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Review on COVID-19 Vaccine: The Game Changer

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ABSTRACT

The world is in the grip of covid-19 pandemic. The outbreak of Coronavirus Disease -2019 (COVID-19), from the city of Wuhan china, spread rapidly in various countries, with many cases reported worldwide. The virus was first identified in the bats and was transmitted to humans through unknown mediators. The novel coronavirus uses the same receptors, the enzyme that converts angiotensin 2 (ACE2) like that of Severe Acute Respiratory Syndrome Coronavirus (SARS CoV) and is widely distributed through the respiratory tract. SARS-CoV 2 belongs to β-coronavirus of the family coronaviridae. The symptoms include breathlessness, fatigue, anxiety and multidisciplinary inflammatory syndrome in children. Treatment of covid-19 with Azithromycin (for bacterial infections like bronchitis and pneumonia), Convalescent plasma (collected from person recovered from covid-19 and transfused to person with active coronavirus), Hydroxychloroquine, chloroquine, Ivermectin, Remdesivir, corticosteroid and Tocilizumab. Vaccines are a new critical tool in the fight against COVID-19 and it is very encouraging to see so many vaccines being effective and progressive. Safe and effective vaccines will be a game changer. The vaccines developed in India are covaxin, covishield, Pfizer-biotech, Moderna, oxford-AstraZeneca. ZyCov-Di, being developed by Ahmedabad based Zydus-Cadila, sputnik V vaccine candidate developed by Dr. Reddy's Lab and Gamaleya national centre in Russia. The covid-19 vaccine produces immunity, as a result of building an immune response to SARS-Cov2 virus. Developing immunity through vaccination means there is a reduced risk of developing the illness and its consequence. Getting vaccinated may also protect people around you. This is particularly important to protect people at increased risk for illness from covid-19, such as healthcare providers, older or elderly adults, and people with other medical condition.

INTRODUCTION

Coronaviruses (CoVs) are a group of related viruses that can cause respiratory tract infection in humans. Until now, there are seven genera of CoVs that are known to infect humans. Four of these genera, including Human Coronavirus 229E (HCoV-229E), Human Coronavirus OC43 (HCoV-OC43), Human Coronavirus NL63 (HCoV-NL63), and Human Coronavirus HKU1 (HCoV-HKU1), only cause relatively mild and self-limiting respiratory symptoms. Alternatively, the other three CoVs, Severe Acute Respiratory Syndrome Coronavirus (SARS-CoV), Middle East Respiratory Syndrome Coronavirus (MERS-CoV), and Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2), are highly pathogenic and can lead to severe respiratory diseases and fatal outcome in infected patients. The first lethal coronavirus SARS-CoV emerged in 2002 in Guangdong Province, China. During the 2002–2004 outbreak, SARS-CoV had infected 8,098 people and resulted in 774 SARS-associated deaths (~10% mortality rate) across 29 countries before it disappeared [1]. In 2012, MERS-CoV emerged in Saudi Arabia. It caused two outbreaks in South Korea in 2015 and in Saudi Arabia in 2018, and still has ongoing reports of sporadic cases nowadays. As of January 2020, there are 2,519 confirmed MERS cases and 866 deaths (~35% mortality rate) across 27 countries. In December 2019, a new type of CoV that can cause severe respiratory illness emerged in Wuhan, China. The World Health Organization named this novel virus SARS-CoV-2 and the disease COVID-19, or Coronavirus Disease 2019. The clinical manifestation of COVID-19 can vary from asymptomatic and mild flu-like symptoms to acute respiratory distress syndrome and death. Long-term pulmonary, cardiological, and neurological complications have also been reported in COVID-19 cases. Compared with SARS-CoV and MERS-CoV, SARS-CoV-2 is highly contagious with an estimated reproductive number of 2.2 (one existing COVID-19 case can cause an average of 2.2 new infections).

