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Microbiology

EFFICACY OF SARS-COV-2 VACCINES - A BIG CHALLENGE ?

KEY WORDS: SARS-CoV-2, vaccine, clinical trials.

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ABSTRACT

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infections and the resulting disease, the coronavirus infectious disease 2019 (COVID-19), have spread to millions of persons worldwide resulting in pandemic. The cases of Covid 19 doesn't seem to end to soon. There are about sixty-two million six hundred nineteen thousand three hundred ninety-ninecases at present in the world with India ranking second after USA with nine million three hundred ninety-three thousand thirty-nine cases.Adoption of infection prevention and control practices such as hand hygiene, respiratory etiquettes, and maintaining social distance are the important strategies for the containment of this deadly and stubborn novel corona virus. The multiple vaccine candidates are under trials, to evaluate their clinical efficacy. The vaccination aims is to generate immunity against COVID-19 and to protect oneself against the disease and limits the spread of disease to close contacts.

Introduction:

Viruses continue to emerge and pose challenges to public health. Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) isthe causative agent of coronavirus infectious disease 2019 (Covid-19).[1] On January 9, 2020, the World Health Organization reported that a novel (new) coronavirus was identified by Chinese authorities. The virus is associated with an outbreak of pneumonia in Wuhan City, Hubei Province, China. The pandemic due to this novel coronavirus has caused mortality in more than1 million, globally. in the first 6 months and has resulted in large loss economically and socially. The incubation period for COVID-19 is around 2 to 14 days with a median time of 4-5 days from exposure to onset of symptoms. The signs and symptoms of COVID-19 vary, but most common symptoms are fever or chills, cough, shortness of breath or difficulty breathing, fatigue, myalgia, headache,loss of taste or smell,sore throat, congestion , nausea or vomiting and even diarrhea in some cases.[2] The gold standard for the diagnosis of SARS- CoV-2 is real-time reverse transcription PCR (rRT-PCR) approved by the WHO and by the US CDC The introduction of serological tests facilitates pandemic management, having an epidemiological role in the thefollow up of cases already infected, in addition to reducing time, costs and workloads in national laboratories and health-care systems. [3] Vaccine is a substance that stimulates a person's immune system to produce immunity to a specific disease thus protecting the person from that disease[4]A vaccine that is safe and effective against SARS- CoV-2is an urgent need of the hour. To prevent further morbidity and mortality associated with COVID-19.[5] In this current scenario, collaborative efforts are being made for vaccine development to expedite preclinical and clinical assessment of candidate vaccines[6]It has been documented that forty four candidate COVID-19 vaccines are in clinical development and one hundred fifty one are in preclinical development.[7]Vaccines require licensing, regulations, equipments, human resources, and thus high expenditure. This becomes a tedious and a time consuming process, resulting in disappointment and

SARS COV-2 VACCINES [4]-

- **GENETICVACCINES**

Usesone or more of the corona virus's own genes to provoke an immune response. Four candidates have been in the first or second stage of human trials.

- **Moderna - Phase II**
- Moderna's mRNA vaccine was tried on eight people in May, As a part of Operation Warp Speed — a US government programme funding five vaccines

- **BioNTech - Phase I, Phase II –**

German company BioNTech is collaborating with USbased Pfizer and Chinese drug maker FosunPharma to develop an mRNA vaccine. Pfizer announced human trials in May, and hopes to have a few million doses for emergency use

- **Imperial College London - Phase I, Phase II** developed a 'self-amplifying' RNA vaccine, which boosts production of a viral protein to stimulate the immune system. They began Phase I/II trials on June 15 and have partnered with Morningside Ventures to manufacture and distribute the vaccine through a new company called VacEquity Global Health.

- **Inovio - Phase I**

In May, American company Inovio published a study showing that their DNA-based vaccine produces antibodies in mice. Phase I trials are underway in the United States and South Korea.

- **PROTEIN-BASEDVACCINES**
- Uses a coronavirus protein or a protein fragment for a immune response.

