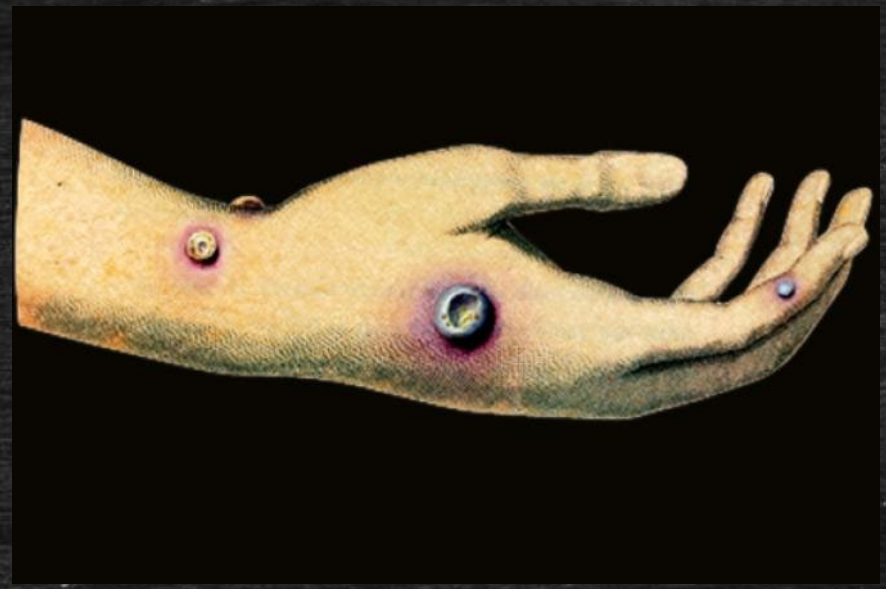

Curious Reactions:

Vaccines- A Brief and Relevant Social History

Larry Aguirre
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Adjunct Instructor of Health

Disclosures and Disclaimers

- Employed by Mendocino College as an adjunct instructor, Redwood Quality Management Company, and contracted with Mendocino Community Health clinics, and Ukiah Juvenile Hall.
- Medical officer for the California Army National Guard.
- The views expressed in this presentation are those of the author and do not necessarily reflect the official policy or position of the Department of the Army, Department of Defense, or the U.S. Government, my employers, or Mendocino College.
- I do not receive funding form any vaccine or pharmaceutical companies.

Smallpox Case Study

- *The smallpox was always present, filling the churchyards with corpses, tormenting with constant fears all whom it had stricken, leaving on those whose lives it spared the hideous traces of its power, turning the babe into a changeling at which the mother shuddered, and making the eyes and cheeks of the bighearted maiden objects of horror to the lover.*

- T.B. Macaulay - *The History of England from the Accession of James II, Vol IV. 1848*

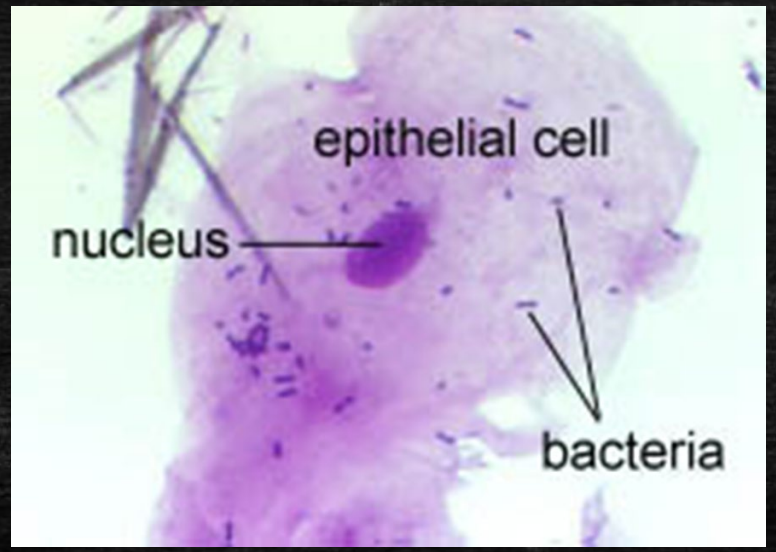
- In the case of London, the Bills of Mortality indicate that smallpox was probably the single most lethal cause of death in the eighteenth century, accounting for 6–10% of all burials.[1]

Smallpox

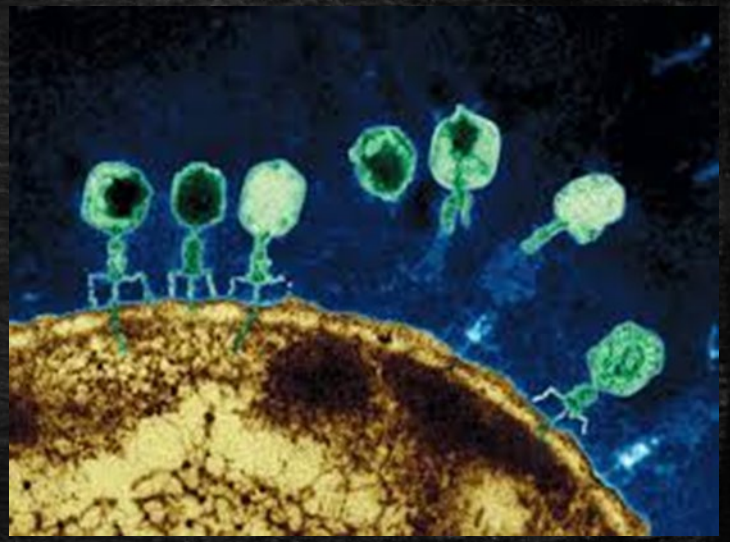
- Variola virus
- Double stranded DNA virus

