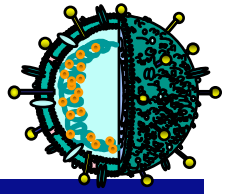

Coronavirus Vaccines

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Introduction

-When this course commenced at the beginning of the pandemic, there was no FDA-approved vaccine for any human coronaviruses.

-Less than a year later, there are many vaccines available for COVID-19. The speed by which the entire vaccine development process takes from preclinical and clinical trials to FDA-approval is indeed unprecedented. Because of these rapid developments, the materials I provided in the original lecture become essentially obsolete.

-As a result, the focus of this topic will be shifted to 3 areas:

1) What types of vaccines are currently available or still under development and how do they work?
2) What are the advantage, disadvantage, efficacy and side effect of various types of COVID-19 vaccines?
3) What are the consideration and concern with regard to the duration of protection, efficacy against SARS-CoV-2 variants, etc.?

-Additional information about COVID-19 vaccine can be found at:

https://www.cdc.gov/vaccines/covid-19/index.html

Types of Vaccines for COVID-19

-There are **Four** main types of COVID-19 vaccines in development:

1) mRNA vaccines

2) Vector vaccines

3) Protein subunit vaccines

4) Whole, inactivated SARS-CoV-2 vaccines

1. mRNA vaccines

-Made by: -Pfizer
-Moderna

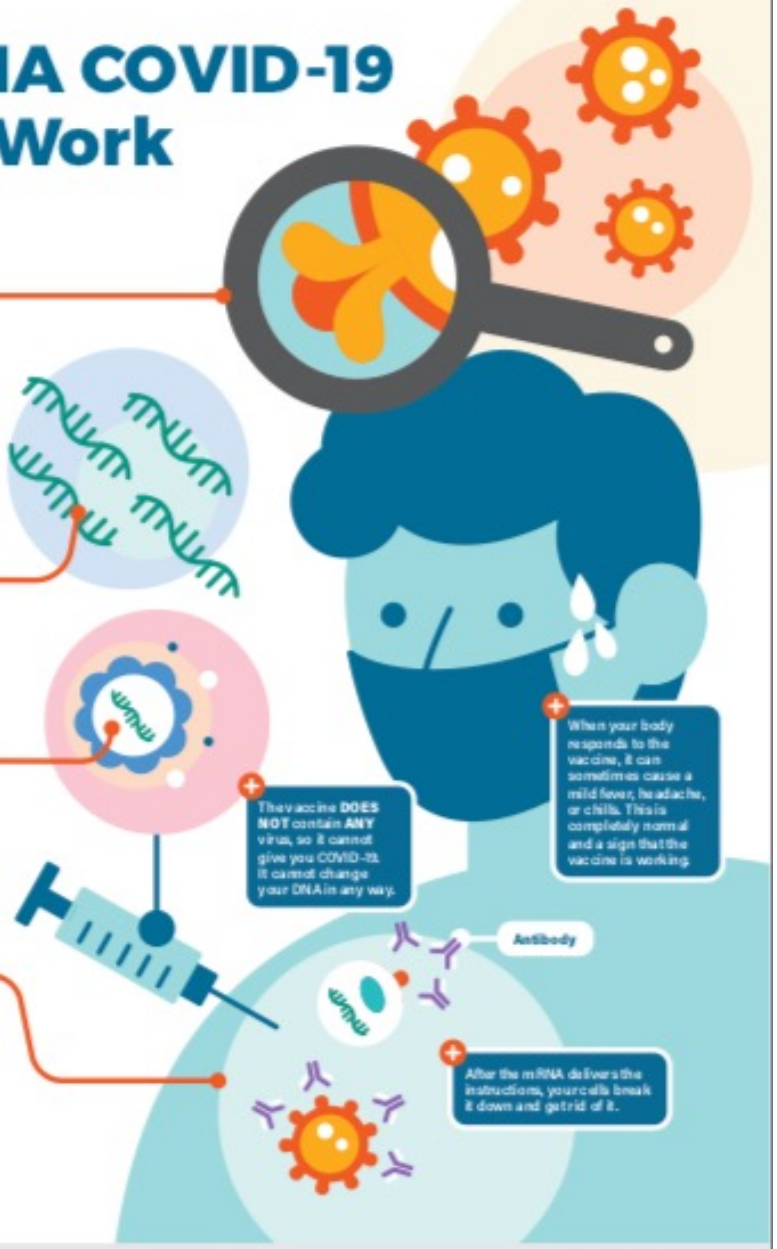
-Doses: 2

-Contains a synthetic mRNA coding for the spike protein of SARS-CoV-2.

