# COVID - 19 Vaccines – Solutions & Challenges

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**Abstract**

With a year almost complete following the arrival of the global threat, the world has adapted to the General measures of prevention with the use of masks, social distancing, and practicing self-hygiene. Another widely discussed topic right from the surfacing of the pandemic is that on the vaccines. On a large scale, the use of vaccines itself has been a matter of debate, but the identification of COVID vaccines, the type of the vaccine, its efficacy, the dosage schedule, the eligible candidates, its safety profile, its impact on the economy and the plausibility of the effective cold chain have been in the limelight among both the general public and the health professionals. This article aims to provide insight into the above addressed topics and shower some light on the possible efficacy of other vaccines for protection against SARS-CoV, which were originally designed to combat other disease conditions.

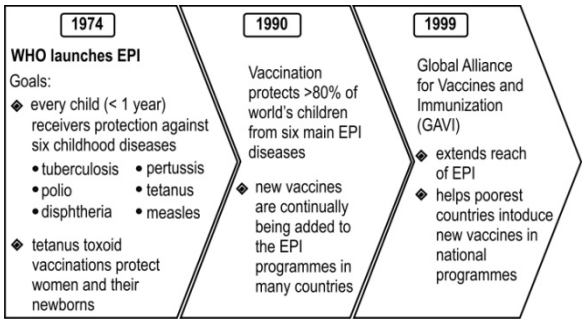
**Introduction**

According to the Centre for Disease Control and Prevention, a Vaccine is defined as a product that stimulates a person's immune system to produce immunity to a specific disease, protecting the person from that disease. Quoting Benjamin Franklin, "An ounce of prevention is worth a pound of cure," vaccines have come a long way in modern medicine as a very effective prevention strategy. Many diseases of deadly or disabling nature have been eradicated, thanks to the timely discovery and effective vaccination protocol. Some landmark vaccines against smallpox, polio, measles, rubella, and so on— the vaccines under trial for the pandemic that's agonizing the world merit detailed discussion.

**History of Vaccines**

Vaccines are the epitome achievement of modern medicine, owing to which the morbidity and mortality from infectious diseases have lowered by a significant level. Historically, Buddhist monks used to drink snake venom to confer immunity to snake bite. Variolation was when the scabs from smallpox infections were grounded and later inhaled or inoculated to facilitate immunity. Though this seemed to reduce the rate of acquiring smallpox, it had the disadvantage of causing the active disease in a few individuals. The article on vaccines would be incomplete, but for the mention of Edward Jenner, the Pioneer in the world of vaccines. On noticing the rare occurrence of the disease in dairy workers., Sir Jenner came up with a hypothesis that the people infected prior with cowpox had a lesser chance of developing the disease. This led to the discovery of the smallpox vaccine, followed by complete eradication of the deadly disease in no time. Following this, Louis Pasteur discovered the rabies vaccine, which led to an armamentarium of later vaccines. Based on the smallpox vaccine's success, the WHO launched the Expanded Programme on Immunization (EPI) in 1974. The main was to protect the children from 6 vaccine-preventable diseases., Tuberculosis, polio, diphtheria, pertussis, tetanus, and measles. Though the vaccines were ruling the medical world, the taste of their benefit could not be felt by the third world countries. This led to the Global Alliance for Vaccines and Immunization development, now called GAVI, the Vaccine Alliance, in the year 2000 by Bill and Melinda Gates Foundation. Since this was instituted, child deaths have halved, and 13 million deaths prevented. The devastating Ebola epidemic made us realize

how ill-prepared the world was to handle an epidemic., leading to the initiation of the Coalition for Epidemic Preparedness Innovation (CEPI) in 2017 to accelerate the development of vaccines against emerging diseases.




**Types of Vaccines:** Immunity can be in two forms., both active and passive immunity. Active immunity is acquired in administering vaccines or after acquiring the disease, while passive immunity comes from antibody administration.

The different types of vaccines are as follows:

**Nucleic Acid Vaccines**

**DNA and RNA Vaccines –** The vaccines in which the DNA or the mRNA sequence are delivered into the cells and directs the recipient cells to produce the viral proteins that do not cause the disease but will stimulate the body to produce antibodies against the same. This has never been clinically tested in humans before. (Fig.1)

**Advantages**

- This method requires only the viral genome to be sequenced. The SARS-CoV genome sequence was identified and published on **January 11, 2020.** Induces both humoral and cellular immune responses.
- They are cheaper to produce as genetic material is easy to mass-produce. It can be used in both immunosuppressed and immunocompromised people as no infectious components are injected.

