The Evolution of Vaccines from Smallpox to COVID

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Learning Objectives

After this lesson you should be able to:

- Name important pioneers in the development of vaccines
- Understand why compulsory vaccination campaigns were necessary
- Distinguish between the three generations of vaccines
- Identify elements of the COVID-19 vaccine campaign

Introduction

To vaccinate is to help the immune system develop protection of a disease using microorganisms or viruses in a weakened, live or killed state. Proteins or toxins from the organism may be used.

The efficacy and safety of vaccines has been widely verified and studied. It is the most effective way of preventing infectious diseases

"vaccination" from the Latin root vaca meaning cow

History – Edward Jenner

Dr. Edward Jenner is known as the pioneer in vaccine history. In 1796 he proposed that someone who contracted cowpox would be immune to smallpox.

He tested this theory by taking cowpox vesicles and infecting an 8 year old boy, James Phipps.

Two months later he was inoculated with smallpox, and it never developed. He was not harmed in the experiment and lived to age 65.

Edward Jenner (1749–1823). Photo courtesy of the National Library of Medicine.

Jenner (continued)…

Two years later in 1798 Jenner distinguished true vs spurious cowpox and created an “arm-to-arm” technique of spreading the vaccine from the patient’s pustule (or abscess).

In the early days there was controversy from medical and religious groups. By 1801 his report was published in 6 languages and over 100,000 people were vaccinated.

The last case of naturally occurring Smallpox was by 3 year old Rahima Banu from Bangladesh in 1975. See photo.

Eradicating Smallpox

The WHO was determined to provide universal vaccinations by 1990 for the following preventable diseases: measles, poliomyelitis, diphtheria, whooping cough, tetanus, and tuberculosis. The WHO has stated measles is so infectious that 100% vaccination is necessary to control it.

Despite decades of mass vaccination campaigns against polio it remains a threat in underdeveloped countries such as India, Nigeria, Somalia, and Afghanistan.

Increasing other public health measures such as improving sanitation facilities and potable water are necessary to further reduce the risk of spreading polio.

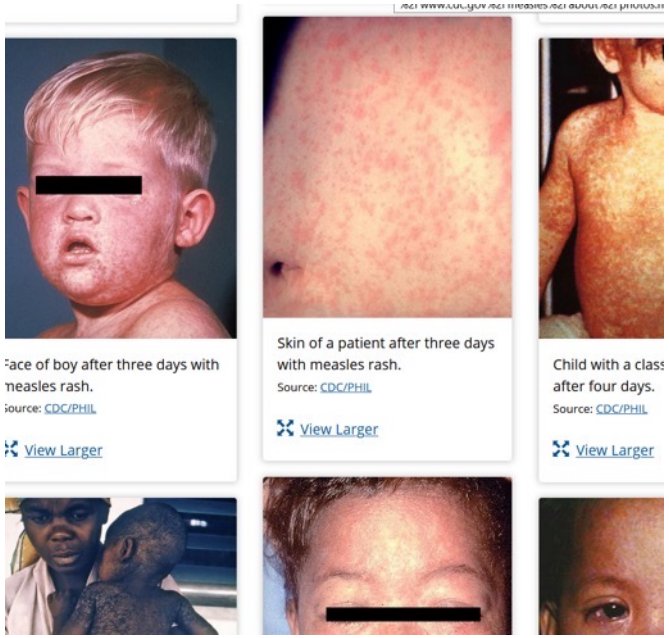


Photo Credit: https://www.cdc.gov/

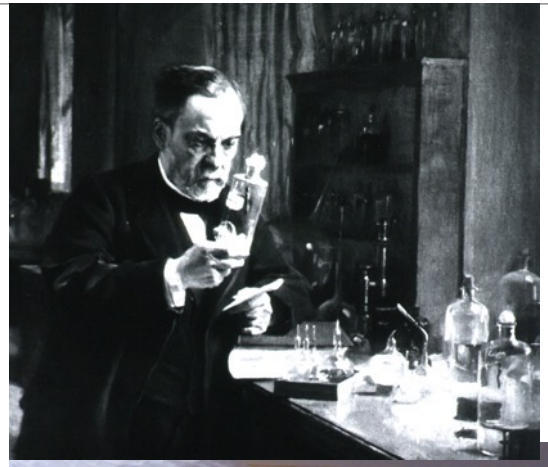
Louis Pasteur

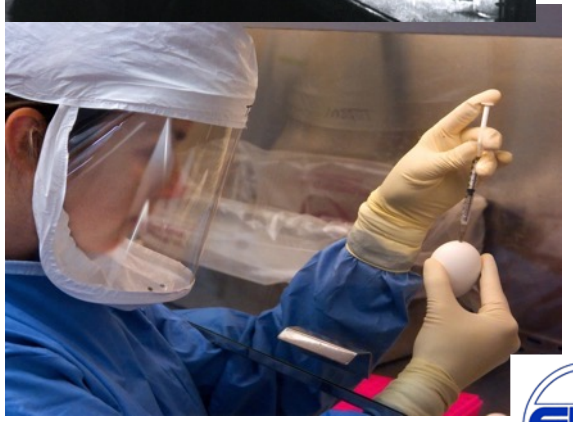
Following Jenner's success, the second generation of vaccines was introduced in the 1880s by Louis Pasteur (for chicken cholera and anthrax).

Eggs: In 1931 Alice Miles Woodruff and Emerst Goodpasture found that fowlpox could be grown in chicken eggs which led the way for scientists to develop other vaccines from eggs such as yellow fever (1935) and the influenza virus (1945).

By 1959 eggs were the standard of virus propagation and not cell cultures or growth medias.

