The Immune System

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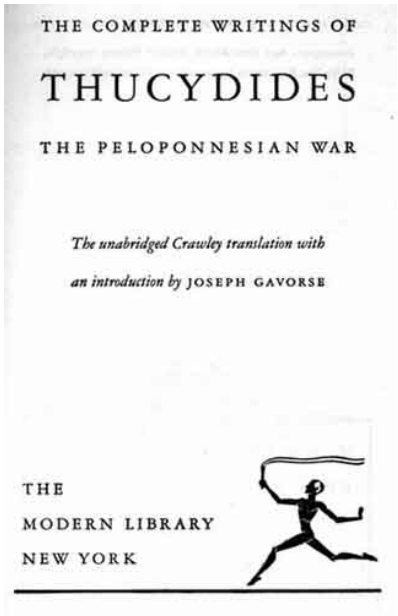
What is the most fundamental (oldest) concept of immunology ?

- Jenner and Smallpox
- Pasteur and Chicken Cholera
- Von Behring & Kitsano and Tetanus antibody
- Mouse pox and cell mediated immunity
- Host Defense (The fight between germs and your body)

430 BC: Thucydides, a great historian of the Peloponnesian war, in describing a plaque in Athen, he wrote that …..
only those who recovered from the plaque could nurse the sick.

"Yet it was with those who had recovered from the disease that the sick and the dying found most compassion. These knew what it was from experience, and had now no fear for themselves; for the same man was never attacked twice--never at least fatally.
And such persons not only received the congratulations of others, but themselves also, in the elation of the moment, half entertained the vain hope that they were for the future save from any disease whatsoever."



Smallpox

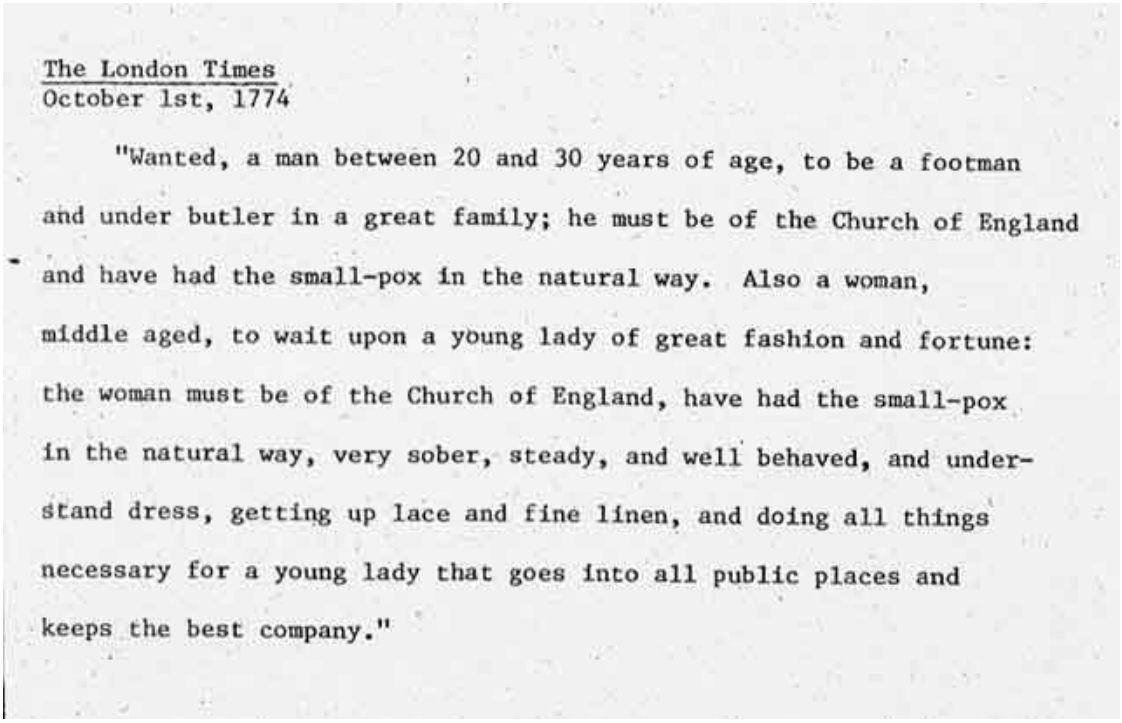
- 20-30% mortality rate
- Estimated death 400,000 annually in Europe end of the 18th century

14th -17th century:
The chinese performed an early form of vaccination they called **variolation**.
The aim was to prevent from smallpox by exposing healthy people to dried crusts derived from smallpox pustules, either by putting it under the skin or by putting it into the nose (inhalation).