The novel beta-coronavirus SARS-CoV-2 is believed to have emerged last year in 2019 in Wuhan from Bats. Crossing the species barrier it entered human beings with furtherance of infection through human to human transmission [2]. The emerging Coronavirus Disease 2019 (COVID-19) pandemic poses a massive crisis to global public health. As of March 11, 2020, there were 118,326 confirmed cases and 4,292 deaths, according to the World Health Organization (WHO). On May 12, WHO reported 4,088,848 confirmed COVID-19 cases and 283,153 deaths globally, showing a dramatic increase in terms of case and death numbers. The World Health Organisation (WHO) has declared the COVID-19 a pandemic. A global coordinated effort is needed to stop the further spread of the virus. A pandemic is defined as

occurring over a wide geographic area and affecting an exceptionally high proportion of the population [3] The COVID-19 caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). SARS-CoV-2 belongs to the β-coronavirus of the family Coronaviridae, and commonly induces respiratory symptoms, such as fever, unproductive cough, myalgia, and fatigue [4-5]. SARS-CoV-2, the coronavirus responsible for COVID-19 is an RNA virus, and these viruses generally have a high mutation rate. Genetic instability has long been considered to represent a challenge to develop effective vaccines against RNA viruses. To better understand the virus, numerous studies have been performed, and strategies have been established with the aim to prevent further spread of COVID-19, and to develop efficient and safe drugs and vaccines [6]. For example, the structures of viral proteins, such as the spike protein (S protein), main protease (Mpro), and RNA-dependent RNA polymerase (RdRp), have been uncovered, providing information for the design of drugs against SARS-CoV-2. In addition, elucidating the immune responses induced by SARSCoV-2 is accelerating the development of therapeutic approaches. In essence, diverse small molecule drugs and vaccines are being developed to treat COVID-19 [7]. SARS-CoV-2, a highly dangerous virus, tends to spread by the inhalation of respiratory aerosols, direct human contact, etc. Social distancing, personal hygiene, frequent hand washing or sanitizing using alcohol (61-70%) based hand-sanitizers, and disinfection of the surfaces are some steps which can protect the individuals from getting infected [8].

The development of SARS-COV-2 vaccines

Due to the urgent need to combat COVID-19, diverse SARS-CoV-2 vaccine types are currently under development, including Inactivated vaccines, Attenuated vaccines, Protein vaccines, Nucleic acid vaccines, Vector vaccines, Subunit vaccines.

Vaccines based on attenuated SARS-CoV-2 viruses

The history of vaccination begins with vaccines based on a living microbe that has been weakened so it can not cause disease. Since attenuated microbes retain the ability to replicate *in vivo* giving rise to a limited disease, they are very effective in stimulating the immune system and inducing a strong and persistent immune memory that is efficacious in preventing infection. Hundreds of millions of people have been protected from disabling and fatal diseases by using attenuated vaccines.

Strategy

This is the most traditional technology exploited in the construction of vaccines. Live attenuated vaccines can be obtained by growing the virus in unfavorable conditions or by generating a genetically weakened version of the virus. However, the attenuation of trillions of viruses is complex and delicate and can be associated with major biosafety risks. Once produced, their storage and handling require carefully observed procedures. The experience with attenuated virus vaccines shows that rare but significant side effects could be expected since attenuated viruses cause disease, even if this is a minor one. The oral route (as in the case of the Sabin polio vaccine) and the intranasal route could induce a mucosal immunity based on secretory IgA and IgM.

Frontrunners

Only three projects of attenuated SARS-CoV-2 vaccines are in active preclinical development at the following institutions:

● The Serum Inst of India, in collaboration with Codagenix, a New York private biotech;

● Indian Immunologicals Ltd, India, in collaboration with the Griffith University, Australia;

● Mehmet Ali Aydunar Univ, Turkey. None of these vaccine projects have yet reached the stage of clinical trials [9].

Vaccines based on the inactivated SARS-CoV-2 viruses

The inactivated SARS-CoV-2 vaccine containing aluminum hydroxide developed by SINOVAC. Vaccines based on killed microorganisms (inactivated vaccines) belong to a very traditional technological platform that has led to numerous vaccines. The vaccines produced using this method are more stable than live attenuated vaccines but their limit is mainly related to the short duration of immune memory which demands inoculation of higher amounts of vaccine or the association of the inactivated microorganism with an adjuvant. The immune response elicited is directed not only against the Spike protein but also against many other SARS-CoV-2 antigens. While the induced response is generally weaker concerning that induced by attenuated viruses, the vaccine is more easily handled, less expensive, and much safer. Inactivated vaccines is conventional vaccines with mature technology and may become the first SARS-CoV-2 vaccine put into clinical use [10].

Strategy

The SARS-CoV-2 is inactivated by exploiting different chemical techniques. All these candidate vaccines are injected intramuscularly.