We still have not been successful in developing vaccines for herpes simplex, malaria (mosquito borne), gonorrhea and HIV.





Revising Vaccines for Safety

The DPT vaccine was a major success in the 1950's to protect the public from diphtheria, pertussis (whooping cough), and tetanus.

It became associated with heavy side effects in the 1990's and wealthy nations become to discourage its use by anti-vaccinations campaigns.

Pertussis outbreaks later increased in many countries. Now this vaccine is called DTaP (2017) after several revisions.

Compulsory Vaccination

Ultimately the goal of vaccinating the public is to eradicate the disease or at least achieve herd immunity.

The idea is if enough of the population is vaccinated the pathogen will be contained.

Some people are not eligible for the vaccine because of medical reasons and anyone who is left, who is eligible, should be vaccinated to make up for the shortage.

Photo Credit: https://www.nlm.nih.gov/exhibition/smallpox/sp_resistance.html

Milestones in Compulsory Vaccination

Vaccination campaigns became more widespread in the early 1800's.

Sweden in 1816: smallpox mandated for children under 2.

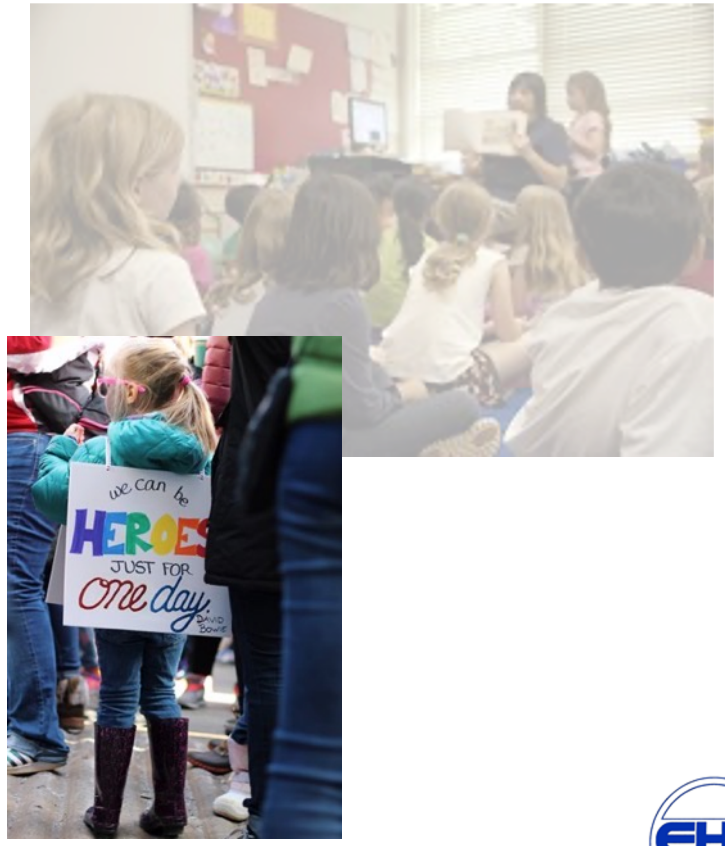
British Government in 1837: from an epidemic that caused 40,000 deaths (vaccination Act of 1840).

England and Wales in 1853: required the smallpox vaccine or face fines.

United States in 1905: in the case of Jacobson v. Massachusetts by the Supreme Court. The court stated laws can be enacted to protect our citizens from communicable diseases. *Only after WWII did compulsory vaccination laws become enforced.*

Controversy

All 50 states in the U.S. require children to receive vaccines to attend public schools (although 47 offer exemptions).



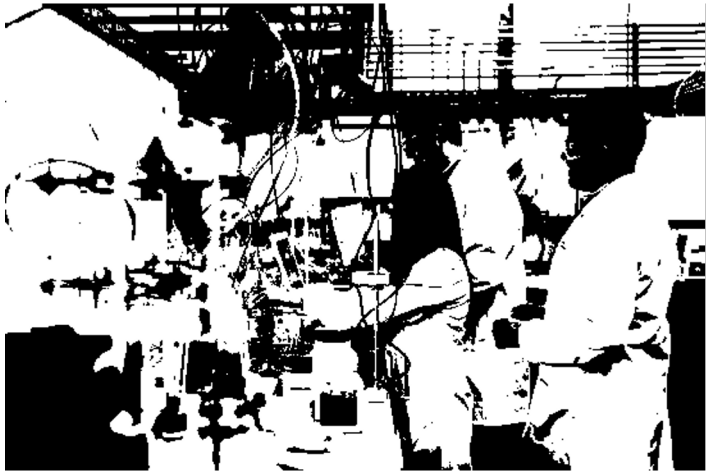
Critics say compulsory vaccination infringes on their medical legal, philosophical or religious rights. Other countries like India opposed vaccines derived from cows.

Balancing public policy over individual liberties is difficult for countries to make but ultimately the decision must be based on the greater good.

Generations of Vaccines:

First Generation: whole organism vaccines. Either live, killed or weakened forms. Live smallpox and polio vaccines introduced killer T-cell responses and helper T-cell response and antibody immunity.

Risk: attenuated forms of the pathogen can convert to danger forms and are *not suitable for those with weakened immune systems* (e.g., HIV). Killed vaccines do not have such risk and T cell responses will not always work.



Generations of Vaccines:

Second Generation: Designed to reduce risk from live vaccines. They consist of protein antigens (tetanus or diphtheria) or recombinant proteins (Heb B surface antigen). They *can* generate the T_h and antibody responses but not the killer T cell responses.