Smallpox

Size comparison



Cheek cell



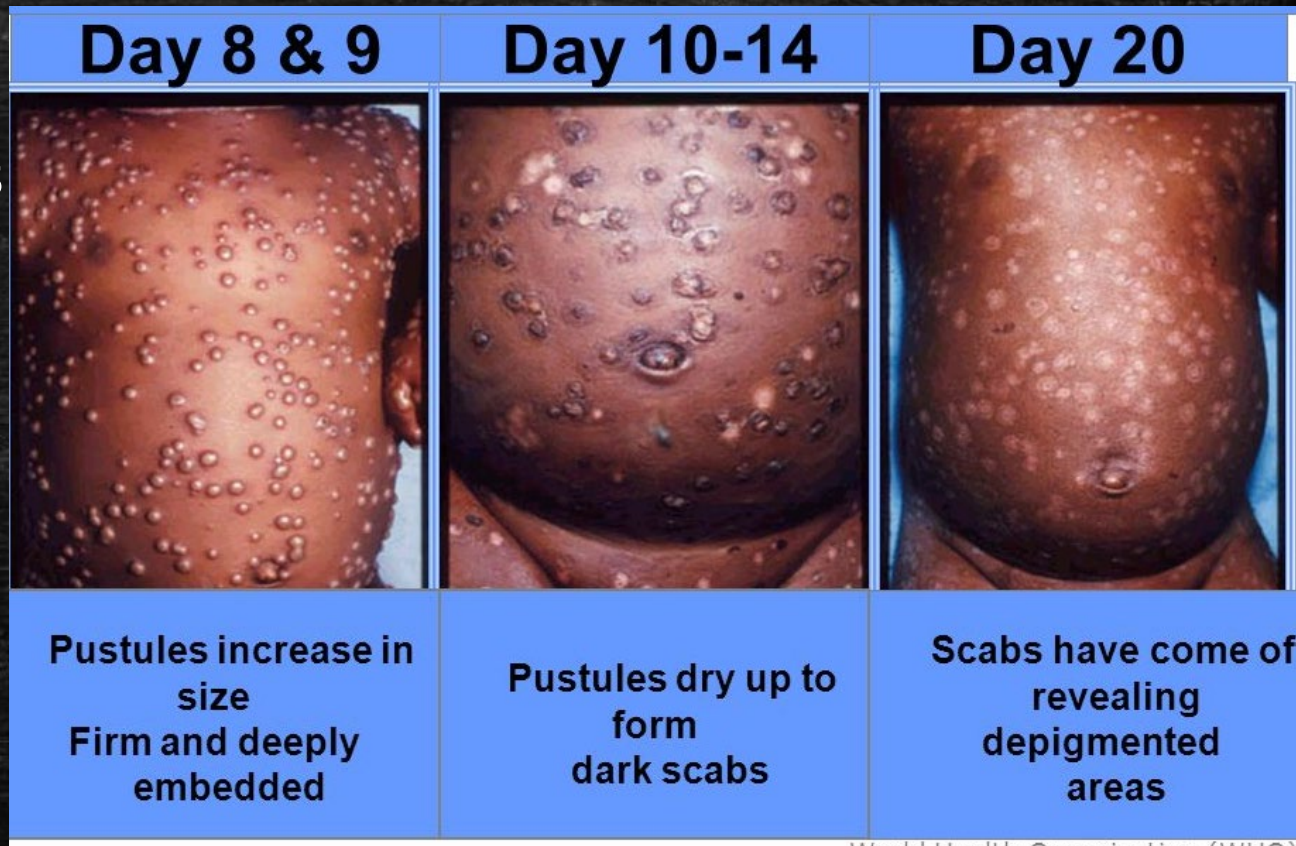
phage

Clinical Manifestations[2]

- Enters the respiratory tract and into to mucus membranes and passing into the lymph nodes with a latent replication cycle of 4-14 days.
- Abrupt severe headache, backache, and fever, followed by sores in the mouth.
- Invades the capillary epithelium of the dermal layers of the skin.

Clinical Manifestations[2]

- Rash -> pustules for 5-8 days, followed by umbilication and crusting.
- Death from toxemia (from immune complexes) and to hypotension.
- Fatality ~ 30%
- Pockmarks in 65 - 80 % of survivors
- Survivors have lifelong immunity.



Ferdinando II de' Medici at his seventh (left) and ninth (right) day of smallpox **(1626).** Justus Suttermans, Galleria Palatina, Florence, Italy.

Early History of Smallpox [3,4]

- Been around since 10,000 BCE with first agricultural settlements.
- It is thought to be mentioned in Chinese and Sanskrit text as early as 1122 BCE.
- It is curiously not well described in classical and biblical sources.
- European sources appear to describe it starting in late antiquity/ early medical period (500-700 CE).
- "The Speckled Monster"
- "Small pockes" 15c England (vs "great pockes" -Syphilis)

Vaccine Precursors [5,6,7]

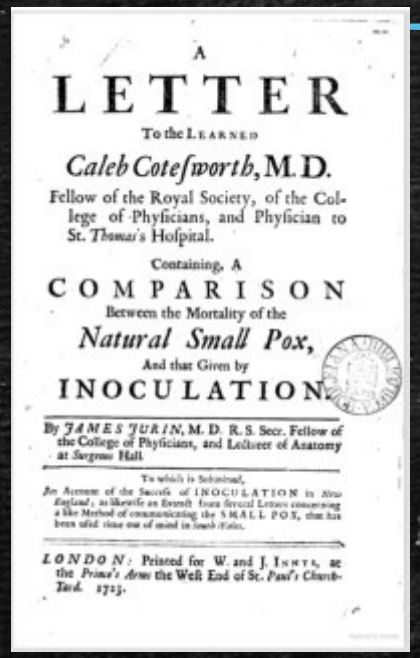
- Lady Mary Wortley Montagu (1689 –1762)
- Wife of British consul in Constantinople.
- In 1717 "The smallpox, so fatal and so general among us, here is entirely harmless by the invention of engrafting."
- Describes parties in which…"nutshell full of the matter…and puts into the vein as much matter as can lie upon the head of her needle."
- This practice thought to Africa, India, and China long before the 18th C.

By George Knapton Dorothy

Vaccine Precursors

- ~1716 Lady Mary's son is inoculated while in Constantinople.
- 1721 Lady Mary's daughter became the first Brittan to be inoculated.
- This would soon be followed by two daughters of the Prince of Wales, (King George II), but not before first performing on condemned felons.
- variolation – Latin *varius* (Channing/spotted) -> variola (smallpox)
- Inoculation- Latin *inoculare* "to graft"
- Boths terms used interchangeably.

