Questions: How do coronavirus vaccines work?
What are the differences?
Why should people get vaccinated?

Immune System Notes

- Concept of microbes/germs and microorganisms
- Microorganisms: We can't live without some; some cause diseases that can make us sick or kill us.
- In the past, people were bad at treating diseases
- Immunity
- How does the immune system work?
    - Major safeguard against infection, illness, and disease
    - Large network made up of cells, tissues, and organs
        - They work together to defend our bodies from anything that could hurt our health
    - Relies on defensive white blood cells called leukocytes
        - These come from our bone marrow
        - bone marrow → bloodstream → lymphatic system
            - The lymphatic system is a network of vessels that help to clear body toxins and waste
        - From 4,000 and 11,000 leukocytes per microliter of blood
        - Leukocytes go through your body and look for harmful signs
            - This system relies on antigens
                - Antigens--molecular traces on the surface of pathogens/foreign substances
                - Leukocytes detect antigens, and the "protective immune response" kicks in
        - Immune response relies on many different types of leukocytes to work effectively
            - classify leukocytes in two main cellular groups:
                - Phagocyte
                    - 1st, the phagocytes cause the immune response by sending macrophages and dendritic cells to the bloodstream
                        - Destroy foreign cells they encounter
                    - Allows phagocytes to identify the antigen on the foreign cells and transmit this information to Lymphocytes
                - Lymphocyte
                    - Causes the defense
                    - Group of lymphocytes called t-cells search for infected body cells

                - Kill them off
            - B-cells use info from the antigens to produce antibodies
                - Special proteins
    - Antibodies:
        - Unique matches to antigens
            - Latch onto antigens like a lock and key, destroying foreign cells
        - B cells produce millions of antibodies that go through the body to attack all of the similar foreign cells
    - High temperatures (fever) and swelling are processes that help aid the immune response
        - Warmer body temperatures = hard for bacteria and viruses to reproduce/spread
            - This is bc they're temperature sensitive
            - When body cells are damaged, they release chemicals that leak fluid into the surrounding tissue--swelling
                - Swelling attracts phagocytes
    - Immune response removes threats in very few days
        - Stops threat from escalating to dangerous levels inside your body
        - The immune system also provides long-term immunity
            - Can use info to recognize invaders/foreign cells in the future
            - Uses the antibodies to get rid of this before it affects more cells
                - This is how you develop immunity to certain diseases
    - Extra basic information:
        - Macrophages-white blood cells that swallow up/digest germs/dead/dying cells
            - Macrophages leave behind parts of invading germs (antigens) and our body identifies antigens as dangerous and uses antibodies to destroy them
        - B-lymphocytes-defensive white blood cells
            - produce antibodies--attack pieces of the virus left behind by macrophages
        - T-lymphocytes-type of defensive white blood cell
            - attack cells in the body that have been infected
- Innate immune system:
    - First line of defense against "invaders"
        - Prevents infections from gaining a solid hold over the body
        - Nonspecific--don't target specific pathogen
        - Innate--built in mechanisms of the human organism
        - Are not acquired over time and lack memory
        - Provide immediate/rapid response
    - Physical Barrier: Immune system's first defense = skin
        - Microbes are normally deflected by the skin
        - Composed of 3 layers of closely packed cells:

- Epidermis
    - Cells packed w keratin--makes the surface tough/resistant to degradation
    - Fatty acids create dry, salty, acidic environments
        - inhibits growth of some microbes/ resistant to breakdown from bacterial enzymes
        - dead cells of epidermis are shed with microbes that may be clinging to them
            - skin cells are replaced with new cells that make a new barrierInfections can occur when the skin barrier is compromised or broken
        - wound = entrance for pathogens that infect the skin tissue around it and spread
- Dermis
- hypodermis

