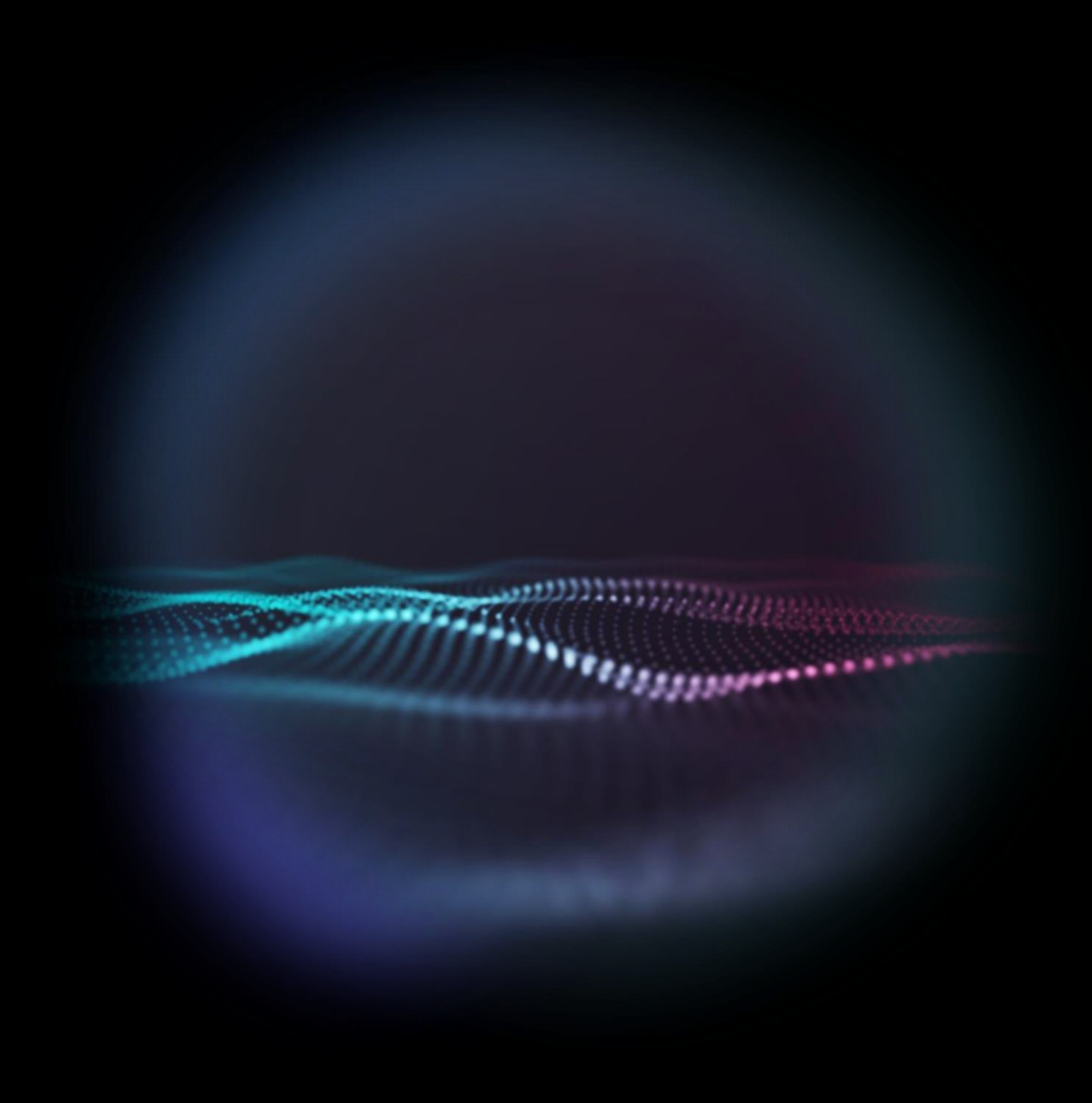

Covid-19 Vaccines

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GRAND ROUNDS LECTURE

JULY 21, 2021*

*UPDATED NOVEMBER 11, 2021

Objectives

- Understand the basics of Covid-19 epidemiology and infection
- Learn about the Covid-19 vaccines currently available (in the United States)
- Understand vaccination efficacy
- Understand vaccination side effects and explore common myths