Vaccine Precursors

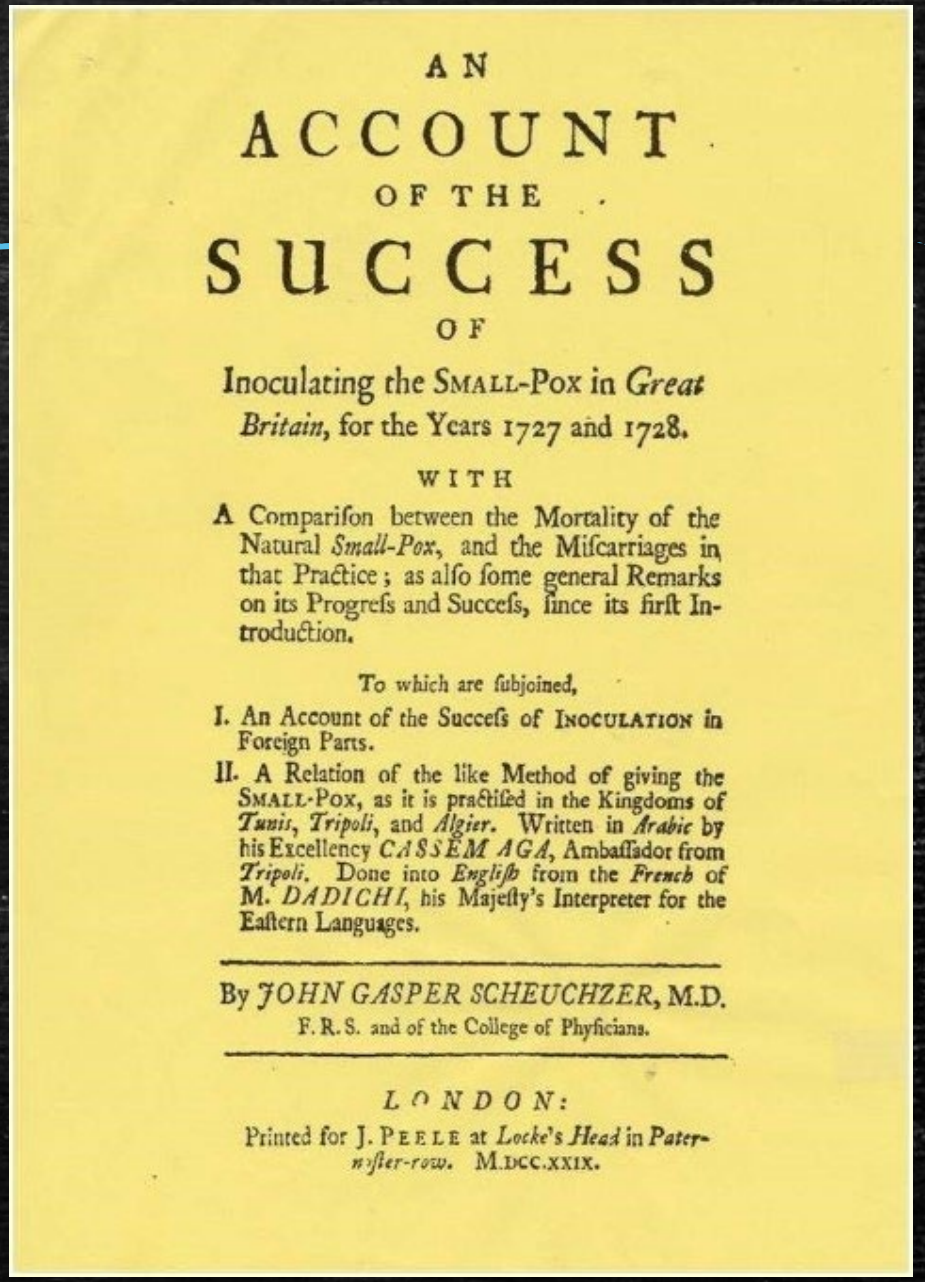


A
LETTER
To the LEARNED
Caleb Cotesworth, M.D.
Fellow of the Royal Society, of the College of Physicians, and Physician to St. *Thomas*'s Hospital.
Containing, A
COMPARISON
Between the Mortality of the
Natural Small Pox,
And that Given by
INOCULATION.
By *JAMES JURIN*, M. D. R. S. Secr. Fellow of the College of Physicians, and Lecturer of Anatomy at *Surgeons Hall*.
To which is Subjoined,
An Account of the Success of INOCULATION in *New England*; as likewise an Extract from several Letters concerning a like Method of communicating the SMALL POX, that has been used there out of mind in South-Wales.
LONDON: Printed for W. and J. INNYS, at the *Prince's Arms* the West End of St. *Paul's* Church-Yard. 1723.

- Several prominent physicians were intrigued by the potential of inoculation.
- Dr. James Jurin of the Royal Society of London showed that 40% mortality in bad epidemics.
- Dr. Thomas Nettleton would observe "Small Pox procured by innoculation….is far less Dangerous than the same Distemper has been for many Years in the Natural Way"

Dr. James Jurin

- The Royal Society that set out to answer the question of whether inoculation/variolation demonstrated clear benefits which outweighed the risk of harm.
- 1722 - 1729 over 129 letters arrived at the Royal Society giving details of both forms of smallpox.
- The final report compiling all the previous reports show "Only 26 of the 1,087 (2%) inoculated individuals had died, while 3,008 of 18,229 (17%) people with natural smallpox perished." [8]



AN

ACCOUNT

OF THE

SUCCESS

OF

Inoculating the SMALL-POX in *Great Britain*, for the Years 1727 and 1728.

WITH

A Comparison between the Mortality of the Natural *Small-Pox*, and the Miscarriages in that Practice; as also some general Remarks on its Progress and Success, since its first Introduction.

To which are subjoined,

I. An Account of the Success of INOCULATION in Foreign Parts.

II. A Relation of the like Method of giving the SMALL-POX, as it is practised in the Kingdoms of *Tunis*, *Tripoli*, and *Algier*. Written in *Arabic* by his Excellency *CASSEM AGA*, Ambassador from *Tripoli*. Done into *English* from the *French* of M. *DADICHI*, his Majesty's Interpreter for the Eastern Languages.

By *JOHN GASPER SCHEUCHZER*, M.D. F. R. S. and of the College of Physicians.

LONDON:

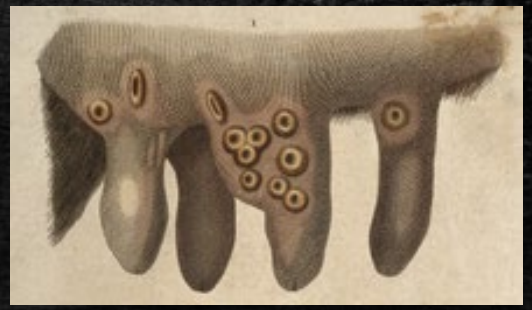
Printed for J. PEELE at *Locke's Head* in *Paternoster-row*. M.DCC.XXIX.

- Physicians developed elaborate and expensive variolation methods.
- 1750 the Sutton family of surgeons developed an easy, inexpensive, and effective method of mass inoculation.
- This led to more widespread inoculation and the observation of one surgeon, John Fewster, who reported on several farmers in Gloucestershire who were resistant to inoculation.
- They all denied having had smallpox but as one old farmer said "I cowpox quite severely, if that makes any difference"." [4]

- There was resistance from some, questioning the moral implications of variolation, particularly among Calvinist who pondered if the efforts interfered with Divine Providence.[5]

Edward Jenner (1749-1823) [4,5,6,9]

- Gloucestershire country Doctor of vaccine fame.
- Son of a Clergyman, who was himself inoculated at 8 and study medicine in London and gained an interest in experimentation.
- Had heard of the findings of Fewster and like others surmised that cowpox may indeed give natural immunity to smallpox.

