

# **PUTTING DEADLY DISEASES OUT TO PASTEUR: A HISTORY OF VACCINES**

**Brittney Waranius DVM MA MPH CPH  
Epidemic Intelligence Service Officer  
Centers for Disease Control & Prevention  
Assigned to: Wyoming Department of Health**



**INFECTIOUS DISEASE  
EPIDEMIOLOGY**

Good morning and welcome to this morning's talk on the history of vaccines. I'm Dr Brittney Waranius, an epidemiologist with the Centers for Disease Control assigned to the Wyoming Department of Health

**Table 1 Recommended Child and Adolescent Immunization Schedule for Ages 18 Years or Younger, United States, 2024**

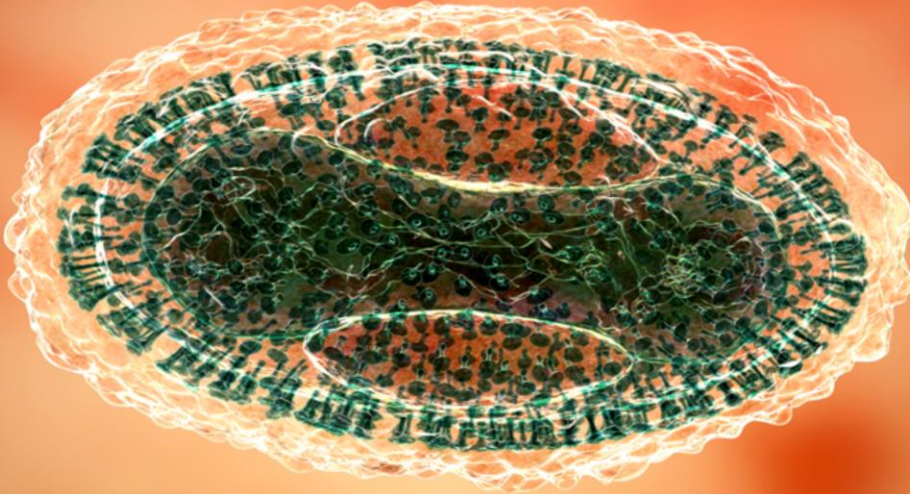
These recommendations must be read with the notes that follow. For those who fall behind or start late, provide catch-up vaccination at the earliest opportunity as indicated by the green bars. To determine minimum intervals between doses, see the catch-up schedule (Table 2).

Vaccine and other immunizing agents	Birth	1 mo	2 mos	4 mos	6 mos	9 mos	12 mos	15 mos	18 mos	19–23 mos	2–3 yrs	4–6 yrs	7–10 yrs	11–12 yrs	13–15 yrs	16 yrs	17–18 yrs	
Respiratory syncytial virus (RSV-mAb [Nirsevimab])	1 dose depending on maternal RSV vaccination status. See Notes					1 dose (8 through 19 months). See Notes												
Hepatitis B (HepB)	1 <sup>st</sup> dose	← 2 <sup>nd</sup> dose →				← 3 <sup>rd</sup> dose →												
Rotavirus (RV): RV1 (2-dose series), RV5 (3-dose series)			1 <sup>st</sup> dose	2 <sup>nd</sup> dose	See Notes													
Diphtheria, tetanus, acellular pertussis (DTaP <7 yrs)			1 <sup>st</sup> dose	2 <sup>nd</sup> dose	3 <sup>rd</sup> dose				← 4 <sup>th</sup> dose →			5 <sup>th</sup> dose						
Haemophilus influenzae type b (Hib)			1 <sup>st</sup> dose	2 <sup>nd</sup> dose	See Notes			← 3 <sup>rd</sup> or 4 <sup>th</sup> dose, See Notes →										
Pneumococcal conjugate (PCV15, PCV20)			1 <sup>st</sup> dose	2 <sup>nd</sup> dose	3 <sup>rd</sup> dose			← 4 <sup>th</sup> dose →										
Inactivated poliovirus (IPV <18 yrs)			1 <sup>st</sup> dose	2 <sup>nd</sup> dose		← 3 <sup>rd</sup> dose →						4 <sup>th</sup> dose					See Notes	
COVID-19 (1vCOV-mRNA, 1vCOV-aPS)	1 or more doses of updated (2023–2024 Formula) vaccine (See Notes)																	
Influenza (RV4)	Annual vaccination 1 or 2 doses																	
Influenza (LAIV4)	Annual vaccination 1 or 2 doses												Annual vaccination 1 dose only					
Measles, mumps, rubella (MMR)					See Notes		← 1 <sup>st</sup> dose →					2 <sup>nd</sup> dose						
Varicella (VAR)							← 1 <sup>st</sup> dose →					2 <sup>nd</sup> dose						
Hepatitis A (HepA)					See Notes	2-dose series. See Notes												
Tetanus, diphtheria, acellular pertussis (Tdap ≥7 yrs)																	1 dose	
Human papillomavirus (HPV)																	See Notes	
Meningococcal (MenACWY-CRM ≥2 mos, MenACWY-TT ≥2years)						See Notes												
																	1 <sup>st</sup> dose	
																	2 <sup>nd</sup> dose	

Here's where we are today. This is the recommended immunization schedule for children and adolescents, and I'm putting it up for the big picture, so need to squint to see the details. This represents the protection we offer for diseases that can cause pain, suffering, or even death. It can seem overwhelming for new parents and practitioners to navigate the vaccine landscape which includes dozens of shots in a child's early years.

And with many of the diseases now occurring at low levels or even eliminated from the United States, it can be easy to lose the forest for the trees. So for the next hour, I'm going to lead us through the early history of vaccines and just how important they remain today to prevent illness and suffering.

# SMALLPOX



## & THE HISTORY OF THE WORLD'S FIRST VACCINE

We'll set the stage by spending the first half of this morning learning about Smallpox, a disease caused by Variola Virus (pictured here). And how the first vaccine in history was designed to combat this incredibly lethal disease.

# ENDEMIC SMALLPOX DISTRIBUTION

4<sup>TH</sup> CENTURY



There is suggestive evidence for smallpox in the remains of mummies from Ancient Egypt and in writings from Ancient Rome. But our first really conclusion evidence comes from medical scholars who described the epidemiology and clinical appearance of smallpox in 4<sup>th</sup> century China



# ENDEMIC SMALLPOX DISTRIBUTION

6-7<sup>TH</sup> CENTURY



6<sup>th</sup> and 7<sup>th</sup> Century Korea, Japan, and India

# ENDEMIC SMALLPOX DISTRIBUTION

10<sup>TH</sup> CENTURY



And 10<sup>th</sup> century Iraq

# ENDEMIC SMALLPOX DISTRIBUTION

10<sup>TH</sup> CENTURY



suggesting that the disease was spreading along ancient trade routes from East to West

# ENDEMIC SMALLPOX DISTRIBUTION

11<sup>TH</sup> CENTURY



By the Middle Ages increasing trade and increased contact from the crusades helped spread the disease across North Africa and Europe

# ENDEMIC SMALLPOX DISTRIBUTION

15<sup>TH</sup> CENTURY



European exploration and colonization continued to spread it to sub-Saharan Africa



# ENDEMIC SMALLPOX DISTRIBUTION

16<sup>TH</sup> CENTURY



Then the Caribbean, Central and South America

# ENDEMIC SMALLPOX DISTRIBUTION

17<sup>TH</sup> CENTURY



To North America

# ENDEMIC SMALLPOX DISTRIBUTION

18<sup>TH</sup> CENTURY



And finally to Oceania, creating a worldwide distribution by the 18<sup>th</sup> century

# SMALLPOX LETHALITY



+

## 1721 OUTBREAK

in Boston killed 8% of the population in a population with outbreaks every 10-20 years.

When Europeans brought the disease to colonial America, outbreaks were sporadic because the cities were small, the population density was low, and there was infrequent contact with Europeans. Boston as a hub for trade with Europe in particular had a series of outbreaks in the 1700s, and the most well known occurred in 1721 when 8% of the population was killed by smallpox in less than a year.

These outbreaks happened approximately every 10-20 years when immunity would wane in the population, while adults may have immunity, the population of children and young adults would grow large enough to be vulnerable

# SMALLPOX LETHALITY



+

## 1721 OUTBREAK

in Boston killed 8% of the population in a population with outbreaks every 10-20 years.



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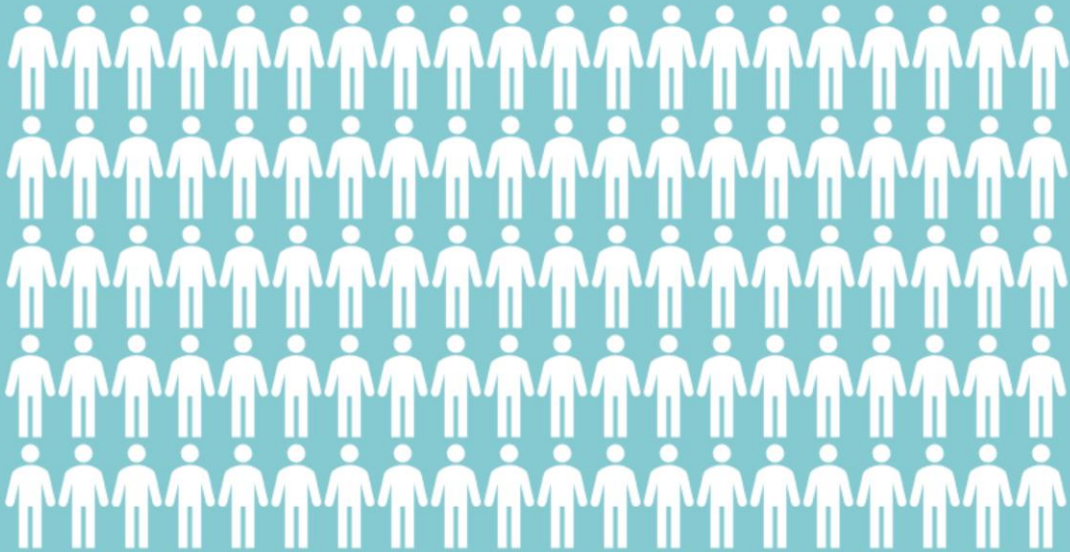
## 1707 OUTBREAK

in Iceland killed approximately 25% of the population in a population with no immunity.

And in areas with no immunity in adults, outbreaks could result in death tolls that were much higher. While Iceland had occasional outbreaks, they were few and far between. So when Smallpox was introduced in 1707 by a sailor, there was no immunity on the island. The resulting outbreak killed 25% of the Icelandic population.

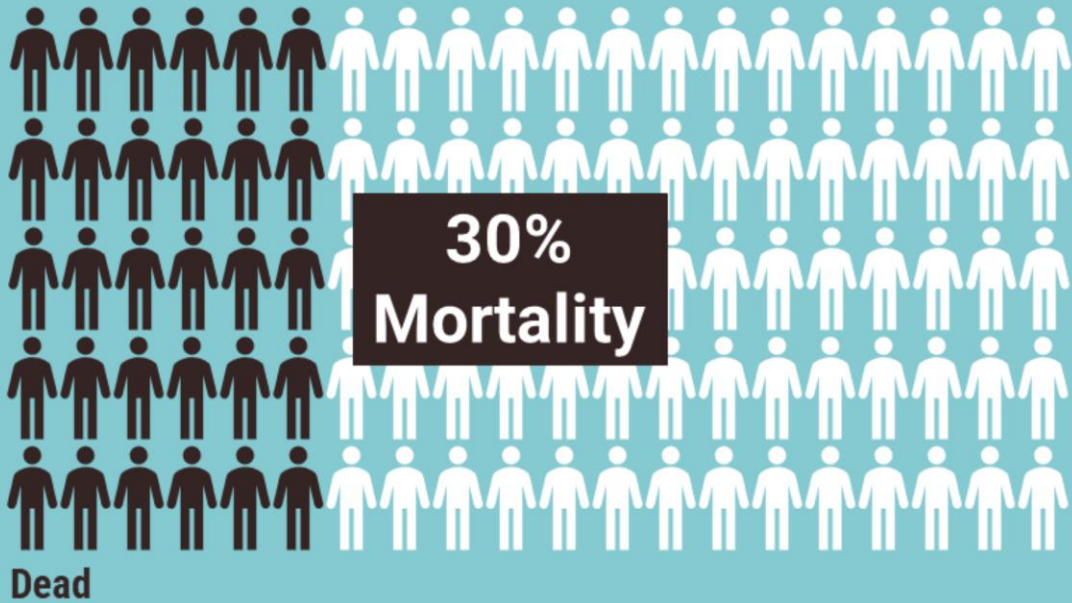


# SMALLPOX COMPLICATIONS



All this is to say, that Smallpox was one of the deadliest diseases in the world prior to the invention of vaccination. Modern studies show that for every 100 people who contracted the disease

# SMALLPOX COMPLICATIONS



On average 30% would die. But death wasn't the only possible consequence of the disease....

# SMALLPOX COMPLICATIONS



For survivors, the most common long-term effect of smallpox was disfigurement. Almost everyone with smallpox was left with some degree of scarring and somewhere between 65-80% of survivors would have scarring to their face.

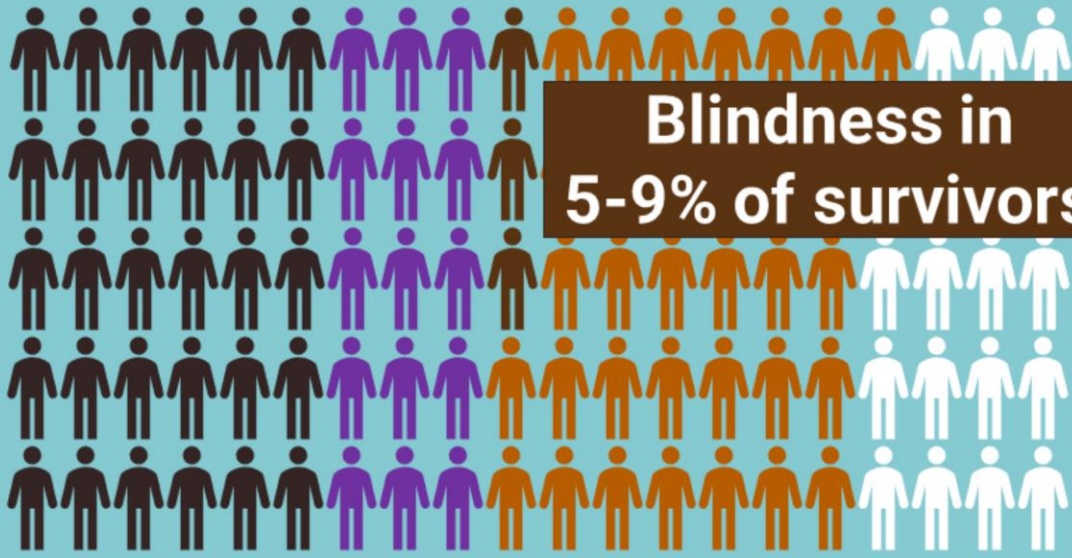
# SMALLPOX COMPLICATIONS



Dead | Severe Disfigurement | Facial scarring

1/3 of the survivors with facial scarring would have severe disfigurement

# SMALLPOX COMPLICATIONS

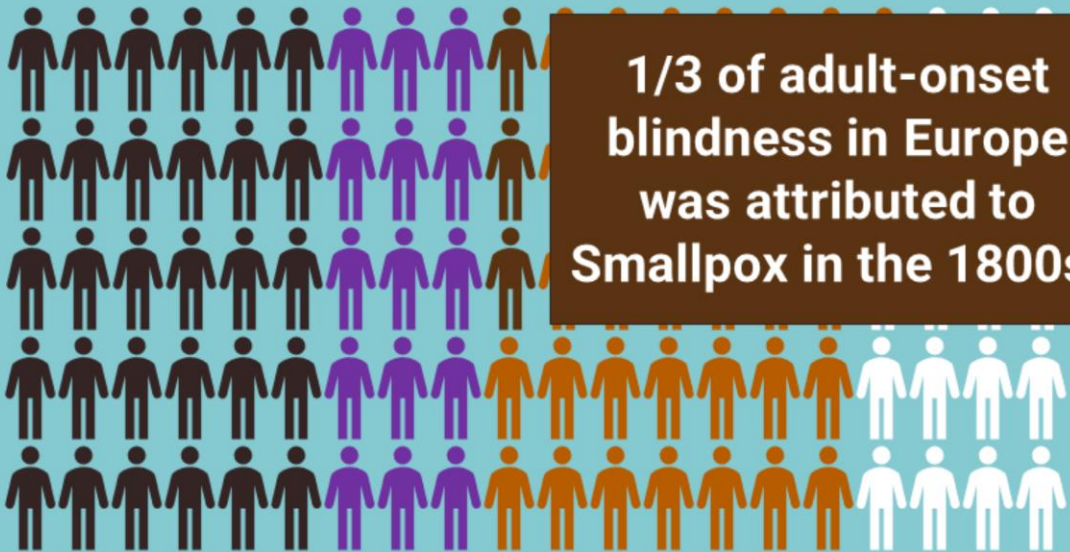


Dead | Severe Disfigurement | Blind | Facial scarring

Blindness was also a very common complication. Studies in the 20<sup>th</sup> century showed for 5-9% of people who contracted smallpox, the disease would spread to their eyes, scar their corneas, and lead to blindness.



# SMALLPOX COMPLICATIONS



Dead | Severe Disfigurement | Blind | Facial scarring

Smallpox was so widespread and so common that it was reported to cause 1/3 of all of the cases of adult-onset blindness in Europe in the 1800s

# SMALLPOX COMPLICATIONS



**Dead | Severe Disfigurement | Blind | Facial scarring | No complications**

So, in our theoretical population of 100 people on my slide, in the event of a smallpox outbreak: Approximately 30 would be dead. About 51 of the survivors would have some type of facial scarring. Of those, approximately 18 people would have severe disfigurement, including about 3 with corneal scarring leading to blindness. And only about 19 people would recover with minimal or no complications.