- Physical Barriier: Inside our bodies, mucus membranes are under constant attack from microbes
    - Line our nose, throat, intestines, and urinary/digestive tracts
    - Mucus catches bad bacteria and destroys it in the stomach or gets rid of it externally--mucociliary escalator
- Mechanical defenses: flushing of urine/tears, eyelashes/eyelids
- Microbiome - Resident bacteria of skin, upper respiratory tract, gastrointestinal tract, genitourinary tract
- Cells in our body have evolved to fight off micro attackers
    - Early responders--macrophages--identify invaders and attack them
        - Give off chemical signals--cytokines--to get reinforcements like neutrophils and other natural killer cells
- Macrophages, neutrophils, and natural killer cells = innate immunity
    - Not specific
    - Sacrifice healthy tissue to contain infection
- **Confused about chemical and cellular defenses as well as pathogen recognition and phagocytosis**
    - **Chemical things that help disrupt infections:**
        - **earwax/chemicals produced in tears**
    - **Cellular:**
        - **Special cells that have little first line duties--blood cells**
- Inflammation and Fever
    - Inflammation is from collective response of chemical mediators/cellular defenses to injury/infection
    - Acute inflammation--short/localized
        - Chronic inflammation--inflammatory response does not work/ result in formation of granulomas

            - 5 cardinal signs of inflammation--erythema, edema, heat, pain, and altered function
                - from innate responses that get increased blood flow to injured/infected tissue.
            - Fever--system-wide sign of inflammation--raises body temp/stimulates immune response.
            - inflammation/fever can be harmful if inflammatory response bad
- Adaptive immune system:
    - Cells recognize what it is and have specific defenses against it
    - Vaccines have been able to eradicate diseases that were once a huge problem
    - Adaptive immunity is gained after being infected or vaccinated
    - Adaptive immunity helps protect the body from pathogens that have not been stopped by the defenses of innate immunity
    - Specific adaptive immunity
        - Once the body is exposed to certain pathogens, it will develop the ability to fight them off by memory
            - Primary response- first exposure
            - Secondary response- the later exposures that have a faster response
        - Dual system
            - Humoral immunity
            - Cellular immunity
        - Antigens are molecules that activate adaptive immunity
            - Their ability to activate adaptive immunity can differ based on its molecular class, molecular complexity and size
            - Antigens possess smaller epitopes
        - Antibodies
            - Glycoproteins found in both blood and tissue fluid
            - Heavy chains and light chains join together to form y shape
            - The “arms” of the y are known as the fab region
                - Fab: “fragment of antigen binding.”
            - Trunk of the y is the Fc region
                - Fc: “fragment of crystallization”
        - Five classes of antibodies
            - IgM, IgG, IgA, IgE, IgD
            - Their five primary functions are: neutralization, opsonization, agglutination, complement activation, and antibody-dependent cell-mediated cytotoxicity (ADCC).

    - Major Histocompatibility Complexes and Antigen presenting cells (not too sure about this)
    - T Lymphocytes and cellular immunity
        - Immature t lymphocytes produced in red bone marrow and travel to thymus

        - Thymic selection
            - 3 step process
            - What t cells mature and exit thymus and enter peripheral bloodstream
    - Lymphocytes and humoral immunity
    - Vaccines
        - Four types of adaptive immunity:
            - Natural active immunity: develops after exposure to pathogens
            - Natural passive immunity: passage of antibodies through birth
            - Artificial passive immunity: transfer of antibodies from one person (or animal) to another human
            - **Artificial active immunity: vaccines**
                - Active immunity: activation of one's own defenses
                - Passive immunity: immunity being transferred to someone
        - Herd immunity: too few individuals in a population who can get infected for the disease to spread properly
        - Variolation
            - Spreading one persons infected material to another
            - Could be risky because more fatal infections could occur
        - Vaccination
            - Developed by Edward Jenner
            - Gave patients infections materials from cowpox
        - Live attenuated vaccines and inactivated vaccines: contain whole pathogens
        - Subunit vaccines, toxoid vaccines, and conjugate vaccines: acellular components with antigens that stimulate immune response

Vaccines:

- How COVID vaccines work
    - The body is left with a store of “memory” t and b-lymphocytes
    - Can cause fever (sign of infection and adaptive immune system)
    - Takes a few weeks
    - Different types of vaccines:
        - mRNA vaccines
            - Contain material from the virus that causes COVID
            - Shows our body how to make harmless protein unique to COVID
            - Our cells make copies of the protein
                - Destroy the genetic material from the vaccine
            - Our bodies recognize the invasive protein and build t/b lymphocytes that remember how to fight the virus
        - Protein subunit vaccines
            - Have harmless pieces/proteins of the virus
                - Causes COVID instead of the entire germ

                - Bodies recognize the invasive protein--build t-lymphocytes/antibodies that remember how to fight the virus
            - Vector vaccines
                - Have modified/different version of the virus
                    - Viral vector: “Shell” of modified virus
                        - Inside--material from the virus
                - genetic material gives cells instructions to make protein (unique to COVID)
                    - our cells make copies of the protein
                    - our bodies build T/b lymphocytes that remember how to fight COVID
- Pfizer-BioNTech
    - People 12 years and older can get it (currently)
    - 2 shots are needed, given 21 days/3 weeks apart
    - You are “fully vaccinated” or “immune” 2 weeks after the second shot
- Moderna
    - People 18 and older can get it (currently)
    - 2 shots are needed, given 28 days/4 weeks apart
    - You are “fully vaccinated” or “immune” 2 weeks after the second shot
- Johnson & Johnson’s Janssen
    - People 18 and older can get it (currently)
    - Only one shot is needed
    - You are “fully vaccinated” or “immune” 2 weeks after

https://www.yalemedicine.org/news/covid-19-vaccine-comparison

3 Main vaccines: Pfizer, Moderna, J&J:
Pfizer
- 95 percent efficiency rate
- It has strict requirements for the temperature it is stored in
- Two shots-21 days apart
- Available for youngest age group (12+)
- Has triggered an allergic reaction in very few people, but cdc makes patients be monitored after getting the vaccine

- Different from the typical vaccine where you insert a disease germ into the body
- mRNA instructs our cells
- Gives a tiny piece of genetic code (mRNA) from the virus to the host cells, which teaches the cell how to make the spike proteins that you see sticking out of the coronavirus
- The spikes penetrate and infect the host cells which stimulates an immune response.
- The cells kick the spike protein into bloodstream which helps the body develop antibodies
- This helps the body develop antibodies and develop memory cells which will recognise and know how to react to the real virus.

Helpful video:
https://www.houstonmethodist.org/blog/articles/2020/dec/how-an-mrna-covid-19-vaccine-works/

Moderna

- 94.1 percent efficiency
- Two main differences from pfizer: can be shipped in standard freezer temperatures and be stored for a while, making it easier to transport. It is also slightly less effective.
- Two shots: 28 days apart
- Same requirements to monitor people as pfizer

- Works very similar to pfizer
- mRNA sends cells instructions to make the spike protein, showing the immune system how to respond to the real covid virus spike protein

Johnson and Johnson

- Easier to store then pfizer and moderna
- Only need one shot
- 72 percent efficient
- Different approach than moderna and pfizer
- A harmless common virus (adenovirus) is engineered as a shell to carry the genetic code on the spike proteins to the cells
- Once the code is inside the cells, they produce a spike protein to train the body's immune system
- This creates antibodies and memory cells that protect against the actual infection

Shots and why they work the way they do:
https://www.popsci.com/health/why-shot-arm/

- Why do we get vaccines in our arms?
    - Wouldn't it be better to get them in our tongues, like the rotavirus vaccine is a little sugar cube type thing, so the b and t-cells are closer to where the invaders would enter bc Coronavirus doesn't enter through your arm
    - Most vaccines are intramuscular injections
        - Some are given orally^^
        - Some are given subcutaneously--just underneath the skin
            - Rubella, mumps, measles
    - Why is the deltoid the place it's given?
    - Muscles have immune cells
        - Muscles make a good vaccine administration site bc of the important immune cells
            - Immune cells can recognize the antigen--or create the blueprint for producing antigens
            - The immune cells pick up the antigens and bring them to the lymph nodes