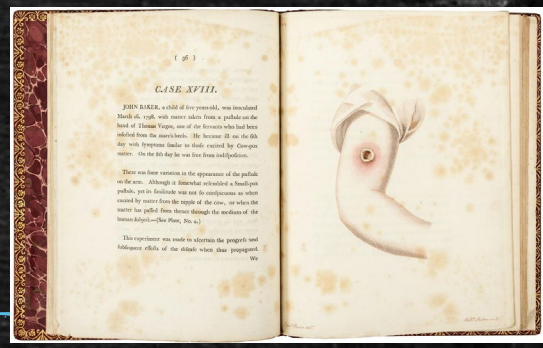


- Cowpox, unlike smallpox, is not very contagious and resulted in a few isolated and fairly benign course.
- Jenner postulated that cowpox inoculation would be safer and still provide immunity to smallpox.
- In May of 1796 Jenner inoculated an 8-year-old boy, James Phillips, with some fluid of a cowpox pustule of a dairy maid (Sarah Nelmes).
- The child developed a slight fever but otherwise made a quick recovery.

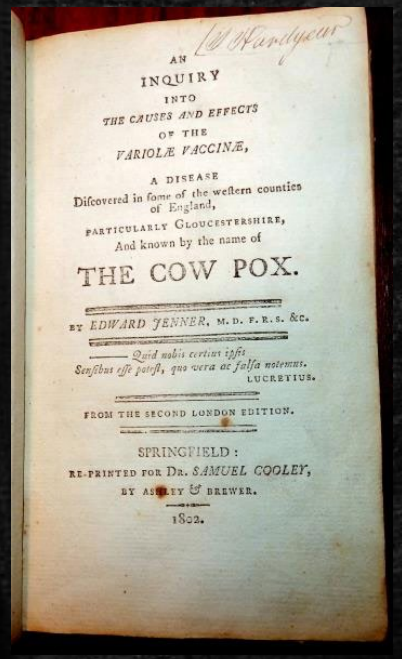
Popperfoto/Getty

hand of Sarah Nelmes
Wellcome Collection

Success! [5,10,11]



- Six weeks later Jenner inoculated this the boy with smallpox, and it did not take.
- Jenner called the cowpox material "vaccine" (from vacca, the Latin for cow) and the process vaccination.
- In 1798 his findings were published and quickly gained attention being published in multiple languages on the continent and in America.
- Jenner's vaccination method proved to be safer and quickly became the preferred method for vaccination.
- By 1799 over 5000 people had been vaccinated in England and in 1803 The Royal Jenner Society was founded to promote vaccination.


AN
INQUIRY
INTO
THE CAUSES AND EFFECTS
OF THE
VARIOLÆ VACCINÆ,
A DISEASE
Discovered in some of the western counties
of England,
PARTICULARLY GLOUCESTERSHIRE,
And known by the name of
THE COW POX.
BY EDWARD JENNER, M.D. F.R.S. &c.
Quid nobis certius istis
Sensibus esse potest, qui vera ac falsa notemus.
LUCRETIUS.
FROM THE SECOND LONDON EDITION.
SPRINGFIELD:
RE-PRINTED FOR DR. SAMUEL COOLEY,
BY ASHLEY & BREWER.
1822.

Not everyone was onboard

published June 12, 1802

'Vaccine Monster' 1807

Social Reactions to Smallpox Vaccine [9,10]

- Napoleon had his Army vaccinated and it became compulsory in Sweden.
- In 1840 the United Kingdom passed its first Vaccination Act which provided free vaccines for the poor.
- The Vaccination Act of 1853 made vaccination compulsory for infants within the first 3 months of life and parents faced fines and imprisonment if they were out of compliance.

Social Reactions

- Resistance to the 1853 Act fallowed almost immediately which included violent riots in some towns and the founding of the Anti-vaccination League in London.
- This did not halt further and more stringent Vaccination Act to be passed in 1857 that extended to compulsory requirments.
- In response to this the AntiCompulsory Vaccination League was founded which focused on what they considered government overreach that infringed on personal liberty and the right to choose.
- The League's efforts included books, newspapers, and the founding of antivaccination journals including the *AntiVaccinator* and an 1885 demonstration in Leicester with up to 100,000 people.

"In Rama there was a voice heard, lamentations and weeping, and great mourning, Rachael weeping for her children, and would not be comforted because they are not."—Matt. II: 2.

The City Papers Cry

VACCINATE! VACCINATE!! VACCINATE!!!

THERE'S MONEY IN IT!!!

TWENTY THOUSAND VICTIMS!!! will be Vaccinated within the next ten days in this City under the present **ALARM!!!**

That will put **$10,000** into the pockets of the Medical Profession.

CLEANLINESS, SANITATION AND HYGIENE ARE "NONSENSE," unworthy of attention by our Board of Health.

FILTHY STREETS, FILTHY LANES, AND FILTHY DRAINS help the Medical Profession.

THERE'S MONEY IN IT!!!

The City Papers Cry

VACCINATE! VACCINATE!! VACCINATE!!!

O tempora, O mores!

August 1885

TRIUMPH OF DE-JENNER-ATION.

[The Bill for the encouragement of Small Pox awaits Third Reading in the Commons.]