## Artists rarely depicted smallpox



*Atlas of Clinical Medicine, Volume 1*  
Sir Byrom Bramwell, 1892

This depiction showing facial scarring was from a medical textbook. This particular patient was not only scarred, but had her eyes removed due to pain and headache resulting from blindness. We almost never see this in images of the day because painters, usually commissioned by the wealthy, wanted to portray their patrons in the best light.

One historian went so far as to call painters the “airbrush artists” of their day because commissioned portraits from the 18<sup>th</sup> and 19<sup>th</sup> century almost never show smallpox scars even though we know they were common.

## Documentation of scarring is easier to find after the advent of photography



Photo credit: L. Dale, India 1975  
World Health Organization

After the advent of photography, it is easier to find documentation of facial scarring, as can be seen in this image from the mid twentieth century of a young Indian woman. Although she recovered from her smallpox infection, her arms and face were permanently scarred.

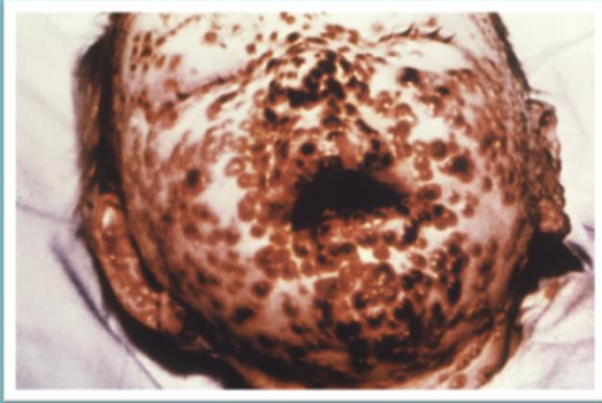


## Disease progression: pustules

Photo credit: Dr John Noble Jr, Bangladesh 1973  
Centers for Disease Control and Prevention

The reason for this extreme scarring is due to the pustules that develop during the course of infection. This photo shows a young girl in Bangladesh at the height of her disease after being infected with smallpox in 1973





# Disease progression: Scabbing

Photo credit: Dr Charles Farm Jr, Wales 1962  
Centers for Disease Control and Prevention

As the infection progressed, it would begin to scab over as we see in this image from the United Kingdom in 1962.

## Disease progression: scarring



Photo credits: Dr John Noble Jr, Ghana 1967  
Centers for Disease Control and Prevention

Eventually those scabs would begin to fall off, leaving behind scars like we see on this on this young boy in Ghana from 1967.

## Severe scarring and blindness were possible



Photo by Don Eddins, Unknown location 1967  
Centers for Disease Control and Prevention

And finally, those scars may create permanent pock marks in the skin, as we see in this patient from 1967 who also experienced lesions on his corneas, leading to permanent blindness.



## EUROPE IN THE 18<sup>TH</sup> -19<sup>TH</sup> CENTURY

**Smallpox caused 10% of all deaths in Cities**

And we can see the brutality of the disease in the 18<sup>th</sup> and 19<sup>th</sup> century from historical records of early modern Europe that show in areas where the disease was endemic, smallpox killed on average about 10% of people in major cities every year.



## **EUROPE IN THE 18<sup>TH</sup> -19<sup>TH</sup> CENTURY**

**Smallpox caused 10% of all deaths in Cities**

**Every year, it was estimated to kill:**

**400,000 Europeans**

Details from various countries historical records show that across Europe, it killed about 400,000 people every year, most of them children.



## **EUROPE IN THE 18<sup>TH</sup> -19<sup>TH</sup> CENTURY**

**Smallpox caused 10% of all deaths in Cities**

**Every year, it was estimated to kill:**

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**10% of all Swedish infants**

While adults could certainly die of Smallpox, it disproportionately impacted the young. In Sweden, records show that it killed 10% of infants every year



## **EUROPE IN THE 18<sup>TH</sup> -19<sup>TH</sup> CENTURY**

**Smallpox caused 10% of all deaths in Cities**

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**400,000 Europeans**

**10% of all Swedish infants**

**1 out of 7 Russian children**

And the records from Russia are even worse. With 1 out of 7 Russian children dying of Smallpox. Every. Single. Year.





# **SMALLPOX WAS AN EQUAL OPPORTUNITY KILLER**

**High and low classes were equally likely to die  
from smallpox.**

Most diseases of the day disproportionately killed the lower classes because of differences in things like hygiene and nutrition. But Smallpox was an equal opportunity killer and you were just as likely to die if you were highborn



# **SMALLPOX WAS AN EQUAL OPPORTUNITY KILLER**



**High and low classes were equally likely to die from smallpox.**

**Between 1694 – 1774, it killed:**

- Queen of England
- Austrian emperor
- King of Spain
- Tsar of Russia
- Queen of Sweden
- King of France

In an 80-year span in early Modern Europe, the disease actually managed to kill the reigning monarchs of six different nations throughout Europe. Their wealth, power, and access to physicians could not save them.



**Henry Wicklin, aged 6 years  
Gloucester smallpox epidemic, 1896**

Photo by H.C.F., Wellcome Collection

**“Parents did not even  
count their children  
until they had survived  
the illness”**

Smallpox was so common among children in London during this time period, that it was said that parents did not even count their children until they had survived the illness. Because the chance of their child not surviving was so incredibly high. For children, especially those under the age of five years, the fatality rate could be as high as 50-60% during outbreaks.

The slide features a light blue background with a thin black border. In the top left, top right, and bottom right corners, there are stylized virus icons. Each icon consists of a central grey circle with several thin grey lines radiating outwards, and a small orange dot positioned above the central circle.

Smallpox was...

**“Unique in its savagery,  
fatality, and universality”**

-Donald R. Hopkins, MD MPH

Because of the horrors it could inflict on people, smallpox was described as unique in its savagery, fatality, and universality. It didn't matter if you were a king or a peasant, an adult or a child, smallpox killed or disfigured millions of people worldwide.

## • EARLY ATTEMPTS AT PREVENTION



## Insufflation

Figure from: Qiu-Hua Li, et al. "Overview of the plague in the late Ming Dynasty and its prevention and control measures." *Traditional Medicine Research* (2020)

Against the backdrop, many civilizations developed ways to try to lessen the impact of the disease. Long before anyone knew about bacteria or viruses, it was common knowledge that people who survived smallpox were immune to the disease. As early as the 5<sup>th</sup> century, we have records that show that smallpox survivors in China were used to care for those who were infected since it was known that they couldn't get sick again.

This knowledge also led early civilizations to try to figure out ways to give people smallpox on purpose, but to give them a less severe version of the disease than through natural infection. One way they did this was through a technique called insufflation.

The oldest records of this practice are from China, which describe the process of taking the scabs or pus from someone suffering from smallpox, drying them out, grinding them up, and blowing them up someone's nose. Sometimes a slightly different process was undertaken but instead of inhaling the scabs or pus, they would scratch them into the arm of an uninfected person.

Records from the 1600s in India also show that when people were infected with a mild case of smallpox, they would take their blankets and wrap them around children who had never been infected with the hopes that it would get the children sick with a mild version of disease.

## • EARLY ATTEMPTS AT PREVENTION



Dr. Clot Bey inoculating himself in Cairo, 1835

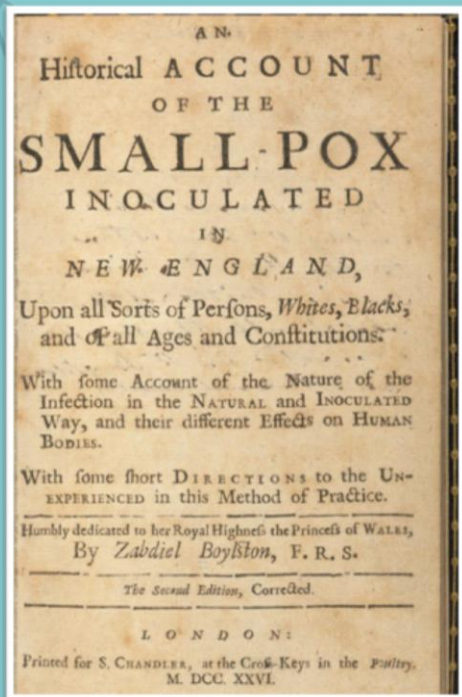
Image Courtesy of: Kasr Al Ainy School of Medicine Museum

## Variolation

But later another technique developed called variolation, which is the precursor to modern vaccination. During this process, a needle would be used to pierce a pustule in someone sick with smallpox, and then that pus would be transferred into incisions made into the forearm or hands.

This process was practiced throughout parts of Asia, Africa, and the Middle East, including the Ottoman empire





## Early accounts of variolation in United States demonstrate its protective effect

And here's the thing about variolation, it worked pretty well. It's hard to quantitatively define the protective effect of variolation was in places where it had been practiced for hundreds of years, but it's much easier to define in places where it was introduced later.

We can see this if we go back to the historical account of the outbreak in Boston in 1721 which is the first year that variolation was used in the American colonies.

The practice of variolation in colonial America is credited to a man known as Onesimus who was enslaved to a Puritan minister named Cotton Mather. Onesimus was from West Africa, where variolation was practiced and he told Mather about the procedure and how it made him immune to Smallpox.

Mather heard similar accounts from other enslaved persons, and also read about similar methods being used in Istanbul. When Boston had its outbreak in 1721, Mather began advocating for its use.

## Smallpox Incidence and Death in 18<sup>th</sup> Century Boston

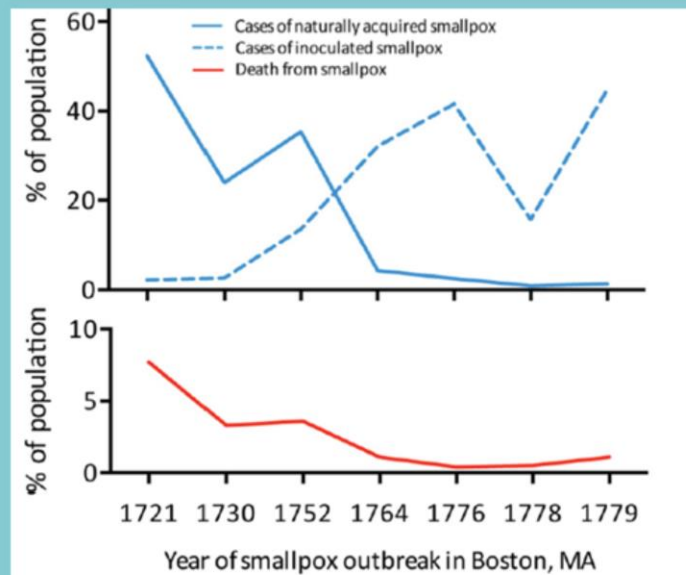


Figure adapted from: Niederhuber, Matthew. "The fight over inoculation during the 1721 Boston smallpox epidemic." *Science in the News* (2014)

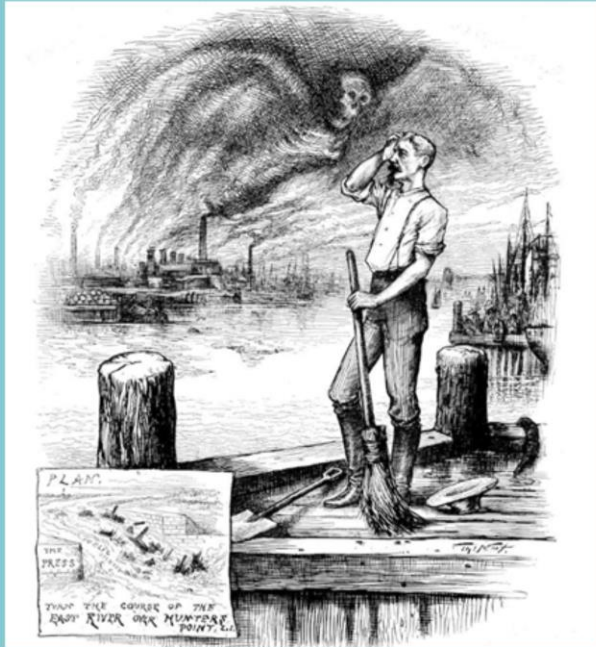
During the outbreak of 1721, over 50% of the population of Boston was infected with smallpox. Most physicians and citizens in Boston were against the idea of variolation since it was new and seemed dangerous, the idea of purposely infecting someone with Smallpox seemed absolutely crazy.

Nonetheless, 287 people were variolated during that outbreak, and records show that only 2% of variolated individuals died. This was much better than the 15% mortality rate of the people who contracted the disease but were not variolated.

Records over the next century from Boston give great data about the number of naturally acquired smallpox cases compared to the percent of the population that was variolated. As we see variolation numbers increasing in the dashed blue line in the top graph, we can see the total number of cases decreasing in the solid blue line.

We can also see the death toll decreasing throughout the years. The red line on the bottom represents the total deaths from smallpox by year. As the percentage of the variolated population increased, the number of cases of naturally acquired smallpox fell. And as those naturally acquired cases fell, so too did the percentage of the population that died of smallpox during each successive outbreak.





Cartoon of Air Pollution Engulfing City  
Thomas Nast, 1880

**Variolation was met with skepticism in Britain due to differences in climate and diet**

The medical establishment in England knew about variolation as early as 1714 from travelers to Istanbul, but physicians did not want to risk trying it in England. At the time, they still didn't know about bacteria or viruses, and the prevailing theory was that smallpox was triggered by environmental factors outside of the body.

So they had concerns that variolation may not work the same on English citizens as it did on people from the Ottoman Empire due to the differences in climate or diet.



**Lady Mary Wortley Montagu**  
Achille Devéria, 1830s

## Lady Mary Wortley Montagu popularized variolation in England

In the end, variolation in England ended up being popularized by an upperclass noblewoman, not a physician. Lady Mary Wortley Montagu was personally victimized by Smallpox in several ways. First, her brother died of the disease. Then, she fell ill with smallpox at the age of 26.

She had been known as a great beauty in London, but smallpox left her with noticeable facial scarring and she permanently lost her eyelashes. This portrait is a great example of how portrait artists in the 1800s airbrushed their patrons – at the time this was painted Lady Mary was well known for having disfiguring facial scars, but there's not a blemish to be seen anywhere on her face.

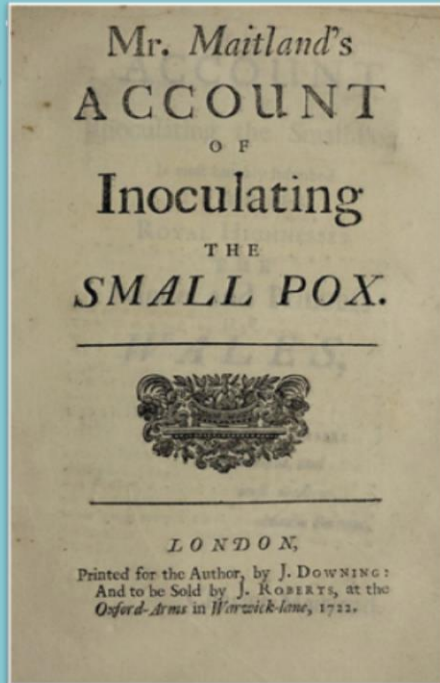


*Lady Mary Wortley Montagu with her son,  
Edward Wortley Montagu, and attendants*  
Jean Baptiste Vanmour, circa 1717

## 1721: Variolation spreads from the Ottoman Empire to England

The year after she contracted smallpox, her husband was appointed as the ambassador to the Ottoman Empire and they moved to Istanbul where she became familiar with the process of variolation. She had her own son variolated while in Istanbul, and he recovered with no issues which convinced her of the practice. She also had an infant daughter, but her daughter was too young to receive variolation while they lived abroad.

They returned to London and a few years later a smallpox outbreak struck. Her daughter was 4 years old at the time, and Lady Mary invited a number of people to watch the process of variolation being performed on her daughter. The King's Physician was in attendance and was impressed enough to suggest that the royal family, who had several young children, undergo variolation during the outbreak.



## Variolation was tested on prisoners & orphans before being given to royalty

Several successful experiments were conducted on prisoners and orphans at the request of the royal physician. Although wildly unethical, medical experimentation on these vulnerable populations was common and accepted practice during this time period.

The experiments were conducted by Charles Maitland, the same physician who had variolated both of Lady Mary's children. After hearing Dr Maitland's report, the royal physician was convinced that the procedure was safe and effective, and the variolation was performed on a prince and princess.

Newspapers followed the experiments as they occurred and covered the successful variolation of the royal children, which led to greater acceptance throughout England. It took about 30 years for variolation to become standard medical practice throughout the country.

**VARIOLATION  
FATALITY RATE:  
2-3%**



Hampstead Smallpox Hospital  
Matthew White Ridley, 1871

While variolation generally caused mild or moderate disease that was easier to overcome, it could cause a severe infection. 2-3% of people who were variolated died from their infections. That percentage is still much better than the 30% on average that might die from a naturally acquired infection.



## RISKING VARIOLATION FOR SURVIVAL (AND BEAUTY)



Circassian Noblewoman  
Abdullah Frères, late 1800s



*Veiled Circassian Beauty*  
Jean-Léon Gérôme, 1876

Nonetheless many people were willing to risk death as a side effect if it meant a much better chance of surviving the disease. Variolation also protected against the other consequences for survivors of smallpox, including decreasing the chance of blindness and scarring. The woman pictured here are from Circassia, an area in the Caucasus Mountains that was part of the Ottoman empire at the time.

Its women had an international reputation for being particularly beautiful, and many of the imperial consorts and the mothers of Ottoman Sultans were ethnic Circassians. Variolation was a very common practice in the region and Circassian women built this reputation for beauty in part likely because they had clear complexions unmarred by smallpox scars

And while it may seem vain by today's standards, sort of like the Botox of its day, having an unmarked face could be important for the outcome of a woman's life in this time period. Women with severely scarred faces were considered unfit for marriage. We see this play out in several famous women of the age.





## Facial scars could impact marriage prospects

*Portrait of Archduchess Maria Elisabeth of Austria*  
Martin van Meytens, 1760s

This is a painting of Archduchess Maria Elisabeth before she contracted smallpox. Her mother was the empress of the Habsburg Empire and her father was the emperor of the Holy Roman Empire. So, she was from the wealthiest, most influential family in the world. You likely have heard of her younger sister of Marie Antoinette.