Frontrunners

Seven vaccine candidates based on variously inactivated SARS-CoV-2 virions are in clinical trials, four of which in Phase III trials and already approved for limited use. When available, reports from Phase II trials suggest that the vaccine is safe and induces a high titer of antibodies. The seven clinical trials are run by:

- Sinovac Biotech, China, this vaccine called CoronaVac is in late-stage Phase III trial and interim results are expected in late November. Meanwhile, CoronaVac has already been approved for limited use among the general Population.
- Sinopharm, China, two of its distinct projects are approved for limited use in the general population.
- Wuhan Inst Biol Products, China, this vaccine has been approved for limited use in the general population.
- Chinese Acad Med Sci, China;
- Bharat Biotech, India, this vaccine, called Covaxin, is in late stage Phase III trial;
- RIBSP, Kazakhstan.

Vaccines based on SARS-CoV-2 proteins

There are several human vaccines based on proteins present on the surface of microbes. Initially, these proteins were purified from the microbes while today, in most of cases, they are produced in vitro exploiting the recombinant DNA technology.

Strategy

The large trimeric aggregates of the Spike protein that protrude outside the virion play an essential role in the docking of the SARS-CoV-2 to human cells. Therefore, the Spike protein or its fragments are the targets of all these vaccines even if in a few cases other SARS-CoV-2

proteins- mostly the nucleoprotein (N) - are also targeted. To activate a robust immune response, often these vaccines exploit adjuvants, either of bacterial or synthetic origin.

Frontrunners

There are very numerous vaccine projects based on SARS-CoV-2 proteins, their fragments, or their fragments combination. At least sixteen candidate vaccines are already in human trials and two in Phase II trial:

- Spike protein or its fragments plus adjuvant Adimmune, Taiwan;
- Bektop, Russia;
- Biotechnology Vector, Russia; Clover Biopharmarm plus GSK adjuvant, China-Italy;
- CoVaxx, US;
- Inst Finlay de Vacuna Vaccine, Cuba plus adjuvant;
- Medigen, Taiwan-US, plus CpG adjuvant;
- Sanofi plus GSK adjuvant, France - Italy;
- The Univ of Queensland, Australia;
- Univ Tübingen, Germany;
- Vaxine, Australia, plus adjuvant;
- West China Hosp Sichuan Univ., China;
- ZFSW Anhui Zhifei Longcom, China, plus adjuvant.
- Proteins carried by nanoparticles Novavax, US, US, Australia, and South Africa, plus adjuvant.
- Oral tablet containing Spike protein fragments Vaxart, US.
- Microneedle skin patch delivering Spike proteins Univ Queensland, Australia

- Spike protein or its fragments inserted in virus-like particles (VLP) SpyBiotech/Serum Institute of India, India.

- Tobacco plant-produced proteins Kentucky Bio Processing, US.

- Tobacco plant-produced proteins in virus like particles (VLP) Medicago plus GSK adjuvant, US – Italy [11].

Naked DNA-based vaccines

The DNA and mRNA-based platforms offer great flexibility in terms of manipulation of the coded antigen and great potential for speed. Currently, there are no DNA vaccines registered for human use; however, DNA vaccines are commonly used in veterinary medicine. These vaccines are stable and can easily be produced in large amounts in bacteria.

Strategy

Once injected into the muscle or skin, DNA plasmids enter human cells, and their ability to enter may be enhanced by a very short local electrical pulse (electroporation). Once entered, plasmid DNA induces the cell to produce temporarily the target protein. In this way, DNA vaccination stimulates the production of antibodies and the activation of killer T cells.

Frontrunners

Six DNA vaccines are entering human trials. All code the Spike protein or its fragments.

- Naked DNA plasmids plus electroporation

Inovio, US;

Genexine, Korea;

Karolinska Inst, Sweden + Inovio, Italy [11].

mRNA-based vaccines

mRNA vaccine is a promising alternative to traditional vaccine approaches due to their safety, potency, quick vaccine-development time, and low-cost production. The procedures to develop the mRNA vaccine include the screening of antigens, the optimization of sequences, modified nucleotides screening, delivery systems optimization, evaluation safety, and

immune response [13]. While messenger RNA (mRNA) has not yet produced any registered vaccine, several vaccine projects exploit this technology for the creation of SARS-CoV-2 vaccines. Unlike DNA, RNA must be transported in various ways to enter the human cell. Once entered, the mRNA vaccine temporarily induces the cell to produce the antigen protein coded by the mRNA.

