COVID vaccination

Peggy L. Carver

Spike protein

RNA, the virus genetic material
Anatomy of a coronavirus

- The ‘spike protein’
  - Allows attachment to host cell
  - Alerts host immune system to fight against it (make antibodies)
  - Target of vaccines!

- Virus mutations (AKA variants)
  - UK (B.1.1.7 variant)
  - S. Africa (B.1.351 variant)
  - Brazil (P.1 variant)
  - Often due to spike protein mutations → more tight binding of spike protein to ACE2 receptor?
  - Have ↑ ‘transmissibility’ (ie can be spread more easily)
  - Have ↑ mortality?
  - Currently covered by vaccines?

ALL viruses MUTATE !!!

www.thelancet.com vol 397 Feb 6, 2021, page 462
What are the different ways to make vaccines?

<table>
<thead>
<tr>
<th>Pfizer / BioNTech</th>
<th>Moderna</th>
<th>mRNA</th>
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<tbody>
<tr>
<td>Oxford / AstraZeneca</td>
<td>Janssen (J&amp;J)</td>
<td>Adenovirus with DNA</td>
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<tr>
<td>Novavax</td>
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<td>Recombinant protein</td>
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**Examples**
- mRNA vaccines work by introducing an mRNA sequence (the molecule which tells cells what to build) to the system which is coded for a specific antigen.
- DNA vaccines use live viruses to carry DNA into human cells.
- Viral vector vaccines use DNA that mimics the virus but are not infectious and, therefore, not a danger. VLP has been an effective way of creating vaccines against diseases such as human papillomavirus (HPV), hepatitis and malaria.
- Virus-like particle vaccines use a part of the virus, in this case the protein component. These vaccines can also be used on almost anyone, including people with weakened immune systems and long-term health problems.
- Protein sub-unit vaccines use the dead version of the virus that causes a disease.

**Traditional approach**
- Examples: flu vaccine, HiB, Polio (inj), Hep A

**Examples**
- MMR
- Varicella
- Zoster
- Yellow fever
- Hep B
- HPV
4 main approaches to COVID vaccine development

- **Genetic-code vaccines**
  - Uses genetic material to instruct cells to start making spike proteins normally found on the outside of the virus. (Pfizer/BioNTech, Moderna)

- **Viral vector vaccines**
  - Uses inactive virus (adenovirus) as a ‘Trojan horse’ to deliver genetic material from the COVID-19 virus (AstraZeneca/Oxford, J & J, CanSino, Gamaleya)

- **Subunit vaccines**
  - Uses little pieces of the virus' surface, rather than a whole dead virus (Novavax)

- **Weakened/inactive vaccines**
  - Traditional approach - uses real weakened or killed virus to stimulate an immune reaction
What happens when you get the mRNA (Pfizer or Moderna) vaccine?

- In our bodies, our naturally created mRNA (messenger RNA) acts like a ‘recipe’ to tell our cells how to make specific proteins.
- The COVID-19 vaccine will not alter your DNA, nor does it enter the nucleus of your cells.
- The mRNA COVID-19 vaccine (Pfizer or Moderna)
  - delivers a ‘recipe’ (lab-developed mRNA) to your cells on how to make the spike protein, telling your body to be on the lookout for the spike protein and to develop an immune response to defeat it. Then, your natural cell processes take over.
  - Within days, the mRNA from the vaccine is destroyed by our cells, leaving no permanent mark on our bodies.
  - After receiving both doses of the vaccine, your body will be prepared to identify and attack the SARS-CoV-2 virus, if it ever enters your system.

What happens when you get the adenovirus (J&J) vaccine

- The adenovirus pushes its DNA into the nucleus of the cell.
- The DNA (gene) for the coronavirus spike protein can be read by the cell and copied into mRNA.
- mRNA leaves the nucleus & the cell reads the mRNA sequence to begin making & assembling viral spike proteins.

What happens when you get the adenovirus (J&J) vaccine

- mRNA leaves the nucleus
- Cell’s molecules read mRNA sequence & begin assembling spike proteins
- Spike proteins, & fragments, go to the cell surface
- The host immune system is alerted by spike proteins to activate immune cells to make antibodies

The Journey of a Vaccine

How a new vaccine is developed, approved, and manufactured

The U.S. Food and Drug Administration (FDA) sets rules for the four phases of clinical research so that researchers can learn about the effects of new therapies while keeping volunteers safe. This includes trials of new vaccines to protect against infection; researchers always test vaccines with adults first.

Phase 1

20-100 healthy volunteers

Researchers try to answer these questions:
- Is this vaccine safe?
- Are there any serious side effects?
- How does the vaccine dose relate to any side effects?
- Is the vaccine causing an immune response?