-The mRNA is coated in soft fatty lipids to protect it and to promote its delivery into cells once administered (intra muscularly). Nevertheless, the mRNA is usually unstable and can be easily degraded. That is why mRNA vaccines need to be kept at a very low temperature.

-Upon injection, the cells take up the mRNAs and express the spike proteins, which then stimulate an immune response, generating antibodies and immune cells that protect from SARS-CoV-2 infection and/or COVID-19.

How mRNA COVID-19 Vaccines Work



Understanding the virus that causes COVID-19.

Coronaviruses, like the one that causes COVID-19, are named for the crown-like spikes on their surface, called **spike proteins**. These **spike proteins** are ideal targets for vaccines.

What is mRNA?

Messenger RNA, or mRNA, is genetic material that tells your body how to make proteins.

What is in the vaccine?

The vaccine is made of mRNA wrapped in a coating that makes delivery easy and keeps the body from damaging it.

How does the vaccine work?

The mRNA in the vaccine teaches your cells how to make copies of the **spike protein**. If you are exposed to the real virus later, your body will recognize it and know how to fight it off.

GETTING VACCINATED?

For information about COVID-19 vaccine, visit: **cdc.gov/coronavirus/vaccines**

CDC

Advantages:

-Because the spike protein is expressed inside cells, like during natural virus infection, it elicits both humoral (antibodies) and cell-mediated immunity, resulting in stronger protection.

-Because the mRNA is synthetic, the spike gene sequence can be changed easily and rapidly at any time, once the existing vaccines are found to be ineffective to a new variant.

Disadvantages:

-Because of the instability nature of mRNAs, mRNA vaccines must be kept at a very low temperature (-20 ^{o}C for Moderna's and -70 ^{o}C for Pfizer's).

-In general, mRNAs have a short half-life in the cells. Once it is translated, the mRNA is degraded. This rapid turn-over of mRNA requires multiple injections to boost immune response. The current Pfizer and Moderna mRNA vaccines require at least 2 doses.

Efficacy:

-Both Pfizer and Moderna mRNA vaccines have an excellent efficacy of protection from COVID-19, even after six months.

-Pfizer's vaccine: 95% efficacy.

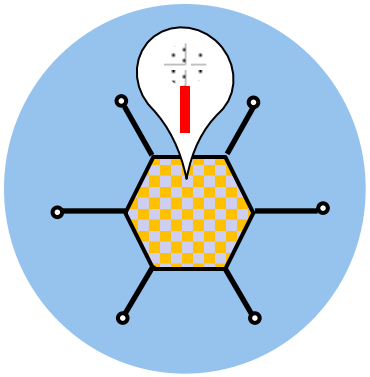
-Moderna's vaccine: 94.1% efficacy.

Side Effect:

-There is no life-threatening side effect reported so far.

-Most of the side effects are similar to mild common cold symptoms, such as tiredness, headache, muscle pain, chills, fever, and nausea.

2. Vector vaccines



-Made by: -Janssen (J&J)(Ad26)
-AstraZeneca (ChAdOx)
-Sputnik (Ad26-Ad5)
-CanSino-BIO (Ad5)

-Doses: 1-2

-Vector vaccines use weakened common cold virus (adenovirus) as a vector to carry the gene coding for the spike protein of SARS-CoV-2.

-Following injection, the recombinant adenoviruses enters the cells and express the spike protein, which then stimulates an immune response, generating antibodies and immune cells that protect from SARS-CoV-2 infection and/or COVID-19.

How Viral Vector COVID-19 Vaccines Work

Understanding the virus that causes COVID-19.

Coronaviruses, like the one that causes COVID-19, are named for the crown-like spikes on their surface, called **spike proteins**. These **spike proteins** are ideal targets for vaccines.

What is a viral vector vaccine?