18th century:
Smallpox was the most infectious disease in Europe killing up to 25% of those infected in numerous epidemics.

Early 18th century: Lady Wortley Montagu, poet and wife of the British ambassador to Turkey, vaccinated her own children.

Stellenanzeige in England 1774



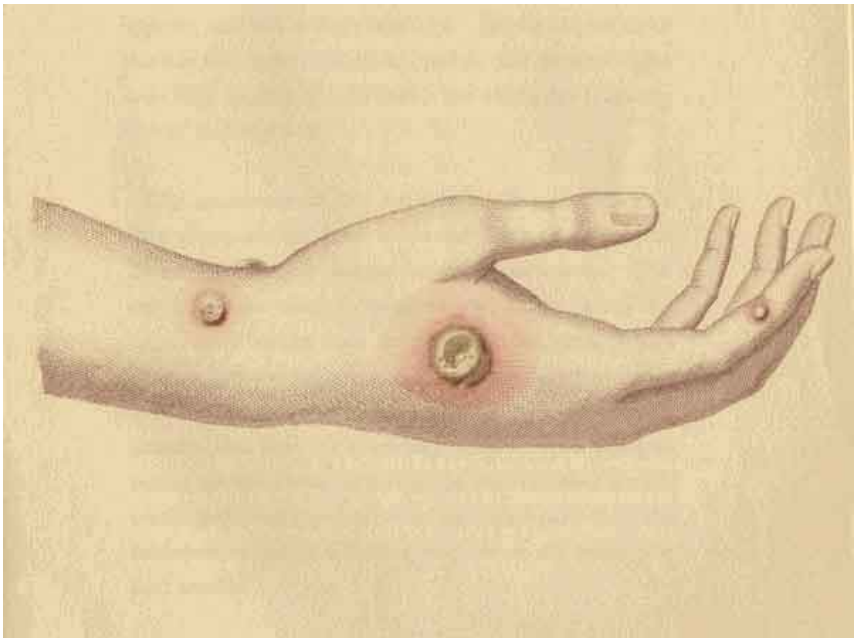
The London Times
October 1st, 1774

"Wanted, a man between 20 and 30 years of age, to be a footman and under butler in a great family; he must be of the Church of England and have had the small-pox in the natural way. Also a woman, middle aged, to wait upon a young lady of great fashion and fortune: the woman must be of the Church of England, have had the small-pox in the natural way, very sober, steady, and well behaved, and understand dress, getting up lace and fine linen, and doing all things necessary for a young lady that goes into all public places and keeps the best company."

Edward Jenner

Late 18th century:
Edward Jenner started noticing similarities between cowpox and smallpox.
He was particularly interested when a milkmaid told him **she wouldn't catch smallpox because she had already had the much milder disease of cowpox** – a common belief amongst rural communities at the time. Jenner's observations of people who had caught cowpox suggested this was true.

In **1796** he deliberately infected a boy, James Phipps, with material obtained from a cowpox lesion. When the boy recovered, he then injected some pus from a smallpox lesion under his skin. The boy didn't catch smallpox.



the 3d day
ms itched conſiderably.
was evidently ſubſiding, and on the
perceptible. No ſymptom of indiſpoſition followed.

To convince myſelf that the variolous matter made uſe of was in a perfect ſtate, I at the ſame time inoculated a patient with ſome of it who never had gone through the Cow-pox, and it produced the Small-pox in the uſual regular manner."