Generations of Vaccines (continued)…

Third Generation: The most current. These are RNA and DNA vaccines. Examples include the Zika virus in 2016, but to mass produce it never came to fruition. Currently studies are underway to develop against HIV with this method.

The COVID-19 vaccine was developed with this method thanks to Operation Warp Speed and the countless researchers worldwide.

CDC Common Side Effects of Any Vaccine

All vaccines have the risk of side effects. The CDC has compiled a list of the following ranked by most to least common:

1) Mild side effects (common)

Mild fever (1 in 4)

Redness, soreness, swelling at the injection site (1 in 4)

Fatigue, poor appetite (1 in 10)

Vomiting (1 in 50)

https://www.cdc.gov/vaccines/vac-gen/side-effects.htm

2) Moderate side effects (uncommon)

Seizure (1 in 14,000)

High fever (over 105 °F) (1 in 16,000)

3) Severe side effects (rare)

Serious allergic reaction (1 in 1,000,000)

Other severe problems such as seizures or brain damage have been reported but they are so rare it is not possible to determine if it was connected to the vaccine or not.

Debunking the Autism Myth

The Lancet published an article in 1998 by an author name Andrew Wakefield. He wrote that 12 patients aged 3-10 developed behavioral symptoms like autism following the MMR vaccine (measles, mumps and rubella) . There was no scientific backing on these claims, and it was later found that Wakefield falsified this information.

Later in 2004, 10 of the original 12 co-authors published a retraction and stated, “We wish to make it clear that in this paper no causal link was established between MMR vaccine and autism as the data were insufficient."

Sources: https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(04)15715-2/fulltext ;https://www.scientificamerican.com/article/straight-talk-about-vaccination/

Debunking the Autism Myth (continued)…

Despite the Lancet retracting article, there are still a substantial number of parents that believe this information. According to Scientific American (2011) 1 out of 4 parents still believe vaccines can cause autism.

To date there have been substantial and validated studies to confirm there is no connection between vaccines and autism. Correcting wrong information, even when overwhelmed with correct and comprehensive information, can be difficult. Since the Wakefield study was published over 20 years ago, Generation Z is likely to capture the latest science in their memory.

COVID-19 Vaccine

SARS-CoV-2 (severe acute respiratory syndrome coronavirus 2), the virus that causes the diseases COVID-19 was first discovered in late 2019.

After research, its genetic makeup was published January 11, 2019, prompting the world to prepare outbreak and create a vaccine.

Multiple governments and pharmaceutical companies around the world worked tirelessly for an effective vaccine.

COVID-19 Vaccine (continued)…

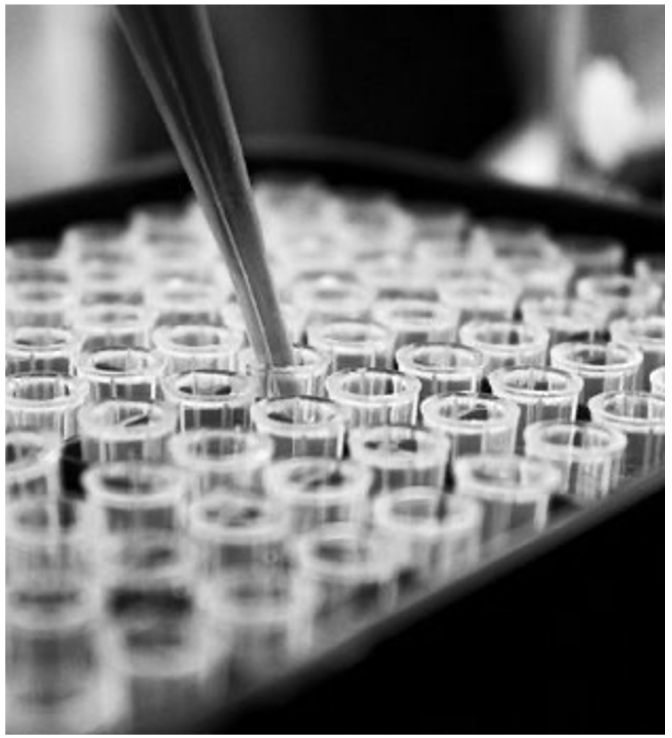
By June 2020, university research groups and international health organizations had invested tens of billions of dollars to create multiple vaccines hoping one would work.

They initially estimated it would not be available for 18 months. The Coalition for Epidemic Preparedness Innovations estimated the US accounted for 40% of this activity, 30% Asia and Australia, 26% Europe and the last amount in South America and Africa.

