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Medi Quest BRS Hospital

A monthly News letter from BRS Hospital

THE RACE FOR COVID VACCINE

Dr.S.Ramesh M.D.,D.C.H.
Consultant Pediatrician
BRS HOSPITAL

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Editors

Dr.B.Madhusudhan,
MS.MCh.,DNB(Plastic)

Dr.S.Ramesh,MD,DCh

28,Cathedral garden Rd,
Nungambakkam,
Chennai - 600 034.
Phone:
044 - 61434250
044 - 61434230
Email:
brsmadhu@yahoo.co.in
Web:
www.brshospital.com

The CORONA pandemic is showing no signs of abating, it has now become common knowledge that only herd immunity or an effective vaccine can halt the progress of this virus.

Herd immunity would be acquired at enormous cost to life, economy and if not an ideal solution, as this view proved detrimental in the UK and Sweden.

Asymptomatic transmission, high infection rate, long incubation period and the realization that COVID 19 could become a seasonal disease makes a vaccine an absolute necessity.

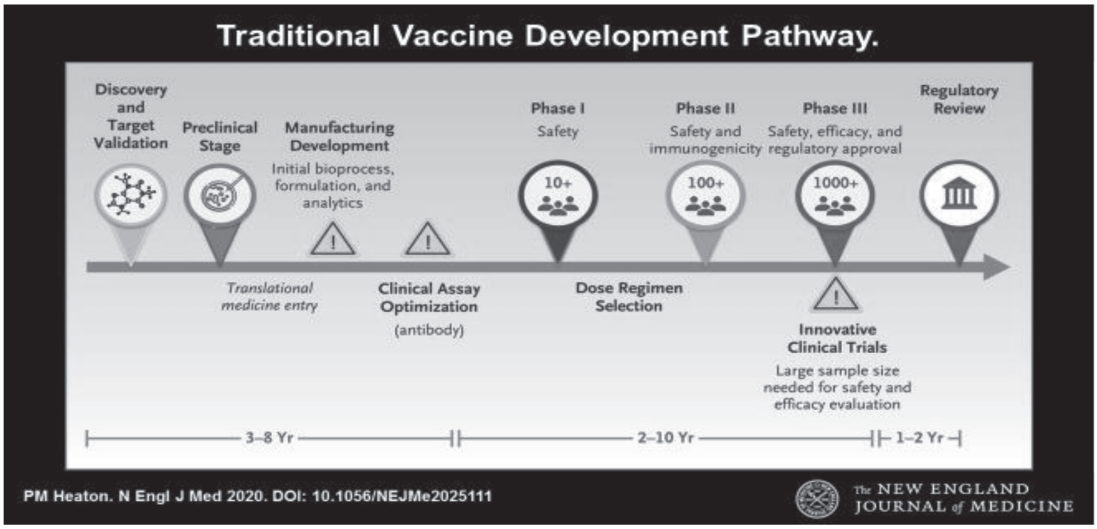
Vaccine Strategies

When designing a vaccine one needs to define the antigen, the adjuvant , the manufacturing system and the delivery strategies.

The rapid development of vaccines is possible because the genome and structural information of SARS-COV2 was made available in record time.

Further more information available from prior development SARS /MERS vaccine candidates has proved useful in the development of SARS-Cov2 vaccine.

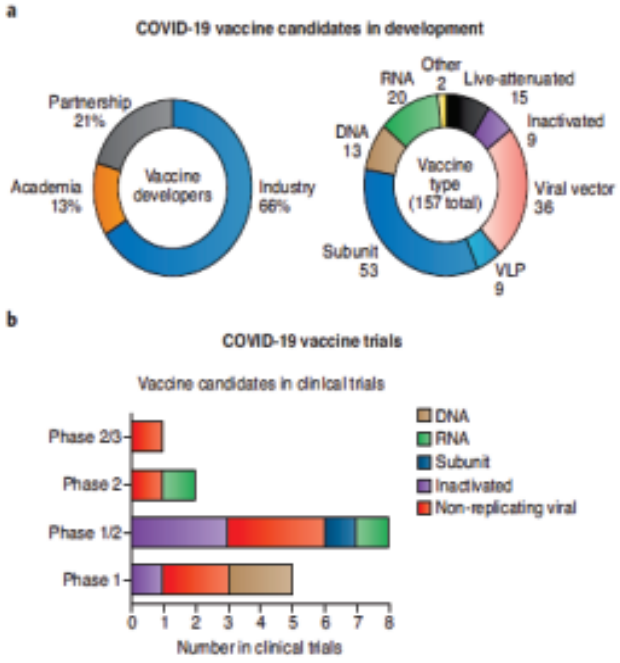
Time frame and strategies of Vaccine Trials.



Current vaccines in development

As of 1st June 2020 157 vaccine candidate are undergoing development by academic labs and industry.

They include
1. Live attenuated vaccines
2. Inactivated vaccines
3. Viral Vector Vaccine
4. Nucleic Acid based vaccines
5. Sub unit vaccines



1. Live Attenuated Vaccine:

PROS: LAV Technology is universally available
CONS: Risk of reversion to pathologic form and cold chain maintenance
Forerunner Live Atttenuated Vaccine in Development Vaccine CDX – CO5 manufactured by Codagenix Incorporation.

2. Inactivated Vaccine:

Heat or chemically inactivated pathogenes
PROS : Safer than LAV`s
CONS : But inactivation results in lower immunogenicity and requirement of multiple dose regimen.
Front Runner: SINOVAC`s vaccine.Phase Three trials are underway in Brazil.

Inactivated vaccine from India:

The front runner is Bharat Bio Tech
Inactivated vaccine developed from the Indian Strain of the novel coronavirus isolatied by NIV PUNE.