Strategy

In most of these vaccine projects, the mRNA is carried by lipid microvesicles (liposomes). Also, in the case of anti-SARS-CoV-2 mRNA vaccines, the target antigen coded by the mRNA is mostly if not only, represented by the Spike protein, its variants, or its fragments. These vaccine preparations have to be kept at −30 to −80 °C.

Frontrunners

There are many vaccine projects based on mRNA and its variants coding the Spike protein, its variants, or its fragments. Two of those have finished Phase III trials. The vaccine mRNA may be carried by:

- Lipid vesicles (Liposomes)

Abogn, China;

CureVac, Germany;

Moderna, US;

Pfizer, US - BioNTech, Two candidate vaccines were tested in parallel, and one finished Phase III trial;

Univ Oxford, UK An inhaled form of the vaccine is also tested but has not yet reached Phase III trial [12].

- Nanoparticles

Arcturus Ther, Singapore.

Vaccines based on viral vectors

The DNA coding for the Spike protein can be conveyed into the cells by viral vectors. By inserting the DNA in a virus, it is possible to exploit the virus's great ability to infect and deliver the mRNA into the human cells.

Strategy

The virus inside which the DNA is inserted may lose its ability to replicate. Since a pre-existing immunity against the virus vector may affect vaccine efficacy, primate viruses (from chimpanzee, gorilla) are often exploited as vectors. In other cases, the DNA is inserted into replication active virus vectors: as these viruses can propagate to some extent, they may induce a more robust immune.

Also in these vaccine projects, the target antigen coded by the DNA is mostly, if not only, the Spike protein, its variants, or its fragments. Commonly, these virus-based vaccines are injected intramuscularly. However, there are numerous and interesting projects aiming at administering the vaccine into the nose by inhalation. If effective, the candidate vaccine could induce a mucosal immunity capable of neutralizing the virus, thus inhibiting its ability to enter the human body [13].

Frontrunners

There are very numerous vaccine projects based on viral vectors that are already in advanced clinical trials. Four of those are currently in Phase III trial or approved for limited use. The vaccine DNA is inserted inside:

A. Engineered non-replicating virus vectors

1. Chimpanzee adenovirus:

AstraZeneca, Univ. Oxford, Sweden-UK-Italy that is also testing a vaccine inhaled form not yet in Phase III trial;

2. Gorilla adenovirus:v

ReiThera, Italy.

3. Human adenoviruses:

● CanSino, China;

● Johnson&Jonhson, US;

● Acad Mil Med Sci, China

● Gamaleya Res Inst, Russia: this vaccine based on two human adenoviruses injected one after the other has been approved for limited use.

4. Adenoviruses specifically modified for nasal spray:

● Beijing Wantai Biol Pharm Enterprise, China;

● Acad Mil Sci, China, two projects;

● Bharat Biotech-Washington Univ, India-US;

● AstraZeneca, Sweden-UK;

● Altimmune, US.

5. Other viruses

B. Engineered replicating virus vectors

1. Injected intramuscularly: ● Measles virus, Merck, US;

● Vesicular Stomatitis Virus.

2. Influenza virus administered by nasal spray:

● Influenza virus:

Univ Hong Kong;

Valavax-Abogn, China;

Beijin Vantal Biol Pharm, China.

Subunit Vaccines

Subunit vaccines contain pathogen-derived proteins (antigens) with immunogenicity that can elicit the host immune system. Subunit vaccine is safe and easily manufactures by recombinant DNA techniques but requires adjuvant to enhance an immune response. So far,

many research institutions initiated the SARS-CoV-2 subunit vaccine, and use the spike glycoprotein S, and its fragments, such as S1, S2, RBD, and nucleocapsid protein as a prime target antigen [14]. Novavax, Inc. developed a candidate vaccine based on S protein. So far, Clover Biopharmaceuticals constructed a SARS-CoV-2 S protein trimer vaccine (S-Trimer) by using its patented Trimer-Tag© technology. Since the RBD of S protein directly bind with the ACE2 receptor on host cells, RBD immunization induces specific antibodies that may block this recognition and effectively prevent the invasion of the virus. Most of SARS-CoV-2 subunit vaccines currently under development use RBD as the antigen. In a study in monkeys, recombinant RBD protein was used to successfully reduce viral loads in the lungs and oropharynx and to prevent MERS-CoV pneumonia [15]. Similar to RBD, the N-terminal domains (NTD) of the S protein, E, M, N, and NSPs proposed carbohydrate receptor-binding activity.