COVID-19 Vaccine (continued)…

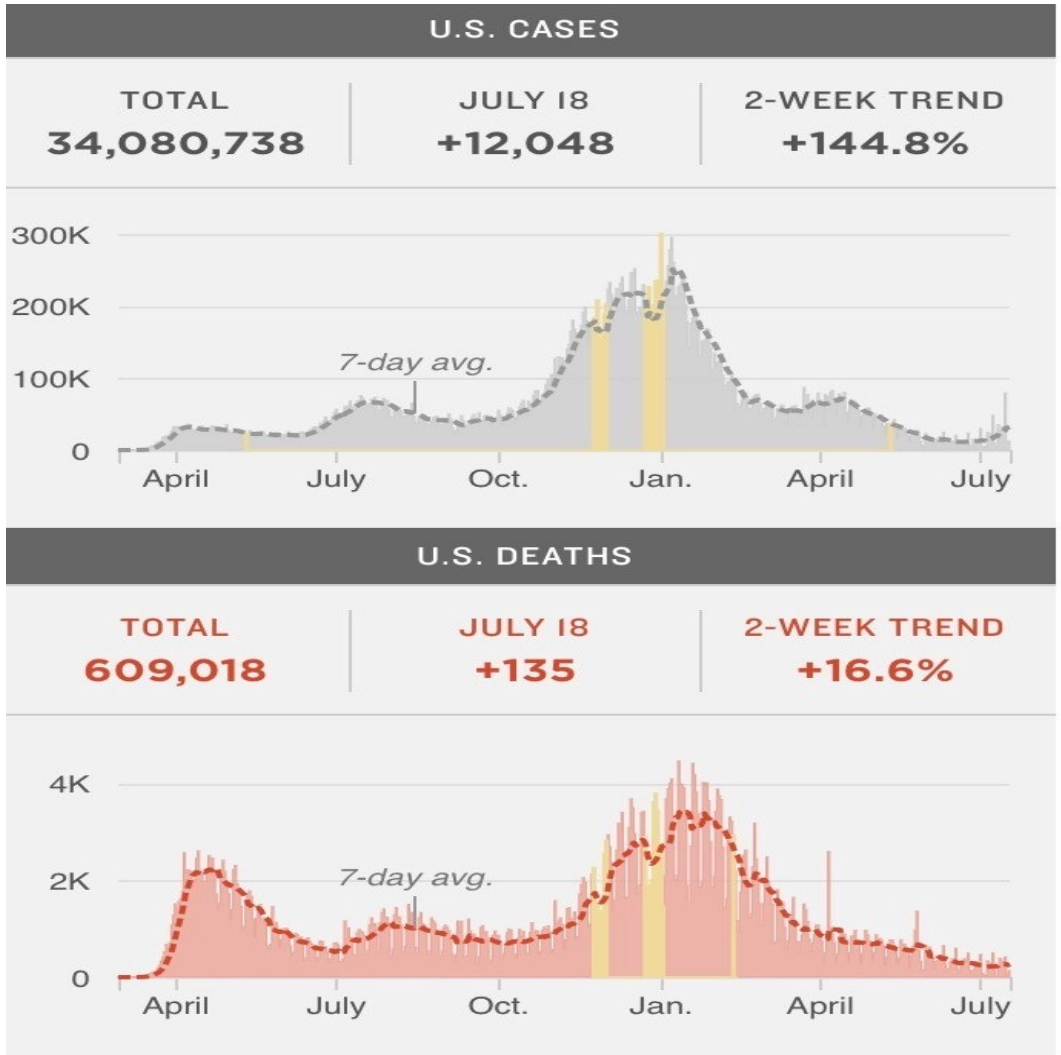
The first four vaccines human trials began in March 2020.

The Pfizer vaccine was first to be approved by (emergency use authorization) EUA for the UK on December 2, 2020, and later the FDA in the U.S. authorized EUA December 11, 2020. One week later the FDA granted EUA for the Moderna Vaccine. Johnson & Johnson would later be approved on February 27, 2021.



COVID-19 Current Update

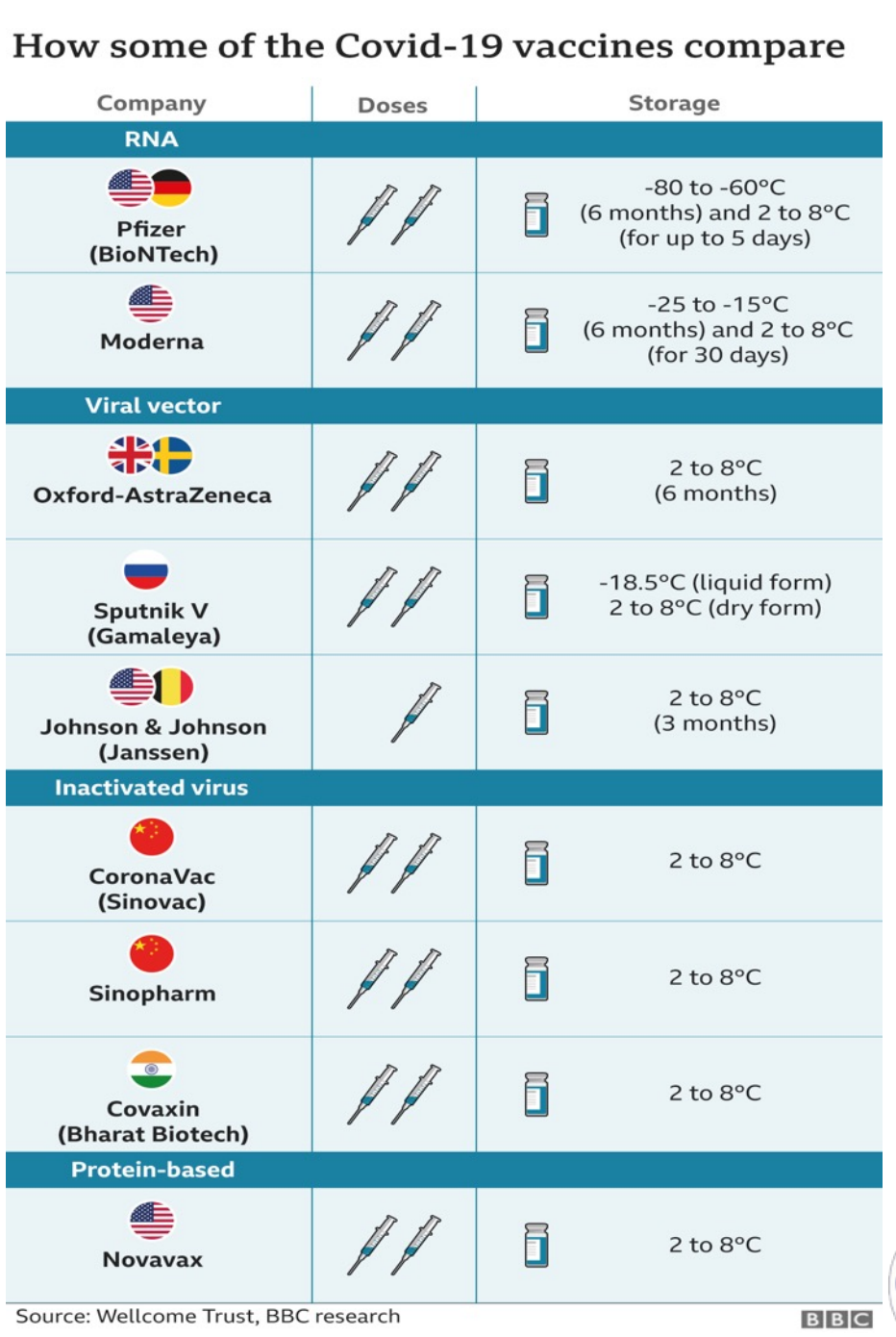
- 34 million U.S. cases total / 609,000 Deaths
- Daily cases 12K / increase 144% (peak 250K/day)
- Daily Death 135 / increase 15% (peak 4K/day)
- 53% fully vaccinated in the U.S.
- 99% new cases in unvaccinated individuals: Avg Age: 40 was 60



