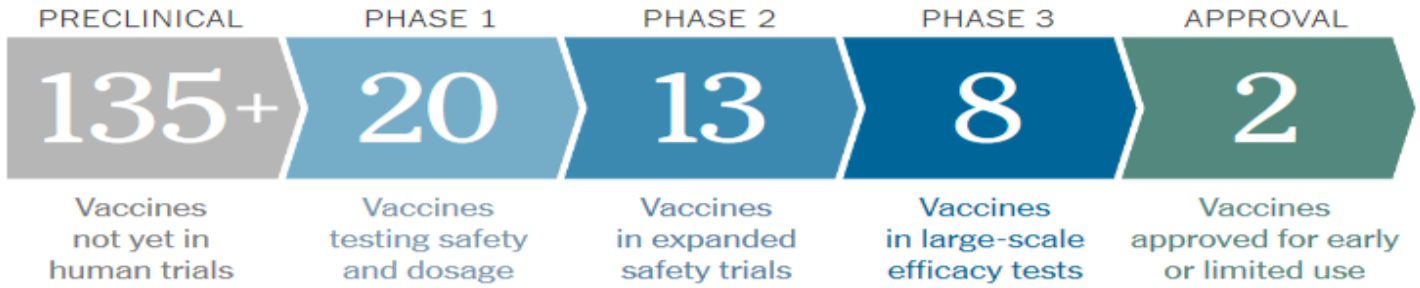
Covid 19 Vaccines

(as of August 20, 2020)

Mount Sinai Health Partners

Worldwide Current State of Vaccine Production & Testing (8/20/2020)*



APPROVED IN SELECT COUNTRIES:

1. China (July 1, 2020) CanSino Biologics - Utilizes Adenovirus 5 viral vector tech
- This company produced a successful Ebola vaccine using this technology
- Only for Chinese military currently
- Limited efficacy with side effects (17% of people with fever >101.3)

2. Russia (August 11, 2020) Gam-COVID-Vac or “Sputnik V”
- Utilizes combination Adenovirus 5 & Adenovirus 26 viral vector technology
- Fast tracked into Phase 3 without Phase 2

* New York Times

Current technologies being actively pursued to produce Vaccines:

NEW & PREVIOUSLY UNSUCCESSFUL TECHNIQUES

- Using Viral Genetic Platforms to get the Spike Protein into the host cell to then generate an immune response
  - DNA or RNA – genetic sequence for the spike protein are "forced" into the host cell – host cell mechanisms then produce the protein which then stimulates immune response
  - Viral Vectors - Using harmless viruses to carry the spike protein genetic sequence into the host cell – host cell then replicates the protein which then stimulates the immune response
    - Adenoviruses are the main vectors (5, 26 or Chimpanzee adenovirus)

PAST SUCCESSFUL TECHNIQUES BUT NOT YET WITH CORONAVIRUSES

- Protein Based Vaccines – (12 vaccines – Phases 1-2)
  - Combine Spike Protein with an adjuvant that stimulates the Immune Response
  - Existing successful vaccines – Cholera, Diphtheria/Tetanus, Hepatitis B Recombinant vaccine

- Whole Virus Weakened (7 vaccines – some in Phase 3)
  - Traditional vaccine technique – attenuated coronavirus to stimulate immune response
  - Merck – would be first oral Covid vaccine; developed approved Ebola vaccine using this technology

- "Repurposed" existing vaccine to promote general host immune response
  - BCG

Most Promising COVID-19 Vaccines

Vaccine Producer	Vaccine Type	Target	Current Phase	Results Published	Projected Available Date	References/ Comment
Moderna**	RNA	Spike protein	III Recruiting	Phase I/II	March, 2021	NEJM 2020 Jul14; NEJMoa2022483
Oxford/ Astrazenaca**	Chimp Adenovirus	Spike protein	II/III Recruiting (9/10/2020 Phase III halted in US; case of transverse myelitis)	Phase I/II	October-December 2020	Lancet 2020 Jul 20: S0140-6736(20)31604-4
CanSino**	Adenovirus 5	Spike protein	III Recruiting	Phase I/II	-	Lancet; Published online July 20,2020 https://doi.org/10.1016/S0140-6736(20)31605-6
Pfizer Bio N Tech**	RNA	Spike protein	II/III Recruiting	Phase I/II	Late 2021	

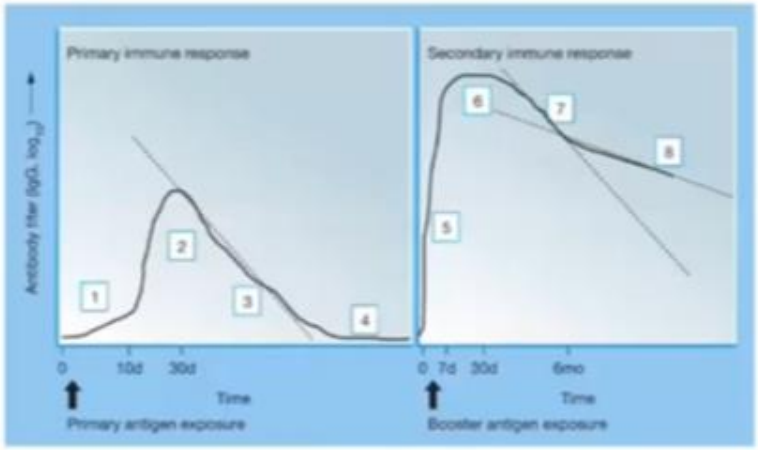
**Adverse Effects Tolerable/Neutralizing Antibody detected; Plus T cell response detected