Even though Maria Elisabeth she was rich, well-connected, and powerful, the disfiguring scars she received after falling ill with smallpox left her considered unfit for marriage. This was particularly unfortunate for her as her family had negotiated with no fewer than five kings and princes to find the best suitor.

She was reportedly just 3 days away from marrying the king of France when she fell ill with smallpox and her marriage contract was cancelled when it became known that her face was severely scarred. And she is certainly not the only woman who this happened to, as there are similar historical accounts from Europe, the Middle East, and Asia.

In a time when women had little to no agency outside of their marriageability, being marred by smallpox could impact their ability to secure a stable future.

# MILKMAIDS IN ENGLAND



**“But what is your fortune,  
my pretty Maid?”**

**“My face is my fortune,  
Sir,” she said.**

From “The Milkmaid”

An old song exhibited and  
explained by R. Caldecott, 1882

Another type of women that were known for their beauty and clear complexions around this era were milk maids in England, young women who's job it was to milk cows on dairy farms.

This is reflected in what is referred to as an “old” song when it was written down in 1882. Called the Milkmaid, the story tells of an impoverished young man who is told by his mother to go and seek a RICH wife. He is infatuated by a young milkmaid in the countryside and considers asking her to marry him. But when asked about what type fortune she has, she responds “my face is my fortune, sir”

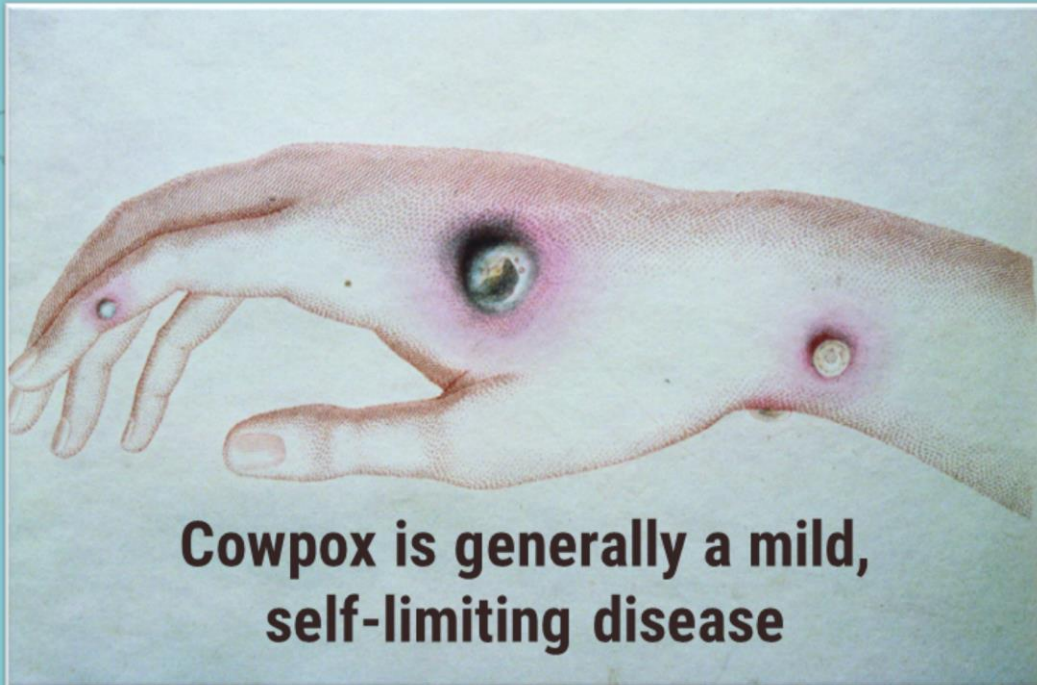


***The Milkmaid***  
William Oliver

“  
**I shall never have smallpox  
for I have had cowpox.  
I shall never have an ugly  
pockmarked face.**  
”

Attributed to a dairymaid by  
Dr. Edward Jenner

Living in the countryside, these women had mostly never been subjected to variolation. Instead they attributed their immunity to their contact with cows. One unnamed milkmaid was allegedly quoted as saying: “I shall never have smallpox for I have had cowpox. I shall never have an ugly pockmarked face.”



**Cowpox is generally a mild,  
self-limiting disease**

Hand of Sarah Nelmes by Dr. Edward Jenner, 1798

Cowpox is generally a mild and self-limiting disease. Lesions appear on the udders of cows, and milk-maids would develop lesions on their hands after milking. Pustules were generally limited to areas with direct skin-to-skin contact and resolved within a few weeks.




***Benjamin Jesty***  
Michael William Sharp, 1805

## **1774: English Farmer deliberately uses cowpox to protect his family from smallpox**

Armed with the folk knowledge that a mild case of cowpox could potentially protect against deadly smallpox, a farmer named Benjamin Jesty deliberately infected his family with cowpox in 1774. Jesty used a needle to scratch pus from a cow's udder into the arms of his wife and two sons. He had previously had cowpox through his farm work and seemed to be immune to smallpox.

Two of his dairymaids who previously had cowpox also never got sick with smallpox even when exposed to family members in the same household that developed the disease. Jesty and his sons would later have their immunity tested through variolation. None of the Jesty's would ever become sick despite having smallpox injected directly into their skin





**1796:  
Physician Edward  
Jenner starts testing  
the first vaccine**



***Edward Jenner***  
John Raphael Smith, circa 1800

It was into this context that Edward Jenner enters the history of vaccination. Jenner had been variolated at a young age, and went on to become a physician, first apprenticing in the countryside where he overheard stories of milk maids saying that cowpox made them immune to smallpox before entering formal studies in London.

After finishing his medical studies he returned to the countryside to practice, and eventually set out to test whether cowpox actually provided immunity. He began testing his theory in 1796.





**Blossom the cow  
kicks off a new  
chapter in medical  
history after giving  
her milkmaid cowpox**

***Blossom***  
Artist unknown,  
possibly Stephen Jenner, circa 1796

Armed with the folk wisdom that cowpox could provide cross-protection for smallpox, Jenner set out to find an infected milk maid. Cowpox was endemic to the county of Gloucestershire in England at the time, and outbreaks only happened sporadically. But in 1796 a cow named Blossom kicked off a new chapter in medical history after giving a young dairy maid named Sarah Nelmes cowpox. After milking Blossom, Nelmes developed a “large pustulous sore” on her hand



***Dr. Jenner performing his first vaccination on James Phipps, a boy of age 8. May 14th, 1796***  
Ernest Board

Jenner used pus from Sarah Nelmes' sore to inoculate an 8 year-old boy named James Phipps through two scratches on his arm. After Phipps recovered, Jenner gave the boy a standard variolation using live smallpox. The boy never developed the disease. Phipps would go on to have variolation performed about 20 times over the course of his life to see if he was still immune, and never developed a case of smallpox.

Unfortunately for Jenner he had to wait 2 years for the cows to cooperate again. When Gloucestershire dairies experienced another cowpox outbreak in 1798, Jenner carried out a series of vaccinations in children showing that he could not only use pus directly from a cow, but also from the children's cowpox lesions to vaccinate against smallpox.



Image Source: Getty Images

**“vacca” → Latin for “cow” +**  
**+**  
**“-ine” → English suffix meaning**  
**“of or pertaining to”**

**Gives us the word**  
**VACC-INE!**

Jenner wanted to coin a new word to distinguish his newly invented process from variolation. And this leads us to how cows helped give vaccines their name. The Latin word for cow is “vacca.” So he took the latin term, and added the English suffix –ine, to give us the word vaccine, meaning a product that comes from cows.



***Smallpox Vaccination***  
Louis-Léopold Boilly, 1807

Jenner published his findings in 1798 with a series of 23 case histories to provide epidemiological as well as experimental evidence to prove that infection with cowpox would protect against smallpox while being much safer. This was the first systematic study of using an altered form of an infectious agent to provide cross-protection against a pathogen.

Although there was some skepticism at first, a number of different investigators had confirmed his theory. By the early part of the 1800s the concept of vaccination had spread throughout Europe and to the Americas. Millions of people were vaccinated in short order and many countries made vaccination mandatory.

# **“The Cow-Pock -or- The Wonderful Effects of the New Inoculation!”**

James Gillray (1756-1815)



Not everyone was happy about this new development though, and there was backlash every step of the way. Lady Mary Wortley Montagu received considerable pushback upon introducing variolation to England, with people attacking the process, her character, and even her looks.

The farmer Benjamin Jesty was ostracized in his hometown, with some in the local population feeling his actions went against the church and were perhaps bordering into witchcraft.

And Jenner’s new vaccination was no different. Some people thought that injecting pus from cows might cause them to develop bovine features, as is depicted in this political cartoon that came out shortly after vaccination was introduced showing people with hooves and horns growing from their faces.





Image reproduced from:  
*Vaccinae vindicia*  
by Robert John Thorton, 1806

## Arguments against the vaccine included both medical and religious skepticism

(some founded and some fantastical)

Some religious leaders felt that injecting material from animals was an affront to god, leading to some incredible theories like the one depicted here. Dr Benjamin Moseley, a vaccination critic, suggested that cowpox injections might lead women to have a romantic interest in bulls and produce half-cow half-human offspring.

Some physicians also objected simply because they were losing income from performing variolations. The most valid opposition however resulted from problems with sanitation. Vaccines could be contaminated with other diseases, like Syphilis, or even with smallpox, because the lancets used to pierce pustules in early vaccination were often reused and poorly cleaned.

Vaccine shortages were also common because cowpox outbreaks was variable and mostly localized to dairy herds in the county of Gloucestershire. Eventually calves were used as a source of material, with the animals being deliberately infected in order to maintain a continuous supply of vaccination material.



***Washington Rallying the Troops at Monmouth***  
Emanuel Leutze, 1857

**“...we should have more to dread from [smallpox], than from the sword of the enemy.”**

-George Washington

Militaries quickly realized that variolation and later vaccination could give them an edge in conflict. George Washington was an early proponent of variolation and ordered the Continental Army to receive the treatment in 1777 after a military loss in Quebec that was partly due to the fact that a large number of the revolutionary soldiers had developed smallpox and were too weak to fight.

In a letter to the director of the medical department of the Army, George Washington wrote that they had more to dread from smallpox than from “the sword of the enemy.”



**“Ah, Jenner,  
I can refuse  
him nothing.”**

-Napoleon  
(allegedly)



***The Battle of Wagram in 1809***

Horace Vernet, 1836

By the time of Napoleon’s campaigns, vaccination was available. In 1805, just seven years after Jenner’s writings on vaccination, Napoleon ordered the vaccination of the entire French Army, and a year later required it for all French civilians as well.

By 1805 Jenner was so famous that he was able to obtain the release of several English prisoners of war from France by writing a letter to Napoleon, who allegedly exclaimed “Ah, Jenner, I can refuse him nothing” because he was so grateful for the invention of the smallpox vaccine.



# Unvaccinated vs Vaccinated

infected on the  
same day in 1901



Image from:  
*Atlas of clinical medicine, surgery, and  
pathology, New Sydenham Society, 1901*

It's hard to argue with the effectiveness of the vaccine, and endemic disease was eliminated throughout many parts of the world. This photo from 1901 in England "shows two boys, both aged 13 years. One was vaccinated in infancy and the other was not vaccinated. They were both infected from the same source on the same day.

While one is in the fully pustular stage, the other had just a few spots and recovered quickly. Changes and improvements had also been made to the vaccine by the time of this photo. Science and laboratory techniques advanced significantly so that we could grow vaccines in culture instead of cows.

Eventually the vaccine was changed from cowpox virus to a different, but related virus named vaccinia virus, which also provided strong cross-protective immunity.

## World-Wide Smallpox Endemic Areas, 1955

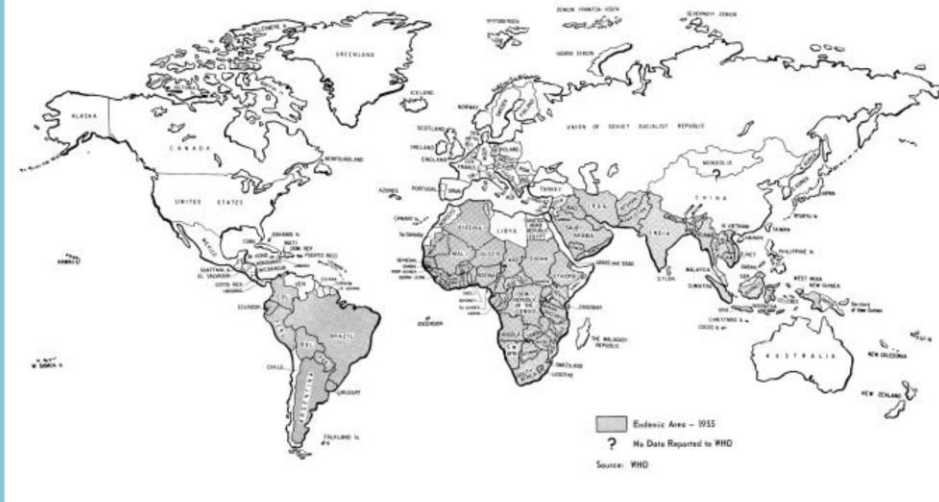


Image from: CDC Public Health Image Library

By the 1950s smallpox had been eradicated from all of Europe and North America, and many other countries. But despite the vaccine, Smallpox remained a significant problem in a number of countries. But in 1959, the World Health Organization started an ambitious plan to eradicate smallpox from the world.



• Image from: CDC Public Health Image Library

After a decade, they had gained some ground, but the virus remained across multiple continents. The campaign had been plagued by a lack of funding, personnel, vaccine supplies, and international cooperation, but progress had been made in many places.



A nomadic Tuareg girl being vaccinated in Mali, 1967

Image from: CDC Public Health Image Library

In 1967, an Intensified Smallpox Eradication Campaign began starting with West African Countries. This photo from the CDC archive is from 1967 in Mali and shows a nomadic Tuareg girl receiving her vaccine.

## World-Wide Smallpox Endemic Areas, 1970

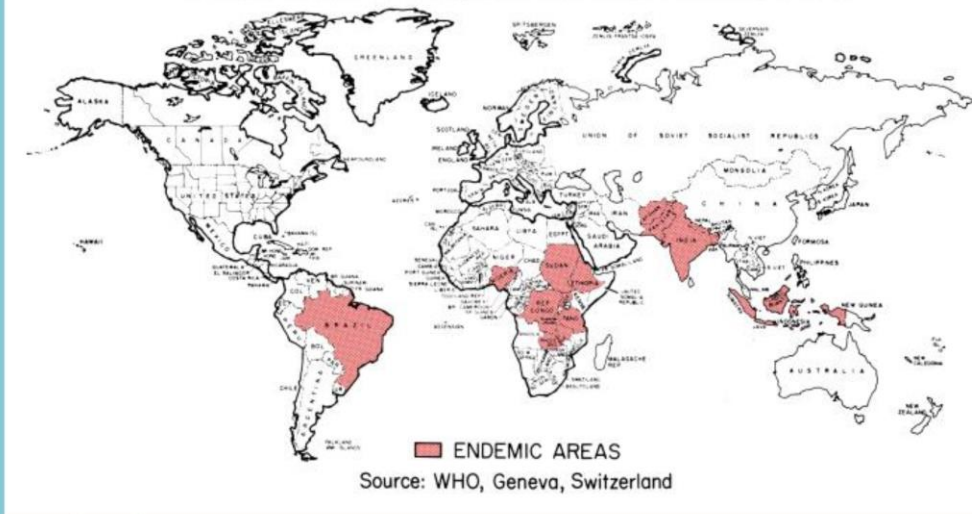


Image from: CDC Public Health Image Library

By 1970 significant progress had been made in eliminating Smallpox from most West African countries.





## World-Wide Smallpox Endemic Areas, 1976



Source: WHO, Geneva, Switzerland

Image from: CDC Public Health Image Library

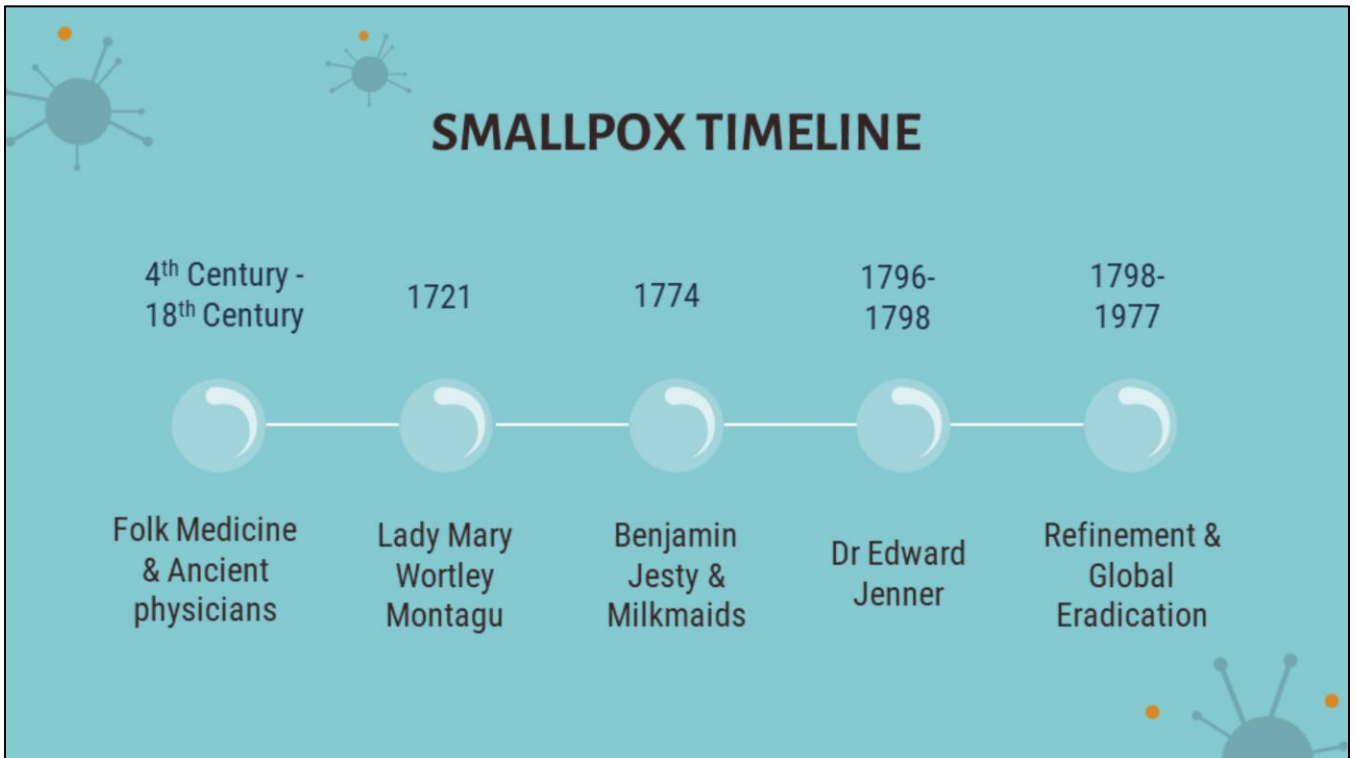
By 1976 it was eliminated from Asia.

