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Worldwide Covid-19 approved vaccines - A comprehensive review on corona virus vaccines

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ABSTRACT

The whole globe remains in the middle of a COVID-19 pandemic. Vaccines save millions of lives each year; we can eliminate COVID-19 only by using vaccines. Vaccines work by training and developing the body's immune system to detect and fight off pathogens. Presently, there are over 50 COVID-19 vaccine candidates in trials across the world. As of December 2020, there are over 200 vaccine candidates for COVID-19 being developed. Of these, at least 52 candidate vaccines are in human trials. There are several others currently in phase I/II, which will enter phase III in the coming months. This article is focussing on the detailed description regarding the various Covid-19 vaccines available around the world.

Keywords: Covid-19 vaccines, Covaxin, Covishield**,** Pfizer-Biontech**,** Sinopharm, Sputnik V, Gamaleya

INTRODUCTION

More than 90 vaccines are being developed against sars-cov-2 by research teams in companies and universities across the world. Researchers are trialling different technologies for manufacture of covid vaccines. At least six groups have already begun injecting formulations into volunteers in safety trials; others have started testing in animals. Nature's graphical guide explains each vaccine design.1-3

THE WHOLE-MICROBE APPROACH INACTIVATED VACCINE

The first way to make a vaccine is to take the disease-carrying virus or bacterium, or one very similar to it, and inactivate or kill it using chemicals, heat or radiation. This approach uses technology that's been proven to work in people, this is the way the flu and polio vaccines are made and vaccines can be manufactured on a reasonable scale. However, it requires special laboratory facilities to grow the virus or bacterium safely, can have a relatively long production time, and will likely require two or three doses to be administered.

LIVE-ATTENUATED VACCINE

A live-attenuated vaccine uses a living but weakened version of the virus or one that's very similar. The measles, mumps and rubella (MMR) vaccine and the chickenpox and shingles vaccine are examples of this type of vaccine. This approach uses similar technology to the inactivated vaccine and can be manufactured at scale. However, vaccines like this may not be suitable for people with compromised immune systems.

VIRAL VECTOR VACCINE

This type of vaccine uses a safe virus to deliver specific sub-parts, called proteins of the germ of interest so that it can trigger an immune response without causing disease. To do this, the instructions for making particular parts of the

pathogen of interest are inserted into a safe virus. The safe virus then serves as a platform or vector to deliver the protein into the body. The protein triggers the immune response. The Ebola vaccine is a viral vector vaccine and this type can be developed rapidly.