            - Carried to the lymph vessels, which transport them to the lymph nodes
                - Lymph nodes contain more immune cells that recognize the antigens from vaccines--this allows the immune system to begin creating antibodies
                - Lymph nodes are located close to the vaccine administration sites--a lot are located under the armpit, which is close to the deltoids
                    - Vaccines given in the thigh don't have to travel far to reach the lymph nodes in the groin
        - When the vaccine is injected into the muscle tissue it is "localized"
            - This allows the immune cells to alert other immune cells
    - Adjuvant--components that "enhance the immune response the the antigen"
        - Vaccines that contain adjuvants must be given in a muscle
            - If not, there can be lots of irritation/inflammation
        - Adjuvants stimulate a stronger immune response
    - Another deciding factor is the size of the muscle
        - Children under three years of age tend to get vaccinated in their thighs bc their arm muscles are not yet large enough to handle it
    - Also, it's just easier!!!!!!

Muscle tissues contain important immune cells that recognise the antigen and stimulate an immune response

Immune cells pick up antigens and present them to lymph nodes

1. Vaccine recognised by immune cells
2. Cells take antigen to lymph vessels
3. Lymph vessels carry the antigen-carrying immune cells to lymph nodes

Vaccines are put in areas close to clusters of lymph nodes

https://news.uchicago.edu/story/how-were-researchers-able-develop-covid-19-vaccines-so-quickly
https://www.cdc.gov/coronavirus/2019-ncov/vaccines/distributing/steps-ensure-safety.html

Why were the vaccines made so fast??

- Initial development
    - Developed in laboratories
    - Virus is similar to other coronaviruses so we could use the information gathered when trying to make a vaccine against those viruses towards the covid virus.
- Clinical trials
    - 3 phases of clinical trials to make sure the vaccine is safe and effective
    - 3 phases done at the same time to make the process faster

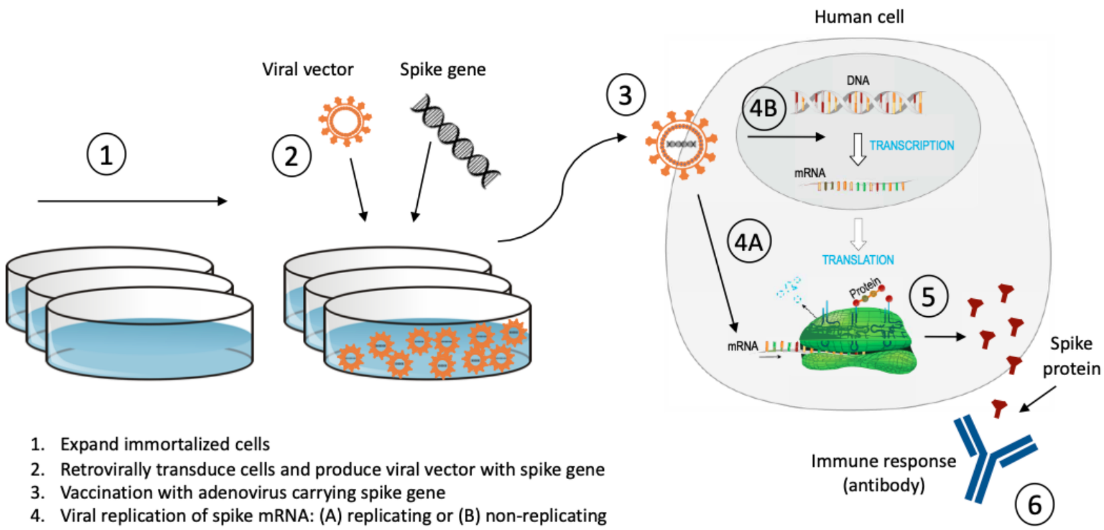
    - No phases were skipped
- Emergency use authorization
    - FDA assesses the results from clinical trials
    - Met their standards so they were granted emergency use
- Manufacturing and distribution
    - Gov invested resources
    - Manufacturing began when the vaccine was still in the third phase of clinical trials
- Tracking Safety Using Vaccine Monitoring Systems
    - After they are distributed, monitoring systems track them to ensure they are safe
    - Some people have no side effects and some people have mild side effects
    - A very small number of people had extreme reactions