## World-Wide Smallpox Endemic Areas, 1977



Image from: CDC Public Health Image Library

And in 1977 the very last case of naturally acquired smallpox occurred in Somalia. In 1980 the World Health Organization declared smallpox eradicated globally due to the vaccination campaign. Smallpox remains the only human disease that we have successfully eradicated from the globe, although significant progress has been made toward eliminating others.



Edward Jenner often gets credit for his medical breakthrough, and for being the father of vaccines, but I'd like to take a moment to keep our medical advancements in perspective. Ancient physicians documented different ways that variolation worked, and Jenner wouldn't have the opportunity to build off of that ancient wisdom if Lady Montagu hadn't pushed for its introduction in England.

Many people in the English countryside knew that getting cowpox could protect them against smallpox. Dr Jenner is the first person to systematically and scientifically prove that vaccination would work, but he was building off of hundreds of years of scientific progress and folk wisdom. And then countless other scientists and doctors continued those refinements until global eradication was possible.



**Montreal's Night-Mayor on  
his Ghostly Rounds**

Julien Henri, 1875

## THE MIASMA THEORY OF DISEASE

After Jenner it would be another 100 years before more vaccines were developed. At this point, we're still at a place in history where people didn't know that germs existed and were the reason for the disease. Much like how people thought smallpox came from diet or the environment, the prevailing theory of the time was that Miasma, a type of "bad air" from the environment caused outbreaks.



**Portrait of Louis Pasteur in his laboratory**

Adrien-Emmanuel Marie, 1885

## 1862: THE GERM THEORY OF DISEASE

The scientific community had known about microbes as early as 1677. Germ Theory, or the idea that these microbes were the cause of disease had been proposed as early as 1762. Many scientists contributed to growing evidence for it over the next century, but would not be proven until 1862 by a scientist named Louis Pasteur.





## 1862: THE GERM THEORY OF DISEASE

### Portrait of Louis Pasteur in his laboratory

Adrien-Emmanuel Marie, 1885


Pasteur invented the process of pasteurization, which is when we use heat, chemicals, or pressure to eliminate microorganisms living in food and beverages. His work on eliminating spoilage bacteria in beer, wine, and milk led to further theories that microbes were responsible for diseases in animals and humans.



## LOUIS PASTEUR INVENTED ATTENUATED VACCINES IN 1879



**FOWL CHOLERA**  
*Pasteurella multocida*



In 1878 Pasteur began to study a disease called Chicken or Fowl Cholera, which is caused by the bacteria *Pasteurella multocida*. Up to 45% of a chicken flock could be killed during an outbreak within a matter of just a few days. Pasteur had been experimenting to prove that bacteria from chickens could be used to infect other animals, including rabbits and guinea pigs.

He was also able to prove that animals that had been infected could become chronic carriers of the disease and continue to infect other animals even after they had recovered fully from their illness.

## LOUIS PASTEUR INVENTED ATTENUATED VACCINES IN 1879



**FOWL CHOLERA**  
Pasteurella multocida



**BACTERIA**  
Weakened through heat or  
exposure to air

In 1879, Pasteur's assistant prepared some bacterial cultures, and then both he and Pasteur went on vacation for a month. When they returned they attempted to grow some new bacteria from those cultures, and Pasteur noted that the bacteria were growing abnormally slowly. He then injected those slow growing bacteria into his chickens.

He injected enough that all of the chickens should have died, but to Pasteur's surprise, almost all of the chickens survived. He concluded that the bacteria had been weakened somehow, and that these chickens might now be immune to fowl cholera.

He prepared a fresh, deadly batch of *Pasteurella multocida* and injected the same chickens with it, and they once again survived. He also injected a new set of chickens with the fresh deadly bacteria to serve as a control group, and all of those chickens died.

The process of weakening a bacteria or virus is known as attenuation. The scientific community knew that a weak form of a disease could produce immunity – that was the whole idea behind using mild cases of smallpox for variolation and later cowpox for vaccination. But the ability to artificially weaken an existing disease was new.

## LOUIS PASTEUR INVENTED ATTENUATED VACCINES IN 1879



**“In the field of experimentation, chance favors only the prepared mind.”**

Louis Pasteur

While this discovery was partly an incredible stroke of luck resulting from Pasteur’s lengthy vacation plans, Pasteur often noted that: “In the Field of experimentation, chance favors only the prepared mind.” Pasteur’s assistant assumed a mistake had been made and wanted to throw out the old, slow-growing cultures but Pasteur stopped him.

He easily could have thrown his old cultures out, or not run a new experiment to compare the immunity of his accidentally vaccinated chickens to a naive flock.

But because of his follow-up, Pasteur’s chickens had given the world the knowledge they needed to start accelerating vaccine production by proving that we can create artificially weak microbes in a lab and then use them to teach our immune system how to survive their more deadly cousins.

## PASTEUR'S VACCINES INCLUDED:



### FOWL CHOLERA

Weakened with exposure to air

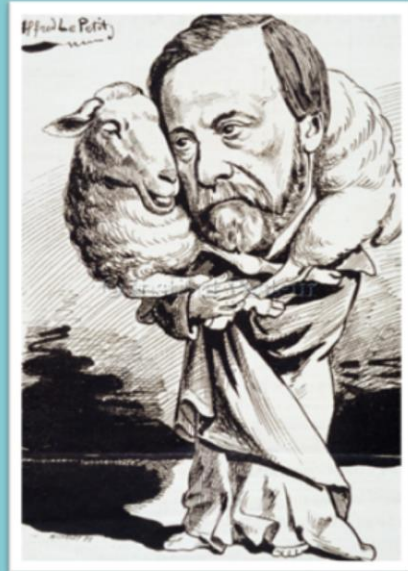
1879



### ANTHRAX

Weakened with chemicals and heat

1881



### *Le bon Pasteur*

Alfred Le Petit, 1882

Armed with the knowledge that he could alter microbes to make them less deadly, Pasteur set out to make more vaccines. By 1881 Pasteur and his team had made a successful vaccine for anthrax in animals. Anthrax is a bacterial disease that killed thousands of animals, especially sheep across Europe in the 19<sup>th</sup> Century, and the team weakened the bacteria by adding chemicals to the culture and heating it.

Pasteur's last name can be translated as "shepherd" in French, and a series of political cartoons began around this time referring to him as Le Bon Pasteur, which translates as The Good Shepherd because of his work in saving animals

## PASTEUR'S VACCINES INCLUDED:



### FOWL CHOLERA

Weakened with exposure to air

1879



### ANTHRAX

Weakened with chemicals and heat

1881



### SWINE ERYSIPELAS

Weakened by passage through rabbits

1883

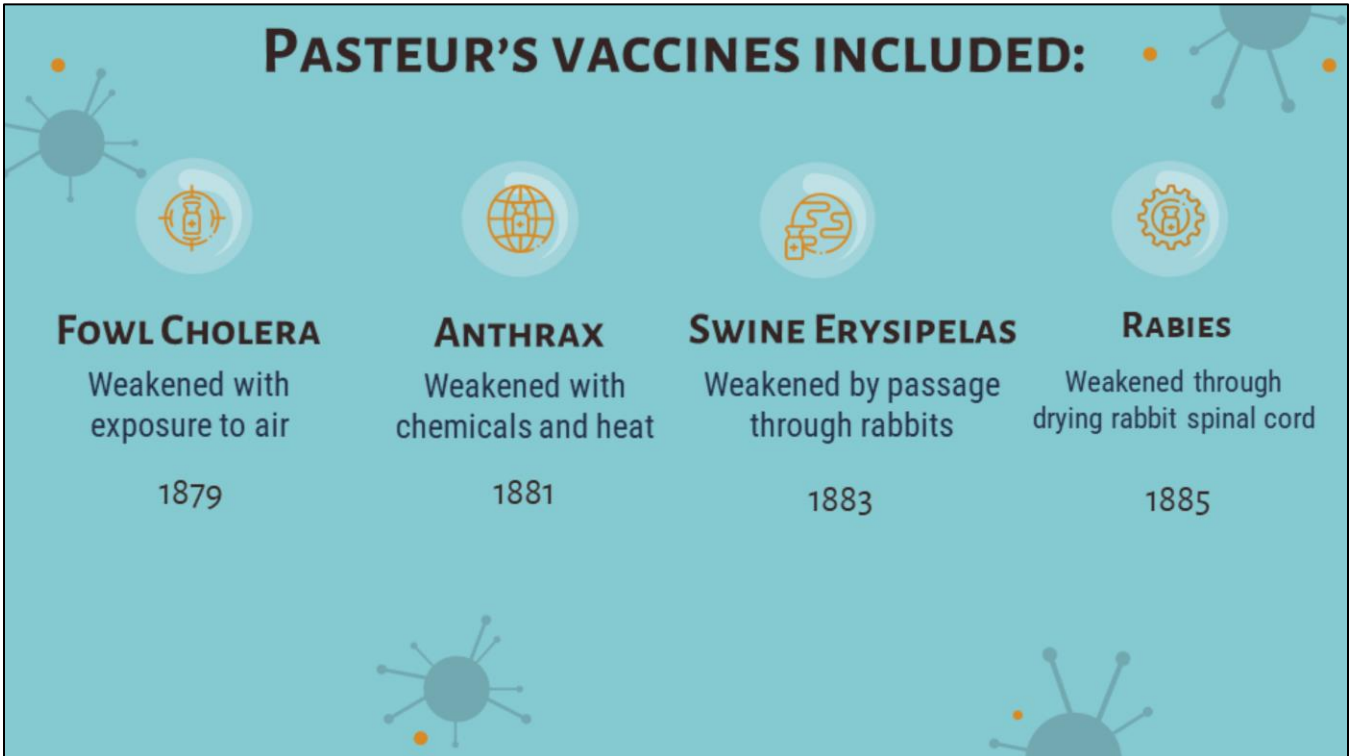


Next up one of Pasteur's students developed a vaccine for a disease of pigs called Swine Erysipelas, another bacterial disease that can kill piglets. Rabbits were infected with the disease, then germs from those rabbits were used to infect another set of rabbits and so on. The resulting bacteria was weak enough to not harm pigs while creating an immune response.

As you can see, the first three of Pasteur's vaccines were made to save livestock. There are a couple of reasons for this – for one, animal testing allowed for controlled conditions to study their theories of vaccination. And another is that there was good money in it – any vaccine that can protect livestock means that farmer's livelihoods and countries economies are protected.

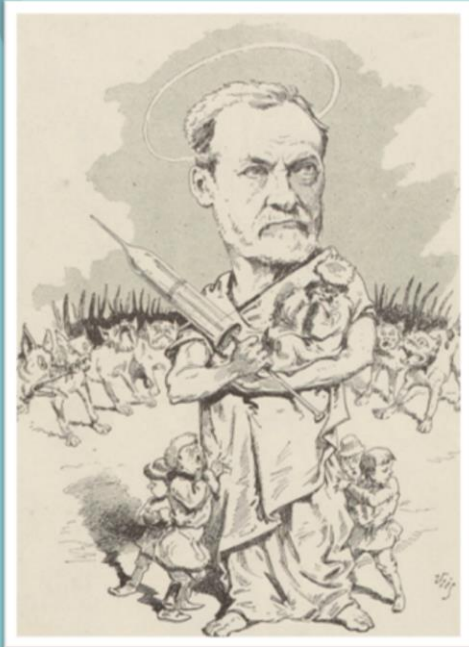


## PASTEUR'S VACCINES INCLUDED:



The last vaccine created by Pasteur's team was a vaccine for rabies. Unlike the other three, rabies is a virus not a bacteria. Viruses hadn't been discovered yet because they were too small to see with the microscopes available in the 19<sup>th</sup> century so it proved much more difficult. Other scientists throughout Europe were busy trying to isolate the agent...

None were ever successful, but there were able to experimentally infect rabbits and monkeys by injecting saliva or tissue from the nervous systems of infected dogs into the brains of other animals. Pasteur built off that work and attenuated the virus by drying out the spinal cord of rabbit and proved that this material could be used to prevent infection by vaccinating 50 dogs and then exposing them to rabies.



**“Every year at the same season, a terror strikes Paris... Rabies draws near, and gains force. Every dog becomes the object of suspicion—the poor dog, good as he is.”**

French journalist  
Clement Bertie-Marriott, 1882

Image courtesy of the Pasteur Institute  
Originally published in *Le Courrier*, April 4, 1886

Pasteur was already internationally famous, but the creation of a Rabies vaccine was a HUGE deal at the time. Here he is, once again pictured as Le Bon Pasteur (The Good Shepherd) this time warding off rabid dogs with a vaccine syringe and protecting small children with a halo over his head. Rabies was an absolutely terrifying disease at the time, and honestly is still pretty terrifying today.

As one 19<sup>th</sup> century journalist said, “every year at the same season a terror strikes Paris... Rabies draws near and gains force. Every dog becomes the object of suspicion, the poor dog, good as he is.”

Even though a small portion of the population would be bitten by rabid animals, there was a lot of hysteria about the disease. In cities being attacked by a rabid dog would make local newspapers. In the countryside foxes and wolves were usually the source of infection.

In one sensational case, a single rabid wolf bit 46 people and 82 cows in one day in the French countryside. While not every person who is bitten by a rabid animal will develop rabies, when a human showed symptoms the disease was 100% fatal.

## RABIES VACCINE TRIALS



Statue of Jean-Baptiste Jupille, 1887  
Photo credit: Doug Briant, 2014

Pasteur's vaccination presented their only chance of survival. There was a lot of controversy over the use of the vaccine at the time, and one of Pasteur's assistants refused to participate with vaccinating human victims of the disease. There was a very valid concern that using the vaccine could give someone rabies, but the only way the vaccine would work is if it was given to someone before they became symptomatic.

The first human successfully vaccinated for rabies was a 9 year-old who had been severely injured by a rabid dog. The second person successfully vaccinated against rabies was the most famous. Jean-Baptiste Jupille, a 15 year-old shepherd had been bitten multiple times while saving a group of young children from a rabid dog in the countryside.

The boy's vaccination received worldwide news coverage, and he was immortalized in a statue at the Pasteur Institute for his bravery. Following news of his survival, desperate people began showing up at Pasteur's laboratory from all over Europe.



## **RABIES VACCINE TRIALS 1885–1898 20,166 VACCINATIONS**

Statue of Jean-Baptiste Jupille, 1887  
Photo credit: Doug Briant, 2014

More than 1,000 people per year received rabies vaccines in the first 13 years that it was introduced which allowed for a comparison of the mortality rates.



Statue of Jean-Baptiste Jupille, 1887  
Photo credit: Doug Briant, 2014

## **RABIES VACCINE TRIALS 1885–1898**

**20,166 VACCINATIONS**

**0.5% MORTALITY RATE IN  
VACCINATED**

Overall, the annual report of the Pasteur Institute showed that of the more than 20,000 people vaccinated, just 0.5% would die. And most of the deaths occurred in people that were already symptomatic when they received the vaccine.





Statue of Jean-Baptiste Jupille, 1887  
Photo credit: Doug Briant, 2014

## **RABIES VACCINE TRIALS 1885–1898**

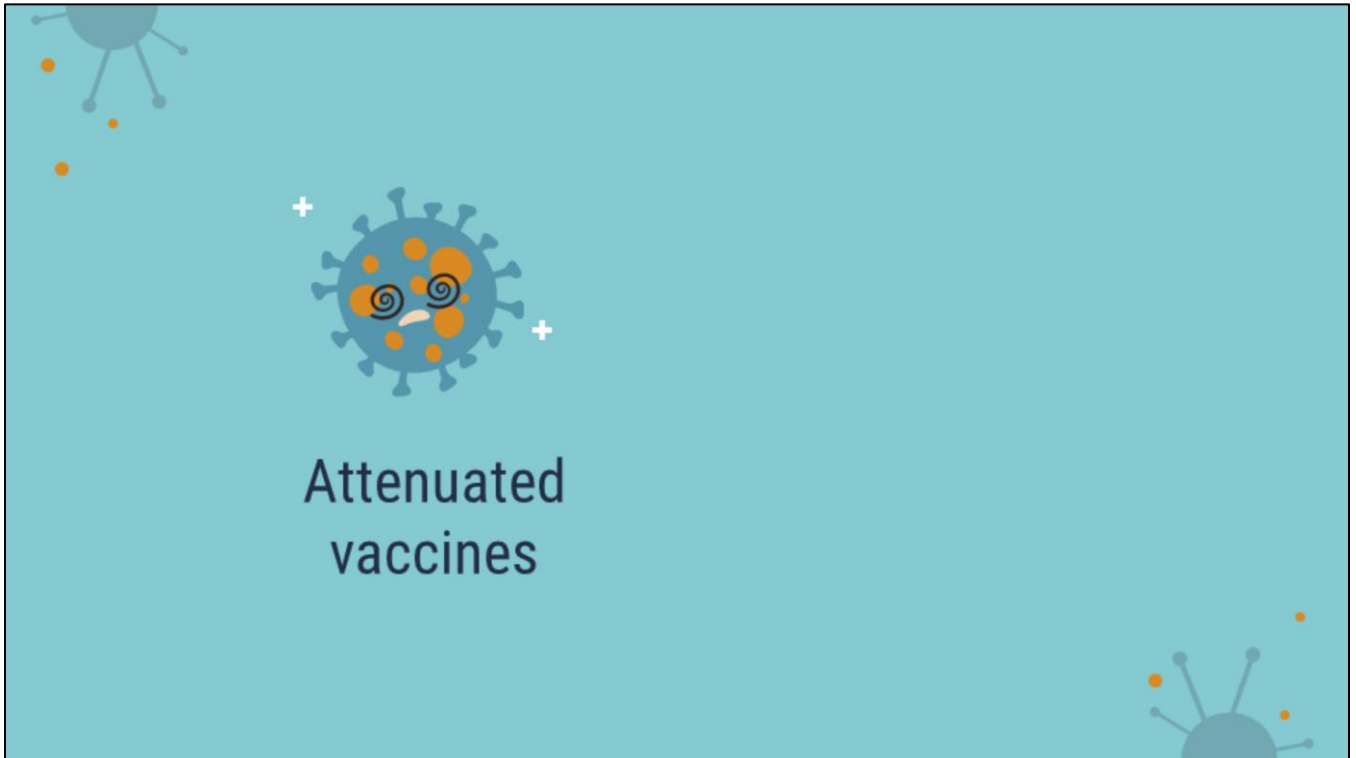
**20,166 VACCINATIONS**

**0.5% MORTALITY RATE IN  
VACCINATED**

**16% MORTALITY RATE IN  
UNVACCINATED**

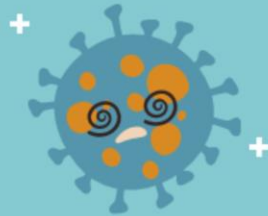
That was much better compared to a death rate of the unvaccinated, who experienced a 16% mortality rate





## Attenuated vaccines

All of the vaccines we've talked about so far were developed with one strategy: attempting to weaken live bacteria or virus so that our immune system can learn to fight against a weaker version of the disease.