For example, the carbohydrate-binding properties of IBV M41 strain related to the NTD of the S protein. Thus, this domain is a candidate antigen for the development of the vaccine [16].

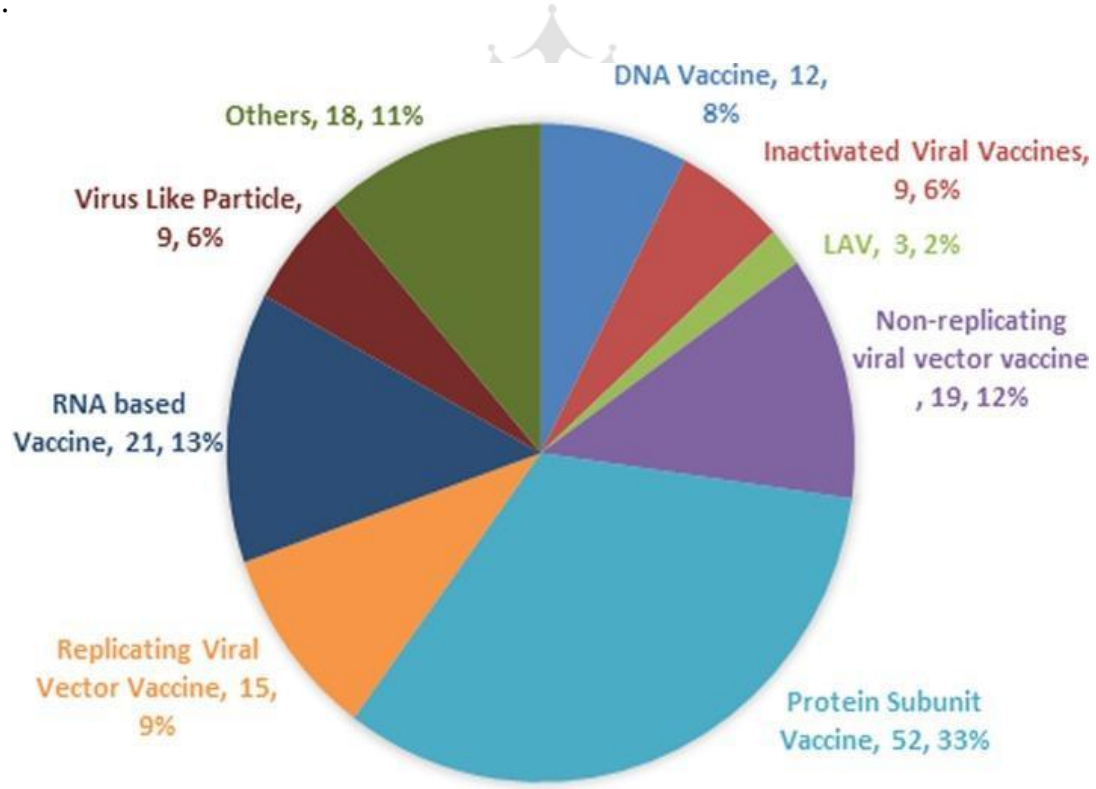


FIG 1: Pie chart showing the different categories of SARS-COV-2 vaccines under research [17].

SAFETY CONCERNS REGARDING VACCINE DEVELOPMENT

The most important criterion of vaccines is safety. Previous experience from the development of SARS-CoV and MERS-CoV vaccines has raised concerns of pulmonary immunopathology correlating with Th2 responses [18]. Th2 is a subgroup of T cells that can secrete Th2-type cytokines, such as interleukin 4 (IL-4), IL-5, IL-10, and IL-13, and aberrant levels of Th2 cytokines can cause immune reactions that lead to eosinophil infiltrations. Inmurine models, four different SARS-CoV vaccines led to the occurrence of Th2-type immunopathology with high eosinophil infiltration, which served as a marker for Th2-type hypersensitivity. This was also observed in mice vaccinated with inactivated MERS-CoV vaccines which had eosinophil infiltrations, with the levels of IL-5 and IL-13 higher than those before vaccination [19]. Moreover, it is proposed that the immunopathologic reaction following vaccination may be partially attributed to the presence of the N protein in the vaccine, but this requires further validation. Recent studies on cytokine changes in patients infected with SARS-CoV-2 also observed increased secretion of Th2 cytokines, which might contribute to lung immunopathology [20-21]. Thus, controlling the T-cell response must be considered when designing vaccines against SARS-CoV-2.