**Disadvantages**

- Since these vaccines have not been used in humans prior, their efficacy in COVID-19 cannot be determined.
- There are concerns that the DNA or RNA might incorporate in the host genome for an extended period than expected and might contribute to mutations and tumorigenesis.
- Strong immune responses might not be elicited because the genetic material needs to cross the cell membranes before it can incorporate into the host genome and might be subjected to quick destruction before they do so.

DNA and mRNA vaccines require a serious cold chain in order to maintain their efficacy and shelf life.

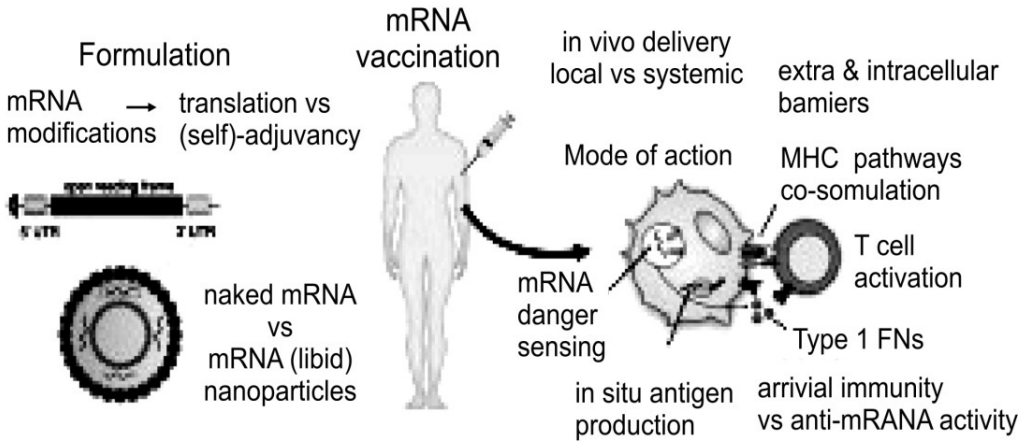



*Figure 1*

**Viral vector vaccines**

These vaccines are made using an inactivated or a harmless viral vector incorporated with a foreign gene of interest against which the immune response needs to be elicited. This is a novel vaccine technology and the example of a viral vector vaccine in Dengvaxia, which uses an attenuated Yellow fever 17D virus strain incorporated with two genes from the dengue virus. Examples of Viral vector vaccines include **Gamaleya- Sputnik, Janssen vaccines,** etc.

**Advantages:** Strong antibody response with both T and B cells

**Disadvantages**

- It cannot be used in immunocompromised individuals.
- It cannot be used in patients with existing antibodies against the attenuated viral vectors.
- Difficult to manufacture, and since it contains genetically modified organisms, it can pose an environmental threat.

**Protein Vaccines**

- Viral subunit vaccines take a part of the pathogen to stimulate an immune response.
- VLP (Virus-like particles) consists of mimicking molecules similar to the virus.
- Split Virus Vaccines in which the viruses are divided and are injected into the body in which they cannot cause a disease

**Viral Vaccines**

- Live attenuated vaccines which contain the live virus but are of much lesser virulence.

Inactivated vaccines in which the virus is inactivated or killed with the help of heat and other chemicals.

**Protocol for Vaccine Development**

**Preclinical trial:** The vaccine is tested in animals for efficacy and safety.

**Phase I clinical trial:** The vaccine is tested in a small group of healthy volunteers.

**Phase II clinical trials:** The vaccine is tested in a group of people of the same age group and sex for whom the vaccine is desired to be used.

**Phase III clinical trials:** The vaccine is tested in a large group of people for its efficacy and safety profile.

**Phase IV trial (or) Post Marketing Surveillance:** This is conducted after the vaccine has been approved for general use. This is done to look out for long-term adverse effects in the population in the long run. (Fig.2)

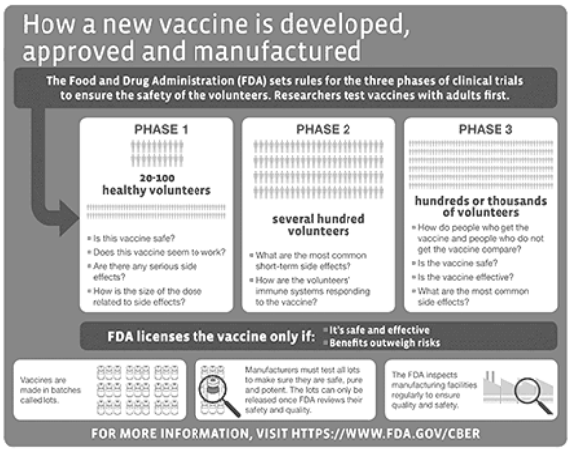



*Figure 2*

**Covid Vaccines in Development**

**Viral Vector Vaccines:**

**Ad5-CoV** contains an adenovirus type 5 vector with spike protein as the antigen

**AZD1222 (ChAD0x1 nCoV-19)** Simian adenoviral vaccine vector with spike protein as the antigen

**Inactivated Vaccines**

**PiCoVacc**

**Inactivated Novel Coronavirus Vaccine**

**Protein Subunit Vaccine:**

**NVX-CoV2373-Novavax**

It's a recombinant full-length spike protein vaccine undergone a phase 3 trial in