- **Novavax - Phase I, Phase II**

In May, US-based Novavax started Phase I/II trials on a vaccine made up of microscopic particles carrying fragments of coronavirus proteins.

- **Clover Biopharmaceuticals - Phase I**

Clover Biopharmaceuticals has developed a vaccine containing a protein from coronaviruses. The vaccine would be taken in conjunction with a so-called adjuvant, made by British drugmaker GSK, to further stimulate the immune system.

- **REPURPOSEDVACCINES**
- These vaccines are already in use for other diseases and may also protect against Covid-19.

- **BCG Vaccine - Phase III**

The Bacillus Calmette-Guerin vaccine was developed in the early 1900s to protect against tuberculosis. The Murdoch Children's Research Institute in Australia is conducting a Phase III trial with it, and several other trials are underway to see if the vaccine partly protects against the coronavirus.

- **VIRALVECTORVACCINES**

- Use a virus to deliver coronavirus genes into cells an provoke an immune response.

- **University of Oxford - Phase II, Phase III**

Supported by Operation Warp Speed, the University of Oxford and the British-Swedish company AstraZeneca are developing a vaccine based on a chimpanzee adenovirus called ChAdOx1. It is going **into phase II/III testing** in England and Brazil.

CanSino Bio - Phase II

- Chinese company CanSino Biologics is testing a vaccine based on the Ad5 adenovirus, in partnership with the Institute of Biology at the country's Academy of Military Medical Sciences. In May, they published a paper in the Lancet — the first time Phase I trial data from any Covid-19 vaccine appeared in a scientific journal.

- **WHOLE-VIRUSVACCINES**

Use a weakened or inactivated version of the coronavirus to provoke an immune response. All three are being developed in China.

- **Sinovac - Phase I, Phase II**

This private Chinese firm is testing an inactivated vaccine called CoronaVac. On June 13, it announced that Phase I/II trials on 743 volunteers found no severe adverse effects and produced an immune response. Sinovac is readying for Phase III trials in China and Brazil.

Sinopharm Phase I, Phase II

State-owned Chinese company Sinopharm has started Phase I/II trials on two inactivated vaccine viruses. The company has announced it has built a facility in Beijing to make up to 200 million doses per year.

- **Institute of Medical Biology - Phase I**

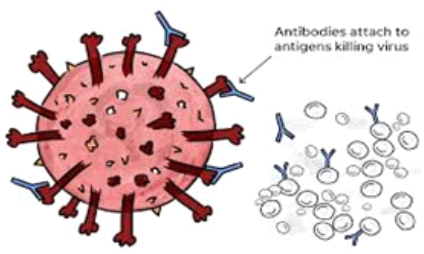
Researchers at the Institute of Medical Biology at the Chinese Academy of Medical Sciences, which has invented vaccines for polio and hepatitis A, are running a Phase I trial of an inactivated virus vaccine for Covid-19 for emergency use by October.

COVID vaccines which have been approved for use are Covaxin (Bharat Biotech), Covishield (AstraZeneca), COVID-19 mRNA vaccine (ModernaTX) and Pfizer COVID-19 vaccine

STATUS IN INDIA

Covaxin (Bharat Biotech) and Covishield vaccine (AstraZeneca), have received DCGI (Drugs Controller General of India) approval for restricted use in emergency situations.

COVAXIN (BBV152) is India's indigenous COVID-19 vaccine. It is developed by Bharat Biotech India Limited, in collaboration with ICMR and NIV Pune. It is a whole virus inactivated vaccine**,** derived from strain of SARS-CoV-2 virus, isolated in NIV, Pune. It covers spike proteins and other antigens targeting the whole surface of virus, expected to provide protection against virus by developing neutralizing antibodies. When administered, immune cells can still recognise the dead virus, prompting the immune system to make antibodies against the pandemic virus.



COVISHIELD-The Oxford-AstraZeneca vaccine is being manufactured locally by the Serum Institute of India, the world's largest vaccine manufacturer. This vaccine is made from a weakened version of a common cold virus (known as an adenovirus) from chimpanzees. It has been modified to look more like coronavirus - although it can't cause illness.