- Many companies used genetically engineered common cold viruses to make COVID vaccines
    - This includes Johnson & Johnson, CanSino Biologics, and the University of Oxford--vector vaccines
    - It was believed that these would be the first vaccines to come out, but this was not true
    - *"As soon as the genetic sequence of SARS-CoV-2 was posted online in January, three groups began independently working on adenoviral vector vaccines for COVID-19: CanSino Biologics, the University of Oxford, and Johnson & Johnson. All three teams are chock full of vaccine veterans, and their COVID-19 programs have garnered global attention for their scale and speed." -Ryan Cross*

- **What do we know about the novel coronavirus's 29 proteins?**
    - Why virus more transmittable
    - 25 percent of people don't show symptoms
    - Studying the rna genome has given some clues about the virus
    - Spike proteins are the key that the virus uses to enter host cells
    - S protein hacks it's way into host cells
    - Amino acid levels of SARS-CoV and SARS-CoV-2 are similar
    - New coronavirus'

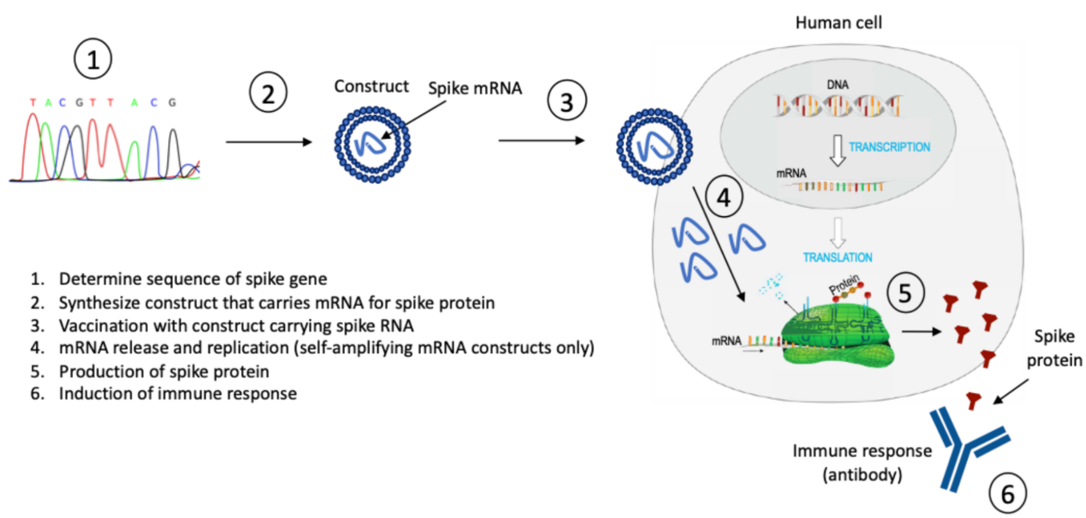
https://lozierinstitute.org/a-visual-aid-to-viral-infection-and-vaccine-production/

Viral Vector-based Vaccine



1. Expand immortalized cells
2. Retrovirally transduce cells and produce viral vector with spike gene
3. Vaccination with adenovirus carrying spike gene
4. Viral replication of spike mRNA: (A) replicating or (B) non-replicating
5. Production of spike protein
6. Induction of immune response

RNA Vaccine



1. Determine sequence of spike gene
2. Synthesize construct that carries mRNA for spike protein
3. Vaccination with construct carrying spike RNA
4. mRNA release and replication (self-amplifying mRNA constructs only)
5. Production of spike protein
6. Induction of immune response