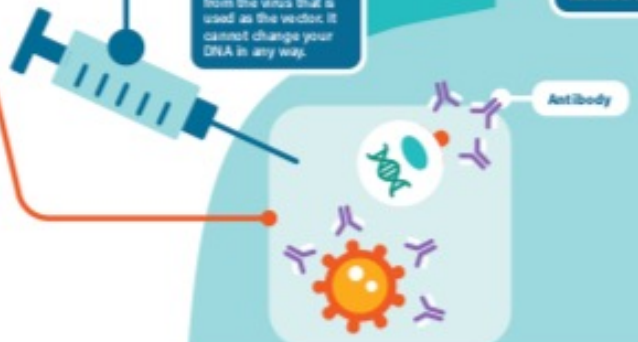
A viral vector vaccine uses a harmless version of a different virus, called a "vector," to deliver information to the body that helps it protect you.

The vaccine **DOES NOT** contain the virus that causes COVID-19 and cannot give you COVID-19. It also cannot make you sick from the virus that is used as the vector. It cannot change your DNA in any way.

When your body responds to the vaccine, it can sometimes cause tiredness, headache, muscle pain, nausea, or mild fever. These are normal signs the vaccine is working.

How does the vaccine work?

The vaccine teaches your body how to make copies of the **spike proteins**. If you are exposed to the real virus later, your body will recognize it and know how to fight it off.



GETTING VACCINATED?

For information about COVID-19 vaccine, visit **cdc.gov/coronavirus/vaccines**

CDC

Advantages:

-As vectored vaccines use a weakened adenovirus as a carrier (that is modified and cannot initiate a productive infection), expression of the spike protein would elicit both humoral (antibodies) and cell-mediated immunity, resulting in stronger protection.

-Also, as the vector virus delivers the target gene (spike) directly into cells, viral vector vaccines do no require adjuvant.

Disadvantages:

-Because viral vector vaccine elicits host immune response not only to the SARS-CoV-2 spike protein but also to vector viral proteins (antigens), use of the same vector for subsequent immunization is less effective or ineffective [Sputnik vaccine used 2 different serotypes of adenoviruses (Ad26, Ad5) for primary and boosting immunization, respectively, so to avoid this pitfall].

-Although the vector virus is weakened, it brings in other vector viral proteins that might cause side effects (in extremely rare cases).

-Require a large quantity, typically 10^{10} to 10^{11} particles, which makes large demands on the manufacturing on global scale.

Efficacy:

-J&J vaccine: 66.3% efficacy overall, 85% effective against severe forms of COVID-19. The efficacy in South Africa trial was lower, at 64%, presumably due to the B.1.351 variant in the region.

-AstraZeneca vaccine: 79% effective against symptomatic coronavirus infections and 100% effective in preventing hospitalization and severe disease. South Africa trial, conducted in ≈2000 people, found an under-25% efficacy against mild and moderate illness from B.1.351 variant.

-Sputnik vaccine: 91.6% efficacy.

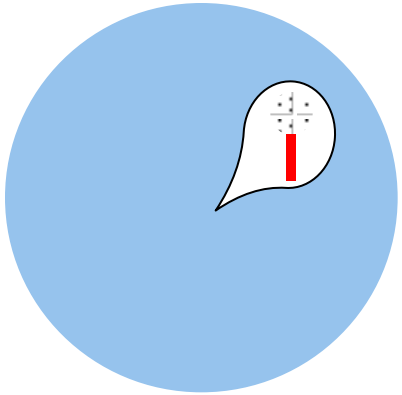
Side Effect:

-Most of the side effects are similar to mild common cold symptoms, such as tiredness, headache, muscle pain, chills, fever, and nausea.

-It was reported that there were 6 severe blood clot cases with 1 death that are associated with J&J vaccine.

-There are under 30 reported cases of serious blood clots among 20 million people given the AstraZeneca vaccine across Europe.

3. Protein Subunit Vaccines



-Made by: -Novavax
-Sanofi

-Doses: 1-2

-Protein subunit vaccines contain only the proteins or fragments of proteins of a target virus, in this case, the spike protein of SARS-CoV-2.

-Genetically engineered insect viruses (e.g. Baculovirus) containing the spike gene are used to infect moths, whose cells then produce the pieces of SARS-CoV-2 spike protein. These are harvested and purified and made into a vaccine.

Advantages:

-Elicits strong humoral immune response (neutralizing antibody production).

-Few side effects.

-Low cost, can be stored with normal refrigerated temperatures.