Covaxin / Covishield vaccine dosage - A dose of 0.5 ml to be given intramuscularly on day 0 and on day 28.

Sero-conversion- An immune response (antibodies) would be expected to develop14 days after second dose of vaccination. This protection is said to last for 6-12 months.

Covaxin / Covishield vaccine storage- 2 to 8°C

As per the latest data, the efficacy of Covishield vaccine is found to be 60-70%.

However, the efficacy of Covaxin has not been made public It is under the final stage of trail.

The Bharat Biotech has been given the permission for conducting phase-3 human clinical trials of the Covaxin . The most common adverse event was pain at the injection site, which resolved transiently. [9,10] The phase-three randomised double- blind placebo-controlled multi-centre trial would be expected to cover around 28,500 subjects aged 18 years and above..

Platform	Type of candidate vaccine	Developer	Coronavirus target	Current stage of clinical evaluation	Non-coronavirus candidates	Current stage of clinical evaluation/
Non-Replicating Viral Vector	recombinant adenovirus expressing Trunctuated S protein (rADV-S)	International Vaccine Institute (IVI)	SARS	Pre-Clinical	N/A	
Replicating Viral Vector	Recombinant measles virus Spike protein	University Health Network, Canada; Center for Disease Control and Prevention (CDC)	SARS	Pre-Clinical		
Replicating Viral Vector	MV-SARS recombinant measles virus vaccine expressing SARS CoV antigen	Institute Pasteur	SARS	Pre-Clinical	West nile, chik, Eobla, Lassa, Zika	Phase III
Protein Subunit	receptor binding domain (RBD) of the SARS- CoV spike (S) Protein	Baylor College Medicine; Sabin; New York Blood Center (NYBC);University of Texas National Institute of Allergy and Infectious Diseases (NIAID)	SARS	Pre-Clinical	N/A	

Protein Subunit	SARS recombinant spike protein plus delta inulin	Vaxine Pty Ltd, Australia	SARS	Pre-Clinical	Ebola, Zika, Influenza, HepB	Phase I
Virus-like Particle	SARS VLPs S protein and influenza M1 protein	Novavax	SARS	Pre-Clinical	RSV, Flu	Phase III
Inactivated Virus	rSARSCoV-E	CNB-CSIC; University of Iowa	SARS	Pre-Clinical	N/A	

DNA	DNA prime–protein S437–459 and M1–20	Institute of ImmunoBo Shanghai Medical College of Fudan University, China	SARS	Pre-Clinical		
DNA	SARS S DNA prime and HLA-A*0201 restricted peptides boost vaccine	Sun Yat-sen University, China	SARS	Pre-Clinical		
DNA	3a DNA vaccine	State Key Laboratory of Virology; Graduate University of Chinese Academy of Sciences	SARS	Pre-Clinical		
DNA	DNA vaccine VRC-SRSDNA015-00-VP ; Biojector used	National Institute of Allergy and Infectious Diseases (NIAID)	SARS	Phase I	Ebola, HIV	Phase I
DNA	DNA S protein + DNA IL2	State Key Laboratoryof Virology, University of Chinese Academy of Sciences	SARS	Pre-Clinical		
DNA	DNA vaccine pIRES-ISS-S1	Jilin University; Academyof Military Medical Sciences	SARS	Pre-Clinical		
DNA	M and N DNA vaccine	National Hospital Organization Kinki-Chuo Chest Medical Center;	SARS	Pre-Clinical		

Non-Replicating Viral Vector	MVA S alone, or MVA-S prime and Ad5-S boost	The Rockefeller University	SARS	Pre-Clinical
Non-Replicating Viral Vector	NC protein add-mixed with MALP-2 by intranasal route and boosting with MVA–NC by intramuscular route	Helmholtz Centre for Infection Research; Technical University Munich; German Center for Environmental Health	SARS	Pre-Clinical