Phase 2

Several hundred volunteers

Researchers try to answer these questions:
- What are the most common short-term side effects of the vaccine?
- What is the body’s immune response?
- Are there signs that the vaccine is protective?

Phase 3

One thousand or more volunteers

Researchers try to answer these questions:
- How do disease rates compare between people who get the vaccine and those who do not?
- How well can the vaccine protect people from disease?

FDA approves a vaccine only if:
- It is safe and effective
- Its benefits outweigh the risks

Phase 4

Treatment is approved by the FDA and made available to the general public.

FDA closely monitors the safety of the vaccine after the public begins using it. Researchers continue to collect data on the vaccine’s long-term benefits and side effects.

Emergency use approval (EUA)
<table>
<thead>
<tr>
<th>Symptomatic COVID</th>
<th>Pfizer / BioNTech</th>
<th>Moderna</th>
<th>Oxford / AstraZeneca</th>
<th>Janssen (J&amp;J)</th>
<th>Novavax</th>
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<tbody>
<tr>
<td>Efficacy</td>
<td>mRNA</td>
<td>mRNA</td>
<td>Adenovirus</td>
<td>Adenovirus</td>
<td>Recombinant protein</td>
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<tr>
<td>original strain</td>
<td>• 95%</td>
<td>• 94.1%</td>
<td>• 62% (SD/SD)</td>
<td>• 72%</td>
<td>• 95.6%</td>
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<td>• 85% 15-28 days after 1st dose</td>
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<td>• 90% (LD/SD)</td>
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<tr>
<td>B1.1.7 variant (UK)</td>
<td>• No impact on efficacy</td>
<td>• Predicted to have no impact</td>
<td>• Predicted to have no impact</td>
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<td>• 85.6% efficacy</td>
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<td>• 0.8-1.46-fold ↓ in neutralizing antibodies</td>
<td>• 6-fold ↓ in neutralizing antibodies</td>
<td>• ~10% efficacy (minimal protection vs mild &amp; moderate COVID)</td>
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<td>B.1.351 variant (S. Africa)</td>
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<td>• 85% after 28 days; 100% after 49 days</td>
<td>• 57% efficacy</td>
<td>• 60% efficacy among HIV- study subjects; 49.5% efficacy vs HI+ &amp; HIV- subjects</td>
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<tr>
<td>Severe COVID</td>
<td>Effectiveness</td>
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<td>1 or 2</td>
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<td>(4 weeks apart)</td>
<td>(4 weeks apart)</td>
<td>(depending on study trial)</td>
<td>(3 weeks apart)</td>
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<tr>
<td>storage</td>
<td>-70°C (-25 to -15°C not yet FDA approved)</td>
<td>-20°C (-25 to -15°C not yet FDA approved)</td>
<td>Regular frig</td>
<td>1-2°C</td>
<td>2-8°C</td>
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<tr>
<td>USA approval status</td>
<td>Emergency use approval (EUA) in Dec 2020</td>
<td>Emergency use approval (EUA) in Dec 2020</td>
<td>In middle of Phase III trial in USA</td>
<td>Meeting for FDA approval Feb 26th</td>
<td>In middle of Phase III trial in USA</td>
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<tr>
<td>Pregnancy</td>
<td>USA/global enrollment in 18+ y/o ongoing</td>
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<td>Pediatric</td>
<td>USA Enrollment complete Dec ’20 (2000 12-15 y/o)</td>
<td>USA Enrollment open (3000 12-17 y/o)</td>
<td>UK Enrollment open (300 age 12+ and 6-12 y/o)</td>
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Adapted from "Your local epidemiologist" [https://yourlocalepidemiologist.com/](https://yourlocalepidemiologist.com/)

LD=low dose; SD=standard dose
Side effects of COVID vaccines

- Rare: anaphylaxis
  - Usually seen with pre-existing PEG (polyethylene glycol) or polysorbate allergy
  - Occurs very quickly after vaccination (so, we monitor for 15-30 minutes after giving vaccine)

Common side effects

On the arm where you got the shot:
- Pain
- Swelling

Throughout the rest of your body:
- Fever
- Chills
- Tiredness
- Headache

Helpful tips

If you have pain or discomfort, talk to your doctor about taking over-the-counter medicine, such as ibuprofen, aspirin, antihistamines, or acetaminophen, for any pain and discomfort you may experience after getting vaccinated. You can take these medications to relieve post-vaccination side effects if you have no other medical reasons that prevent you from taking these medications normally. It is not recommended you take these medicines before vaccination for the purpose of trying to prevent side effects, because it is not known how these medications may impact how well the vaccine works.