Covid-19 Epidemiology

- Numbers via Johns Hopkins Coronavirus Resource Center Covid-19 Dashboard (as of week of 11/7/21)
- Globally
  - Cases: 250.4 million
  - Deaths: 5.1 million
- United States
  - Cases: 46.6 million
  - Deaths: 755,636

JHU Covid-19 Dashboard
https://coronavirus.jhu.edu/map.html

Covid-19 Epidemiology

- Numbers via Johns Hopkins Coronavirus Resource Center Covid-19 Dashboard (as of week of 11/7/21)
- Los Angeles
  - Cases: 1,501,527 (#1)
  - Deaths: 26740 (#1)
- Other top counties: Cook (Chicago), Maricopa (Phoenix), Miami-Dade

JHU Covid-19 Dashboard
https://coronavirus.jhu.edu/map.html

Covid-19 Infection: Symptoms

Non-specific, mimics multiple other viral and bacterial respiratory infections

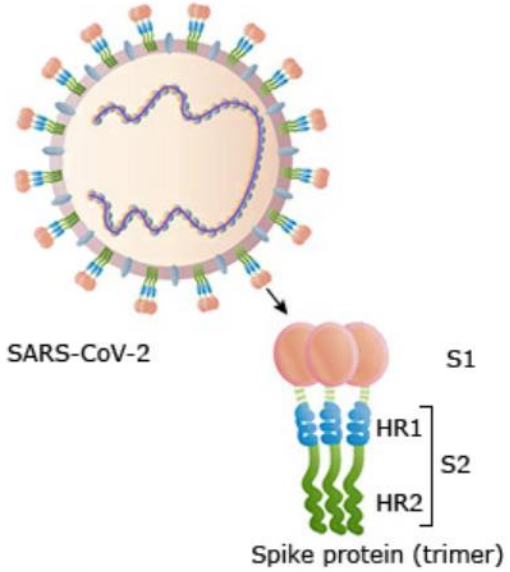
- Fever
- Cough
- Myalgias
- Shortness of breath
- Chills/rigors
- Sore throat
- Headache
- Ageusia
- Anosmia
- Diarrhea
- Nausea/vomiting
- Rhinorrhea/congestion
- Fatigue
- Confusion

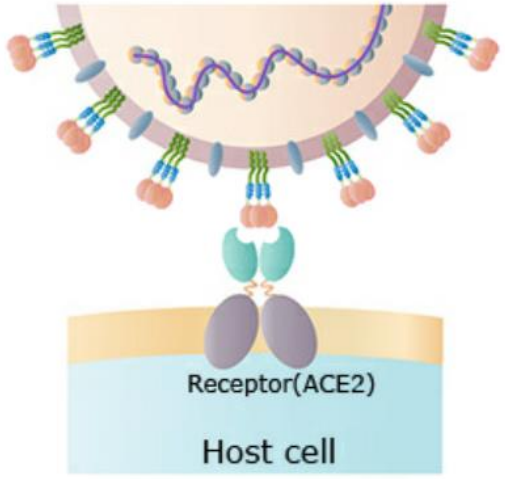
McIntosh, UpToDate 2021

Comorbidities of Severe Infection

- Cancer
- HIV
- CVA
- COPD/other lung conditions
- Diabetes
- Pregnancy
- Smoking (including prior hx)
- Heart Disease
- Immunosuppressive medications
- Organ transplant
- Substance use disorders
- Down syndrome
- Obesity/overweight
- CKD
- Dementia/other neurologic conditions
- Kids: some metabolic, neurologic, chronic conditions

McIntosh, UpToDate 2021





Covid-19 Virology

- The virus: SARS-CoV-2
  - Type of coronavirus
  - Related to SARS virus (2002-3)
  - Enveloped +strand RNA virus
- Spike protein
  - Mediates binding to host cell to initiate infection
  - Binds to host cell protein: angiotensin converting enzyme 2 (ACE2)