## Attenuated vaccines

1796: Smallpox

1881: Anthrax

1884: Rabies

1896: Cholera

1938: Yellow Fever

1963: Poliovirus

**1963: Measles**

**1967: Mumps**

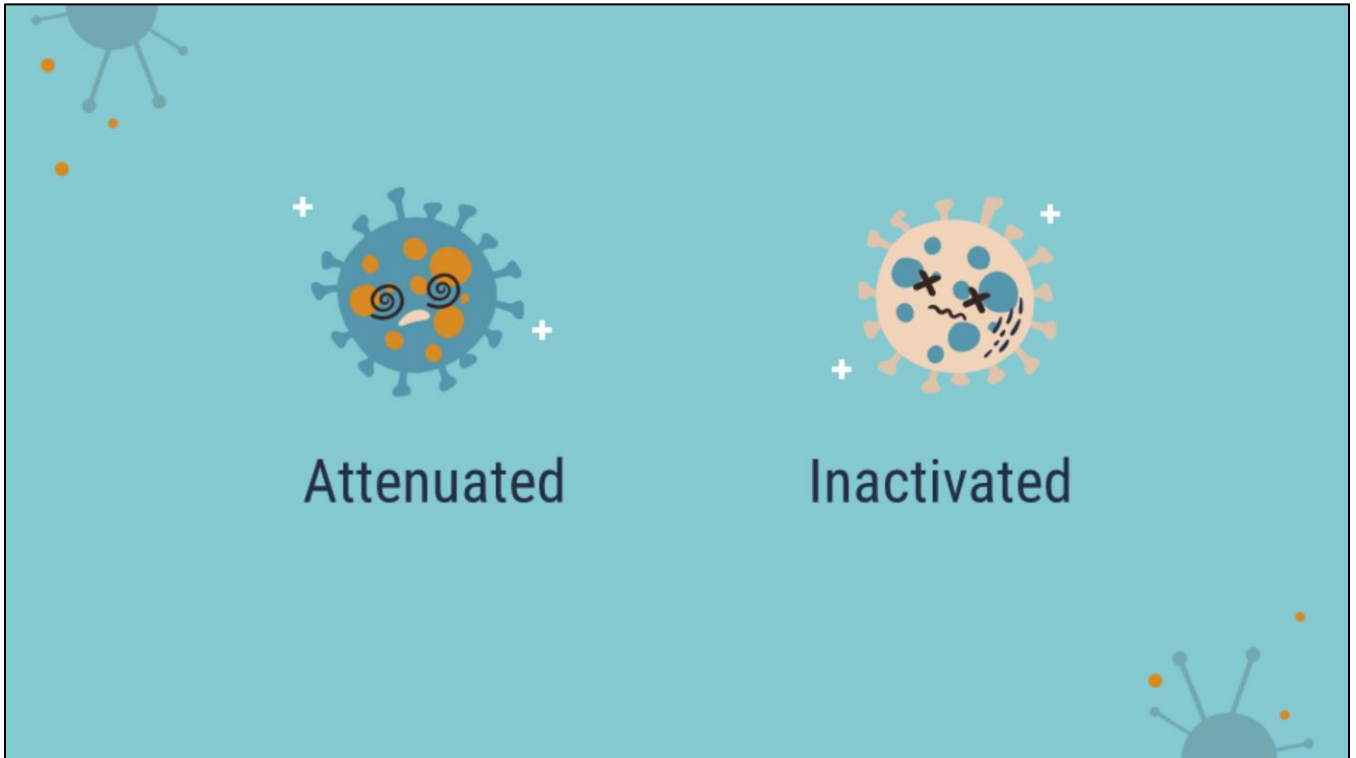
**1969: Rubella**

1971: Adenovirus

**1984: Chickenpox**

1998: Rotavirus

I'm not going to have time this morning to go the history of every single vaccine, but many vaccines we use today still use this principle including the vaccines for Measles, Mumps, Rubella, and Chickenpox



Instead of modifying the microbe, we also have the option of killing it so that it is not able to cause any disease, and then letting our immune system try to learn how to protect itself after injecting the dead organism. Killed vaccines were introduced at the same time that Pasteur was trialing his attenuated vaccines.

## The first inactivated vaccines provided very short-term immunity, didn't work well and caused awful side effects



1884

Cholera



1896

Typhoid



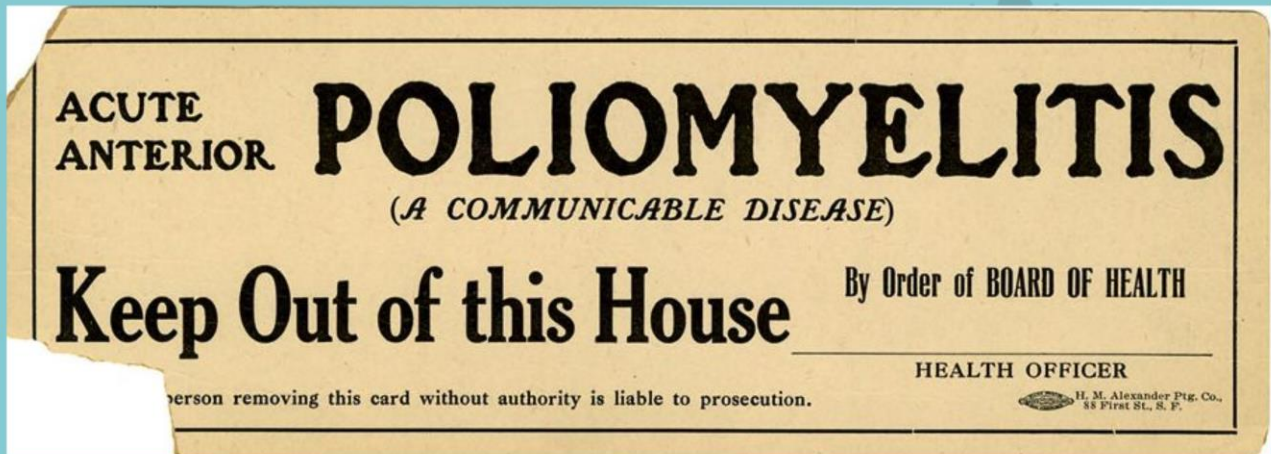
1897

Plague

But unfortunately most of these original vaccines only provided very short-term immunity, did not work well, and had many awful side effects including severe skin infections at the site of injection

This includes attempted vaccines for cholera, typhoid, and plague but none worked well and were soon abandoned. It would take almost 60 more years of scientific advancement before a truly effective inactivated vaccine was developed for the first time.

## 1900s: POLIO OUTBREAKS BEGIN IN THE U.S.



Quarantine Order posted in San Francisco circa 1910

Image courtesy of The National Library of Medicine

Until the mid-20<sup>th</sup> century, inactivated vaccines continued to progress but were pretty unimpressive. A vaccine for Yellow Fever was attempted but abandoned. The first vaccines for influenza were developed at the end of World War II but weren't terribly protective in the long term because influenza mutates constantly.

So when poliovirus started sweeping the United States in the 20<sup>th</sup> century scientists at the time felt strongly that an attenuated live vaccine would probably be needed. Polio is a viral infection that had historically infected infants. But as our sanitation systems improved, exposure to polio started to be delayed.

Starting in 1916 there were outbreaks every summer in the United States because people had not been exposed to the disease as infants. This led to people being quarantined in their homes by Health Departments as we see in this quarantine order from San Francisco circa 1910.

## 1940S-1950S: POLIO OUTBREAKS INTENSIFY

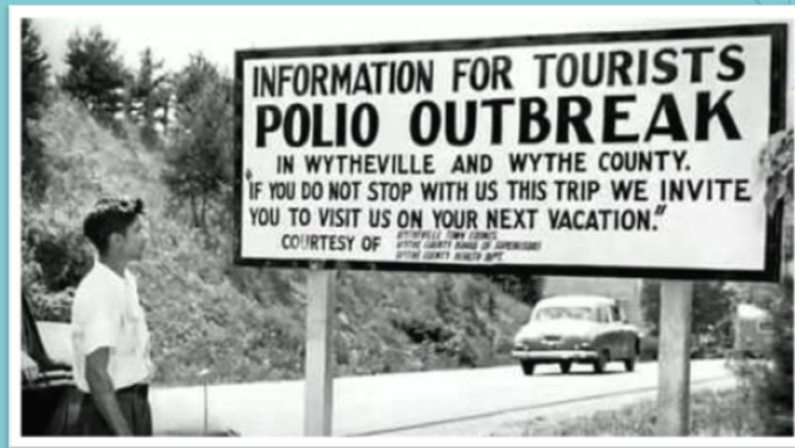


Image courtesy of Visit Wytheville / [visitwytheville.org](http://visitwytheville.org)

By the 1930s, scientists began looking for a cure. Because polio only naturally infects humans, it was really hard for scientists at the time to figure out how to grow the virus in a lab because they had previously only used animal tissue to grow microbes. As they searched, the outbreaks intensified throughout the 1940s and 1950s causing panic. Towns would shut down public places where kids would congregate, like pools and parks.

And entire towns may ask visitors to stay away as we see in this billboard from Wytheville, Virginia that experienced the most concentrated outbreak of polio in US history in 1950. An oral history from Wytheville referred to 1950 as the “summer without children.” Parents kept their children inside, people distanced themselves. The local tourism industry shut down. Businesses, swimming pools, the local theater and public facilities closed.

The streets were deserted. Farmers were afraid to take the livestock to market. The local baseball team cancelled their season. People were afraid to touch money, washed their hands constantly, had their groceries delivered. Families sent their young children to stay with relatives or friends out of town whenever they could.

The nearest hospital to Wytheville was 80 miles away, but it was segregated meaning that black patients were denied admission and had to be driven nearly 300 miles for care.



## PARALYTIC POLIO RAVAGES COMMUNITIES



Images courtesy of The Centers for Disease Control and Prevention

The virus is usually very mild in young children but can kill or paralyze older children and adults. In children over the age of 5, 1 out of 1000 would become paralyzed by the disease, and for adults the chance of paralysis was just 1 in 75. Outbreaks peaked in 1952 when there were nearly 60,000 cases.

A little more than 5% the infected died, and close to half of the survivors experienced some type of paralysis. This could result in lifelong disabilities like this girl whose leg atrophied after infection. Some patients also required the use of an Iron Lung, a type of mechanical respirator.

If they never regained control of the muscles needed for breathing, patients could be stuck in them for their whole lives – the record holder spent 42 years of his life in an Iron Lung.



**Jonas Salk, 1956**

Photo credit: Yousuf Karsh

Courtesy of the Smithsonian Institution

**Dr. Jonas Salk believed  
that an inactivated  
vaccine could provide  
immunity to polio**

The race for a vaccine became very dramatic. Dr. Jonas Salk had worked on the inactivated influenza vaccine when he was younger and held the view that you did not need to be infected with a live virus to develop immunity.

Salk felt that a killed vaccine would create the immunity needed to break the ongoing national outbreaks, the trick was just finding a way to inactivate the virus without destroying its ability to produce an immune response. It also had the advantage of being quicker and easier than making an attenuated vaccine. Salk's polio vaccine was ready to go and licensed for use by 1955.

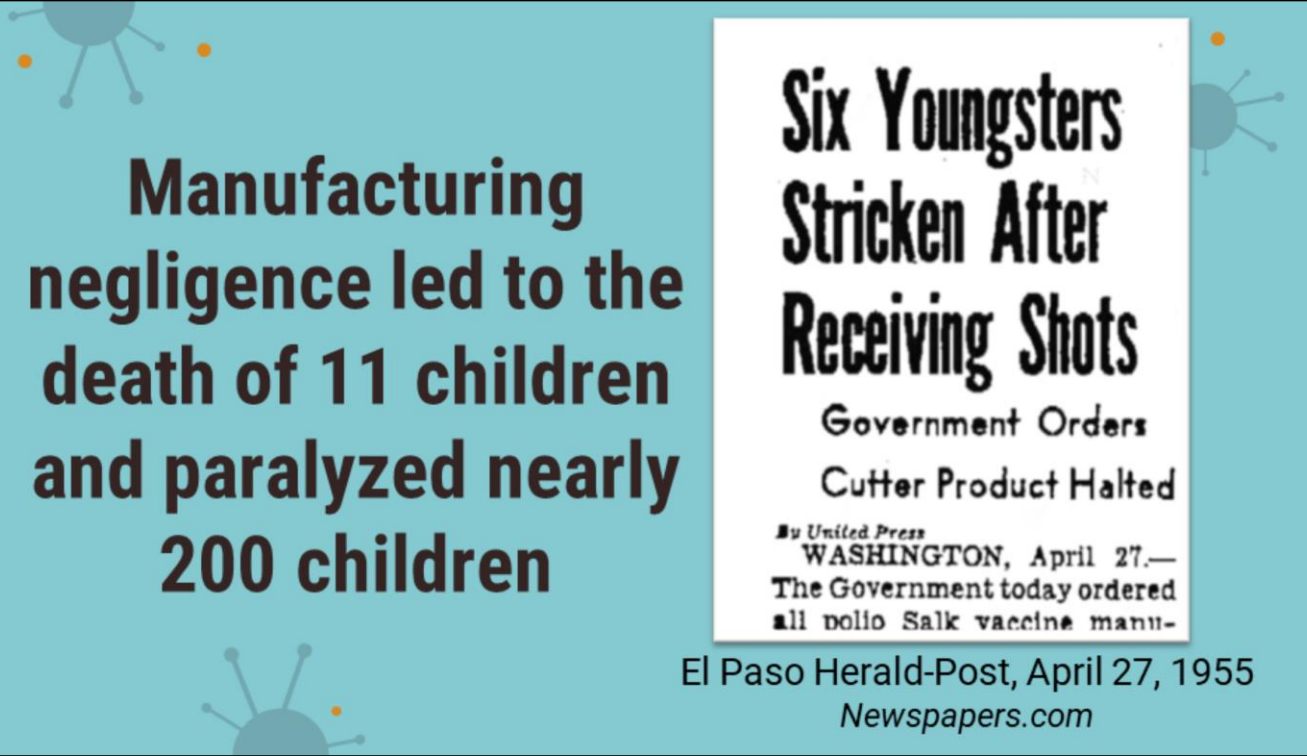
# Salk's inactivated vaccine was 80-90% effective



Image credit: March of Dimes

As Salk's vaccine went to trial, hundreds of thousands of children were signed up. The vaccine was tested on 600,000 children and proved to be 80-90% effective. The results were announced at a raucous news conference and the nation was riveted. The scientific community however, was upset with the roll out of the vaccine.

With the results announced at a press conference instead of a scholarly journal, many also felt that this spit in the face of the scientific process where other scientists could evaluate the results of the experiment. Some felt that Salk was elevated to the role of "Celebrity scientist" and appropriate credit was not being given to the many, many hard-working people working across the country helping to develop the vaccine.

The background of the slide features several stylized virus icons, each consisting of a central grey circle with several thin grey lines radiating outwards, and a few small orange dots scattered around. These icons are positioned in the top-left, top-right, and bottom-left corners of the slide.

**Manufacturing  
negligence led to the  
death of 11 children  
and paralyzed nearly  
200 children**

**Six Youngsters  
Stricken After  
Receiving Shots**

**Government Orders  
Cutter Product Halted**

*By United Press*  
**WASHINGTON, April 27.—**  
The Government today ordered  
all polio Salk vaccine manu-

El Paso Herald-Post, April 27, 1955  
*Newspapers.com*

To make matters worse, disaster struck within just a few weeks of the vaccines official licensing when children began dying. It turned out one of the six companies manufacturing the vaccine did not appropriately inactivate the virus.

Instead of injecting a killed microbe, thousands of children had potentially been vaccinated with live, full power polio virus. In the end 200 polio cases resulted from those vaccines, 11 died, and almost all of the victims were severely paralyzed.



Photo credit: WHO/Pasteur Merieux

**Dr. Albert Sabin believed that an attenuated live virus would be needed to provide immunity to polio**

There were other scientists working on developing vaccines at this time as well. Dr. Albert Sabin was a rival of Dr. Salk and immediately called for all of inactivated vaccines to be pulled from the market when news of the vaccine-associated outbreak broke. He strongly believed that a weakened live-virus would be needed to provide immunity safely.