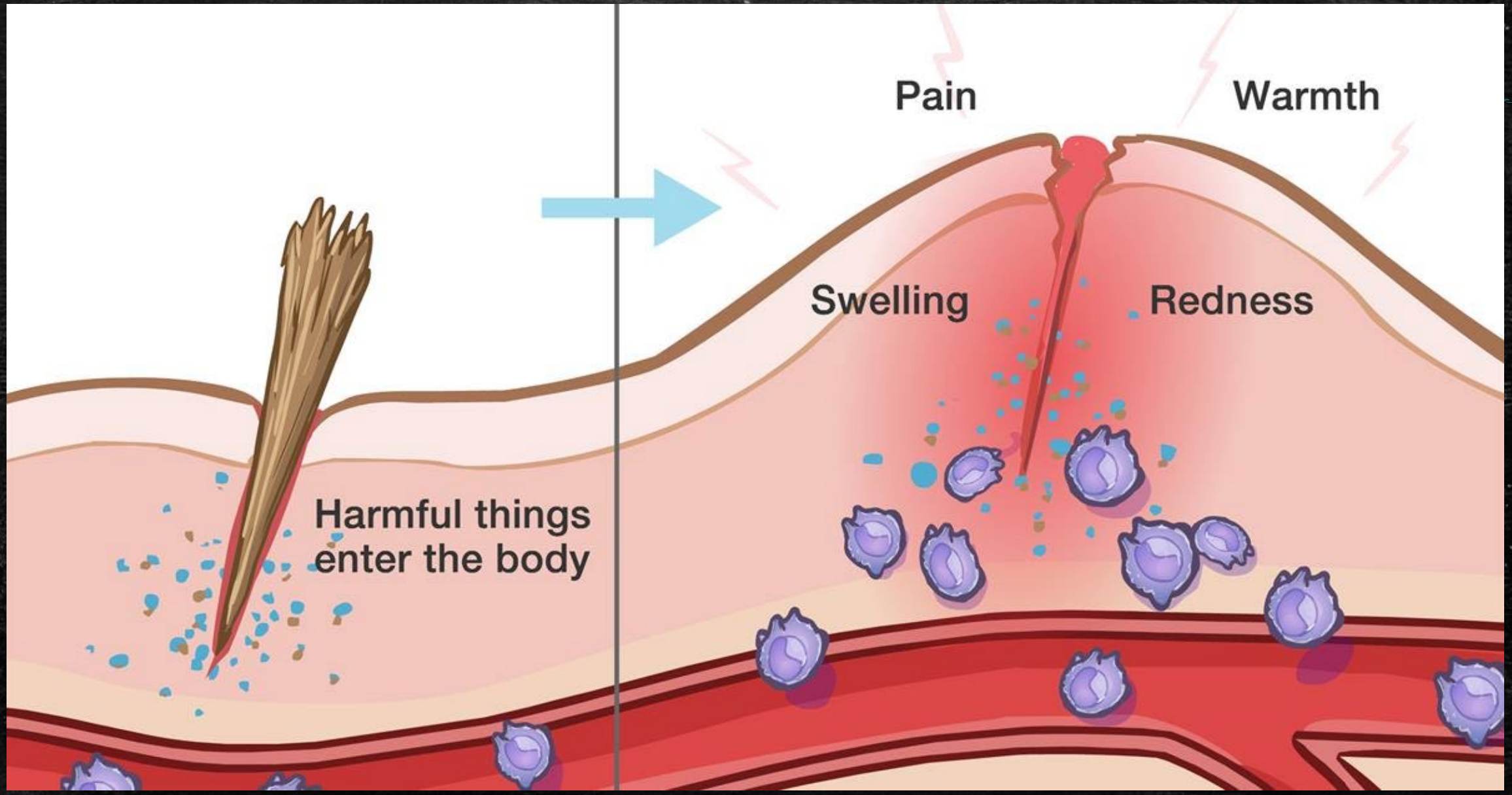
1898

- The League's efforts were successful, resulting the establishment of a royal commission to hear grievances as well as evidence in favor of vaccination.
- After **7 years of hearing extensive testimony** the commission reported that vaccination does protect against smallpox but also advised the removal of penalties for non-compliance.
- "A new **Vaccination Act in 1898** removed cumulative penalties and introduced a conscience clause, allowing parents who did not believe vaccination was efficacious or safe to obtain a certificate of exemption."
- END OF PART I

How does Immunity Work?

- There are several ways the body protects from infection.
- Non-specific such as the skin, but also include more complicated immune responses such as inflammation and fever.
- For vaccinations to work it requires the response of our specific immunity that includes **antibodies** that have been tailored to attack a specific pathogen such as influenza or smallpox.

Nonspecific Immunity

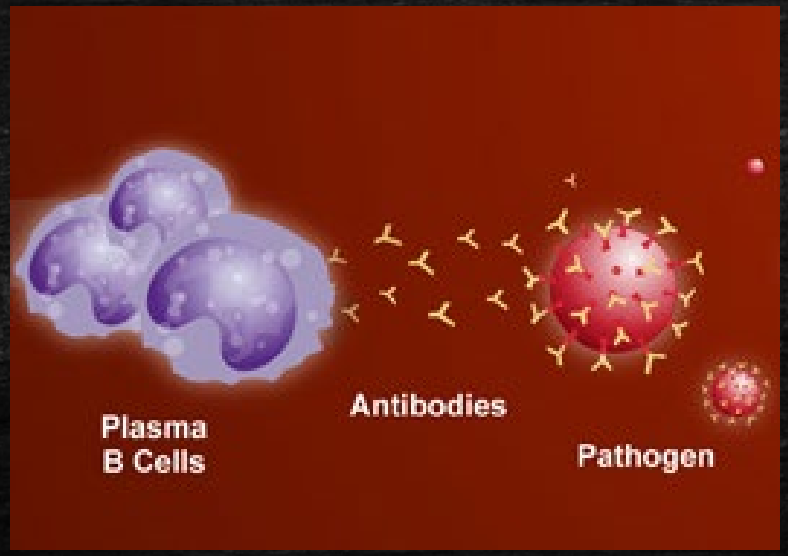


- Other White Blood Cells (WBC) that will mount a specific antibody response to the invading bacteria.

- An antibody is a protein structure that can be produced by a WBC and used to attack an invader (e.g., virus, bacteria).

- The problem is that to work properly they need to have specific structure that will attach to the invader so that it can be incapacitated.

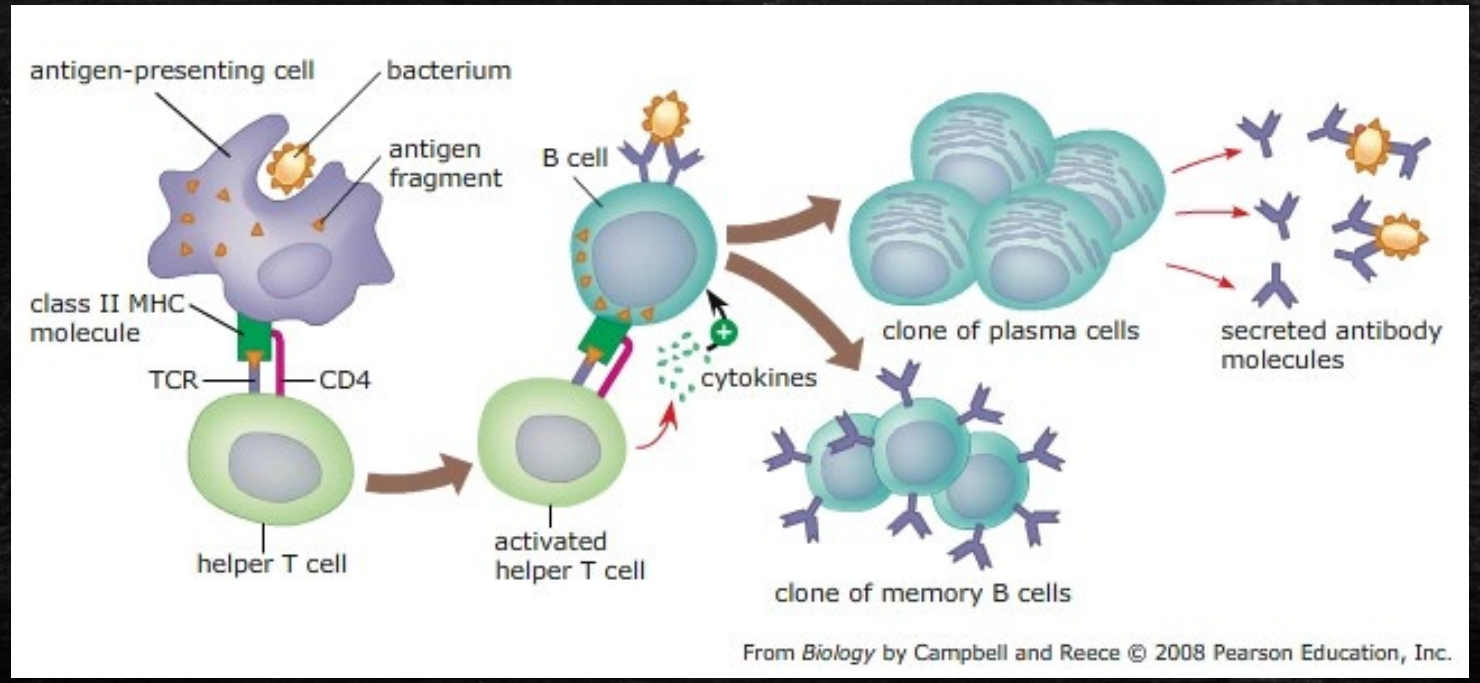
- The other problem is that it takes time for WBC to produce a coordinated response, especially against an invader it has never seen before.