Vaccine Types:

- Currently approved under emergency authorization in the United States:
  - Moderna
  - Pfizer
  - Johnson and Johnson

- In approval process:
  - Novavax



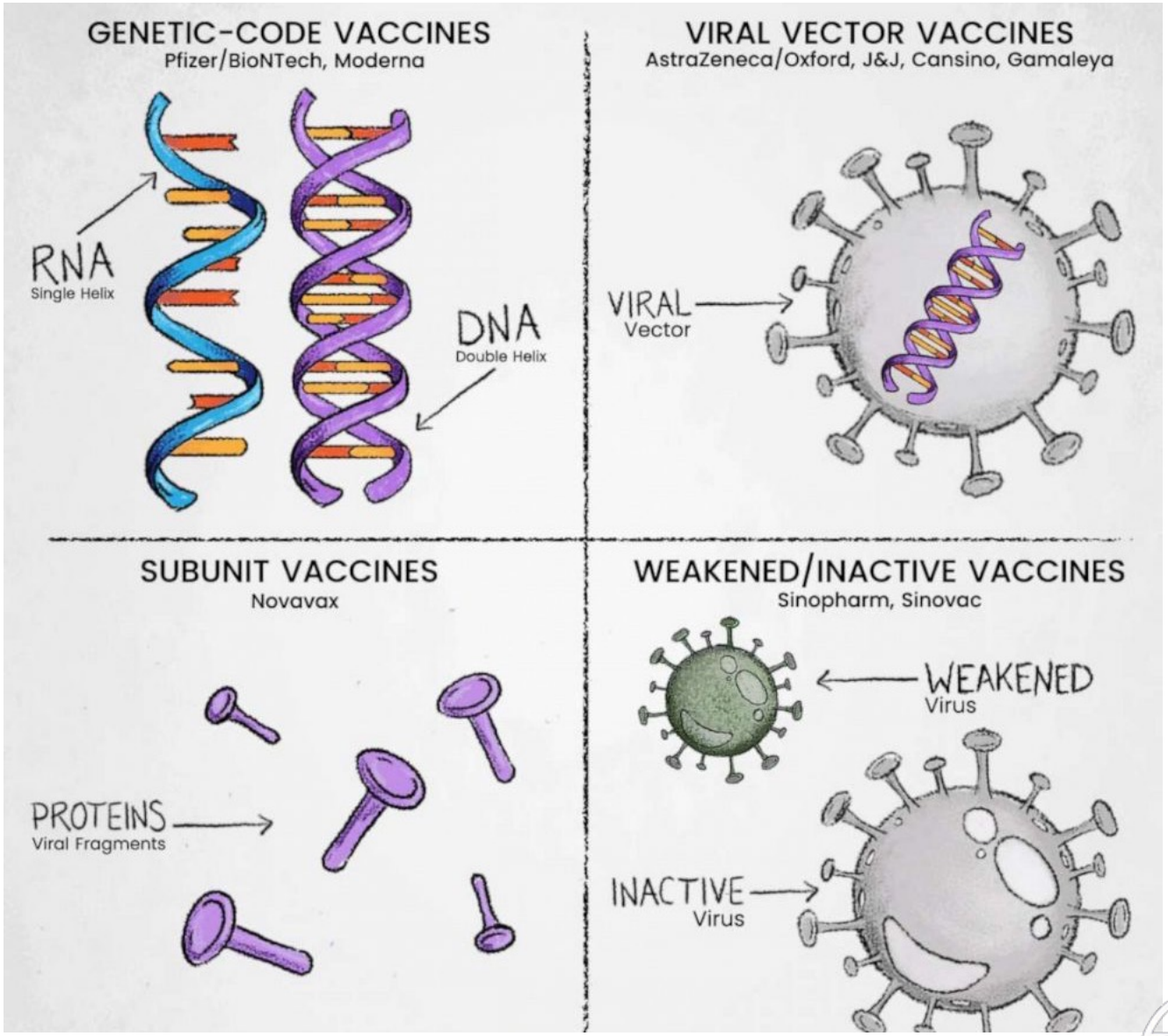
How some of the Covid-19 vaccines compare