Name of vaccine: Covaxin Phase I human trials have commenced in July 2020 results are awaited.
Zydus Cadila
This company is also making an inactivated vaccine. Approved for human clinical trials progress is awaited.

3.Viral vector vaccine:

Principle : Non replicating viral vectors containing coding sequence for spike protein are the template for the vaccine. Vaccine when introduced in the human body , makes it produce the spike protein, subsequently a immune response is generated to spike protein and hence to Sars CoV-2.

ChAdOx1 n Cov-19

This is the first vaccine in Western world to reach phase 3trials. ChAdOx1 nCov-19 vaccine developed by Oxford University in Partnership with Astra Zeneca. It is a Chimpanzee adenovirus vectored vaccine expressing the SARS-Cov2 spike protein.

Phase 1/2 trials for this vaccine was done between April 23rd and May 21st 2020, 1077 participants were enrolled and assigned to receive either ChAdOx1 nCov-19 (n=534) at a dose of $5x10^{10}$ virus particles or Men ACWY (n=534). (Note: Men ACWY is a meningococcal vaccine).
10 participants assigned to non – randomized group received two doses of ChAdOx1 nCov-19 vaccine at day 1 and 28.

Findings: Local and systemic reaction were more common in the ChAdOx1 nCov-19 group and including pain, feeling feverish, chills muscle ache, headache and malaise and were reduced by use of prophylactic paracetamol. There were no serious adverse effects.

Antispike IgG responses rose by day 28 and were boosted following a second dose. Neutralizing antibody response were detected in more than 90% tested after the first does. After a booster dose, all participants had neutralizing antibodies by day 56. Neutralizing antibodies correlated strongly with antibody levels measures by ELISA.
T cell responses peaked on day 14 resulting in marked increase in spike specific effector T.Cell response
Phase 3trials for this vaccine are underway.The results of which are expected.
Serum Institute of India has partnered with Oxford University to produce the vaccine in India.

Russian Adenovector Vaccine

Two adenoviral vector vaccines are under development in Russia
i. rAd26 consists of a recombinant adenovirus vector based on the human adenovirus type 26, containing the SARS-CoV-2 S protein gene .
ii. rAd5 Component, consists of a vector based on the human adenovirus type 5, containing the SARS-CoV-2 S protein gene.
iii. Three trials were conducted .In two trials these vaccines were used separately. in a single dose.

In the third trial rAd26 was given on day 1 and rAd5given on day 21.
The results of these studies are officially anticipitated.

4.Nucleic Acid Vaccines

Nucleic Acid based vaccines deliver the genetic code for in situ production of viral proteins. This includes both mRNA and DNA vaccines.

a.Moderna's mRNA vaccine

Moderna`s vaccine (mRNA 1273) is the front runner. The candidate vaccine encodes the stabilized SARS-Cov2 spike protein (S-2P antigen)
Phase I trials of mRNA 1273 have been completed 2doses of vaccine were given on day 1 and day 28 at a dose of 25mcg, 100mcg or 250mcg.

Vaccine safety:

No serious adverse events were noted .Solicited systemic adverse events were more common after the second vaccination. Local adverse events, when present were mild or moderate.
Binding antibody IgG geometric mean titers to S-2P

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increased rapidly after the first vaccination with sero conversion in all participants by day 15.
Receptor binding domain specific antibody responses were similar in pattern.

Neutralisation Antibody response was assessed by (PsVNA) and (PRINT) assays. PsVNA response was detected in half the participants after 1st vaccination and a dose effect seen.
After second vaccination, PsVNA response was seen in all participants.
At day 43, wild type virus neutralizing activity capable of reducing SARS- Cov-2 infectivity by 80% or more by PRINT assays, was noted.

T cell Responses:

This vaccine elicited CD4 T cell responses with expression of Th1 cytokines with minimal (Th2) cytokine expression. CD8 T cell responses to S-2P were detected at low levels.
Phase 2 trial of mRNA 1273 in 600 adults evaluating doses of 50mcg and 100mcg is ongoing.
From what information we have from Phase 1 trial the investigations favour a two dose schedule.
A large phase III trial expected to evaluate a 100mcg dose is anticipated.

b.DNA vaccine:

Front runner is Inovio Pharmaceutical, with then Phase I clinical trial commenced on April 6th 2020 for COVID -19 DNA vaccine INO-4800.

5.Sub unit vaccine:

Sub unit vaccines constitute minimal structural components of SARS- Cov-2 that can prime protective immune responses. SARS-Cov-2 sub unit vaccine candidates are formulations of full length S.protein or S1/S2 sub units with adjuvants for enhanced immunogenicity.

a)From Noyavax Company NVx- Cov 2373

Preliminary immunogenicity and safety results expected in July 2020.
NVx-Cov 2373 uses recombinant nano particle technology to generate antigen from the spike protein and contains Saponin based Matrix- MTM adjuvant to enhance the immune response and stimulating neutralizing antibodies.

b)VLP vaccines:

Virus like particles are non infections multi protein structures that are engineered to self assemble from viral structural proteins. VLP mimic the conformation of authentic native viruses without being infectious, since they do not carry any viral genetic material. When presented with in a host immune system, VLP evoke effective immune response without triggering the side effects associated with the native virus.
Additionally they can be used as carrier proteins of foreign antigens, in COVID Scenario the foreign antigen are spike protein.
Medicago and iBio are using Nicotiana benthamiana (tobacco leaves) to produce VLPs using the S.Protein.

At the time time of going to press the Oxford Vaccine , Moderna's mRNA vaccine and Russian Covid Vaccines are in the front of the race. In India the results of COVAXIN are awaited eagerly.

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