- Luckily, our body has a system to mount a complicated and coordinated attack against invaders it is familiar with.

- There are specialized WBC (memory cells) that can quickly reproduce and mount an antibody attack to invaders it has seen in the past.

- This explains why for many infections once we have had exposure to them, we are able to fight them off quickly and effectively, meaning we have immunity.



How do Vaccines Achieve Immunity? [12]

- For vaccines to be effective they must induce an immune response that will prevent or greatly reduce the virulence of infectious agents such as virus and bacteria.
- They must achieve this safely and effectively.

Types of Vaccines

- **Live-attenuated vaccines**

  - Smallpox, Measles, mumps, rubella (MMR) , Chickenpox

- **Inactivated vaccines**

  - Flu injection, Hep A

- **Subunit/recombinant/ polysaccharide/ conjugate vaccines**

  - HPV, Hep B, Meningococcal

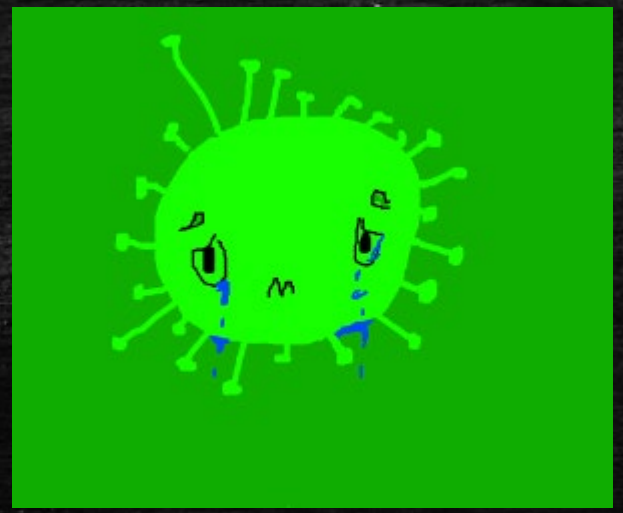
- **Toxoid vaccines**

  -Tetanus, Diphtheria

Live-attenuated vaccines

Smallpox, Measles, mumps, rubella (MMR) , Chickenpox

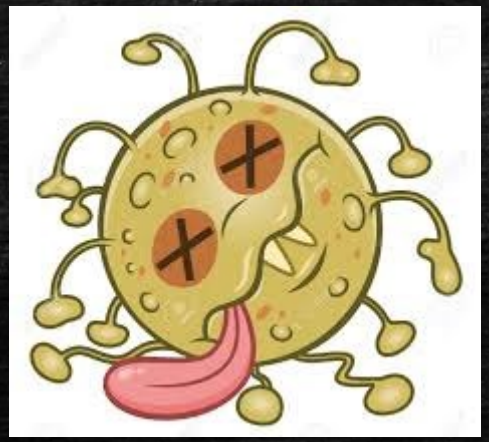
- Live vaccines use a weakened (or attenuated) form of the germ that causes a disease.
- Because these vaccines are so similar to the natural infection that they help prevent, they create a strong and long-lasting immune response. Just 1 or 2 doses of most live vaccines can give you a lifetime of protection against a germ and the disease it causes



Inactivated vaccines

Flu injection, Hep A

- Inactivated vaccines use the killed version of the germ that causes a disease.
- Vaccines usually don't provide immunity (protection) that's as strong as live vaccines. So you may need several doses over time (booster shots) in order to get ongoing immunity against diseases.



Subunit / recombinant / polysaccharide/ conjugate vaccines

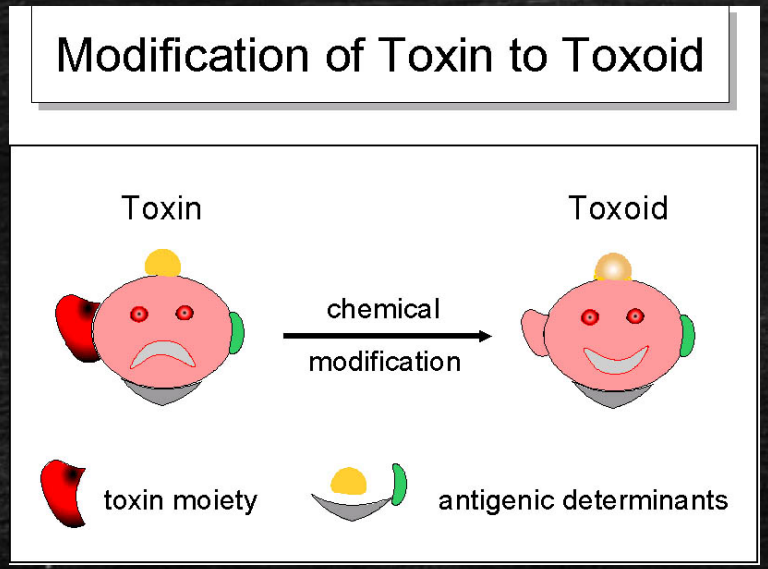
HPV, Hep B, Meningococcal

- Subunit, recombinant, polysaccharide, and conjugate vaccines use specific pieces of the germ — like its protein, sugar, or capsid (a casing around the germ).
- Because these vaccines use only specific pieces of the germ, they give a very strong immune response that's targeted to key parts of the germ.

Toxoid vaccines

Tetanus, Diphtheria

- A chemically modified toxin from a pathogenic microorganism, which is no longer toxic but is still antigenic and can be used as a vaccine.



Contemporary Vaccine Hesitancy [13,14]

- Concern for side effects.
- Perceived lack of need.
- Concern they are ineffective.
- Vaccines will overload the immune system.
- Distrust of government and healthcare systems.
- Believing natural immunity is better.