Company	Doses	Storage
RNA		
Pfizer (BioNTech)		-80 to -60°C (6 months) and 2 to 8°C (for up to 5 days)
Moderna		-25 to -15°C (6 months) and 2 to 8°C (for 30 days)
Viral vector		
Oxford-AstraZeneca		2 to 8°C (6 months)
Sputnik V (Gamaleya)		-18.5°C (liquid form) 2 to 8°C (dry form)
Johnson & Johnson (Janssen)		2 to 8°C (3 months)
Inactivated virus		
CoronaVac (Sinovac)		2 to 8°C
Sinopharm		2 to 8°C
Covaxin (Bharat Biotech)		2 to 8°C
Protein-based		
Novavax		2 to 8°C

Source: Wellcome Trust, BBC research

BBC

Vaccine Delivery Methods



COVID-19 Vaccine development

Key Terms

- **Vaccine Efficacy**: refers to how well a vaccine performs in a carefully controlled clinical trial.
- **Vaccine Effectiveness**: describes its performance in real-world observational studies
- Evidence demonstrates that the authorized COVID-19 vaccines are both efficacious and effective against symptomatic, laboratory-confirmed COVID-19.
- Breakthrough infection in fully vaccinated individual is determined by symptoms, not a positive test.
- **Vaccine Primary Goals**
    1. Death
    2. Severe Illness

Vaccine Development

- **Animal Challenge Studies:** Rhesus macaque challenge studies provided the first evidence of the potential protective effects of Pfizer-BioNTech, Moderna, and Johnson & Johnson/Janssen COVID-19 vaccines against SARS-CoV-2 infection, including asymptomatic infection.
- **Clinical Trials (Efficacy):** subsequently demonstrated the authorized COVID-19 vaccines to be efficacious against laboratory-confirmed, symptomatic COVID-19 in adults, including severe forms of the disease, with evidence for protection against asymptomatic SARS-CoV-2 infection as well
- **Real-world vaccine effectiveness:** Multiple studies from the United States and other countries demonstrate that a two-dose COVID-19 vaccination series is highly effective against SARS-CoV-2 infection (including both symptomatic and asymptomatic infections) and sequelae including severe disease, hospitalization, and death. Early evidence for the Johnson & Johnson/Janssen vaccine also demonstrates effectiveness against COVID-19 in real-world conditions.

Vaccine Trial & Real Word Effectiveness Studies

Clinical Trials:

- All approved vaccines showed an overall efficacy of 65-95%
- Near 100% efficacy for death.
- >89% efficacy for severe illness.
- In the clinical trials, no participants who received a COVID-19 vaccine died from COVID-19; the Moderna and Johnson & Johnson/Janssen trials among adults ≥18 years each had COVID-19 deaths in the placebo arm.

Real World Effectiveness Studies:

- General Population
- Healthcare Workers
- Long-Term Health Care
- Multiple studies from the United States and other countries demonstrate that a two-dose COVID-19 vaccination series is highly effective against SARS-CoV-2 infection (including both symptomatic and asymptomatic infections) and sequelae including severe disease, hospitalization, and death.
- Major reductions in SARS-CoV-2 infections among those receiving two doses of COVID-19 vaccine even when community transmission was increasing
- Studies from the United Kingdom **found significantly reduced likelihood of transmission to household contacts from people infected with SARS-CoV-2 who were previously vaccinated for COVID-19.**

Vaccine Safety

- COVID-19 vaccines are **safe and effective**.
- Millions of people in the United States have received COVID-19 vaccines under the most intense safety monitoring in U.S. history. (338 million doses)
- VAERS accepts reports of any adverse event following any vaccination.
- Reports of adverse events to VAERS following vaccination, including deaths, do not necessarily mean that a vaccine caused a health problem.

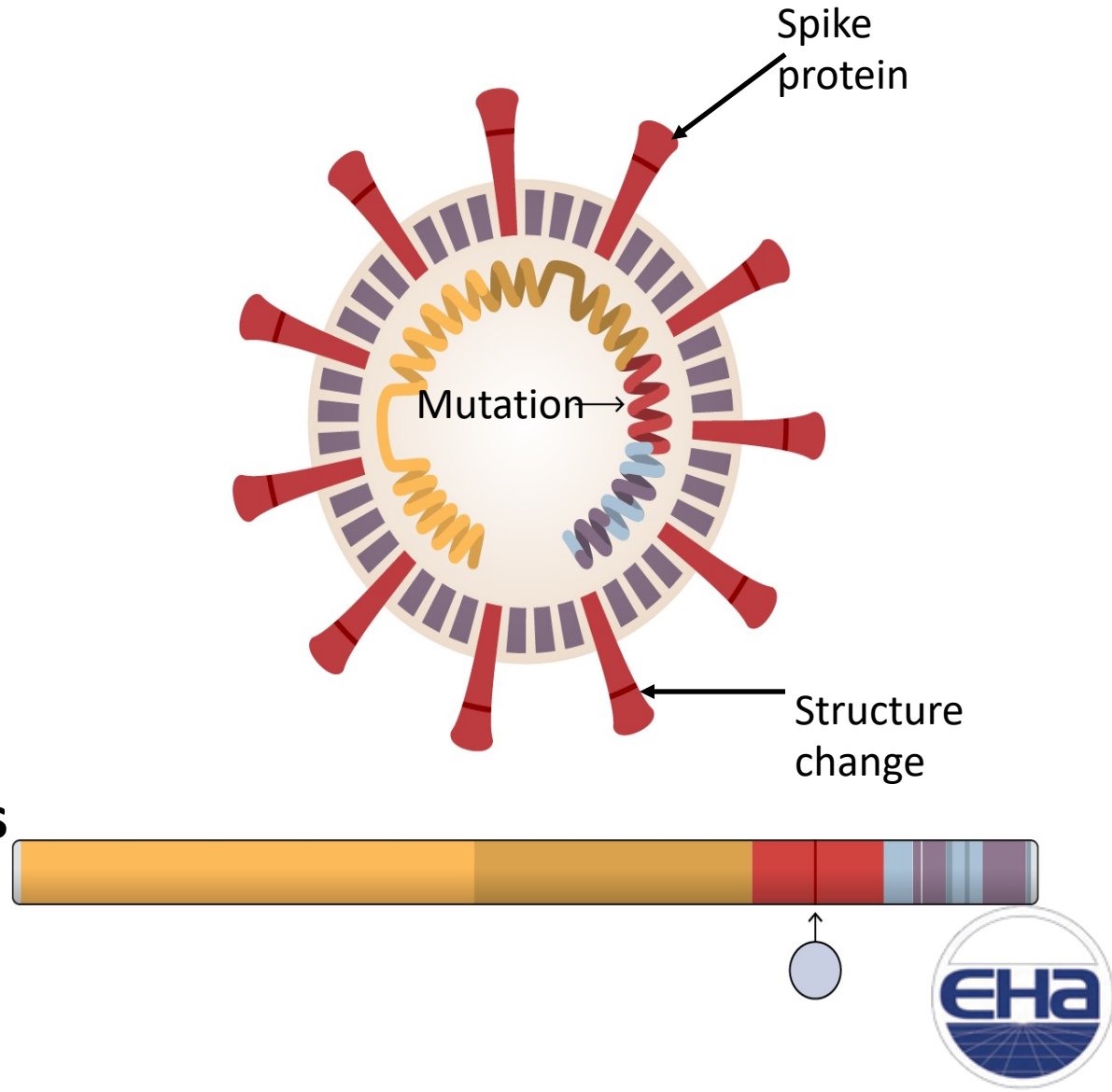
VAERS Vaccine Adverse Event Reporting System
www.vaers.hhs.gov