McIntosh, UpToDate, 2021

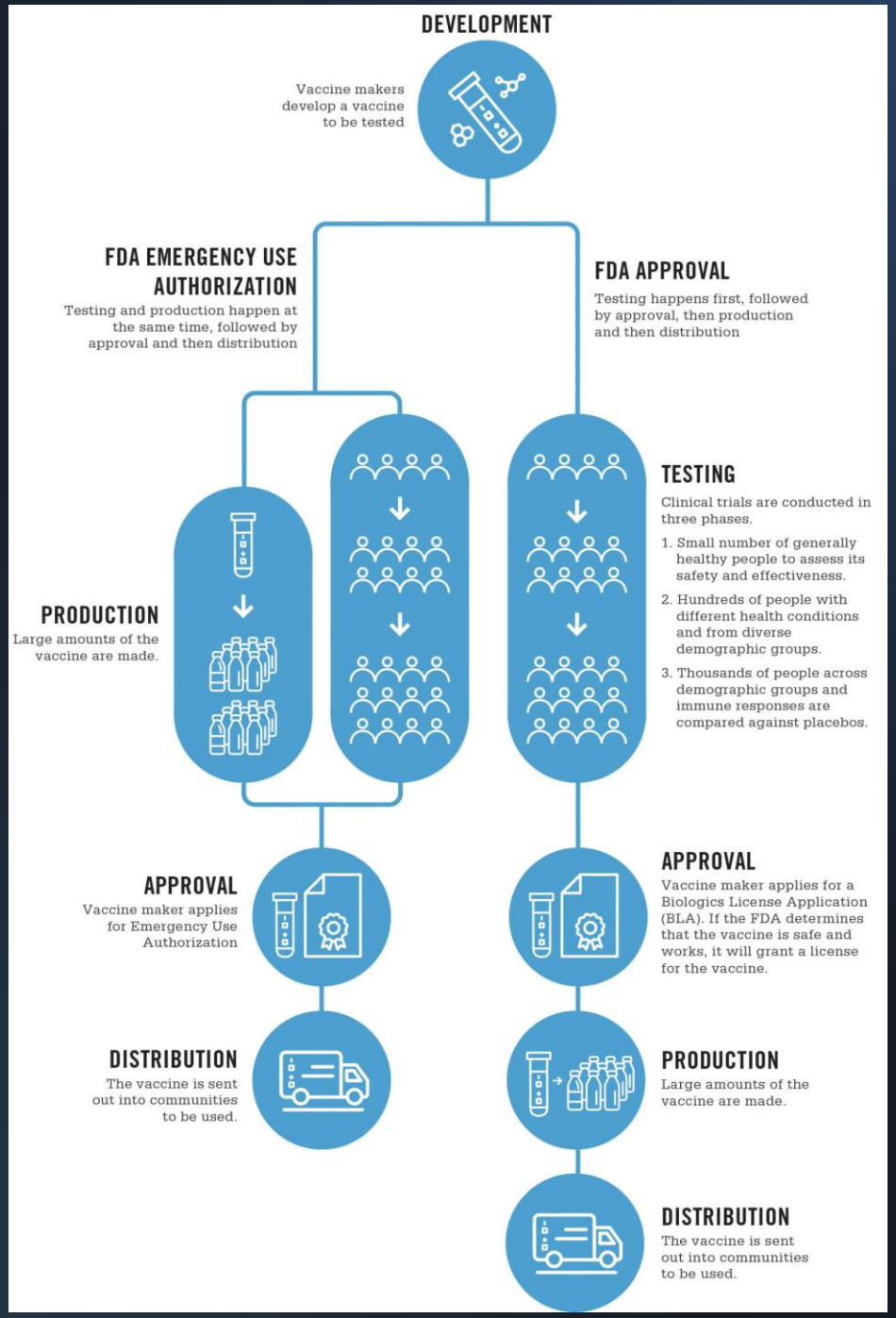
Variants

- Multiple variants of SARS-CoV-2 are currently circulating globally
  - Classified by mutations in the **spike** protein
- Variants of concern in the United States
  - B.1.1.7 (Alpha, UK), B.1.351 (Beta, South Africa), P.1 (Gamma, Japan/Brazil)
  - B.1.617.2 (**Delta**, India)→ >>**95% of current cases**
- Variants are of concern for one or more of the following
  - Increased transmissibility
  - Reduced susceptibility to neutralizing antibody treatments
  - Reduced neutralization by vaccine-induced antibodies
  - Evidence of increased disease severity

CDC, “Variant Classifications and Definitions” 7/2021

Vaccines Available in the U.S.