Risk Mitigation [15]

- clinical trials and FDA approval.
- National Vaccine Injury Compensation Program (VICP). Most Vaccines.
- Countermeasures Injury Compensation Program (CICP) - Many other vaccines including COVID.
- Informed consent at time of visit. Health screens by exam and checklists.
- Vaccine information sheet (VIS)

Clinical Trials

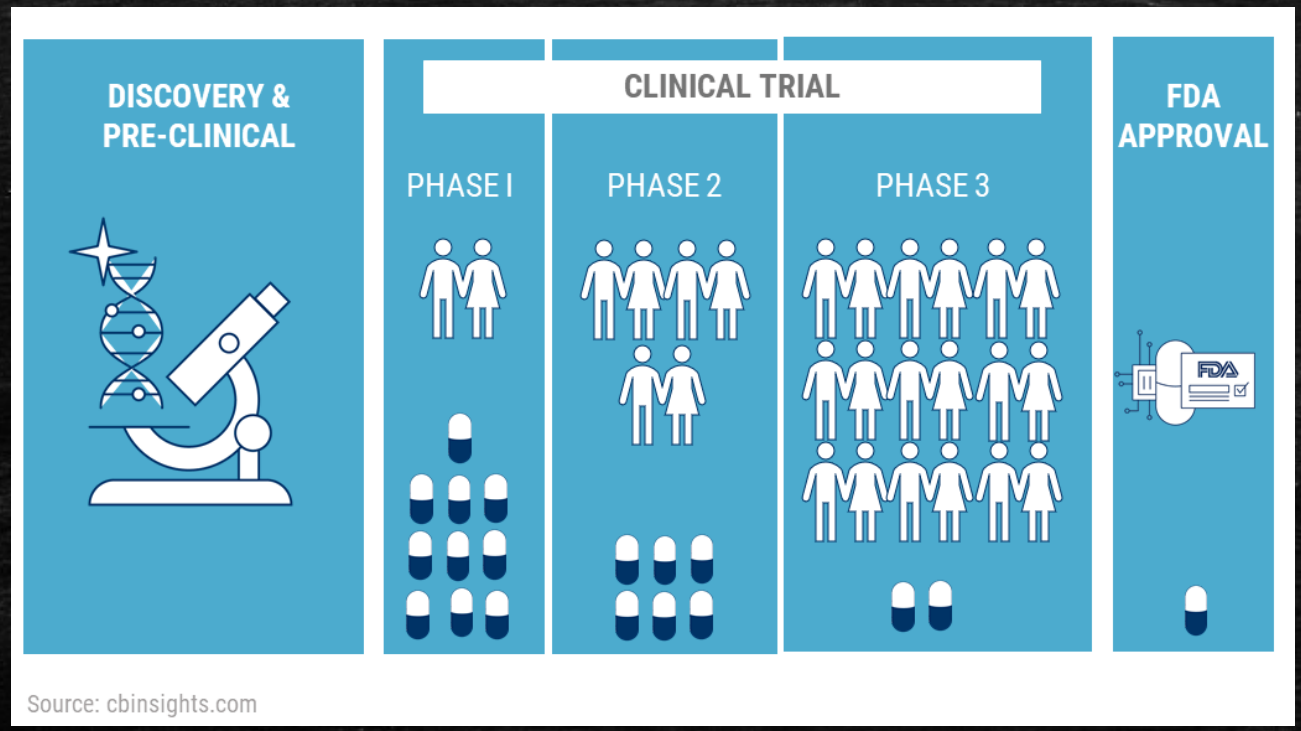
- Institutional Review Boards (IRBs). Informed consent. Clinical team.
- Phase 1: Safety - very small number of participants. Evaluate the drug's overall safety and determine the safest dose of the drug.
- Phase 2: Larger group of people (up to several hundred), to see if it's effective and safe. If results from this phase show that the new drug or device may be just as beneficial or more beneficial than the existing drug or device to treat the same or similar ailments, then researchers can move to Phase 3.
- The FDA estimates that about 33% of medications move on to phase III. [16]

Clinical Trials

- Phase 3: Large groups of people. Confirm the drug's efficacy, monitor side effects, compare it to other commonly used treatments or to a placebo, and collect information to ensure safe use of the drug or treatment.
- Placebos are often used in clinical trials as an inactive control so that researchers can better evaluate the true overall effect of the drug treatment under study.
- Double-blind -neither the participant nor the investigator knows which medication the participant is taking. This helps to eliminate bias when interpreting results.

Clinical Trials

- Phase 4: After FDA approval- designed to evaluate the long-term risks and benefits of a medication. Determine more about the side effects, interactions with other drugs, and how well it works when it's more widely used.



Side Effects [17,18,19]

- Common side effects
- Autism?
- Mercury?
- It will cause the disease it is trying to prevent?
- Overwhelm immune system?
- Uncommon serrious adverse events:

  - Allergic reactions, Seizure, Guillain-Barre

Other Considerations [20]

- **Herd Immunity-** occurs when a significant portion of a population becomes immune to an infectious disease, limiting further disease spread.
- Some cannot be vaccinated, including some children, because they are immune compromised. Those who can be vaccinated can help protect those that cannot.

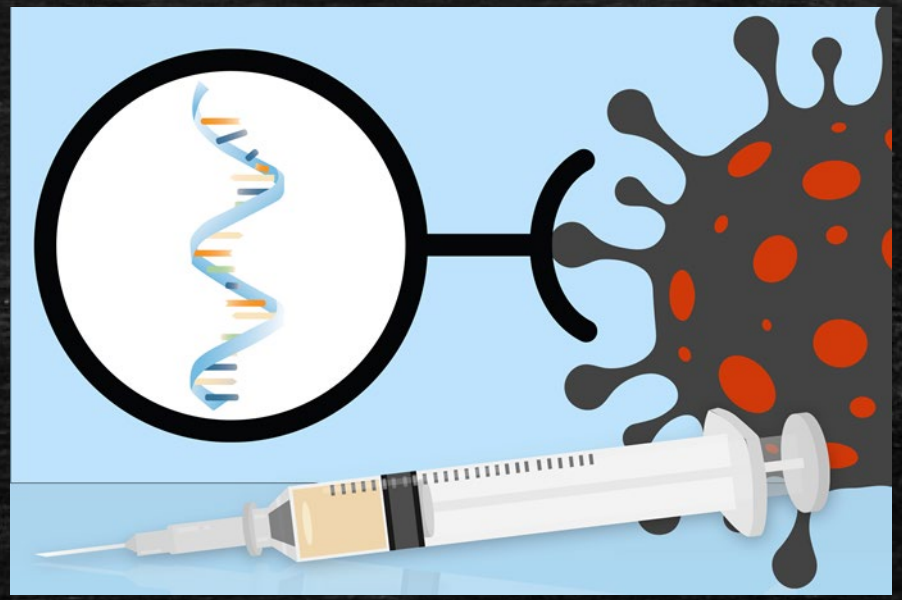
Efficacy of Vaccines [21]

