubella vaccination (used mainly in low-income countries), has resulted in a substantial decrease in measles cases and measles deaths.[11-13]

2. DTP - Diphtheria, Tetanus and Pertussis Vaccine

- Diphtheria is an infection caused by the bacterium Corynebacterium diphtheriae and can block the airway and create a barking cough as in croup. Whooping cough or pertussis or the 100-day cough, is a highly contagious bacterial disease. Tetanus, known as lockjaw, is a bacterial infection characterized by muscle spasms.
- DTP is a kind of grouping of vaccines against three infectious diseases in humans: diphtheria, pertussis (whooping cough), and tetanus.
- The vaccine ingredients include diphtheria and tetanus toxoids and either eliminate whole cells of the bacterium that causes pertussis or pertussis antigens.
- Trade Names - Adacel, Boostrix, Revaxis, etc.
- The route of administration is intramuscular. Three doses of 0.5ml for primary immunization are injected on three separate occasions at 4-6 week intervals. The first dose to be given at about six weeks of age. Two booster doses of 0.5ml are given after 12 months and between the age of 4-6 years.
- Common adverse effects consist of soreness where the vaccine was given, fever, prickliness, loss of appetite, and vomiting. Most disadvantages are slight to moderate and may last from one to three days.[14-16]

3. TB Vaccine BCG - Bacillus Calmette Guerin Vaccine

- Tuberculosis (TB) is a transmissible infection that generally attacks your lungs and can also spread to other parts of your body, like your brain and spine. *Mycobacterium tuberculosis* is a bacteria which causes this infection.
- The vaccine was established by Albert Calmette and Camille Guérin, who named their invention Bacillus Calmette-Guérin, or BCG. BCG vaccine produces an immune response that partly protects infants and young children from severe tuberculosis.
- BCG vaccine is an attenuated vaccine. It is given as an intradermal injection at the insertion of the deltoid muscle.
- Dose- Child: 0.05 ml single dose soon after birth as possible Or If child is over one year old: 0.1 ml single dose
- Adverse Effects: fever, headache and swollen glands. More serious complications, such as boils or bone inflammation.[17-20]

4. **Hepatitis A & B Vaccine**

- Hepatitis A is a communicable disease of the liver caused by Hepatovirus A, a type of epidemiologic hepatitis. Hepatitis A vaccine is a vaccine that stops hepatitis A. Two doses are suggested beginning after the age of one. It is given by intramuscular injection.
- Hepatitis B is a serious liver infection produced by the hepatitis B virus (HBV). For some people, hepatitis B infection becomes chronic and lasts more than six months. Chronic hepatitis B raises your risk of evolving liver failure, liver cancer or cirrhosis. Hepatitis B vaccine is generally given as 2, 3, or 4 shots. Infants should get their first dose of hepatitis B vaccine soon after birth and will generally complete the series at 6 months of age. Vaccine is inactivated or attenuated.
- Trade Names for Hepatitis A Vaccine - Biovac A, Havrix, Vaqta, etc.
- Trade names for Hepatitis B Vaccine - Heplisav B, Engerix B, Recombivax HB, etc.
- Twinrix is a vaccine that acts against both hepatitis A and hepatitis B, manufactured by GlaxoSmithKline Biologicals. The full common name is hepatitis A (inactivated) & hepatitis B (recombinant) vaccine, which is given over three doses.
- Adverse Effects: Pain, tenderness, redness, swelling at the injection site, fever, headache, nausea, diarrhoea, loss of appetite,and dizziness may occur.[21-23]

5. **Chronic Kidney disease vaccine**

- Infection is a major cause of sickness and mortality in patients with chronic kidney disease. Chronic infections such as hepatitis B virus (HBV) can lead to severe problems upon immunosuppression given for the treatment of glomerular diseases or the prevention of kidney transplant rejection.
- **Vaccination immunology in CKD patients**[24]

a. **Hepatitis B vaccine:** Prevention of HBV infection helps the outcomes of CKD patients, and this can be achieved via effective HBV vaccination. A four-dose regimen is suggested for Engerix in CKD patients.