Most Promising COVID-19 Vaccines

Vaccine Producer	Vaccine Type	Target	Current Phase	Results Published	Projected Available Date	References/ Comment
Wuhan*	Inactivated Virus Vaccine	Whole virus	III Recruiting	Phase I/II	End 2020	
Sinovac*	Inactivated Virus Vaccine	Whole virus	III Recruiting	Phase I/II		
Harvard-Deaconess J & J	Adenovirus 26	Spike	I/II Recruiting			
Murdoch Children's Inst (Australia)	BCG	--	III Recruiting			BCG may Partly Protect against Covid-19

*Adverse Effects Tolerable/Neutralizing Antibody detected

Detectable Antibody to SARS CoV2 appears to be short-lived – This is the BASIC IMMUNE RESPONSE?



Plotkin *Vaccines*, 7th edition

Antibody Immune Response

Primary Immune Response - Does not last, especially to a novel virus

Secondary Immune Response – More robust and of longer duration

T cell Immune Response

Also part of Primary Immune Response; may be of greater importance at re-exposure

Both produced by primary exposure to the virus & may quickly be undetectable

Both are there and ready to respond in the event of re-exposure

Concerns & Questions

What we know:

- Three vaccines thus far have produced neutralizing antibody & T-cell Stimulation data
  - Moderna RNA, CanSino Adeno5 & Oxford Astra Zeneca Chimp Adeno) and MORE
- May indicate that a Coronavirus vaccine in humans is possible
- Has been shown to prevent infection in lab animals (some after one dose; others require two)
- Strong neutralizing antibody response in the laboratory

What we don't know:

- Does this response in a lab test guarantee that the vaccine will prevent disease?
- **Minimal viral mutation at this time – more broad based vaccines might offer more protection vs Spike Protein specific vaccines**
- Will the mild side effect profile continue when more patients receive the vaccine?
- What will the efficacy be in real world trials? How long does the immune response last?
- Who goes first?
- Ethically cannot deliberately expose healthy people to the virus to determine infection prevention – rely on the ongoing prevalence of CoVid-19 to determine efficacy (since we do not have a TREATMENT for the infection should the person get sick)

And Perhaps MOST IMPORTANTLY- Will People agree to GET the Vaccine?

- Recent estimate by UCSF that 50% of people considering declining the vaccine
- BUT Phase III recruitment trials around the world have already achieved many of the target number of patients

Appendix

Genetic Virus Vaccines

Process:

- Introduce DNA or RNA sequences with the instructions for making spike protein into the host cell
- Genetic material is “zapped” into the cell using electroporation (validated technology which briefly opens up pores in the cell membrane)
- Host cell mechanism then produces the spike protein (harmless without the virus attached)
- These proteins then provoke an immune response
- NO evidence that this genetic material alters host genetic code

DNA/mRNA vaccines track record:

  - Technology has been around for decades
  - Some success in licensed vaccines for pigs, dogs, poultry
  - Attempted in humans against HIV, flu, malaria vaccines- NONE successfully

Status of two RNA based vaccines with further along:

  - Moderna – Phase III recruiting; July data showing neutralizing antibody
  - Pfizer Bio N Tech – Phase I recruiting

Viral Vector Vaccines

Process:

- Use harmless Virus to carry the Coronavirus genetic sequence instructions into the host cell
- Host cell then produces the Spike protein which then provokes an immune response
- Merck developed an oral version using this technology for Ebola

Viral Vectors used:

- Adenovirus 5
  - Common Adenovirus; many people have antibody against this
  - Higher dose needed to prompt immune response (with more side effects; may not last?)
  - CanSino Biologics – Version approved for Chinese Military; other version in Phase I/II recruiting; has neutralizing antibody data July 20, 2020
- Adenovirus 26
  - Less common virus; lower dose needed; more favorable side effect profile
  - Harvard/Deaconess Johnson & Johnson vaccine – Phase I/II combined
- Chimpanzee Adenovirus
  - Oxford Astra-Zeneca – Phase III recruiting; has neutralizing antibody data

Other Vaccine Technologies:

Protein Based Vaccines

- Combine Spike Protein onto Microscopic Particles and use of adjuvants stimulate a deep immune response
- Hepatitis B Recombinant Vaccine is based on this technology – Antigen from Human Plasma
- Novavax – Recombinant whole Spike Protein + Adjuvant
- Currently in Phase I/II Recruiting

Attenuated or Inactivated Whole Virus

- Produce a weakened virus grown in cell culture and inject into the host to generate an antibody response
- Each year need to repeat this process: example Flu vaccine
- But also to produce all other vaccines live or attenuated/dead

Repurposed

- BCG to promote a general immune response that in turn leads to temporary enhanced protection

Sources: Will update

- VuMedi
- Source: COVID-19 Vaccine Update: When Can We Really Expect it?
- Amesh Adalja, MD
  Johns Hopkins Bloomberg School of Public Health, Baltimore, MD
- NYT Coronavirus Tracker updates