Vaccine Safety

- **Side Effects:** Normal reaction to vaccines, symptoms may include:
  - Fever
  - Muscle Soreness Body Aches/Fatigue
  - Rash
  - Not all individuals have side effects, does not mean the vaccine is not working.
  - Does not require medical attention and resolves in 12-48 hours
- **Adverse Health Effects:**
  - Requires medical attention
  - Not very common

What is a Variant?

- Viral variants are a normal occurrence due to mutations in the virus genetic material.
- Variants are expected to occur.
- Can change the structure of spike (attachment) proteins on the virus surface.
- Can increase transmissibility or decrease effectiveness of treatments/vaccines.
- Can do the opposite.
- **All approved vaccines in the United States work on the circulating variants.**



Variant Classification

1. Variant of Interest (VOI) – variant with specific genetic markers that have been associated with changes to receptor binding, reduced neutralization by antibodies generated against previous infection or vaccination, reduced efficacy of treatments, potential diagnostic impact, or predicted increase in transmissibility or disease severity.
2. Variant of Concern (VOC) – A variant for which there is evidence of an increase in transmissibility, more severe disease (e.g., increased hospitalizations or deaths)
3. Variant of High Consequence (VOHC) – A variant of high consequence has clear evidence that prevention measures or medical countermeasures (MCMs) have significantly reduced effectiveness relative to previously circulating variants. **Currently there are no SARS-CoV-2 variants that rise to the level of high consequence**

Current Variants of Concern in the United States

- **B.1.1.7 (Alpha)**: This variant was first detected in the United States in December 2020. It was initially detected in the United Kingdom.
- **B.1.351 (Beta)**: This variant was first detected in the United States at the end of January 2021. It was initially detected in South Africa in December 2020.
- **P.1 (Gamma):** This variant was first detected in the United States in January 2021. P.1 was initially identified in travelers from Brazil, who were tested during routine screening at an airport in Japan, in early January.
- **B.1.617.2 (Delta)**: This variant was first detected in the United States in March 2021. It was initially identified in India in December 2020.

Delta Variant

Twice as contagious as previous variants.

More severe illness in unvaccinated individuals.

Greatest risk of person-to-person transmission is between unvaccinated individuals.

Current vaccines available in the U.S. and U.K. are effective against the delta variant.

Vaccinated individuals are highly protected against severe illness and death.

Update: Breakthrough cases with disease can occur but are a small percentage and symptoms are typically mild.

UPDATE: The CDC is investigating the extent a fully vaccinated person can asymptomatically transmit the Delta variant. Changes in recommendations enacted while research is ongoing.

State Comparison: Cases, Hospitalization, Death: Vax vs Non-Vax

State	Share of Overall Cases Among Fully Vaccinated	Share of Overall Cases Among Not Fully Vaccinated*
Alaska	4.0%	96.0%
Arizona	5.9%	94.1%
Arkansas	3.6%	96.4%
California	1.4%	98.6%
Connecticut	0.2%	99.9%
Delaware	1.0%	99.0%
District of Columbia	1.3%	98.7%
Idaho	1.2%	98.8%
Indiana	1.1%	98.9%
Maine	1.3%	98.7%
Massachusetts	1.0%	99.0%
Michigan	1.6%	98.4%
Montana	3.2%	96.8%
Nebraska	0.4%	99.6%
New Jersey	0.2%	99.8%
New Mexico	1.2%	98.9%