UK and Have shown the efficacy of 95% with original strain compared to 85% against B117UK Variant.

Similarly, In South Africa, Phase ll b trial has proved the efficacy of 60% against South African B1351 variant

**mRNA Vaccine**

**BNT162b2 (Pfizer) & mRNA 1273 (Moderna)**

These are all Novel mRNA vaccines delivered through a lipid Nanoparticle and expresses Spike Protein. They are said to have an efficacy of 94.1 to 95%. Local and systemic adverse Events are common after the second dose.

**DNA Vaccines**

**INO-4800**

**Plasmid DNA oral vaccine**

**Indian Vaccines:**

**ChAdOx1 nCoV-19/AZD1222**

This vaccine utilizes Chimpanzee adenovirus as a vector that expresses Spike protein. This It is administered 4weeks apart and approved in various countries like UK, EU & Brazil. It is Said to have an efficacy of 62.1% with standard doses of vaccine. The adverse events are not Different between the vaccine and control groups. It is manufactured by Serum Institute, India, with technical collaboration by Astra Zeneca.

**Covaxin - BBV152**

It's an inactivated virus developed by Bharat Biotech in collaboration with ICMR. It has undergone phase 1 & 2 trials on 380 Patients with Good seroconversion on Day 56 (92.9%), administered 28 days apart and currently under phase 3 trial. It is an inactivated whole virus vaccine is killed by a reagent (Alum).

**Others**

Zydus Cadila makes another vaccine, a DNA vaccine **ZyCovD**, administered as an injection. This vaccine is also in the Phase 3 trial.

Other vaccines like **Sputnik V** is a Russian vaccine, an adenovirus vector vaccine and Reported an efficacy of 91.5%. Sinopharm (Approved in UAE) and Sinovac are inactivated Virus-based Vaccines from China, both are administered in two doses 28days apart.

Both Covishield and Covaxin are given as 0.5ml doses intramuscularly on days 1 and 29, i.e., 28 days apart. The Indian vaccines have a favorable setting in our country owing to the fact that the mRNA vaccines might need strict cold storage techniques. At the same time, both the Covishield and Covaxin require only normal refrigeration temperatures of 2-8 degrees Celsius.

Most of these vaccines discussed above are being planned to be given in 2 doses because of the phenomenon of immunological memory and anticipation. When the body is exposed to the virus or after the first dose of the vaccine, the immune response is weak and is slow to develop. The body then creates a memory of the attack in the form of memory B cells. The second time the body encounters the pathogen, there is a quick and a heightened immune response owing to the already created memory. This thus explains the theory of two-dose vaccination.

**Target Group:** The vaccine is being administered to the high-risk groups as the health care professionals, the frontline workers like the sanitation workers, the police officials, other bureaucrats. The vaccine will later be extended for the use of the general public above the age of 16 years.

**Safety Profile:** The COVID 19 mRNA vaccine, which is being planned to be used in the UK, is going to be given in 2 doses of 0.3 ml, 21 days apart. The adverse effect profile of this vaccine is as under:

Very common: Headache, arthralgia, myalgia, injection site pain, fatigue, chills, pyrexia, redness at the injection site.

Uncommon: Lymphadenopathy, malaise, nausea, Bells palsy

A similar safety profile is expected for our Indian vaccines as well though its safety profile is currently under study.

**Additional Effects of other Vaccines:** Vaccines like BCG and oral polio vaccines have been shown to have immunomodulatory effects and hence may have an effect on the prevention of COVID-19. Measles vaccine trials are also underway. The above trials are being conducted in countries like Australia, Netherlands, and South Africa. Oral polio vaccines are being considered in the USA.

## Conclusion

Herd immunity is defined as the reduction of the infection or disease in the unimmunized segment as a result of immunizing a proportion of the population. Estimates suggest that around 60 to 70 percent of the population needs to be immune for effective herd immunity, the best way to achieve the above is via vaccination. Keeping the above studies in mind, a vaccine with a proven safety profile after phase III of trials is welcome.

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