Generally speaking, modified live virus vaccines provide stronger immunity that is longer lasting, meaning that boosters would not be needed. Live virus vaccines could be administered by oral drops which would simulate the way that people normally got sick from polio. It's a harder task to develop however, and it took Sabin six years longer to develop his vaccine than Salk





## **Sabin's vaccine was used to vaccinate 77 million children in the USSR in 1959 and became the preferred vaccine worldwide**

Photo credit: Bettmann Archive / Getty Images

Because so many children in the United States were already vaccinated for polio, Sabin ended up testing his vaccine in the Soviet Union so that the true efficacy could be determined. By the end, 77 million children in the USSR were vaccinated with the oral vaccine and the country credited him with effectively eliminating the disease.

The injectable killed vaccine developed by Salk never had any issues again, and it's what we still use in the United States today. But Sabin's vaccine would become more popular worldwide

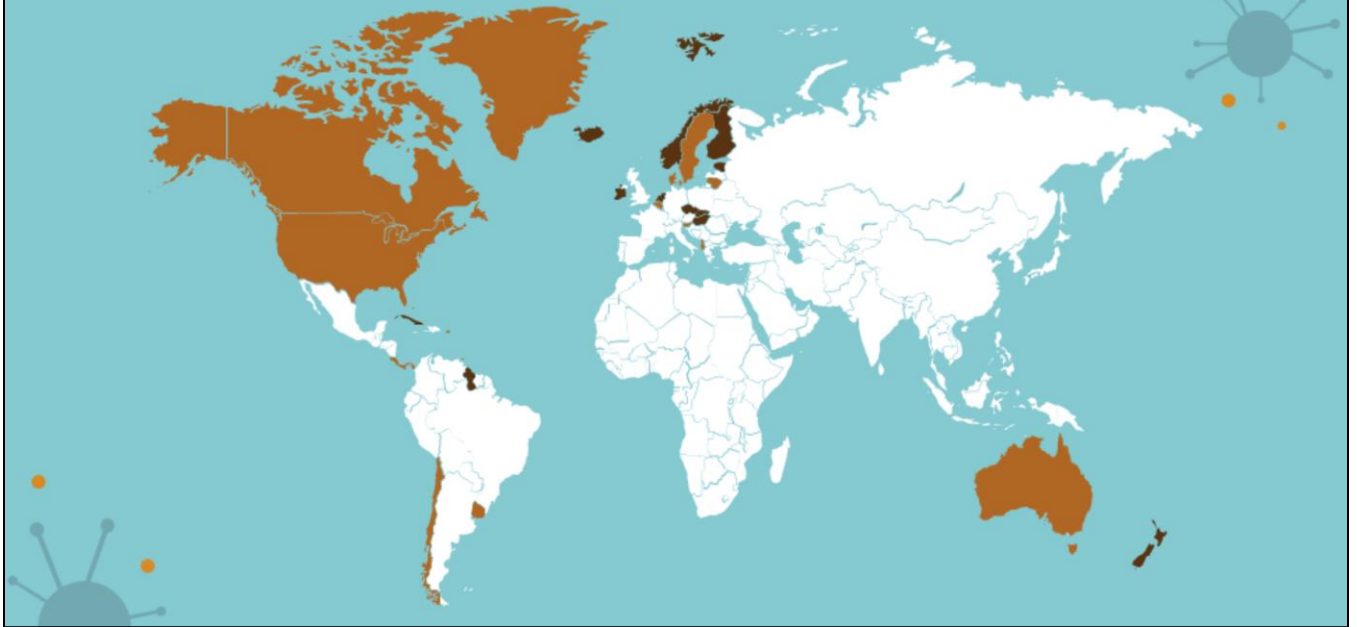


## PARALYTIC POLIO ELIMINATION 1960S



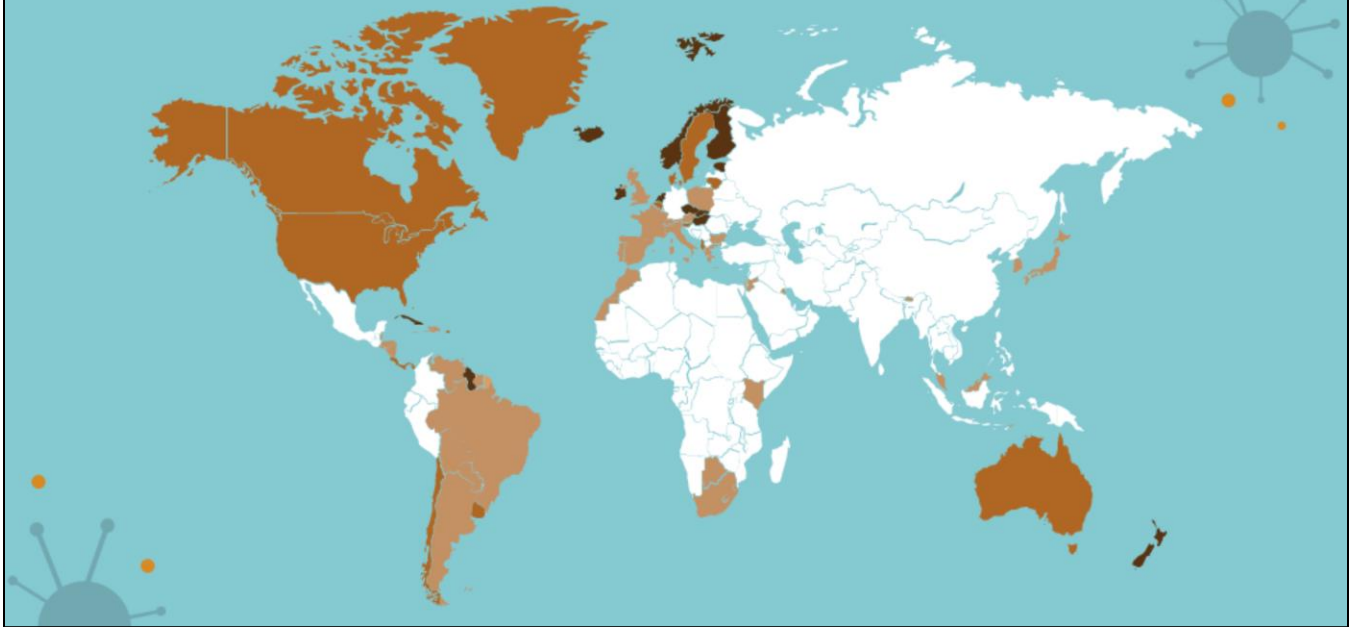
By the 1960s only a few countries had eliminated polio

# PARALYTIC POLIO ELIMINATION 1970S



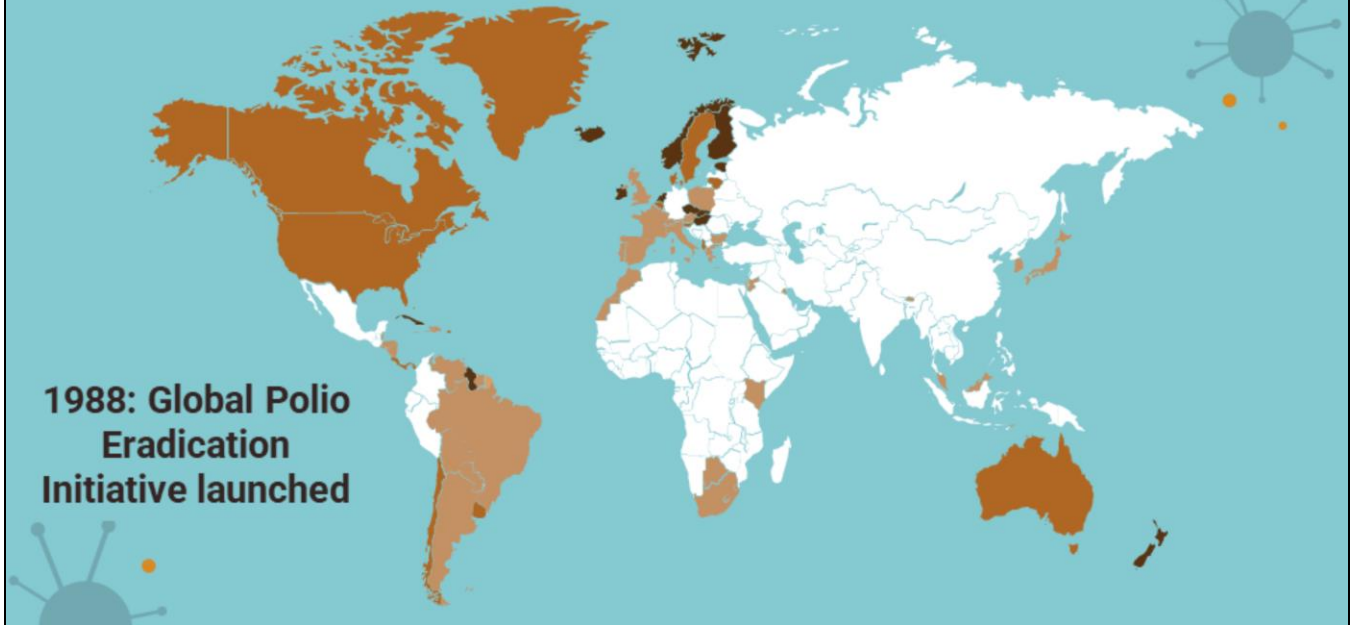
But the number grew steadily by the 1970s,

## PARALYTIC POLIO ELIMINATION 1980S



And in the 1980s through country level efforts to vaccinate children.

# PARALYTIC POLIO ELIMINATION 1980S



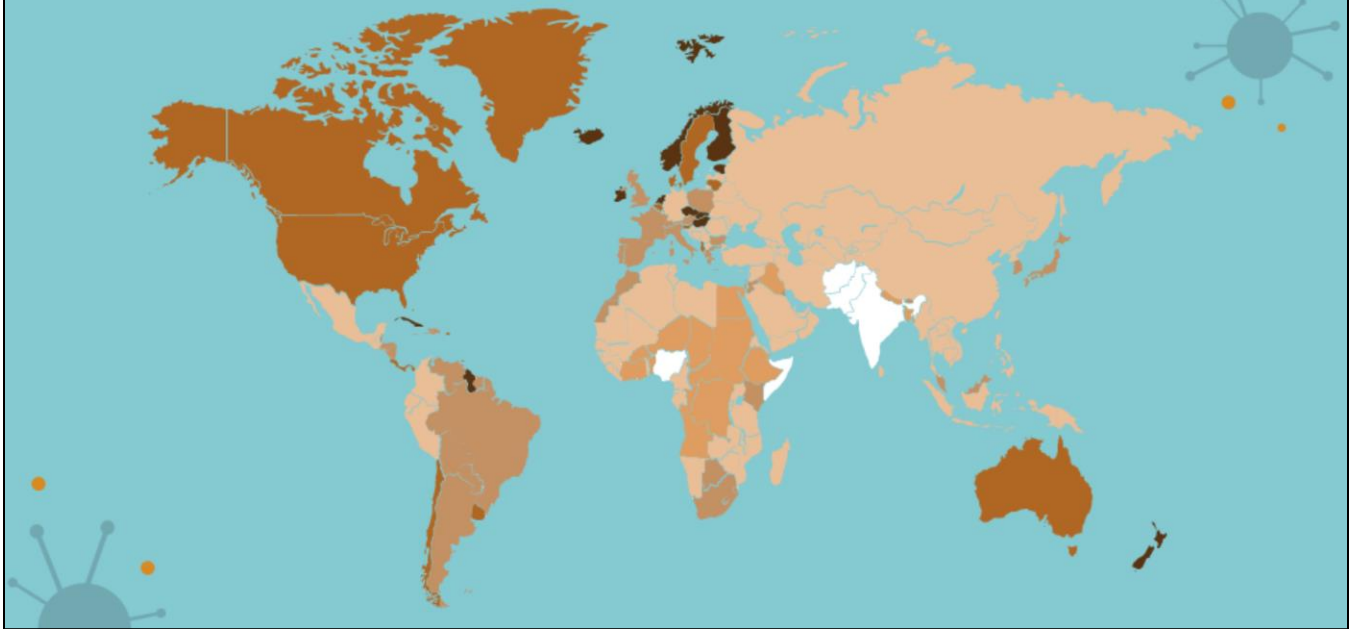
In 1988 the Global Polio Eradication Initiative was launched by the World Health Organization

# PARALYTIC POLIO ELIMINATION 1990S



Which helped to quickly eliminate polio across most of the world by the 1990s...

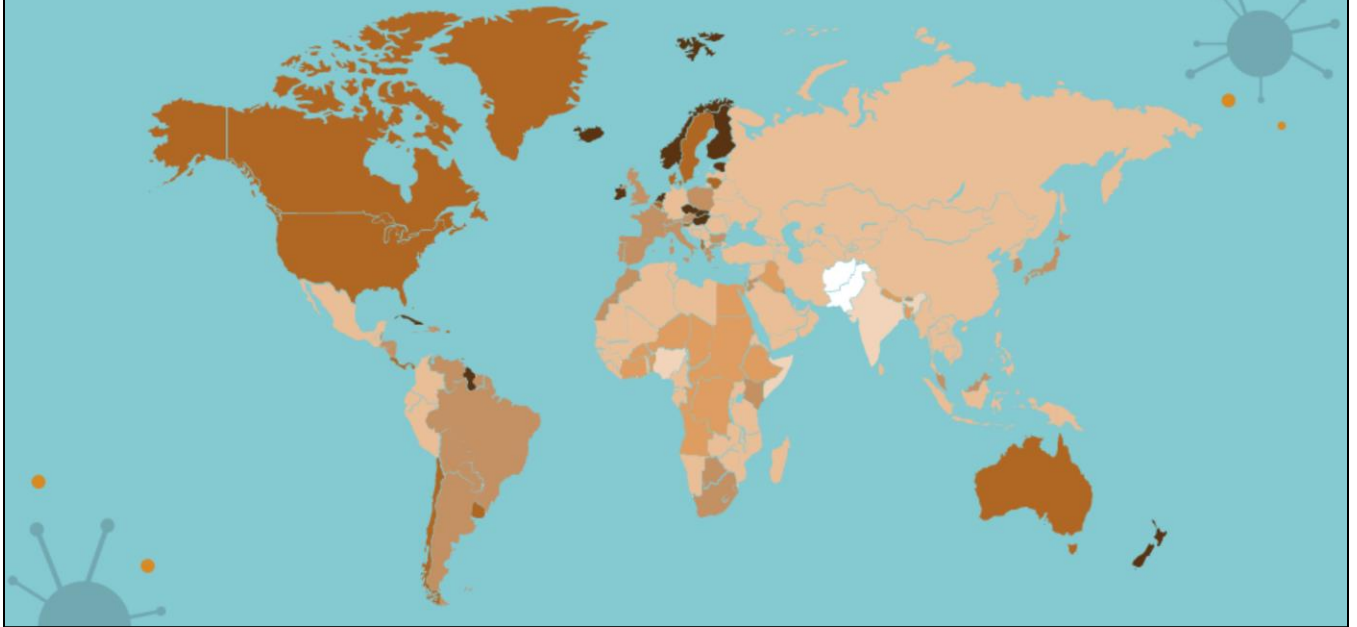
# PARALYTIC POLIO ELIMINATION 2000S



And the 2000s

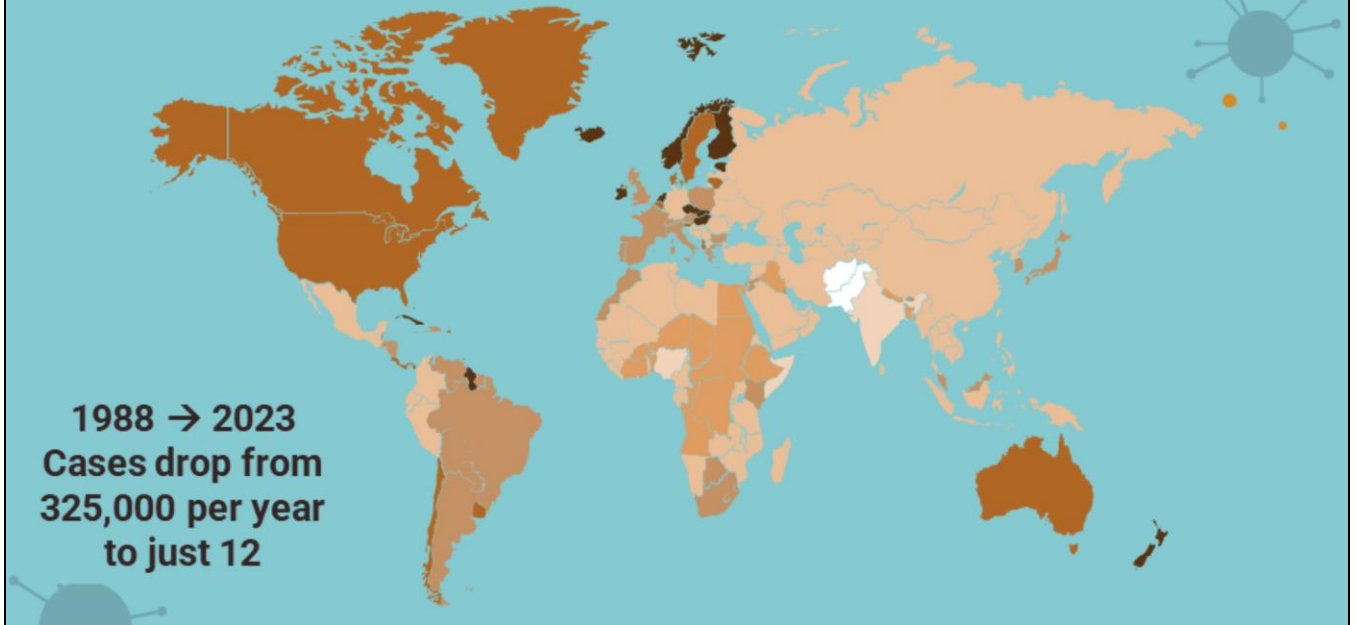


# PARALYTIC POLIO ELIMINATION 2010S



Polio was nearly eradicated worldwide by the 2010s.