- Three vaccines currently approved for use in the United States by the Food and Drug Administration (FDA):
  - **Pfizer/BioNTech:** Two dose series, plus booster (ages 5 y+)
  - **Moderna:** Two dose series, plus booster (ages 18 y+)
  - **Johnson & Johnson/Janssen:** Single dose, plus booster (ages 18 y+)
- Considered fully immunized **two weeks** after initial series



Emergency Use Authorization

- Moderna and J+J covid vaccines currently in use in the US have been approved by the FDA under an emergency use authorization (EUA)
  - Due to public health emergency
- **Covid-19 vaccine fully FDA-approved (as of Aug 23, 2021)**
- This differs from standard licensing mostly in timing and duration of manufacturing and administrative procedures
  - Does NOT reduce requirements for Phase I-III clinical trials

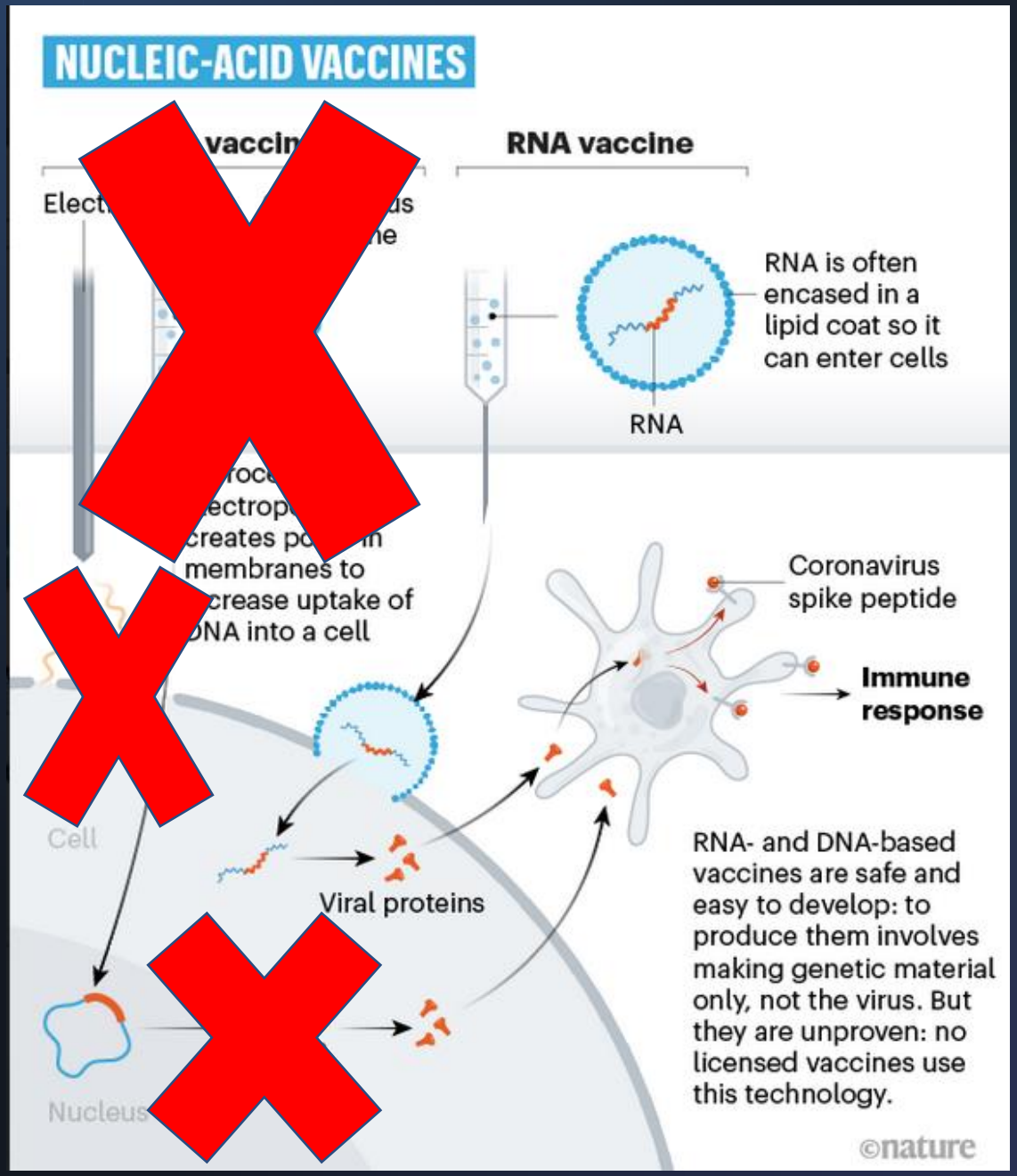
UNC Covid-19 Vaccine Hub, 2/2021

Mechanism of Action: Pfizer, Moderna

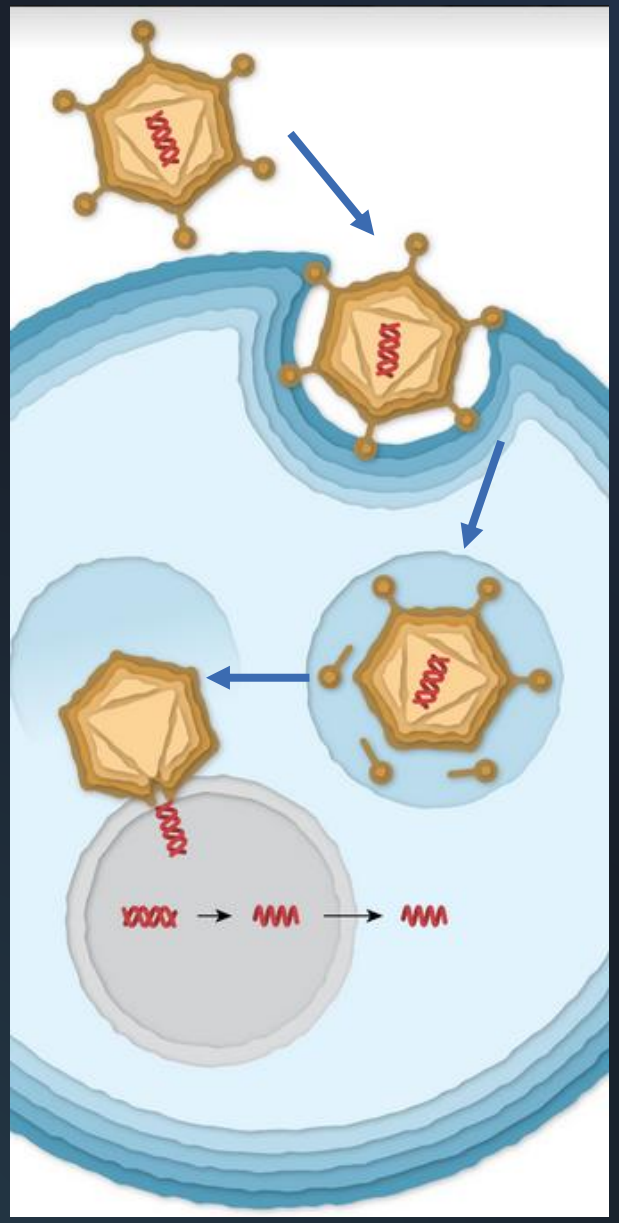
- Use **mRNA** to induce human cells to create **spike proteins** to induce antibody response
- Pfizer: 2 doses, 21 days apart, injected into deltoid, then booster at least 4-6 mo later for high-risk groups
- Moderna: 2 doses, 28 days apart, injected into deltoid, then booster at least 4-6 mo later for high-risk groups