While the humoral immune response induced by vaccines may represent a potent approach of conferring protection against CoV infection, an abnormal antibody response may also result in physical deterioration of patients. In SARS-CoV-infected macaque models, vaccine-induced S-specific IgG resulted in severe Acute Lung Injury (ALI) because IgG disturbed the inflammation-resolving response of macrophages and the blockade of Fc γ-receptor (FcγR) reduced such influence.

Moreover, deceased patients displayed higher titers of NAbs and faster NAb responses which dropped more quickly than in recovered patients during the acute infection, potentially triggering a systematic breakdown of the immune system and exerting the immunopathologic effects on the lung and spleen [22]. Consistently, patients severely infected with SARS-CoV-2 frequently exhibited more robust IgG responses and increased antibodies titers, which linked with the worst clinical condition and suggested Antibody-Dependent Enhancement (ADE) of SARS-CoV-2 infection [23]. Whether SARS-CoV-2 vaccines will cause abnormal antibody responses is currently unknown and additional research is required to address the potential lung damage caused by SARS-CoV-2 vaccine candidates.

Age is known to influence vaccine immunity. Vaccinated aged animals that were challenging to immunize also displayed eosinophilic immune pathology in the lungs. Worse still, neutralizing titers were significantly reduced in aged vaccinated groups compared to young groups. In essence, elderly populations with underlying diseases including diabetes, hypertension, and cardiovascular disease are at high risk for infection by SARS-CoV-2. Given the severity of disease in elderly people, aged animal models are essential for the preclinical validation of vaccines.

RISKS ASSOCIATED WITH FAST TRACK VACCINE EVALUATION

The administration of a new vaccine must always be carefully associated with a rigorous study of its safety. This is particularly important because a vaccine is not a drug for sick people at risk of dying, but rather a treatment that is given to those who are well to prevent the risk of falling ill.

The race to develop a COVID-19 vaccine is not only justified but necessary. However, the time required to evaluate the dangers and risks that may arise from a new vaccine must be included in its development. In some cases, vaccines prepared against other coronaviruses or other viruses have worsened the disease and have induced T helper 2-type immunopathology. These issues must be carefully evaluated and excluded before a new COVID-19 vaccine is distributed to combat the pandemic or its subsequent outbreaks. These basic considerations take on special importance when inappropriate political pressures may lead to accelerating the evaluation of vaccine safety.

Claiming to have won the race to develop a COVID-19 vaccine or the distribution of a candidate vaccine to clusters of the population before all data from clinical trials are obtained and carefully analyzed can be dangerous and erode trust in both the vaccine and regulatory bodies. In this weird contest, the pledges put forward both by pharmaceutical companies and the director of the US Objective Warp Speed to keep rigorous efficacy and safety standards as an absolutely central issue in COVID-19 vaccine development are reassuring.

VACCINES

INACTIVATED VACCINES

Advantages:

1.Can be easily produced and stably express conformation-dependent antigenic epitopes.
2.It can be used along with Adjuvants to increase their immunogenicity.

Disadvatages:

1.The unimportant antigen may skew the immune

SUBUNIT VACCINES

Advantages:

1.May protect immunized animals from viral infection.
2.Do not have any live component of the viral particle.

Disadvantages:

1.May have limited efficacy and make immune

VECTOR VACCINES

Advantages:

1.Can infect APCs directly, and is physically and genetically stable.
2.Show highly specific gene delivery into the host cell with a vigorous immune response.

Disadvatages:

1.May induce prior immunity to the vector

DNA VACCINES

Advantages:

1. Enhances humoral and cellular immune responses.
2.Is stable, and can be easily prepared and harvested in large quantities.

Disadvatages:

1.The safety and efficacy of vaccines for use in

RNA VACCINES

Advantages:

1.Can be rapidly developed and have potential for low-cost manufacture.
2.Safe and well-tolerated; Highly adaptable to new pathogen; Native antigen expression.

Disadvatages:

1.The properties of mRNA may influence its cellular delivery and organ distribution.