b. **Influenza vaccination:** A trivalent vaccine consists of virus strains H1N1, H3N2 and one strain of influenza B, while the quadrivalent vaccine consists of an additional strain of influenza B. Vaccination with a high-dose influenza formulation in hemodialysis patients was associated with reduced hospitalization rates compared with standard-dose vaccination.

c. **Pneumococcal vaccination:** Two types of pneumococcal vaccines are mostly available, namely the pneumococcal polysaccharide vaccine (PPSV) and pneumococcal conjugate vaccine (PCV).

d. **Herpes zoster vaccination:** The two zoster vaccines currently available include the live-attenuated vaccine (LZV) Zostarax, and the inactivated recombinant vaccine with adjuvant (RZV) Shingrix. Both vaccines can be administered in CKD patients, although RZV is preferred due to its higher efficacy and longer-lasting immunity.

- Adverse effects - Nausea, Vomiting, Loss of appetite, Fatigue and weakness, Sleep problems, Changes in how much you urinate, Decreased mental sharpness, Muscle twitches and cramps, Swelling of feet and ankles.

5. Cancer Disease Vaccine[25]

- Cancer is the unlimited growth of abnormal cells anywhere in a body. Anything that may cause a normal body cell to develop irregularly can cause cancer; general categories of cancer-related or causative agents are chemical or toxic compound exposures, ionizing radiation, pathogens, and human genetics. Cancer is the second most common cause of death worldwide. Among the various types of cancers, lung, breast, prostate, and colorectal cancers are the most common.

- **Types of cancer**

a) Breast cancer
b) Prostate cancer
c) Skin cancer (melanoma)
d) Colon cancer
e) Lung cancer

Table 2: List of FDA-approved preventive cancer vaccines.[26]

Name of the Vaccine	Cancer Type Prevented
Cervarix	HPV-related anal, cervical, head and neck, penile, vulvar, and vaginal cancers.
Gardasil-4	HPV-related anal, cervical, head and neck, penile, vulvar, and vaginal cancers
Gardasil-9	HPV-linked anal, cervical, head and neck, penile, vulvar, and vaginal cancers
Bacillus Calmette–Guérin (BCG)	Early-stage bladder cancer(through local instillation into the bladder)
Sipuleucel-T(Provenge)	Prostate cancer

- Cancer vaccines can be grouped as preventive and therapeutic. Preventive vaccines are used to avoid any future infections, whereas therapeutic vaccines are used to cure a person with active disease.
- A cancer screening programme is a much more costly and complex undertaking than an early diagnosis programme. Therefore, where capitals are limited, and where most cases are analysed in late stages, early diagnosis of the most often cancers, linked to suitable treatment, is likely to be the best option to lower premature deaths and suffering due to cancer. Considering the price of cancer drugs and the survival rate, mutation of proteins that are involved in cancer development, and resistance pathways, therapeutic vaccines have promise in the upcoming cancer therapy.
- Adverse effects - Fatigue, Hair loss, Easy bruising and bleeding.Infection, Anemia (low red blood cell counts),Nausea and vomiting, Appetite changes, Constipation.[27]