Theſe

Jenner`s documentation

SUMMARY OF JENNER'S CASES

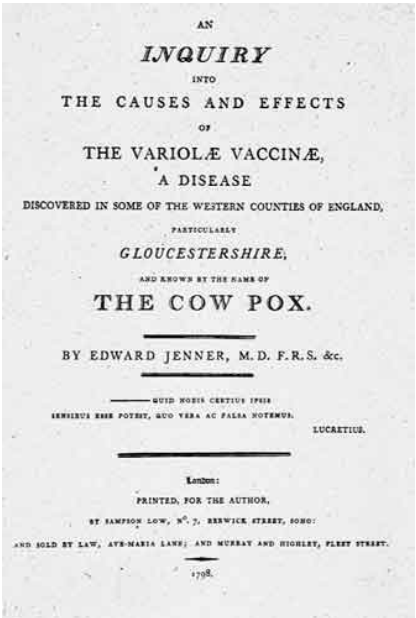
CASE	DATE	PATIENT	SOURCE	PASSAGE	IMMUNITY
XIX	March 16, 1798	William Summers (5♂)	From Cow	1	Yes
XX	March 28, 1798	William Pead (8♂)	From Summers	2	Probably
XXI	April 5, 1798	Hannah Excell (7♀)	From Wm Pead	3	Unknown
XXII	April 12, 1798	John Macklove (1½♂)	From Excell	4	Unknown
		Robert Jenner (11 mo♂)	From Excell	4	Unknown
		Mary Pead (5♀)	From Excell	4	Unknown
		Mary James (6♀)	From Excell	4	Unknown
XXIII		J. Barge (7♂)	From Mary Pead	5	Probably

SUMMARY OF 23 CASES REPORTED BY
EDWARD JENNER IN HIS BOOK:
"AN INQUIRY INTO THE CAUSES AND EFFECT OF THE
VARIOLAE VACCINAE" 1798

CASES I THROUGH XII
19 PEOPLE WITH HISTORY OF COWPOX WERE IMMUNE TO SMALLPOX INOCULATION

CASES XIII THROUGH XV
3 PEOPLE WITH HISTORY OF "GREASE" WERE NOT TOTALLY IMMUNE

CASES XVI AND XVII
MAY 14, 1796 JAMES PHIPPS (8♂) INOCULATED FROM HAND OF SARA NELMES, A DAIRYMAID. (WHO GOT DISEASE FROM A COW)
JULY 1, 1796 (AND SEVERAL MONTHS LATER) INOCULATED WITH SMALLPOX WITHOUT PRODUCING DISEASE



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.

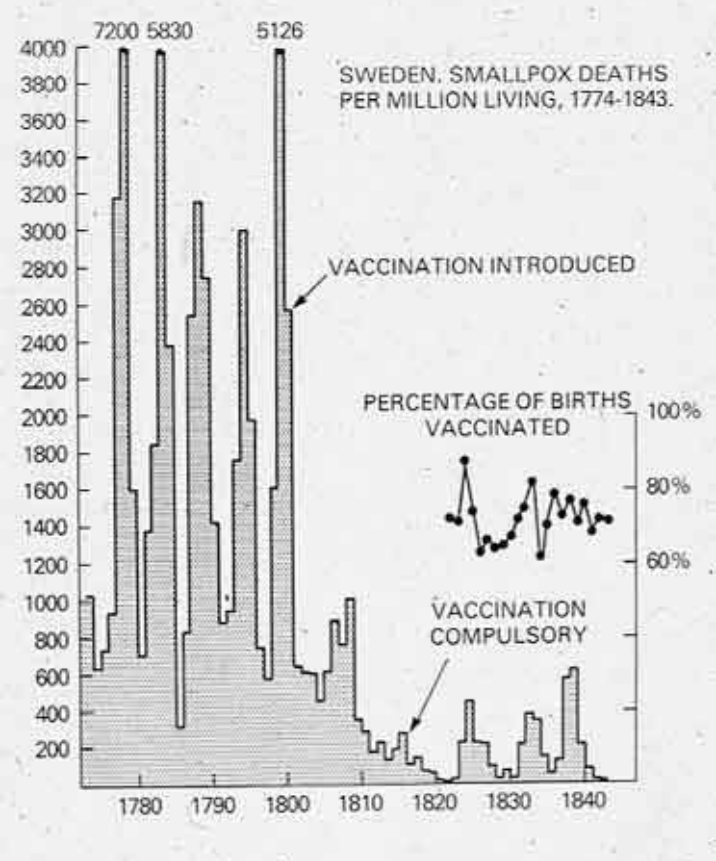
BY EDWARD JENNER, M.D. F.R.S. &c.

QUID NOBIS CERTIUS IPSIS
SENSIBUS ESSE POTEST, QUO VERA AC FALSA NOTEMUS.
LUCRETIUS.

London:
PRINTED, FOR THE AUTHOR,
BY SAMPSON LOW, N°. 7, BERWICK STREET, SOHO:
AND SOLD BY LAW, AVE-MARIA LANE; AND MURRAY AND HIGHLEY, FLEET STREET.
1798.