LIVE ATTENUATED VACCINES (LAV)

Advantages:

1.It has the intrinsic ability to stimulate the immune system by inducing the toll-like receptors (TLRs) namely: TLR 3, TLR 7/8, and TLR 9. 2.It can be derived from “Cold Adapted” virus strains, reassortants, and reverse genetics.

Table No. 1: comparative chart of different covid-19 vaccines.

Name of vaccine	Type of vaccine	Efficacy in phase 3 trial	Dosing	Storage	Special points
Moderna	Encapsulated mRNA Vaccine	94.1% (US/UK strain)	0.5ml-2doses 28 days apart	-20°C 6month +2-8°C 30days	mRNa encoding for the spike protein is protected in a lipid nanoparticle. Once absorbed, the cell expresses the spike protein resulting in immune response
Biotech /Pfizer	Encapsulated mRNA Vaccine	95% (US/UK strain)	0.3ml-2doses 21 days apart	-70°C 6month +2-8°C 5days	
Sinopharm	Inactivated Virus Vaccine	79% (US/UK strain)	2 doses 3 weeks apart	+2-8°C	SARS-CoV2 is chemically inactivated with a chemical called beta-propiolactone, so it cannot replicate but all the proteins remain intact.
Novavax	Virus-like particle vaccine	89% (US/UK strain)	2 doses 21 days apart	+2-8°C 3months -20°C 2years	Nanoparticles are coated with synthetic spike protiens. An additional element called adjuvant is added which allows to boost the immune reaction.
Oxford/ AstraZeneca	Viral vector vaccine	82% (US/UK strain)	2 doses 12weeks apart	+2-8°C 6months	dsDNA encoding for the spike protein is protected in a safe virus. The infected cell expresses the spike protein which leads to immune response.
SputnikV/ Gam-Covid-Vac	Viral vector vaccine	91% (US/UK strain)	0.5ml-2 doses 28 days apart	+2-8°C 3month -20°C 2years	
Johnson &Johnson	Viral vector vaccine	72% (US/UK strain)	1 dose	+2-8°C 3month -20°C 2years	

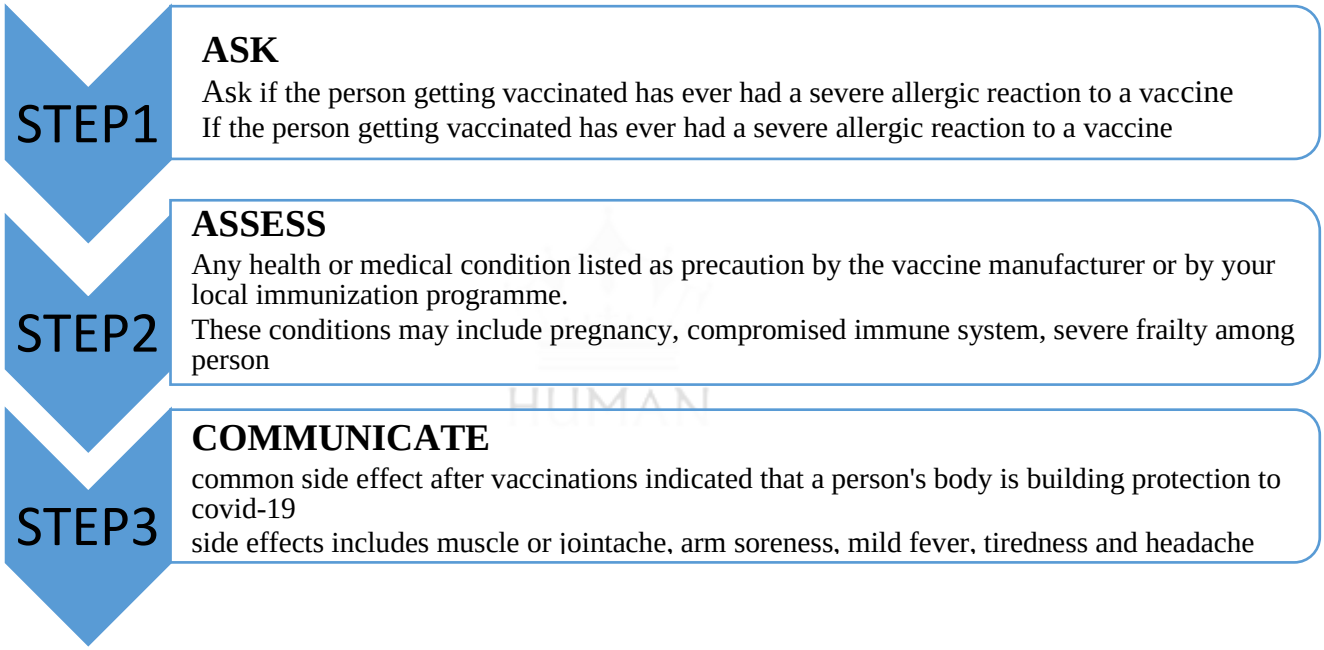
Table No. 2: Comparative chart of different covid-19 vaccines, under Indian Government