State	Share of Overall Hospitalizations Among Fully Vaccinated	Share of Overall Hospitalizations Among Not Fully Vaccinated*
Alaska	5.0%	95.0%
Arkansas	4.7%	95.4%
California	0.8%	99.2%
Delaware	0.6%	99.4%
District of Columbia	0.5%	99.5%
Illinois	1.6%	98.4%
Indiana	0.6%	99.4%
Michigan	1.3%	98.7%
Montana	2.3%	97.7%
New Jersey	0.1%	99.9%
New Mexico	0.3%	99.7%
Oklahoma	0.7%	99.3%
Oregon	3.2%	96.8%
Rhode Island	4.2%	95.8%
Tennessee	0.9%	99.1%
Utah	4.6%	95.4%
Vermont	1.4%	98.6%
Virginia	1.6%	98.4%
Washington	2.2%	97.8%

State	Share of Overall Deaths Among Fully Vaccinated	Share of Overall Deaths Among Not Fully Vaccinated*
Alaska	2.3%	97.7%
Arizona	1.0%	99.0%
Arkansas	2.6%	97.4%
California	0.2%	99.8%
Connecticut	0.1%	99.9%
Delaware	1.3%	98.7%
District of Columbia	1.4%	98.7%
Illinois	2.0%	98.0%
Indiana	1.0%	99.0%
Michigan	2.7%	97.3%
Montana	3.1%	96.9%
New Jersey	0.1%	99.9%
New Mexico	0.3%	99.7%
Oklahoma	0.4%	99.6%
Oregon	0.9%	99.2%
Tennessee	0.5%	99.5%
Utah	1.4%	98.6%
Virginia	1.5%	98.5%
Washington	2.1%	97.9%

BREAKING NEWS

U.S. Food and Drug Administration's (FDA) Vaccines and Related Biological Products Advisory Committee (VRBPAC) voted unanimously to recommend the FDA grant Emergency Use Authorization (EUA) for a booster dose of COMIRNATY® (COVID-19 Vaccine, mRNA) in individuals 65 years of age and older and individuals at high risk of severe COVID-19. The committee recommended that the additional dose be administered at least six months after the two-dose series. The panel also agreed that healthcare workers and others at high risk for occupational exposure should be included in this EUA.

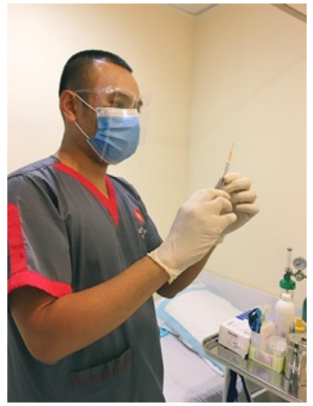
Source: https://www.pfizer.com/news/press-release/press-release-detail/fda-advisory-committee-votes-unanimously-favor-comirnatyr

COVID-19 Vaccine MYTHS: Facts vs Fiction

Myth - The COVID-19 vaccines were rushed through development and approval and can not be trusted.

- **Fact -** The mRNA method for the first two vaccines approved have been in development for over a decade.
- **Fact -** Current technology allowed for complete sequencing of the SARS-CoV-2 virus's DNA quickly. Accelerating identification of the proteins.

- **Fact -** The entire world has focused resources (money) and technology on development of the vaccines.
- **Fact** -Clinical trials were properly designed and performed easier due to the large number of cases in the population. This allowed for quicker testing of efficacy. The trials for currently approved vaccine deemed them safe and effective.
- **Fact -**Vaccine production started before approval was achieved due to country paying in advance for the vaccines.



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COVID-19 Vaccine MYTHS: Facts vs Fiction

Myth- The vaccine can give you COVID-19

- **Fact -** It is not possible to get COVID-19 from the vaccine. None of the vaccines use a live version of the SARS-CoV-2 virus; only provided the body with instructions (mRNA) to make proteins in order for your body to initiate an immune response.
- **Fact-** Fever, headache, body aches are normal possible responses to a vaccine for some individuals. They are signs the vaccine and body has initiated an immune response (vaccine is working!).

COVID-19 Vaccine MYTHS:
Fertility Myth

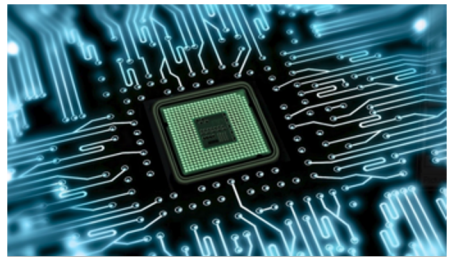
Myth: Antibodies to SARS-CoV-2 virus spike protein which is the target of all vaccines will also bind to placental proteins preventing pregnancy.

- **Fact -** The two proteins are completely different, and it is biologically impossible for this to occur.
- **Fact -** Pregnant women have contracted Covid-19. The body produces the same antibodies during natural active infection. No increases in miscarriages have been observed. This directly contradicts this myth as increases in miscarriages would be expected.
- **Fact -** 23 Women in the Pfizer clinical trial who received the vaccine as part of the trial successfully became pregnant with no complications due to the vaccine.

COVID-19 MYTHS: Facts vs Fiction
Tracking and DNA Manipulation Myths

Myth- Vaccine was developed to track individuals or will insert tracking microchip.

- **Fact-** this myth originates with comments from Bill Gates, who suggested digital vaccine records so that verification could be done quickly.



Conclusion

Vaccines have been largely responsible for the worldwide eradication of smallpox and eliminating such diseases as polio and tetanus. However, small groups have disputed the safety of vaccines in the early 2000's and have now led to diseases such as measles to resurface in America.

Thanks to international efforts, three COVID-19 vaccines were developed and approved for EUA in the United States as of this writing. This radically slowed the progress of the COVID-19 Pandemic in 2021 allowing major cities to reopen.

To date over 600,000 people have been killed from COVID-19 in the U.S.

For more information on this and other public health consulting needs visit us at https://www.ehagroup.com/ or call us at 410-484-9133.

Thank You

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