Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

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Editorial

Timelines of COVID-19 vaccines

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World Health Organisation discussed the "Top Threats to Human Health in 2019," and developed a strategic plan to meet the challenges. Among the communicable diseases. Emerging and Re-emerging viral pathogens causing Global Pandemic with devastating results were emphasised. Severe Acute Respiratory Syndrome Coronavirus-2 (SARS- Cov-2) has caused a pandemic of Coronavirus disease - 19 (Covid-19) with global public health and economic crisis.[1] There is an urgent need for diagnostic and therapeutic countermeasures and rapid development of a vaccine for prevention and control of this formidable disease. Since the WHO notification of first case of this disease on 31st Dec, 2019 and a complete genome sequence of the virus on Jan 5, 2020, global attempts to produce a suitable vaccine are ongoing in scores of laboratories.

Most of the Coroviruses in humans including COVID-19 are derived from bats and there is a variable similarity between them. The whole genome sequence of COVID - 19 has about 50% similarity to that of MERS- CoV. The novel virus is a single strand RNA which attaches to the human cell using through angiotensin converting enzyme 11 (ACE-2) receptors like Middle East respiratory syndrome (MERS) and severe acute respiratory syndrome (SARS). There is a continuing evolution of this virus globally including the ones seen in Eastern India. The geographic distribution, and severity of disease and risk of subsequent waves caused by these genomic variants is currently unknown.

1. Phases of vaccine development[2,3]

Various phases of vaccine development are:

Preclinical trials are done in suitable animals for safely and efficacy by challenge studies.

Clinical Studies are made in 4 phases:

Phase I: Vaccines are given to a limited number of human volunteers with emphasis on safety and also to monitor the immune response. Phase II: This is done by vaccine administration to a few hundred volunteers of various age groups to further study safety and efficacy. Phase III: It is done by giving vaccine to thousands of volunteers to monitor protection and safety. Finally the data is analysed and evaluated for submission to regulatory authorities for approval. Phase IV: It is post-marketing surveillance for protection and any adverse events.

The whole process may take several years. However, in an emergency situation as now, it can be compressed by simultaneous phase 1 to 3 trials and scientific collaboration in various institutions. Around 200 vaccine candidates are under active development and 15 are in human clinical trials.

2. Virus vaccine candidates

1. Inactivated Virus Vaccines: virus may be inactivated by treatment with heat or a chemical but viral surface proteins are left intact. However, it may not be potent immunogenic and repeat doses may be required. Example: Salk vaccine.
2. Live attenuated vaccine: virus is modified so that it is immunogenic but avirulent (Sabin Poleo vaccine).
3. Non-replicating Viral Vector Vaccines: genes of viral proteins are identified and put into a harmless carrier virus to be delivered into the host cell which make the viral protein and stimulate immune system of the host. University of Oxford with AstraZeneca are using this approach.
4. Replicating Viral Vector Vaccines: the harmless viral vector may multiply in the host, produce copies of vaccine proteins and produce protective antibodies. Used for Ebola vaccine.
5. RNA Vaccine: RNA codes for the spike protein on the surface of COVID- 19. RNA vaccine stimulates immune system to produce protective antibodies against viral S protein.

3. DNA vaccine

Carries genetic instruction to host cells to produce RNA which in turn stimulates immune system to produce antibodies.

4. Protein subunit vaccine

The actual viral protein is injected and immune system produces corresponding protective antibodies. Novavax is using this approach.

5. Repurposed Vaccine[4–7]

Bacillus Calmette-Guerin (BCG) vaccine is a live attenuated vaccine against tuberculosis. It is the most used vaccine used in the world and ~ 85%. Children in India are vaccinated at birth. Various epidemiological studies show that it significantly reduces

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Table 1
Candidate Vaccines.

Candidate Vaccine	Sponsor	Trial Phase
AZD1222 (adenovirus ChAdox1)	The University of Oxford	II/III
mRNA-1273 (RNA based)	Moderna Inc.	II/III
BNT 162	Pfizer, BioNTech	I/II
CoronaVac: inactivated virus	SinoVac Biotech	I/II
RNA vaccine: self-amplifying	Imperial College	I/II
Inactivated vaccine	Sinopharm	I/II
BBIBP-CoRV	Sinopharm	I/II
AD5-NCoV Adenovirus 5	CanSino Biologics	I
INO 4800 (DNA-based)	Inovio	I
mRNA-based	CureVac	I
AD26. CoV–S (Adenoassociated virus 26)	Johnson & Johnson	Pre-clinical
NVX-CoV2373 (Adenoassociated virus)	Novavax	Pre-clinical

disseminated tuberculosis and its mortality in infants. This is due to protection by BCG against unrelated respiratory pathogens and neonatal sepsis. BCG activates innate cells which engulf and kill virus. (Trained Immunity). Another related organism, Mycobacterium vaccae also has protective action in mouse model and humans against tuberculosis when used for immunotherapy. BCG enhances innate immunity and may reduce viral load of COVID-19 and may reduce cytokine storm. BCG has a general boosting effect. Some ecological studies do suggest a "link between prior BCG vaccine and recorded cases of COVID-19". However, more studies are required. Professor David Levine from University of California, Berkeley states that there is a "shred of evidence" from studies in Spain and Italy that BCG may protect against COVID-19.

6. Timeline of vaccines[8–10]

As of now around 200 vaccines are under development. However, only 11 are in Phase I, 8 in Phase II and 3 in Phase II/III. Others are in preclinical phase. (Table 1).

Indian Council of Medical Research (ICMR) has partnered with Bharat Biotech International Limited for developing indigenous Covid-19 vaccine, Serum Institute of India has partnered with AstraZeneca and Oxford University to supply AZD 1222 vaccine for supply of vaccine to India.

Frantic efforts are being made to have the vaccines at the earliest. It is expected that we may have these in place by early next year. However, there are several logistical and policy dilemmas: affordability, fair distribution in various countries, priority of professional individuals, dosage, vaccine hesitancy, repeat doses, and prohibitive cost.

Declaration of Competing Interest

The author has nothing to disclose.

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