# PARALYTIC POLIO ELIMINATION 2020S



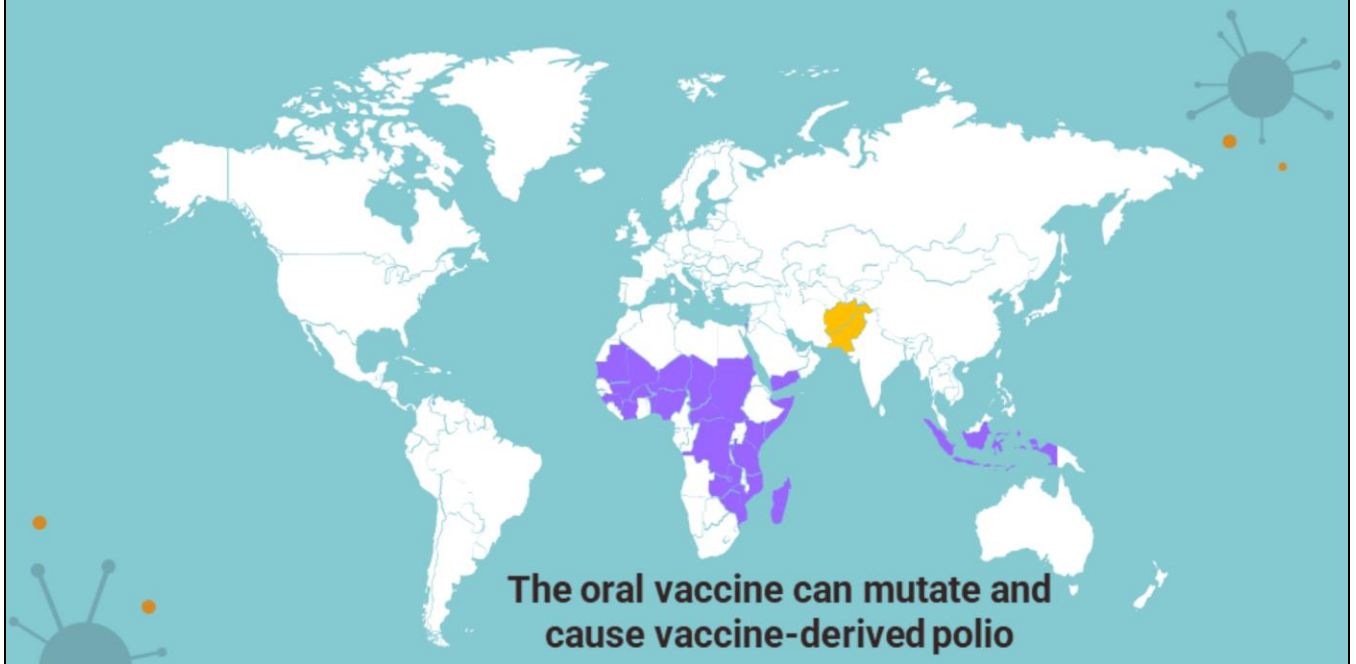
And from 1988 to 2023, global cases of polio dropped from 325,000 to just 12 total worldwide.

## PARALYTIC POLIO ENDEMIC COUNTRIES



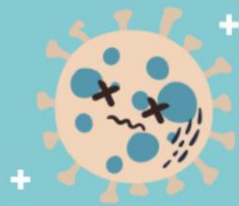
But wild type polio is still endemic in one location today – the border region of Afghanistan and Pakistan.

## PARALYTIC POLIO CASES - 2023



The live oral vaccine developed by Sabin is still the preferred vaccine in most of the world – it provides better immunity, doesn't require boosters, and it's easier to store and administer by lay people. But one of the drawbacks of the attenuated live virus is that it can mutate inside of the human body. So, it sometimes reverts back to a more potent infectious form and can cause outbreaks of vaccine-derived virus.

This is a map of countries that had polio cases just last year. While wild type polio is limited to Afghanistan and Pakistan; all of the countries in purple had cases that were caused by the mutated vaccine strains of the virus. Global work is still continuing to eradicate polio completely.



## Inactivated vaccines

- 1945: Influenza**
- 1955: Poliovirus**
- 1980: Rabies**
- 1991: Hepatitis A**
- 1992: Japanese Encephalitis**

To avoid the issues with mutated vaccine-derived poliovirus, many countries with robust healthcare access, including the United States, continue to use Salk's inactivated polio vaccine today. Other inactivated vaccines include influenza, hepatitis A, and Japanese encephalitis. We also switched to an inactivated rabies vaccine in 1980 for safety reasons. Because rabies is 100% fatal, we want to make sure that there is no chance of accidentally inducing disease due to a mutation in a modified live-virus vaccine.



Attenuated



Inactivated



Sub-unit

**use just part of the  
pathogen to cause an  
immune response**

Attenuating a live microbe or killing it aren't the only tricks we have up our sleeves for developing vaccines. Instead of teaching our immune system how to recognize an entire germ, we can also teach it how to recognize just a part of the microbe. Because a subunit vaccine doesn't contain a whole pathogen, there is no risk of introducing the disease, which makes these vaccines safer and easier to manufacture than other types.





Watercolor by Richard Cooper, 1912

## **DIPHTHERIA: THE STRANGLING ANGEL OF CHILDREN**

The first disease that made it clear that we could do this was Diphtheria. Diphtheria was primarily a disease of childhood and was sometimes called The Strangling Angel of Children because inflammation in the airways could cause children to slowly suffocate to death. By the late 1800s in the United States approximately 100,000 cases occurred every year and 15% of the children infected died.



## 1889: DIPHTHERIA ANTITOXIN IS DEVELOPED IN GUINEA PIGS

Photo credit: Bettmann Archive / Getty Images

In 1888, two of Pasteur's students demonstrated that the symptoms came not from the bacteria itself, but from toxins that the bacteria produced. A race began to try to figure out how to combat the effects of the toxin, and scientists in Germany developed a treatment in guinea pigs.

They took the blood of guinea pigs that were given sub-lethal doses and injected their blood serum into sick guinea pigs. Scientists didn't know it yet, but blood serum contains the antibodies that our body produces, so by injecting antibody laden serum into sick animals gave them what they need to fight the disease but without teaching their immune system how to defeat the pathogen itself

## LARGE SCALE PRODUCTION OF DIPHTHERIA ANTITOXIN CAME FROM HORSES



Photo credit: otsphoto/Adobe Stock

The problem with guinea pigs in moving forward with treatment is that they are very small. This makes them a great lab animal, but not so great for producing antitoxin on a large enough scale to use in the thousands of children who were getting sick every year. And this is where horses come into our story. Compared to an average 2 lb guinea pig, the average horse weighs in at more than 1000 pounds.

Large scale production of antitoxin began in 1893 using horse blood. Horses were injected with diphtheria and once they had sufficient time to mount an immune response, their blood was harvested and spun down so their serum could be used in humans.

# THE RACE TO SAVE NOME, ALASKA FROM DIPHTHERIA

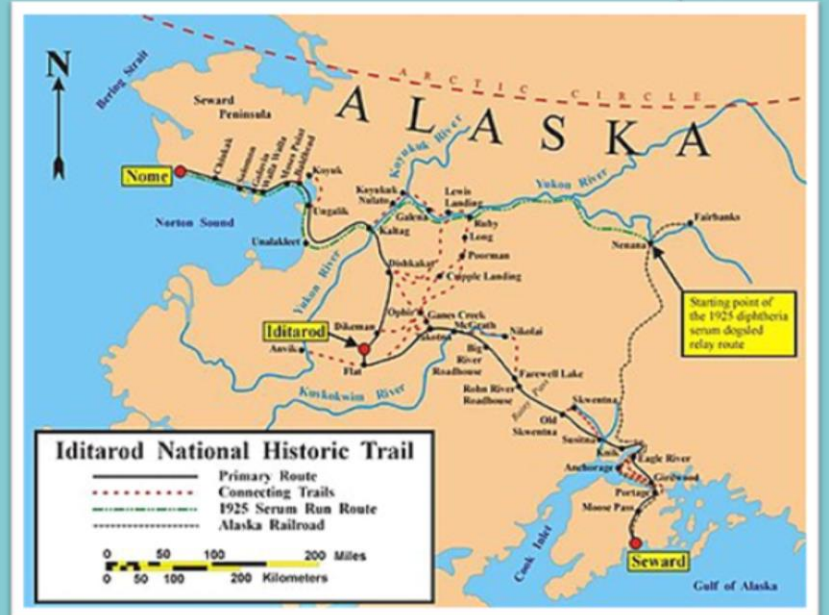


Image credit: U.S. Bureau of Land Management

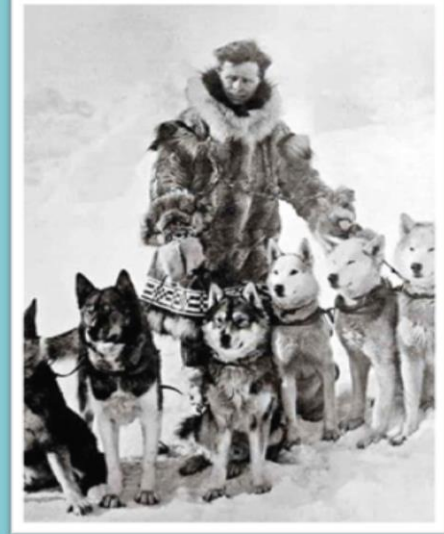
It became clear that the antitoxin greatly improved a child's chances of living, and the serum from horse blood reduced the death rate by half. The problem with antitoxin, is that you had to live somewhere where it was available to benefit from it. While patients in an outbreak could eventually get antitoxin, the first patients experiencing symptoms may not be so lucky.

This problem came to a head in an outbreak in Nome, Alaska during the winter of 1925. Because the sea was frozen, antitoxin could not be shipped to the community directly. Antitoxin had to be sent instead by boat from Seattle to Seward, on the southern coast, then by train to inland Alaska, and finally by a relay team of dog mushers that had to cross the final 671 miles as fast as possible to prevent widespread death in the town's children.

## 1925 SERUM RUN TO NOME



**Gunnar Kaasen & Balto**  
Brown Brothers, 1925



**Leonhard Seppala, Togo, and sled team**  
Carrie M McLain Museum, circa 1924

A severe winter storm plagued the dog team relay, with windchill as low as -85 degrees Fahrenheit. Many dogs died and all of the mushers suffered frostbite. The mushers and their dogs became national celebrities, and several books, news stories, movies have been made to honor the two most important lead sled dogs, Togo and Balto.

Gunnar Kaasan and his dog Balto often get a lot of the credit because they ran the last leg of the relay to Nome. But Leonhard Seppala and his team were the most important team in the relay – with his lead dog Togo, Seppala ran the longest distance, including the most treacherous across frozen rivers, covering 170 out of the 671 miles.

The trip would normally take a dog sled team 30 days, but the mushers & dogs raced day and night to get the serum to Nome in just 5. Every year the Iditarod dog sled race is run to commemorate this act of heroism.



# DIPHTHERIA BECOMES THE FIRST TOXOID VACCINE

**1904: Horses**

**1907: Guinea Pigs**

**1923: Humans**



**Extraction of diphtheria serum from horse blood at the Behring factory in Marburg**

Fritz Gehrke, ca 1895

It was clear that a vaccine would be preferable to the antitoxin – it would be far better for people’s immune systems to be able to fight off the toxin instead of relying on a horse to create antibodies

The diphtheria bacteria couldn’t be used to make a vaccine in the same way that others had worked because the bacteria itself didn’t make people sick, just the toxin it produced once it was in the body, so scientists had to figure out a way to make a vaccine for a toxin for the first time.

A German physician named Paul Ehrlich had worked extensively on making diphtheria antitoxin effective. During his experiments he discovered that the chemical formalin could render the toxin into a toxoid – an inactive form. Diphtheria toxoids were used to vaccinate horses as early as 1904, and experiments in 1907 proved that it could produce immunity in guinea pigs.

It took about 20 years to prove that this could also be applied to humans. Immunity in humans was finally achieved in 1923 with a toxoid that had been rendered harmless through the application of chemicals and heat.



# SUB-UNIT VACCINES

## 20<sup>TH</sup> CENTURY DEVELOPMENT

- Toxoid
  - Polysaccharide
  - Conjugate
  - Recombinant
- Other
    - purified protein
    - acellular extracts
    - virus like particles
    - outer membrane vesicles
    - synthetic peptides

The realization that we did not need to use a whole microbe to create a vaccine opened a whole new line of development for sub-unit vaccines. Once we'd established toxoid vaccines, we experimented a host of different strategies for sub-unit vaccine development.

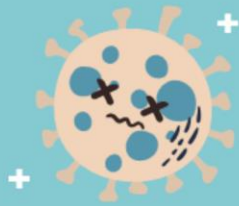
# SUB-UNIT VACCINES

## 20<sup>TH</sup> CENTURY DEVELOPMENT

- Toxoid
  - Other
  - Recombinant
    - synthetic peptides
- icles

Any sub-unit can work as long as it is antigenic!

but they all basically boil down to scientists taking some part of the microbe to create a vaccine. Any sub-unit can work to as long as it is antigenic, or capable of producing an immune response.



## Sub-unit vaccines

**1913: Diphtheria**

**1914: Whooping cough**

**1924: Tetanus**

**1936: Pneumococcal**

**1954: Anthrax**

**1969: Meningococcal**

**1981: Hepatitis B**

**1985: Haemophilis Influenza Type B**

**2006: HPV**

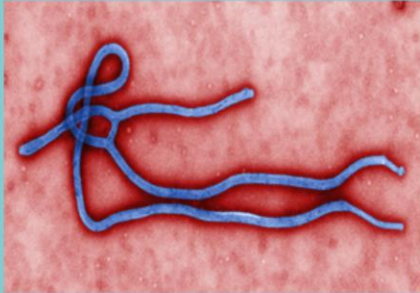
**2006: Shingles**

**2015: Malaria**

After developing the diphtheria vaccine, an additional 10 sub-unit vaccines were licensed using different techniques for diseases such as whooping cough, tetanus, pneumococcal and meningococcal disease, hepatitis B, HPV, shingles and... most recently, for malaria.

## FUTURE AREAS OF DEVELOPMENT: TEACH YOUR BODY HOW TO MAKE SPECIFIC TYPES OF PROTEINS

### VIRAL VECTORS



Trials: 1984

1<sup>st</sup> FDA licensed vaccine:  
Ebola (2017)

*Image credits: CDC/Cynthia Goldsmith*

The newest types of vaccines use DNA or mRNA to teach your own body how to make specific types of proteins.

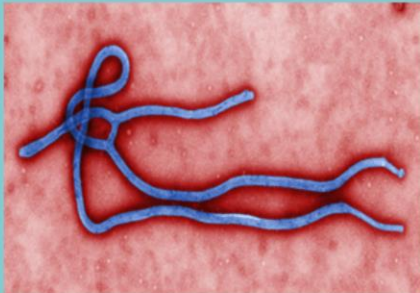
Viral vectors take a harmless virus and then insert DNA from a pathogen into its genetic code. This viral vector acts like a natural infection to your body, so your immune cells scoop it up and create protection not only against the viral vector, but also to the DNA from the real pathogen that you want protection from.

We've been trialing vaccines like these since 1984. Currently there are only two vaccines for human use licensed using this technology in the United States— one is for Ebola and one is for COVID. Like we've seen with other historic diseases, many vaccine types are used in animals extensively before they bridge over to human vaccinations, and viral vector vaccines are no different with many different vaccines available since the 1990s for dogs, cats, horses, livestock, and birds.

# FUTURE AREAS OF DEVELOPMENT:

TEACH YOUR BODY HOW TO MAKE SPECIFIC TYPES OF PROTEINS

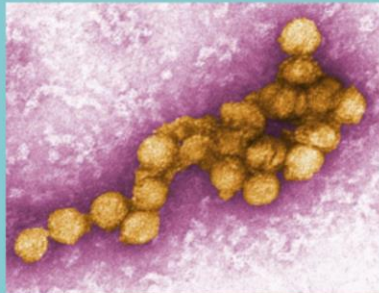
## VIRAL VECTORS



Trials: 1984

1<sup>st</sup> FDA licensed vaccine:  
Ebola (2017)

## DNA



Trials: 1993

1<sup>st</sup> USDA licensed vaccine:  
West Nile Virus (2005)  
veterinary use

Image credits: CDC/Cynthia Goldsmith

CDC/Pierre Rollin

DNA vaccines work in a similar way – but instead of using a harmless virus to get the DNA of the pathogen into your cells, they use something called a plasmid. Plasmids are small molecules that are normally found in cells, and when they are injected into your body your immune cells will go pick them up

and then make the antigens themselves from the DNA inside. So instead of growing antigens in culture or inside of something harmless like a yeast like we do for sub-unit vaccines, DNA vaccines trick your body into making them.

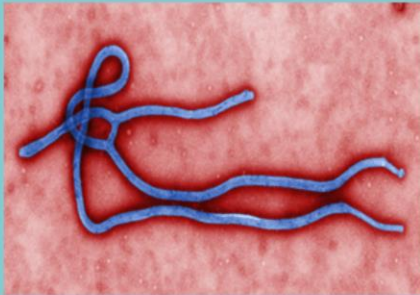
We've been trialing vaccines like these since 1993 in animals. Currently there is only one vaccine licensed for human in India, but none in the United States.

But the number of DNA vaccines in veterinary medicine is very high – the first licensed vaccine of this type in the United States was for West Nile Virus nearly 20 years ago. And if you can name an animal, chances are there is a DNA vaccine licensed for use in that species. This includes dogs and cats, horses, birds, and livestock. There are even DNA vaccines licensed for use in fish and raccoons.