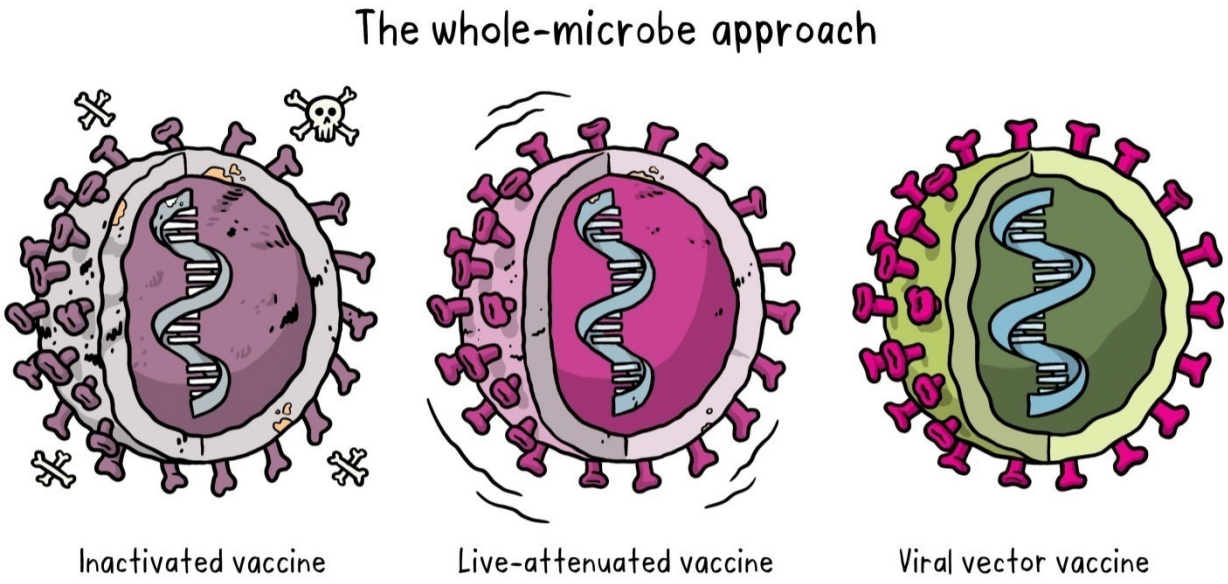

Fig 1: The whole microbial approach

OVERVIEW

The genetic sequence of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) was published on January 11, 2020, and the rapid emergence of research and collaboration among scientists and biopharmaceutical manufacturers followed. Various methods are used for vaccine discovery and manufacturing. As of April 6, 2021, The New York Times Coronavirus Vaccine Tracker lists 3 vaccines in emergency use in the United States. Several other vaccines are approved for full use (outside the United States) and 22 vaccines are in phase 3 clinical trials globally.[1] A number of antiviral medications and immunotherapies are also under investigation for coronavirus disease 2019 (COVID-19). The FDA has granted EUAs for 3 SARS-CoV-2 vaccines since December 2020. Two are mRNA vaccines – BNT-162b2 (Pfizer) and mRNA-1273 (Moderna), whereas the third is a viral vector vaccine – Ad26

DIFFERENT COVID-19 VACCINES

COVISHIELD -OXFORD/ ASTRAZENECA VACCINE

Name is COVISHIELD, manufactured by Serum Institute of India Pvt. Ltd. The vaccine is made from a weakened version of a common cold virus (known as an adenovirus) from chimpanzees. Covishield produced by genetical engineering i.e ChAdOx1 viral vector technology in adenovirus that normally causes the common cold in chimpanzees.

The COVISHIELD vaccination course consists of two separate doses of 0.5 ml each. The second dose should be administered between 4 to 6 weeks after the first dose. However, there is data available for administration of the second dose up to 12 weeks after the first dose from the overseas studies. It administered with intramuscular (IM) injection only. It can be stored in 2-8^{0}c for 6 months

The COVISHIELD Vaccine includes the following ingredients: L-Histidine, L-Histidine hydrochloride monohydrate, Magnesium chloride hexahydrate, Polysorbate 80, Ethanol, Sucrose, Sodium chloride, Disodium edetate dihydrate (EDTA), Water for injection.

POSSIBLE SIDE EFFECTS

Very Common mild side effects for few peoples are tenderness, pain, warmth, redness, itching, swelling or bruising where the injection is given, generally feeling unwell, feeling tired (fatigue), chills or feeling feverish, headache, feeling sick (nausea, joint pain or muscle ache, Common, a lump at the injection site, fever, being sick (vomiting), flu-like symptoms, such as high temperature, sore throat, runny nose, cough and chills. [7,8]

COVAXIN -BHARAT BIOTECH VACCINE

COVAXIN, India's indigenous COVID-19 vaccine by Bharat Biotech is developed in collaboration with the Indian Council of Medical Research (ICMR) - National Institute of Virology (NIV). The indigenous, inactivated vaccine is developed and manufactured in Bharat Biotech's BSL-3 (Bio-Safety Level 3) high containment facility.

The vaccine is developed using Whole-Virion inactivated vero cell derived platform technology. Inactivated vaccines do not replicate and are therefore unlikely to revert and cause pathological effects. They contain dead virus, incapable of infecting people but still able to instruct the immune system to mount a defensive reaction against an infections.

COVAXIN is included along with immune-potentiators, also known as vaccine adjuvants, which are added to the vaccine to increase and boost its immunogenicity.It is a 2-dose vaccination regimen given 28 days apart. It is a vaccine

with no sub-zero storage, no reconstitution requirement, and ready to use liquid presentation in multi-dose vials, stable at 2-8°C. Pre-clinical studies: Demonstrated strong immunogenicity and protective efficacy in animal challenge studies conducted in hamsters & non-human primates. For more information about our animal study, please visit our blog page on Non-Human Primates.