Non-Replicating Viral Vector	Heterologous Adenoviral prime boost AdHu5 s AdC7-nS	University of Manitoba; University ofPennsylvaniaSchool of Medicine;Southern Research Institute; Fox Chase Cancer Institute	SARS	Pre-Clinical
Non-Replicating Viral Vector	VEEV replicon particles expressing the SARS-CoV S	University of North Carolina at Chapel Hill, USA	SARS	Pre-Clinical
Non-Replicating Viral Vector	Recombinant DI expressing S Protein	National Institute ofInfectious Diseases, Japan	SARS	Pre-Clinical
Protein Subunit	Recombinant trunctuated S-N fusion protein	Beijing Institute ofGenomics	SARS	Pre-Clinical

Protein Subunit	Recombinant peptide N223 on liposomes	Saitama Medical University; Josai University; Nippon Oil and Fat Corporatin; National Institute of Infectious Diseases, Japan	SARS	Pre-Clinical	
Protein Subunit	Recombinant TM-truncated S Protein	Chinese Center for Disease Control andPrevention; Canadian Science Centre for Human and Animal Health	SARS	Pre-Clinical	
Protein Subunit	Trimeric Spike protein	HKU-Pasteur Research Centre; The University of Hong Kong; National Institutes of Health; Centers for Disease Control and Prevention; CombinatorX	SARS	Pre-Clinical	N/A

Virus-like Particle	Chimeric VLP (S protein SARS plus E, M and N proteins of mouse hepatitis virus)	University of Texas Medical Branch (UTMB)	SARS	Pre-Clinical	N/A	
Virus-like Particle	Recombinant trimeric S Protein	The John Hopkins University School of Medicine, USA	SARS	Pre-Clinical	N/A	
Inactivated Virus	purified inactivated Vero-cell SARS vaccine	Institute of Microbiology and Epidemiology, National Vaccine and Serum Institute; Beijing Genomics Institute (BGI); Harbin Institute of Veterinary Medicine	SARS	Pre-Clinical	N/a	

Inactivated Virus	Formalin- and UV inactivated virus vaccine	Baxter Vaccines, Austria	SARS	Pre-Clinical	N/A	
Inactivated Viral Vector	RABV-SARS	Thomas Jefferson University	SARS	Pre-Clinical	Filoviruses, Hendra	Pre-Clinical
Inactivated Virus	whole virus	Sanofi	SARS	Pre-Clinical	Influenza and others	Licensed Product

Inactivated Virus	-propiolactone inactivated virus vaccine	National Institute of Allergy and Infectious Diseases (NIAID); University of Virginia	SARS	Pre-Clinical	NA
Live Attenuated Virus	Live attenuated vaccine Nsp16 mutant lacking 2'-OMTase	University of North Carolina	SARS	Pre-Clinical	N/A
Live Attenuated Virus	Live attenuated SARS-CoV MA- ExoN	University of North Carolina	SARS	Pre-Clinical	N/A
Inactivated Virus	ISCV	Sinovac Biotech Ltd (/Beijing Kexing Bio-product), Chinese Centre for Disease Control and Prevention; Chinese Academy of Medical Sciences	SARS	Phase I	N/A

Inactivated Virus	Formalin- and UV inactivated virus vaccine	Baxter Vaccines, Austria	SARS	Pre-Clinical	N/A	

Conclusion:

In order to respond quickly and effectively to the COVID-19 pandemic, a broad range of candidate COVID-19 vaccines are being investigated globally using various technologies and platforms. These include viral-vectored, protein subunit, nucleic acid (DNA, RNA), live attenuated and inactivated vaccines. Some of these candidates have entered clinical trials. There are currently more than 50 COVID-19 vaccine candidates in trials. WHO is working in collaboration with scientists, business, and global health organizations through the ACT Accelerator to speed up the pandemic response.. People most at risk will be prioritized. While working towards rolling out a safe and effective vaccine fairly, the essential public health actions must be continued to suppress transmission and reduce mortality.

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