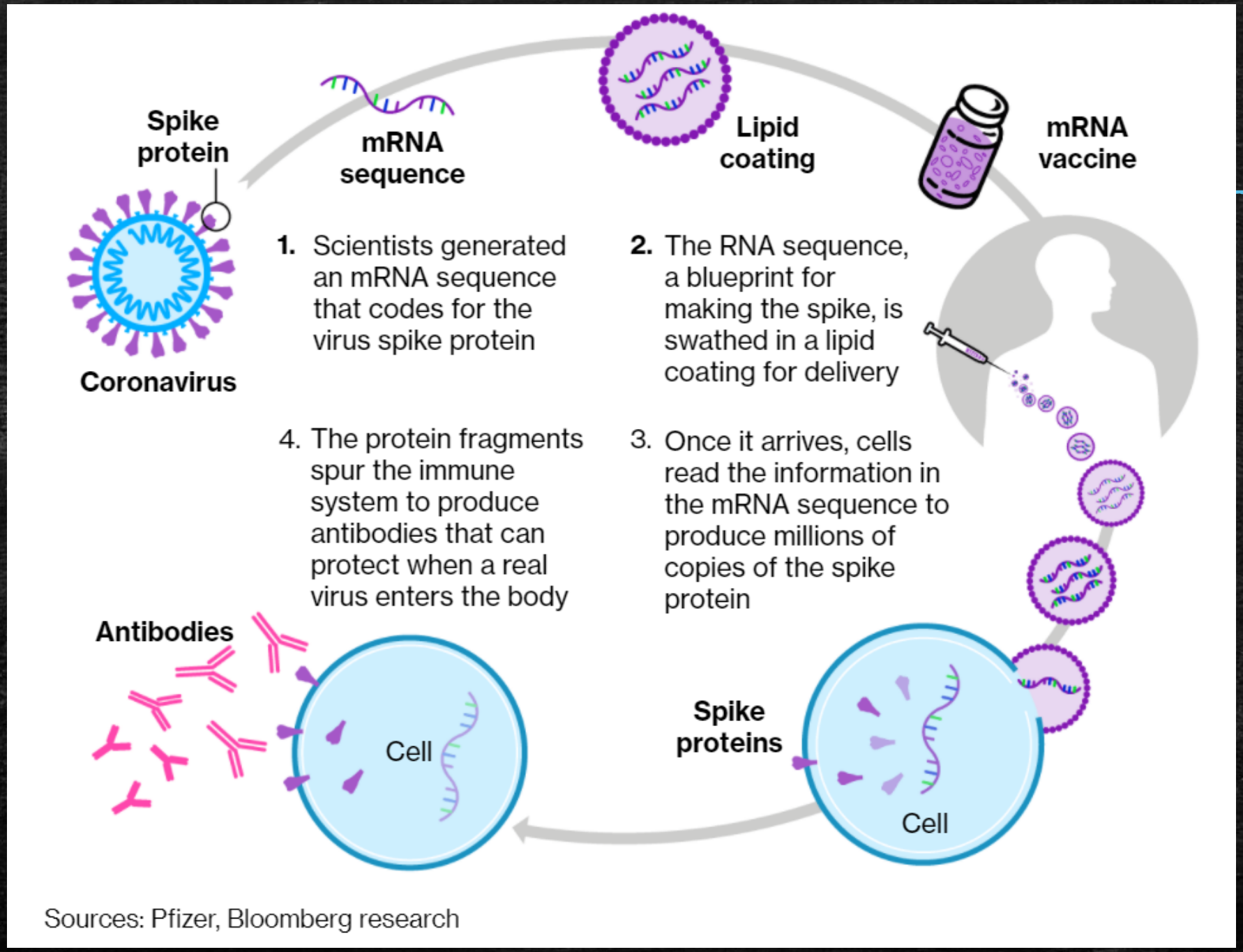
Vaccine-Preventable Disease	Prevaccine No. (y)				Vaccine Date(s), y[f]	Most Recent Postvaccine Reported No.	
	Estimated Annual Average		Peak				
	Cases[b]	Deaths[c]	Cases[d]	Deaths[e]		Cases, 2006[g]	Deaths, 2004[h]
Diphtheria	21 053 (1936-1945)	1822 (1936-1945)	30 508 (1938)	3065 (1936)	1928-1943	0	0
Measles	530 217 (1953-1962)	440 (1953-1962)	763 094 (1958)	552 (1958)	1963, 1967, 1968	55	0
Mumps	162 344 (1963-1968)	39 (1963-1968)	212 932 (1964)	50 (1964)	1940s, 1967	6584	0
Pertussis	200 752 (1934-1943)	4034 (1934-1943)	265 269 (1934)	7518 (1934)	1914-1941	15 632	27
Poliomyelitis, acute	19 794 (1941-1950)	1393 (1941-1950)	42 033 (1949)	2720 (1949)	1955, 1961-1963, 1987	0	0
Poliomyelitis, paralytic	16 316 (1951-1954)	1879 (1951-1954)	21 269 (1952)	3145 (1952)	1955, 1961-1963, 1987	0	0
Rubella	47 745 (1966-1968)	17 (1966-1968)	488 796 (1964)	24 (1968)	1969	11	0
Congenital rubella syndrome	152 (1966-1969)	Not available	20 000 (1964-1965)	2160 (1964-1965)	1969	1	0
Smallpox	29 005 (1900-1949)	337 (1900-1949)	110 672 (1920)	2510 (1902)	1798	0	0
Tetanus	580 (1947-1949)	472 (1947-1949)	601 (1948)	511 (1947)	1933-1949	41	4

[a]Footnote letters correspond to Box 1.

Covid-19 / SARS-CoV-2 / "The Rona" [22,23]

- A New approach: Messenger RNA vaccines
- Pfizer-BioNTech
- Moderna




Spike protein
Coronavirus
mRNA sequence
Lipid coating
mRNA vaccine
1. Scientists generated an mRNA sequence that codes for the virus spike protein
2. The RNA sequence, a blueprint for making the spike, is swathed in a lipid coating for delivery
3. Once it arrives, cells read the information in the mRNA sequence to produce millions of copies of the spike protein
4. The protein fragments spur the immune system to produce antibodies that can protect when a real virus enters the body
Antibodies
Cell
Spike proteins
Cell
Sources: Pfizer, Bloomberg research

- Researchers have been studying and working with mRNA & DNA vaccines for decades. Interest has grown in these vaccines because they can be developed in a laboratory using readily available materials. This means the process can be standardized and scaled up, making vaccine development faster than traditional methods of making vaccines.
- Future mRNA vaccine technology may allow for one vaccine to provide protection for multiple diseases, thus decreasing the number of shots needed for protection against common vaccine-preventable diseases.
- Beyond vaccines, cancer research has used mRNA to trigger the immune system to target specific cancer cells.

Hey-What Happened to Smallpox?

- 1967 WHO began the global initiative to eradicate smallpox.
- Oct 26 1977 the last naturally occurring case is reported in Somalia.
- Sept 11 1978 Janet Parker was the last person to die of smallpox. She worked at Birmingham University Medical School in England.
- Dec 9 1979 WHO decrees smallpox is eradicated.
- locations where it is stored : CDC in Atlanta, & VECTOR Institute) in Koltsovo, Russia.
- The Strategic National Stockpile (SNS)external icon has stockpiled enough smallpox vaccine to vaccinate every person in the United States.

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