COVAXIN includes the following ingredients: COVAXIN contains 6µg of whole-virion inactivated SARSCoV-2 antigen (Strain: NIV-2020-770), and the other inactive ingredients such as aluminium hydroxide gel (250 µg), TLR 7/8 agonist (imidazoquinolinone) 15 µg, 2-phenoxyethanol 2.5 mg, and phosphate buffer saline up to 0.5 ml. The vaccine (COVAXIN) thus has been developed by using inactivated/killed virus along with the aforementioned chemicals.The vaccine received DCGI approval for Phase I & II Human Clinical Trials in July, 2020.

POSSIBLE SIDE EFFECTS

Mild side effects that have been reported for few peoples with the Bharat Biotech COVID-19 (COVAXIN) include: Injection site pain, Swelling, Redness, Itching Headache Fever Malaise, body ache Nausea Vomiting Rashes [9]

BNT162b2 -PFIZER-BIONTECH

Name is BNT162b2, manufactured by Pfizer, Inc., and BioNTech, it is an mRNA vaccine. It should be administered in 2 shots, 21 days apart. It Should be given in the muscle of the upper arm. Dosing is 0.3ml. It should be stored in -70°c for 6 months, 2-8°c for 5 days.

The FDA has authorized the emergency use of the Pfizer-BioNTech COVID-19 Vaccine to prevent COVID-19 in individuals 16 years of age and older under an Emergency use authorization (EUA)

The Pfizer-BioNTech COVID-19 Vaccine includes the following ingredients: mRNA, lipids ((4-hydroxybutyl)azanediyl)bis(hexane-6,1-diyl)bis(2-hexyldecanoate), 2 [(polyethylene glycol)-2000]-N,N-ditetradecylacetamide, 1,2-Distearoyl-sn-glycero-3-phosphocholine, and cholesterol), potassium chloride, monobasic potassium phosphate, sodium chloride, dibasic sodium phosphate dihydrate, and sucrose.Based on evidence from clinical trials, the Pfizer-BioNTech vaccine was 95% effective at preventing laboratory-confirmed COVID-19 illness in people without evidence of previous infection.

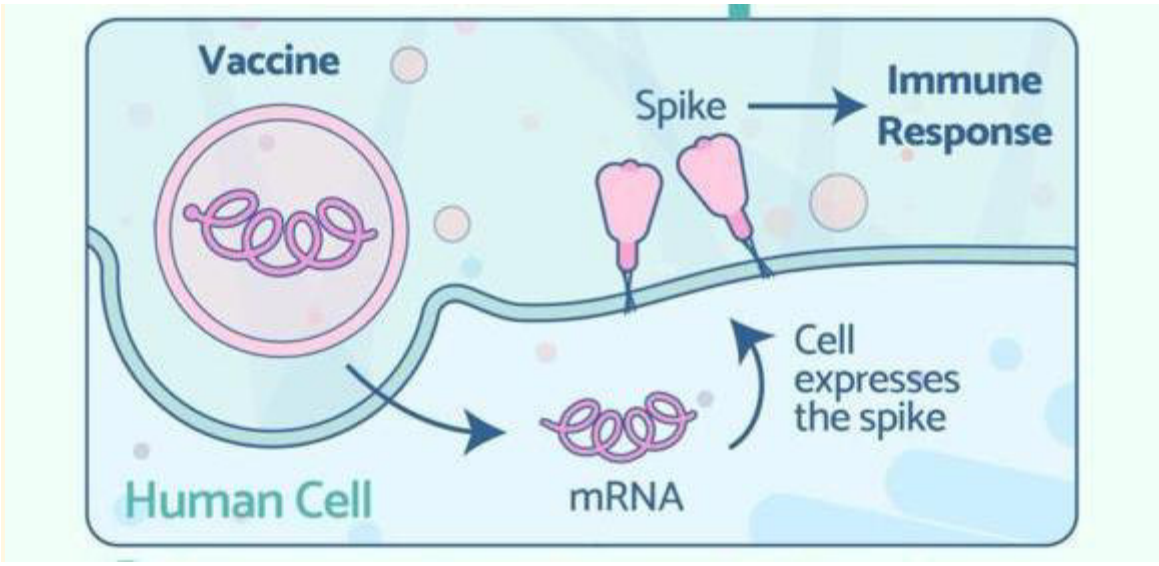

Fig 2: Mechanism of vaccine action

POSSIBLE SIDE EFFECTS

In the arm where you got the shot:Pain, Redness, Swelling. Throughout the rest of your body:Tiredness, Headache, Muscle pain, Chills, Fever, NauseaThese side effects usually start within a day or two of getting the vaccine. Side effects might affect your ability to do daily activities, but they should go away in a few days.[4]