Indicators	COVISHIELD	COVAXIN
Types	Recombinant covid-19 vaccine based on viral Technology	Whole-vaccine inactivated coronavirus vaccine
No of doses in each vial	10	20
Shelf life	6 months	6 months
Expiray date available on vial	Yes	Yes
Vaccine Vial Monitor (VVM)	Not available	Not available
Route	Intramuscular (IM) injectable	Intramuscular (IM) injectable
Physical appearance of vaccine	Clear to slightly opaque, colorless to slightly brown	White translucent
Dose	0.5 ml each dose	0.5 ml each dose
Course	2 doses	2-doses
Schedule	4 weeks apart	4 weeks apart
Vaccination during pregnancy	Not recommended	Not recommended
Vaccination <18 years of age	Not recommended	Not recommended
Vaccination to lactating mothers	Not recommended	Not recommended
Storage and transportation	+2ºC to +8ºC at all levels	+2ºC to +8ºC
Shake test	Not applicable	Not applicable
Freeze sensitive	Yes	Yes
Discard the vial, if	Solution is discolored or visible particles are observed	Presence of particulate matter or other coloration
AEFI	Some mild AEFI may occur like injections site tenderness, myalgia, malaise, pyrexia, chills, athralgia, nausea	Some AEFI may occur like injection site pain, nausea and vomiting, dizziness, tremors, cold, cough.
Instructions	Paracetamol may be used to provide symptomatic relief	Shake well before use Use of chloroquine and

	from post vaccination adverse reactions. As with other intramuscular injections, COVISHIELD should be given with caution to individuals with thrombocytopenia	corticosteroids may impair antibody response.

Roadmap to monitor and report COVID-19 SIDE EFFECTS

BEFORE VACCINATION



AFTER VACCINATION

STEP4

VACCINATE

STEP5

OBSERVE

The vaccinated person for 15 min-tell them where and to report severe reactions

observe people with a past vaccine allergy for 30 minutes,after they have been approved by a specialist

STEP6

INFORM

inform your supervisor immediately of any unsuspected or severe reaction during the observation period or reported later.

complete an electronic or paper Adverse events following immunization (AEFI) form, available online at investigation.gvsi-aefi-tools.org.

health officials will then investigate the event.

PROPHYLAXIS AND TREATMENT:

❖ As prevention is better than cure, to stop the spread of this deadly virus, clean hands with soap and water frequently and use alcohol-based hand rub.

❖ Maintain social-distancing approximately 6 ft from anyone you see the symptoms such as sneezing or coughing.

❖ Use of face cover or mask in public place or while sneezing or coughing,

❖ Avoid unnecessary visits to hospitals, nursing home, or health care system to function more effectively.

CONCLUSION:

Vaccines saves millions of lives each year. Vaccines work by training and preparing the body's natural protection - the immune system – to acknowledge and fight off the viruses. After vaccination if body is later exposed to those disease-causing germs, then the body immediately destroys them, preventing illness. The widespread threat of SARS CoV-2 has spawned challenges to develop safe and effective vaccines for preventive use. As of 18 February 2021, at least seven different vaccines across three platform have ruled out in countries. At the same time more than 200 additional vaccines candidates are in development of which more than 60 are in clinical development. Vulnerable population are the first

priority for vaccination. Before receiving validation from WHO and national regulatory agencies, COVID-19 vaccines must undergo rigorous testing in clinical trials to prove that they meet internationally agreed benchmarks for safety and effectiveness. The only aim is to end this phase of covid-19 pandemic by speeding up the development of safe and effective vaccine against covid-19, supporting the building of manufacturing capabilities and working with government to ensure fair and equitable allocation of the vaccines for all the countries. Overall, it has been a remarkable chapter in vaccine development with widespread collaboration and partnership in race against virus.

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