To reduce pain and discomfort where you got the shot:
- Apply a clean, cool, wet washcloth over the area.
- Use or exercise your arm.

To reduce discomfort from fever:
- Drink plenty of fluids.
- Dress lightly.

When to call the doctor

In most cases, discomfort from fever or pain is normal. Contact your doctor or healthcare provider:
- If the redness or tenderness where you got the shot increases after 24 hours
- If your side effects are worrying you or do not seem to be going away after a few days

Taking pain relievers (Tylenol, ibuprofen, etc) before / after vaccination

- It is recommended **not to take pain relievers PRIOR to vaccination**. Having said that, the minimum data we have is in kids with other vaccines, and the immune response with COVID is different (which, could be good or bad).

- Given the common incidence of fever and/or pain after the COVID vaccine, a lot of study patients likely took it (even if told not to in the protocol…) and they had great responses.

- **After** vaccination it is thought to be OK to take pain relievers, but there is little data on timing. (For that matter, we have little data on this even with regular (nonCOVID) vaccines.)

Symptomatic pregnant women with COVID-19 have an ↑ risk of more severe illness

- Pregnant women are at ↑ risk:
  - ICU admission
  - need for mechanical ventilation
  - death
- COVID-19 (infection or vaccine) does not cause infertility or miscarriages
  - Antibodies to COVID-19 spike protein (from getting the virus or from getting vaccinated) have not been linked to infertility
  - No ↑ risk of miscarriage with COVID-19 during pregnancy
  - The virus’ spike protein does not attach to the placenta and cause miscarriage.

Vaccination during pregnancy or breastfeeding

- The mRNA vaccines do not contain virus particles.
  - Within hours or days our bodies eliminate mRNA particles used in the vaccine, so these particles are unlikely to reach or cross the placenta.
  - The immunity that a pregnant individual generates from vaccination can cross the placenta, and may help to keep the baby safe after birth.

- Vaccines currently available under EUA
  - Vaccine trials did not deliberately include pregnant or breastfeeding individuals
  - A trial is ongoing.
  - There are no safety data specific to use in pregnancy

- Should pregnant / breastfeeding women get vaccinated?
  - The CDC recommends vaccination
  - Several professional societies have advocated vaccination.
  - Pregnancy testing should not be a requirement prior to receiving any EUA-approved COVID-19 vaccine.

Would the vaccine cause you to test positive for COVID-19?

- Vaccines currently in clinical trials in the United States won’t cause you to test positive on **viral tests**, which are used to see if you have a current infection.
- ‘false positive’ results can occur with **antigen** tests, esp if users do not follow the instructions for use.
- If your body develops an immune response, which is the goal of vaccination, there is a possibility you may test positive on some **antibody** tests.
  - Antibody tests indicate you had a previous infection and that you may have some level of protection against the virus.
  - Experts are currently looking at how COVID-19 vaccination may affect **antibody** testing results.
Why are there usually 2 doses?

For those without prior COVID
- Dose # 1 ‘primes’ the immune system
- Dose # 2 induces a vigorous immune response and production of antibodies
- Dose # 2 adverse reactions > dose # 1

Better immune response
- Dose # 1 ↓ risk of symptomatic infection ~50% (Pfizer vaccine) to 80% (Moderna vaccine).
- Dose # 2 (either vaccine) ↓ risk ~95%

For those with prior COVID, dose #1 usually has more adverse reactions than dose 2

What about missing the 2nd dose?
- A delay of 3-7 days for 2nd dose is probably ok
- CDC: up to 42 days between Pfizer or Moderna doses
- UK: spacing of 12 weeks best for AstraZeneca

Concern that partial immunization could help new coronavirus variants to develop

https://www-scientificamerican-com.proxy.lib.umich.edu/article/is-it-safe-to-delay-a-second-covid-vaccine-dose/
Michigan vaccination priority groups

<table>
<thead>
<tr>
<th>Phase</th>
<th>People covered</th>
<th>Dec</th>
<th>Jan</th>
<th>Feb</th>
<th>March</th>
<th>April</th>
<th>May</th>
<th>June</th>
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<th>Oct</th>
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<th>Dec</th>
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<tr>
<td>1A</td>
<td>Healthcare workers</td>
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<td>Long term care residents and staff</td>
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<td>1B</td>
<td>75 years and over not covered in Phase 1a</td>
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<td>Prioritized Frontline Responders</td>
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<td>School and child care staff</td>
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<td>Agriculture and food processing workers</td>
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<td>Other essential frontline workers</td>
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<td>1C</td>
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<td>18-64 with COVID-19 risk factors/pre-existing</td>
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Preexisting conditions = COPD, hypertension, chronic kidney disease, heart disease, diabetes, obesity, & other high risk conditions