mRNA-1273 -MODERNA VACCINE

Name: mRNA-1273, Manufactured by ModernaTX, Inc. it belongs to mRNA Type of Vaccine, It should be administered as 2 shots, one month (28 days) apart. It should be administered in the muscle of the upper arm. Dosing is 0.5ml. It should be stored in -20°c for 6 months, 2-8°c for 30 days

The Moderna COVID-19 Vaccine contains the following ingredients: messenger ribonucleic acid (mRNA), lipids (SM-102, polyethylene glycol [PEG] 2000 dimyristoyl glycerol [DMG], cholesterol, and 1,2-distearoyl-sn-glycero-3-phosphocholine[DSPC]), tromethamine, tromethamine hydrochloride, acetic acid, sodium acetate trihydrate, and sucrose.

Based on evidence from clinical trials, the Moderna vaccine was 94.1% effective at preventing laboratory-confirmed COVID-19 illness in people who received two doses who had no evidence of being previously infected. The vaccine appeared to have high effectiveness in clinical trials (efficacy) among people of diverse age, sex, race, and ethnicity categories and among persons with underlying medical conditions. Although few people in the clinical trials were admitted to the hospital, this happened less often in the people who got the Moderna vaccine compared to people who got the saline placebo.

POSSIBLE SIDE EFFECTS

In the arm where you got the shot: Pain, Redness, Swelling. Throughout the rest of your body: Tiredness, Headache, Muscle pain, Chills, Fever, Nausea. These side effects usually start within a day or two of getting the vaccine. Side effects might affect your ability to do daily activities, but they should go away in a few days.[5]

JNJ-78436735-JOHNSON & JOHNSON'S JANSSEN:

Name: JNJ-78436735, Manufactured by Janssen Pharmaceuticals Companies of Johnson & Johnson. It belongs to Viral Vector type vaccine. It should be administered as single shot through the muscle of the upper arm. At 2-8°c it shall be stored for 3 months. At -20°c it shall be store for 2 years.

The Janssen COVID-19 Vaccine includes the following ingredients: recombinant, replication-incompetent adenovirus type 26 expressing the SARS-CoV-2 spike protein, citric acid monohydrate, trisodium citrate dihydrate, ethanol, 2-hydroxypropyl-β-cyclodextrin (HBCD), polysorbate-80, sodium chloride.

The J&J/Janssen vaccine was 66.3% effective in clinical trials (efficacy) at preventing laboratory-confirmed COVID-19 illness in people who had no evidence of prior infection 2 weeks after receiving the vaccine. People had the most protection 2 weeks after getting vaccinated.The vaccine had high efficacy at preventing hospitalization and death in people who did get sick. No one who got COVID-19 at least 4 weeks after receiving the J&J/Janssen vaccine had to be hospitalized.Early evidence suggests that the J&J/Janssen vaccine might provide protection against asymptomatic infection, which is when a person is infected by the virus that causes COVID-19 but does not get sick.

POSSIBLE SIDE EFFECTS

In the arm where you got the shot: Pain, Redness, Swelling. Throughout the rest of your body: Tiredness, Headache, Muscle pain, Chills, Fever, Nausea These side effects usually start within a day or two of getting the vaccine. Side effects might affect your ability to do daily activities, but they should go away in a few days.[6]

BBIBP-CorV -SINOPHARM VACCINE

In early 2020, the Beijing Institute of Biological Products created an inactivated coronavirus vaccine called BBIBP-CorV. Clinical trials run by the state-owned company Sinopharm showed that it had an efficacy rate of 79 percent. China approved the vaccine and soon began exporting it to other countries. It should be administered in two shots between 21-28 days interval through the muscles of the upper arm. It shall be stored in 2-8°c.