- **Ok for booster vaccine to be of a different brand than initial series**

CDC, “Understanding mRNA Covid-19 Vaccines,” 3/2021

Mechanism of Action: mRNA Vaccines



Callaway, *Nature*, 4/2021



Graphic adapted from: Corum & Zimmer, NYTimes, 5/2021

Mechanism of Action: Johnson & Johnson

- Single-dose vaccine, injected into deltoid; then booster 4-6 mo later
- Uses attenuated **adenovirus-26 (viral vector)** to induce cells to create **spike proteins** leading to an antibody response
  - Attenuated adenovirus has DNA for spike protein incorporated into genome
  - Virus enters host cell and injects DNA into host nucleus
  - Spike protein is transcribed to mRNA
  - mRNA leaves nucleus and cell produces spike protein
  - Adenovirus vector **cannot replicate**

CDC, “Understanding Viral Vector Covid-19 Vaccines,” 4/2021

Common Side Effects

- **At injection site:** pain, erythema, swelling
  - For relief: cool compresses, move arm around
- **Systemic:** fevers, chills, myalgias, fatigue, nausea, headaches
  - For relief: hydration, acetaminophen, NSAIDs, antihistamines
  - Avoid taking meds before shot for prophylaxis
- Symptoms typically resolve within a few days
- Ok to get second shot even if you felt sick after first shot
  - Exception: severe allergic reaction