Disadvantages:

-May require multiple boost.

-Require adjuvants.

-Lack of T cell-mediated immunity.

Efficacy:

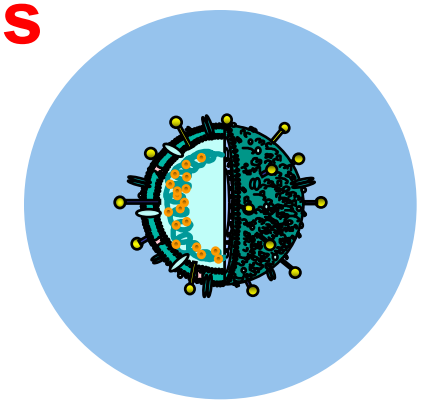
-Novavax's UK trial, with more than 15,000 participants ages 18 to 84, found that the vaccine had an efficacy of 96.4% against the disease caused by the original strain and 86.3% against the B.1.1.7 variant first identified in the UK.

Side Effect:

-There is no life-threatening side effect reported so far.

-Most of the side effects are similar to common cold symptoms.

4. Whole, Inactivated Vaccines



-Made by: -Sinovac
-Sinopharm

-Doses: 1

-Whole inactivated virus vaccines are made from the SARS-CoV-2 that are grown in cell cultures. The virus is then killed (inactivated) using a chemical or heat, and then made into a vaccine that can be injected to elicit an immune response.

Advantages:

-Elicits neutralizing antibodies.
-Simple and traditional process for making vaccine.
-Can be stored with normal refrigerated temperatures.

Disadvantages:

-Takes longer to make because batches of coronavirus must be first grown under biosafety conditions.
-Lack of T cell-mediated immunity.

Efficacy:

-The efficacy for SinoVac varies from 50.4% to 91.25% in various large-scale trial countries:

- -In Turkey: 91.25%
- -In Indonesia: 65.3%
- -In Brazil: 50.4%.

-Sinopharm vaccine: 79% effective in Phase 3 trial.

- -An interim report from the United Arab Emirates Phase 3 trial: 86% effective.

Side Effect:

-Only minor fatigue or discomfort, no more than 5%.

What Do We Know About the Current COVID-19 Vaccines So Far?

-Most of the current experimental vaccines appear effective against COVID-19, and at a minimum, in preventing severe disease, hospitalization, or death.

-Most of the current experimental vaccines have mild side effects, with common cold symptoms.

-Severe side effects are very rare, only found in a few severe blood clotting cases with 1 death associated with J&J vaccine and fewer than 30 cases with AstraZeneca vaccine, both of which use Adenovirus vector. This implies that blood clotting might be associated with the vector adenovirus, although further prove is necessary to establish this cause-effect relationship.

-Limited clinical data indicate that current vaccines are effective against several variants circulating globally, albeit with reduced efficacy at various degrees.

A Final Thought About the Future of COVID-19 Vaccines and the Evolving Landscape of the Pandemic

As a virologist studying coronaviruses over the past 30 years, I have some thoughts about the great promises and potential challenges in the development of COVID-19 vaccines:

Promises:

-With a number of efficacious vaccines currently in use and more in the pipelines and mass campaign for vaccination, herd immunity can be achieved in the not-too-distant future, at least in the developed nations, which will be critical in controlling the pandemic.

-The ability to change the spike sequence in a vaccine seamlessly and rapidly, especially for mRNA vaccines, allows an effective control of the pandemic, even for the ever-evolving SARS-CoV-2.

Potential Challenges:

-Partial immunity (which does not completely neutralize the virus and prevent infection) elicited from vaccination or natural infection will drive the virus to make more mutations in the spike proteins, as we have already seen the rise of many variants during the pandemic, which may eventually render the current vaccines ineffective.

-Without effective measures to break the transmission chain, SARS-CoV-2 will likely, unfortunately, not disappear from the human populations. This will pose a significant challenge in vaccine development at multiple levels and global scale.

-While to date we do not have enough information about the duration of protection elicited by vaccines or natural virus infection, based on previous animal coronavirus studies showing that reinfection is common and immunity is short-lived, COVID-19 vaccines likely need to be changed in the spike sequence and administered more frequently, like the flu vaccines.

With the COVID-19 Vaccines on Hand We Will Have a Better Tomorrow