## FUTURE AREAS OF DEVELOPMENT:

TEACH YOUR BODY HOW TO MAKE SPECIFIC TYPES OF PROTEINS

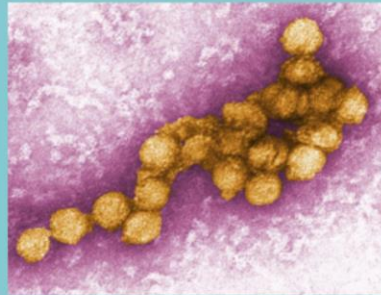
### VIRAL VECTORS



Trials: 1984

1<sup>st</sup> FDA licensed vaccine:  
Ebola (2017)

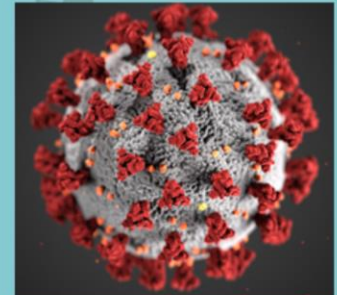
### DNA



Trials: 1993

1<sup>st</sup> USDA licensed vaccine:  
West Nile Virus (2005)  
veterinary use

### mRNA



Trials: 2001 (cancer) /  
2008 (microbes)  
1<sup>st</sup> licensed vaccine:  
COVID-19 (2021)

Image credits: CDC/Cynthia Goldsmith

CDC/Pierre Rollin

CDC/Alissa Eckert & Dan Higgins

And last but not least we have mRNA vaccines. These became famous after being licensed for the first time during the COVID-19 pandemic.

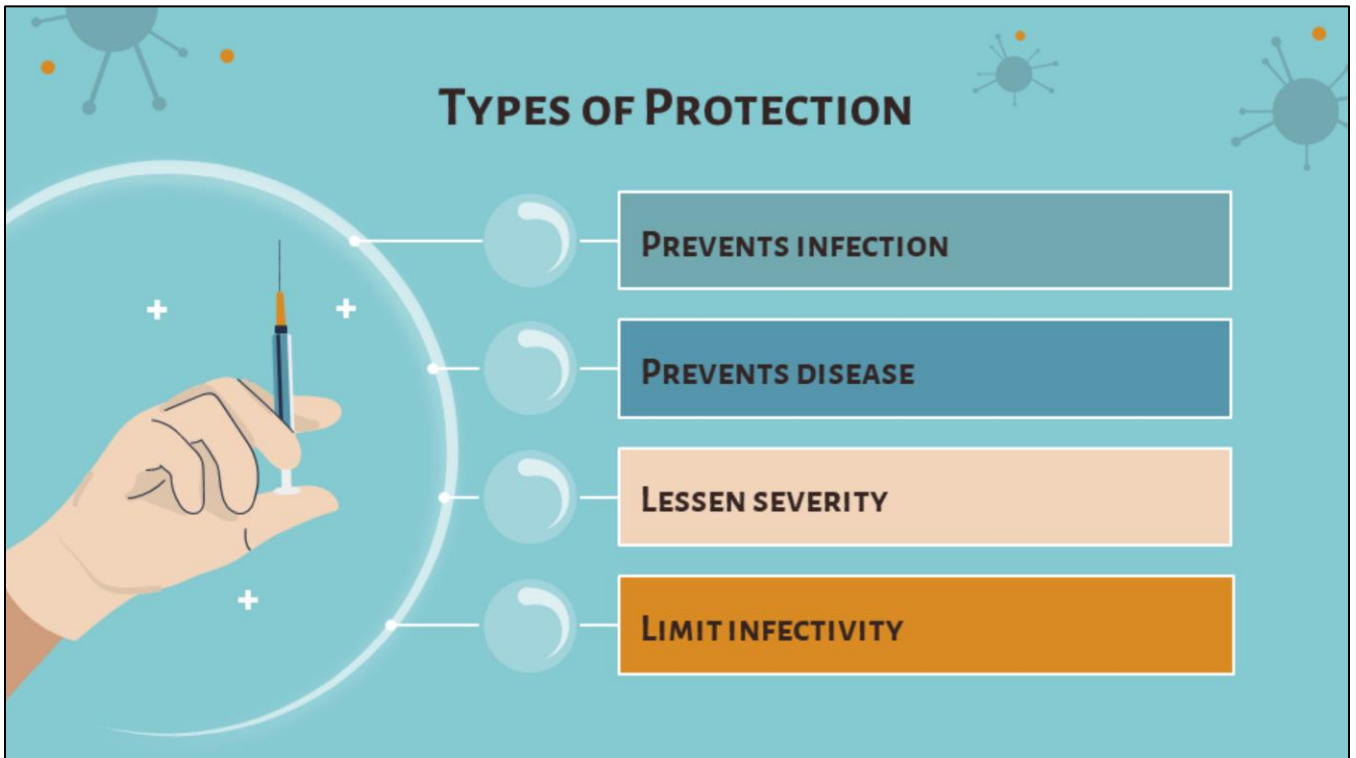
Again these work in a similar way to the viral vector vaccines and DNA vaccines. But instead of injecting DNA like with the others, we're injecting a copy of a molecule called messenger RNA. The immune cells pick up this mRNA and start making antigens associated with the pathogen.

Unlike DNA vaccines however, this is only a snippet of genetic code. mRNA breaks down after its used by your cells, so the material doesn't stick around and can't do anything other than tell your immune cells to make one specific protein.

mRNA vaccines began trials in 2001 for cancer and in 2008 for infectious microbes. The first licensed vaccine was in 2021 for COVID-19, but mRNA vaccine trials have been ongoing for many other infectious diseases for more than 15 years.

(\*\*An mRNA vaccine for RSV was approved shortly before this presentation)





Unsurprisingly, all these different types of vaccines can offer different types of protection. A common misconception in the public is that if you've been vaccinated you'll never be infected at all. That may or not be true. Some vaccines absolutely prevent infection – if you've been vaccinated, the microbe will be killed by your immune system before the infection takes hold.

Some may not be able to prevent you from being infected, but they will prevent you from getting sick. For toxoid vaccines for example – your body doesn't really care about the bacteria because those don't make you sick directly, instead the vaccine is designed to prevent you from getting sick by targeting the toxin.

Vaccines can also lessen the severity of disease if you do get sick. This is something that we see really commonly with the seasonal flu vaccine. Last years flu vaccine was only about 54% effective at preventing infection, which is the goal. But it's still worth getting because people who get the flu vaccine are much less likely to be hospitalized or fall severely ill than those who haven't been vaccinated.

There are also some vaccines that limit how much of the microbe you put back out into the environment. That's not generally a goal of vaccination, but it is a nice side effect that helps prevent other people around you from getting sick.

Now that we've covered all of the ways we've manipulated microbes to our advantage over the last few centuries, we'll wrap up by talking a little bit about the impacts here in Wyoming as well as nationally.

## THE IMPACT IN WYOMING

**“ During the last three months I have administered Pertussin vaccine to about one hundred children. As near as I can tell now about seventy-five percent have proven successfully protected against disease. One outstanding fact which has been shown is that the ones who did become infected after the inoculation has had a very short and mild attack. ”**

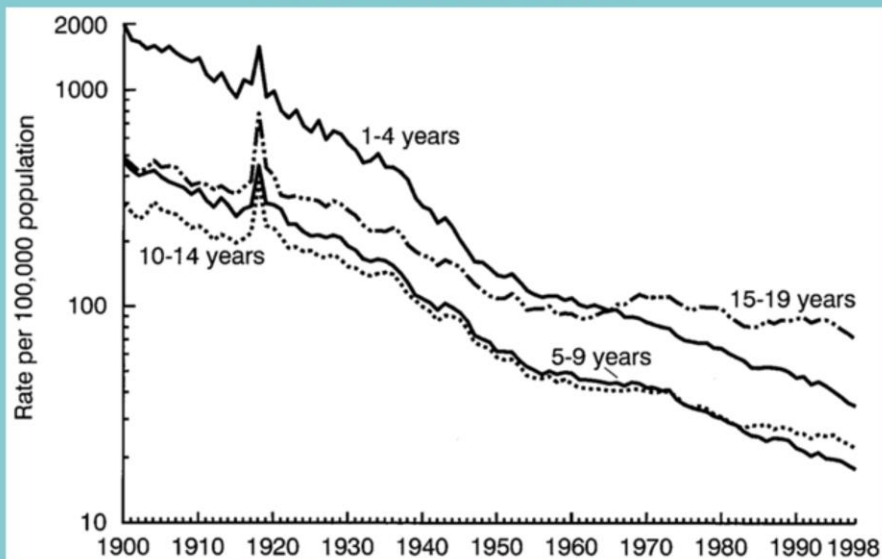
- Dr J.L. Wicks

Health Officer for Uinta County, 1932

We can see the differences of protection types talked about in the history of Wyoming. One Health Officer in Uinta County sent in his annual report in 1932 and said that after vaccinating one hundred children in the country against pertussis, also known as Whooping cough, that about 75% of them seem to have been successfully protected against disease.

And for the remaining 25% who were noted to become infected after inoculation, they only had a “very short and mild attack” of illness.

## NATIONAL IMPACT



### Age-adjusted death rates: United States 1900–1998

Figure from: Guyer, Bernard, Mary Anne Freedman, Donna M. Strobino, and Edward J. Sondik. "Annual summary of vital statistics: trends in the health of Americans during the 20th century." *Pediatrics* 106, no. 6 (2000): 1307-1317.

And we can see that protective effect in action by looking at the national death rates over the last century for children. We can see back here in 1900, 2,000 out of every 100,000 infants and toddlers died every year. Over the course the century it dropped all the way down to about 25 out of every 100,000.

Putting it another way that's the equivalent of saying that 1 out of every 50 died in 1900 versus 1 out of every 4,000 by the end of the century. And that downward trend is seen in all of the age categories, including infants, children and teenagers.

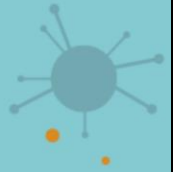
Vaccines certainly don't get all the credit for that, we can also thank things like better living conditions, sanitation, nutrition, and healthcare. But we also know historically and even in the modern day in parts of the world that don't have good access to vaccines, that a very large percentage of deaths in children under the age of 5 are due to vaccine-preventable illness.

## Vaccine preventable diseases reported in Wyoming

1941-1944

Disease	Total cases
Chicken Pox	3011
Diphtheria	119
Rubella	810
Measles	7683
Meningococcal	82
Mumps	3143
Polio	78
Smallpox	7
Typhoid	38
Whooping Cough	1367

Population approx. 220,000



Within Wyoming's statistics we can see a dramatic drop in infections as well. The ten diseases up on the slide all have childhood vaccinations. In the early 1940s more than 16,000 cases were reported for these diseases during the 4-year period from 1941 to 1944.

## Vaccine preventable diseases reported in Wyoming

1941-1944

2019-2022

Disease	Total cases
Chicken Pox	3011
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Population approx. 220,000

Disease	Total cases
<b>Chicken Pox</b>	<b>25</b>
Diphtheria	0
Rubella	0
Measles	0
Meningococcal	0
Mumps	0
Polio	0
Smallpox	0
Typhoid	0
<b>Whooping Cough</b>	<b>45</b>

Population approx. 580,000

By 2022, the population of Wyoming had more than doubled, but 8 of those diseases didn't have a single case and the remaining two, Chicken Pox and Whooping Cough combined, accounted for just 70 TOTAL cases in the entire state over the course of 4 years.

## THE IMPACT IN WYOMING

**“ This is the fourth year of the diphtheria prophylaxis campaign in Sweetwater County, and I have not had one case of diphtheria reported in the County during the year 1932. It is gratifying to be able to place Diphtheria by the side of Smallpox and Typhoid Fever as one of the diseases which no community needs to be afflicted with if known preventive measures are efficiently carried out. ”**






- J.H. Goodnough, M.D.  
Health Officer of Sweetwater County, 1932

This was a long process started in the early 1900s. The Health Officer for Sweetwater County was particularly pleased with the introduction of the diphtheria vaccine.

By 1932 they had been vaccinating children for 4 years in the County and did not have a single case during that year. He described that “It is gratifying to be able to place Diphtheria by the side of Smallpox and Typhoid Fever as one of the diseases which no community needs to be afflicted with if known preventive measures are efficiently carried out.”



## MINIMUM ESTIMATED HERD IMMUNITY THRESHOLDS






MEASLES		90%
DIPHTHERIA		83%
RUBELLA		83%
SMALLPOX		80%
POLIO		80%

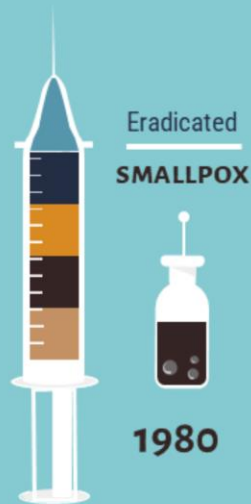


And those preventative measures helped eliminate several childhood diseases in the United States. To ensure that there is no disease transmission, a certain percentage of the population needs to be vaccinated so that the disease can't spread within the community.

This is known as herd immunity, and it generally ranges from 80-95% depending on the pathogen. Over the course of the twentieth century, the work of public health and clinical practitioners like you, helped to ensure that those herd immunities were met for a variety of diseases.






# MINIMUM ESTIMATED HERD IMMUNITY THRESHOLDS

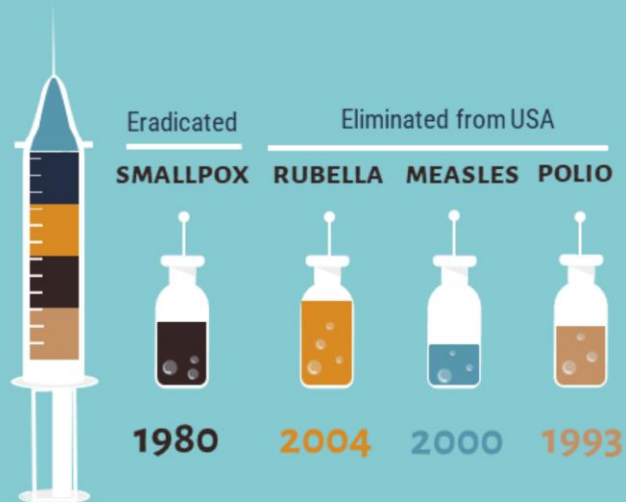
MEASLES		90%
DIPHTHERIA		83%
RUBELLA		83%
SMALLPOX		80%
POLIO		80%



As I mentioned earlier, Smallpox was eradicated globally






# MINIMUM ESTIMATED HERD IMMUNITY THRESHOLDS

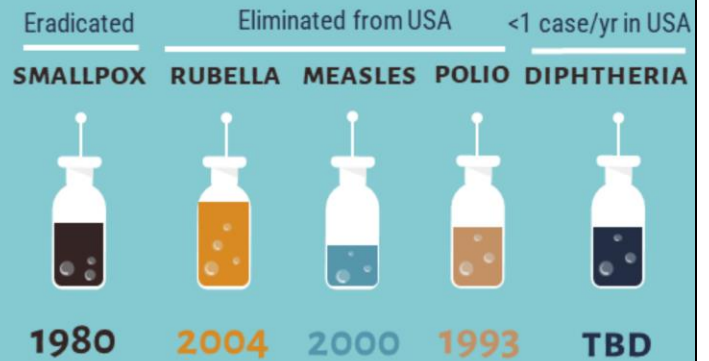
MEASLES		90%
DIPHTHERIA		83%
RUBELLA		83%
SMALLPOX		80%
POLIO		80%



Polio, measles, and rubella were all eliminated from the United States as well. Although it's possible that may come back as some locations, like pockets of southern California and New York City, have vaccination rates that have fallen below 90% and imported cases have been able to cause small scale outbreaks.

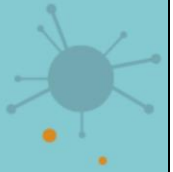
# MINIMUM ESTIMATED HERD IMMUNITY THRESHOLDS

MEASLES		90%
DIPHTHERIA		83%
RUBELLA		83%
SMALLPOX		80%
POLIO		80%



And diphtheria is tantalizingly close to be eliminated. From 1996 to 2018, just 14 total cases were reported in the United States over the course of 22 years, making the number of cases reported annually less than 1 per year for the entire country.

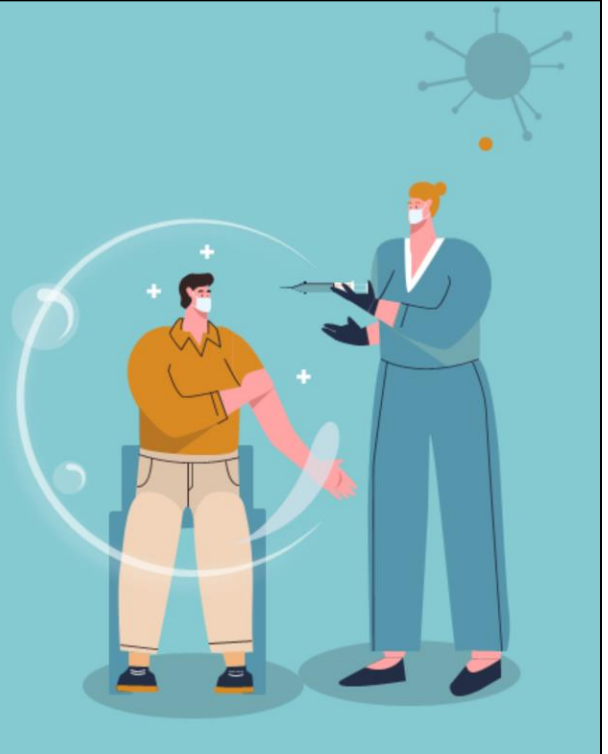
**“ It should not be forgotten that eternal vigilance is the price of freedom... The babies born each year must be protected in their turn if Wyoming is to remain free from this disease. ”**



Wyoming State Health Officer  
*Eleventh Biennial Report of the Wyoming  
State Board of Health, 1931-1932*

And I'll close with the words of the Wyoming State Health Officer in 1932 about vaccination: It should not be forgotten that eternal vigilance is the price of freedom... The babies born each year must be protected in their turn if Wyoming is to remain free from... disease.

# THANK YOU



I hope you enjoyed reflecting on how far we've come in fighting vaccine preventable diseases. Thank you very much for your time and attention this morning.



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