CDC, “Common SEs After…Vaccination” 6/2021

Rare Potential Side Effects: Pfizer, Moderna

- Myocarditis, pericarditis
  - Mostly affects males
  - Mostly affects those ages 30 or younger
  - Typically, mild course and responds quickly to trt
  - Rates in people ages 12-29 y (after two doses)
    - Male: 41 cases in 1,000,000 (vs 2.4 cases in ages 30+)
    - Female: 4.2 cases in 1,000,000
  - **Compared to non-infected patients, covid-19 infection overall increases risk of mycarditis 16x, for pts 16-39 y, risk is 7x higher**

Edwards & Orenstein, UpToDate, 6/2021

Rare Potential Side Effects: Johnson & Johnson

- Rare, but serious, plausible causal relationship between J&J vaccine and condition called thrombosis w/ thrombocytopenia syndrome (TTS)
  - 7 per 1,000,000 women ages 18-49
  - Rarer in men and women ages 50+
  - Similar mech to HIT, also noted w/ AstraZeneca vaccine
- Guillain-Barre Syndrome (GBS)
  - Initial studies support link, though benefits >risk, caution if hx GBS

Edwards & Orenstein, UpToDate, 6/2021 &
CDC J&J Vaccine Overview & Safety, 6/2021

Who can receive the Covid-19 vaccine?

- People as young as young as 5 years old, depending on the vaccine (as of 11/7/21)

Authorized For	Pfizer-BioNTech	Moderna	J&J / Janssen
4 years and under	No	No	No
5–11 years old	**Yes**	No	No
12–17 years old	**Yes**	No	No
18 years and older	**Yes**	**Yes**	**Yes**

CDC, “Vaccines for Children and Teens” 11/2021

Who can receive the covid-19 vaccine?

- Immunocompromised: Yes, in some cases vaccine response may be blunted→ **extra dose of vaccine recommended** (3rd of mRNA vaccine or 2nd of J+J)
- Pregnant people: Yes!
  - High risk for severe covid illness, preterm birth, and possibly other adverse birth outcomes
  - ACOG recommends that pregnant people “have access to” covid vaccines

CDC, “FAQs about Covid-19 Vaccination,” 6/2021
& ACOG Practice Advisory, 12/2020

Contraindications to vaccination

- **Not many**
- Allergy to any ingredients in vaccine (on CDC's website)
- Severe allergic response within 4 h of prior vaccine administration
  - Isolated hives >4 h after a dose unlikely due to vaccine
- Within 90 days of monoclonal antibody trt
- After illness, wait until recovered and have met criteria to end isolation
- Under 5 y of age (not currently approved)

Edwards & Orenstein, UpToDate, 6/2021

Cautions for vaccination

- GBS after prior vaccines
- Recent history of HIT/TTP
  - Consider mRNA vaccine over J&J
- Prior hx of DVT/PE, thrombophilic disorders is NOT a contraindication to getting any of the vaccines

Edwards & Orenstein, UpToDate, 6/2021

Efficacy

- Efficacy at preventing lab-confirmed covid-19 (clinical trials) (as of 7/2021)
  - Pfizer: 95% (16 y +), also 90% efficacy in reducing severe illness
  - Moderna: 94.1% (18 y+), high efficacy in reducing severe illness
  - J&J: 66.3%, but high efficacy in reducing severe illness
- All trials showed high efficacy across different racial/ethnic groups
  - Studies were majority white, non-Hispanic
  - J&J trial most diverse

CDC Covid-19 Vaccine Overview & Safety pages, 6/2021

Boosters: If you received Pfizer/Moderna

- **Should** get a booster shot:
  - Adults ≥65 years
  - Adults ≥18 years who live in long-term care facilities
  - Adults 50-64 years with certain high-risk conditions (DM, cancer, HIV, Down's, ESRD, etc→ full list on CDC website)
- **May** get a booster shot:
  - Adults 18-49 years with certain high-risk conditions (same as those listed above)
  - Adults 18-64 years in high-risk occupations (eg first responders, education staff, grocery store workers, corrections offers, postal service, etc→ full list on CDC website)
- **When to get it:** at least 6 months after 2nd dose
- **Which one:** Pfizer, Moderna, or J+J