BBIBP-CorV works by teaching the immune system to make antibodies against the SARS-CoV-2 coronavirus. The antibodies attach to viral proteins, such as the so-called spike proteins that stud its surface.To create BBIBP-CorV, the Beijing Institute researchers obtained three variants of the coronavirus from patients in Chinese hospitals. They picked one of the variants because it was able to multiply quickly in monkey kidney cells grown in bioreactor tanks.

Once the researchers produced large stocks of the coronaviruses, they doused them with a chemical called beta-propiolactone. The compound disabled the coronaviruses by bonding to their genes. The inactivated coronaviruses could no longer replicate. But their proteins, including spike, remained intact. The researchers then drew off the inactivated viruses and mixed them with a tiny amount of an aluminum-based compound called an adjuvant. Adjuvants stimulate the immune system to boost its response to a vaccine.

Inactivated viruses have been used for over a century. Jonas Salk used them to create his polio vaccine in the 1950s, and they're the bases for vaccines against other diseases including rabies and hepatitis A.

POSSIBLE SIDE EFFECTS

There are no published studies yet that have focused on Sinopharm vaccine side effects. But as with other 'inactivated' vaccines the side effects appear to be mild.Anecdotally, people report a sore arm and minor swelling, with others feeling fatigue or symptoms similar to a cold, which pass in a few days.[10,11]

SPUTNIK V - GAMALEYA VACCINE

The COVID-19 vaccine Sputnik V (Gam-COVID-Vac) is an adenoviral-based, two-part vaccine against the SARS-CoV-2 corona virus. Sputnik V uses a weakened virus to deliver small parts of a pathogen and stimulate an immune response. The Sputnik V (Gam-COVID-Vac) vaccine reduces the time taken for the actual development of immunity to SARS-CoV-2, the virus behind the COVID-19 pandemic.

It is a vector vaccine based on adenovirus DNA, in which the SARS-CoV-2 corona virus gene is integrated. Adenovirus is used as a "container" to deliver the corona virus gene to cells and start the synthesis of the new corona virus's envelope proteins, "introducing" the immune system to a potential enemy. Sputnik V is a two-component vaccine in which adenovirus serotypes 5 and 26 are used. A fragment of tissue-type plasminogen activator is not used, and the antigen insert is an unmodified full-length S-protein. Sputnik V vaccine is produced with the HEK293 cell line. The vaccine should be administered intramuscularly in two doses of 0.5 ml each with interval of 21 days. The vaccine has to be stored at -20°C for 2 years, it shall be stored in 2-8^{0}c for 6 months.

The active components are a modified replication-defective adenovirus of a different serotype (Serotype 26 for the first component and serotype 5 for the second), modified to include the protein S-expressing gene of SARS-CoV-2. The ingredients include Tris-(hydroxymethyl)-aminomethane, Sodium chloride, Sucrose, Magnesiumchloride hexahydrate, Disodium EDTA dihydrate, Polysorbate 80, Ethanol, and Water.

The quality and safety of the Sputnik V vaccine are, among other things, assured by the fact that it uses a 4-stage purification technology that includes two stages of chromatography and two stages of tangential flow filtration. This purification technology helps obtain a highly purified product that goes through mandatory quality control, including control for RCA or any additives presence.

Control for RCA is carried out not only for the finished product but also at all stages of production, including the viral seed. Sputnik V team believes that its purification technology is the best among all vaccines and is one of the pillars for vaccine safety. Furthermore, only E1 and E3 type non-replicating adenoviral vectors, which are harmless for the human body, are used in the Sputnik V vaccine production. Sputnik V cell lines: Design and Development: HEK293 cells; Production: HEK293 cells.