6. Polio Vaccine

- Poliomyelitis or polio, is an infectious disease caused by the poliovirus. It causes Muscle weakness resulting in an inability to move and this disease spreads by fecal-oral route. The World Health Organization (WHO) recommends all children be fully vaccinated against polio.
- Polio vaccines are vaccines used to stop poliomyelitis (polio). Two types are used, an inactivated poliovirus given by injection and a weakened poliovirus given by mouth (OPV). The inactivated polio vaccines are very safe. Slight redness or pain may arise at the site of injection. The disease is preventable with the polio vaccine, but multiple doses are required for it to be effective.
- Trade names for Polio vaccines - Ipol, Poliovax, and others.
- The first polio vaccine, known as inactivated poliovirus vaccine (IPV) or Salk vaccine, was established in the early 1950s. This vaccine comprises a killed virus and is given by injection. During that time, infants have received four doses of the vaccine. Many other countries continue to use the oral polio vaccine because it is more inexpensive and easier to administer, allowing more people to get the vaccine. It also provides better community immunity.
- Pulse Polio is an immunisation campaign formed by the government of India to eliminate poliomyelitis (polio) in India by vaccinating all children under the age of five years against the polio virus. The project fights polio through a large-scale, pulse vaccination programme and also monitoring for poliomyelitis cases.[28,29]

7. Covid-19 Disease Vaccine

- COVID-19 disease is affected by a Coronavirus called SARS-CoV-2. It is predominantly a respiratory illness that can infect other organs. People with COVID-19 may experience a wide range of symptoms from mild to severe categories. Symptoms might appear 2 to 14 days after exposure to the virus.
- A COVID‑19 vaccine is a vaccine considered to provide acquired immunity against severe acute respiratory syndrome coronavirus 2 (SARS‑CoV‑2).
- Remdesivir is available in established countries as a particular antiviral medication that has been shown to be effective in reducing symptoms and accelerating recovery from COVID-19 disease, it is expensive in most parts of the world and is in inadequate supply, such that much of the world expects an inexpensive and effective antiviral drug.
- The treatment for COVID-19 trusts on the management of the symptoms attentive to the symptomatic management of the patients which include changeable secondary infections by the administration of broad-spectrum antibiotics, aeration, and fluid control.

Table 3: Different vaccine available for COVID-19.[30]

a) Covaxin vaccine	b) Covishield vaccine
Manufacturer/developer: Bharat Biotech Vaccine type: Inactivated Administration method: Intramuscular injection Side effects: Headache, weakness, fever, body ache, abdominal pain, nausea and vomiting, faintness, sweating, cold, cough and swelling on the site of injection.	Manufacturer/developer: AstraZeneca, Serum Institute of India Vaccine type: Viral vector Administration method: Intramuscular injection Side effects: Pain or inflammation at the injection site, Headache, Tiredness, Muscle or joint aches, Fever, Chills, Nausea.

- Several companies have started the expansion of antiviral and vaccines for COVID-19. Different methods have been undertaken to progress an effective vaccine for COVID-19 such as attenuated virus, viral proteins, viral nucleic acid, virus-like particle, peptide, viral vector (replicating and non-replicating), and recombinant proteins.
- The most important challenge post-vaccine development will be the fair circulation of the vaccines globally. Recovering plasma therapy and monoclonal antibody therapy are also being tested and can be the potential therapeutic modality for the administration and inhibition of COVID-19. However, they might benefit only the hospitalized patients and will not be usually useful for the population.
- Research study is investigating the long-lasting protection against SARS-CoV-2.[31]

CONCLUSION

Vaccines have successfully reduced the boost of diseases and the death rate related to infectious agents such as cancer, tetanus, polio, measles, rubella and hepatitis, etc. Vaccines are proved to be among the safest and significant public health interventions. DTP and MMR are combination vaccines. Cancer is a fatal disease all over the world, considering the price of cancer drugs and the survival rate, therapeutic vaccines have promise in the upcoming cancer therapy. The first polio vaccine was given by injection, but most countries continued to use the oral polio vaccine because it is more economical and easier to administer, allowing more people to get the vaccine. BCG vaccine is the only licensed vaccine for the prevention of TB. The treatment of covid-19 now is worldwide based on various vaccines including covaxin and covishield which also has some side effects.

New vaccines undergo rigorous testing before receiving FDA approval and like other medicines and medical interventions, vaccines also carry some risk. Current and potential new vaccines protect against contagious and noncontagious diseases, but not all future vaccines have the equivalent spillover effects. Vaccination is a highly effective and easy way to keep ourselves healthy.

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