CDC, "Covid-19 Vaccine Booster Shots," 10/2021

Boosters: If you received Johnson & Johnson

- **Should** get a booster shot:
  - Adults ages ≥18 years and older who received a prior J+J vaccine
- **When to get it:** at least 2 months after shot
- **Which one:** Pfizer, Moderna, or J+J

CDC, “Covid-19 Vaccine Booster Shots,” 10/2021

Immunocompromised people

- Moderately to severely immunocompromised people ages ≥12 years and older should may not mount an effective antibody response to initial vaccine series/dose
  - In contrast, immunocompetent people generally had excellent antibody response after initial doses
  - An **additional dose** improves immune response of initial series while a **booster dose** is for those who had good response, but immunity waned over time
- **Who is moderately to severely immunocompromised?**
  - Active cancer treatment for tumors or blood cancers
  - Organ transplant on immunosuppressive therapy
  - Active immunosuppressive therapy (eg high-dose steroids, some rheum meds)
  - Stem cell transplant within the last 2 years
  - Primary immunodeficiency syndrome (eg DiGeorge, Wiskott-Aldrich,etc)
  - Advanced or untreated HIV

CDC, “Covid-19 Vaccines for Moderately to Severely Immunocompromised People,” 10/2021

Immunocompromised people

- **When to get additional dose:** 28 days after last dose
  - In contrast to boosters, which are administered 2-6 months later
- **Which one to get**
  - **Pfizer/Moderna:** Aim to get the same one you got in the initial series (eg all should be from same manufacturer)→ if this is not logistically possible for pt, ok to mix/match
  - **J+J:** No formal recommendation on whether booster dose is necessary (presenter comment: would just tell patients for now to get a booster dose of any vaccine)
- What about boosters for immunocompromised patients?
  - Not enough data yet on needing both an additional dose and a booster; for now, additional dose 28 days later is only recommendation

CDC, “Covid-19 Vaccines for Moderately to Severely Immunocompromised People,” 10/2021

Covid-19 Vaccination Myths

- “The vaccine alters your DNA”
  - *FALSE:* The mRNA in the Pfizer/Moderna vaccines never enters the cell’s nucleus and does not interact w/ DNA in any way.
  - The J&J viral DNA does not integrate into human DNA.

- “The vaccine causes covid-19”
  - *FALSE*: No vaccines contain live covid virus, and so cannot, even theoretically, induce covid-19 infection.

CDC, “Understanding mRNA Covid-19 Vaccines,” 3/2021 & “Understanding Viral Vector Covid-19 Vaccines,” 4/2021

Covid-19 Vaccination Myths

- “I don’t need a vaccine because I was already infected”
  - *FALSE:* It is unclear how long immunity from infection lasts and some studies show vaccination boosts immunity in those who were infected.
    - Wait until isolation period over to get vaccine
- “The vaccine will effect my ability to get pregnant in the future”
  - *FALSE:* There is **absolutely no** scientific evidence backing claims that covid vaccination causes infertility. ACOG recommends vaccination to all eligible people.

CDC, “FAQs about Covid-19 Vaccination,” 6/2021
& ACOG Practice Advisory, 12/2020

Covid-19 Vaccine Distribution

(as of week of 11/7/21)

JHU Covid-19 Dashboard, 11/2021
https://coronavirus.jhu.edu/map.html

Vaccination Rates Globally

- *As of week of 11/7/21*
- 7.3 billion doses have been administered worldwide
- Most distributed doses: China (> 2 billion)
- Highest rate of fully vaccinated people: Gibraltar (97.5%)

JHU Covid-19 Dashboard & US News & World Report updated 11/2021

Vaccination Rates Locally

- *As of week of 11/7/21*
- United States
  - 57.2% fully vaccinated
  - 430.9 million doses of vaccine administered
- Los Angeles County
  - 72% fully vaccinated (85% among 65+)
  - 13.4 million doses of vaccine administered

US News & World Report/ OurWorldinData updated 11/2021 & LA County DPH 11/2021

Role of the Physician

- Recent polling suggests that 85% of people trust their personal physician
  - Rates are similar regardless of political party affiliation (NPR/Ipsos 12/2020)
- As a PCP, you can help increase vaccination rates and combat obstacles to vaccination including
  - Conspiracy theories circulating online
  - Inconsistent messaging from politicians
  - Overall vaccine hesitancy
- **Speak to your patients regularly about getting vaccinated!**

Martin, AAFP, 2/2021

Thank you!

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