POSSIBLE SIDE EFFECTS

Serious adverse events or those requiring hospital admission were rare in both the placebo and vaccine groups and none were considered associated with vaccination, the researchers said. Adverse effects were mild, including flu-like symptoms, pain at injection site and weakness or low energy.[12-14]

Table 1: Different worldwide Vaccines details

Name	Manufacturer	Type of vaccine	Efficacy rate
BNT162b2	Pfizer-BioNTech	mRNA	95%
mRNA-1273	Moderna	mRNA	94.5%
Ad26.COV2.S	Janssen (Johnson & Johnson)	Viral vector	66%
Covishield*	Serum Institute of India (Oxford-AstraZeneca)	Viral vector	81.3%
Covaxin	Bharat Biotech	Inactivated	80.6%
BBIBP-CorV	Sinopharm (Beijing)	Inactivated	79.34%
Inactivated (Vero Cell)	Sinopharm (Wuhan)	Inactivated	72.51%
Ad5-nCov	CanSino	Viral vector	65.28%
Sputnik V	Gamaleya	Viral vector	91.6%

***Covishield is the Oxford-AstraZeneca vaccine produced for India**

If you have had a severe allergic reaction (anaphylaxis) or an immediate allergic reaction to any ingredient in the vaccine you are scheduled to receive, you should not get that vaccine. If you have been instructed not to get one type of COVID-19 vaccine, you may still be able to get another type. Learn more information for people with allergies.You should get your second shot as close to the recommended 3-week or 4-week interval as possible. However, your second shot may be given up to 6 weeks (42 days) after the first dose, if necessary. This represents a huge change in the conventional pathway of vaccine development which usually takes 5–10 years timescale. Along with speeding up the development process, it is equally important to evaluate the effectiveness and safety of vaccine at each step, and this has been the major hurdle for researchers in establishing the vaccine's efficacy so far. However, the phase 3 trial will play a major role in establishing the vaccine that is safe and effective in a large and diverse population. Finally, the animal models specific for COVID-19 should be established in

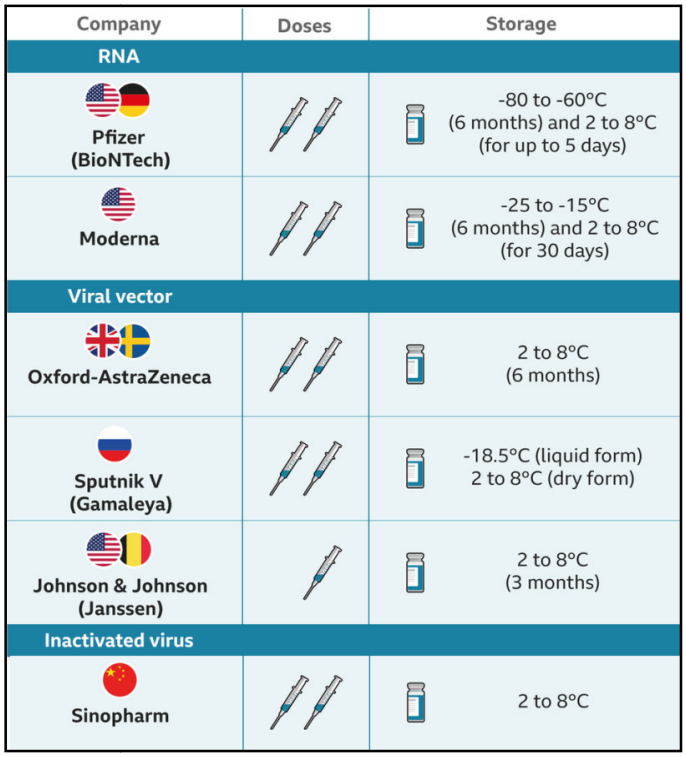

Fig 3: Vaccine dose & strage

CONCLUSION

The need of the hour is to develop a safe and effective COVID-19 vaccine which can induce an appropriate immune response to terminate this pandemic. It is the universal priority to spot the international funding mechanisms to support the development, manufacturing, and stockpiling of the coronavirus vaccines. This pandemic should serve as the guidepost to the international research community to not only acknowledge the outbreak but also indurate the following coronavirus crossing into mammals. A pan-coronavirus vaccine is urgently needed as the delay of vaccine rollout even by one week will accompany millions of deaths. Furthermore, it appears to be a scientifically feasible task with the newly available vaccines in due time. Also it's the responsibility of the entire world to get vaccinated. By doing the 100-percentage vaccination only we can able to eradicate the corona virus from the earth.

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