These experiments afforded me much satisfaction, they proved that the matter in passing from one human subject to another, through five gradations, lost none of its original properties, J. Barge being the fifth who received the infection successively from William Summers, the boy to whom it was communicated from the cow.

Smallpox death statistics from Sweden



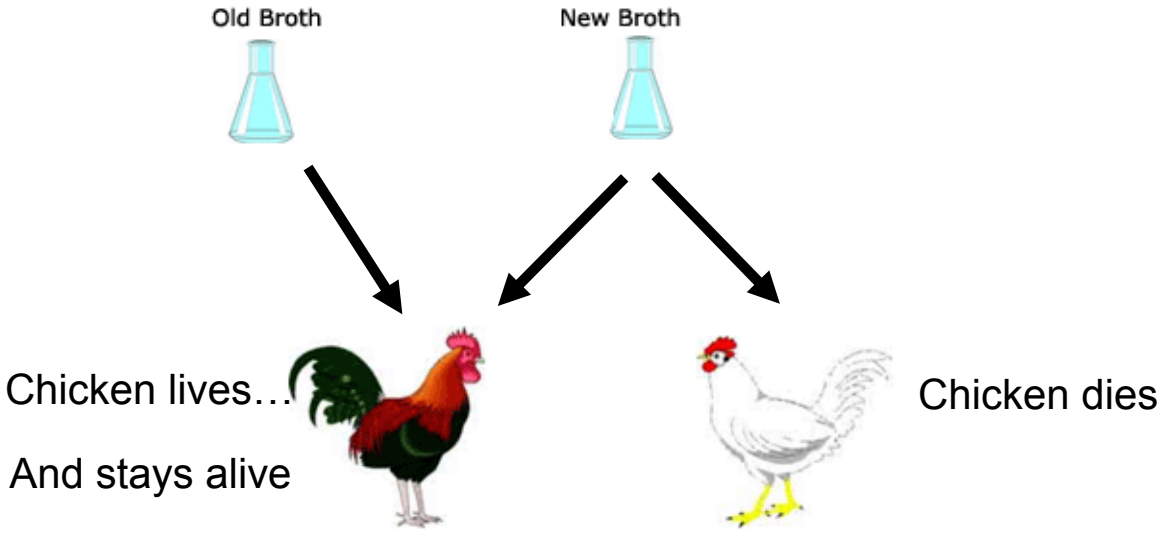
Smallpox Eradication

May 14, 1796
Jim Phipps vaccinated by Edward Jenner
October 26, 1977
Last case of Smallpox discovered in Somalia
May 8, 1980
WHO declares the world free of smallpox

"When meditating over a disease, I never think of finding a remedy for it, but, instead, a means of preventing it."

Louis Pasteur

Late 19th century, Pasteur succeeded growing the bacterium thought to cause fowl cholera. Chickens infected with the bacteria developed cholera. He found that an old culture induced mild disease and chickens recovered.
The same chickens also survived after reinfection with a fresh culture of bacteria. He called this **vaccination**



The beginning of modern immunology…

1881: Pasteur vaccinated one group of sheep with heat-killed Bacillus anthracis (anthrax). He then infected vaccinated and unvaccinated sheep with virulent bacilli.
All vaccinated survived and all unvaccinated died!!!

1885: Pasteur went on to use this method to develop a vaccine against rabies, which protected a young boy, J. Meister, from bites of a rabid dog.

However, Pasteur did not understand how vaccination worked

Emil von Behring and S.Kitasato
• 1890 discovered the antitoxins of diptherie and tetanus

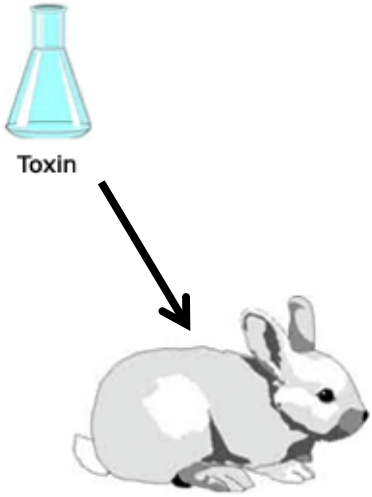
Corynebacterium diphteriae (discovered 1883 by E. Klebs) killed 70% of infected children

1891: Serumtherpay saved the life of many children

1901: von Behring received Nobel Price (4 years before Koch)

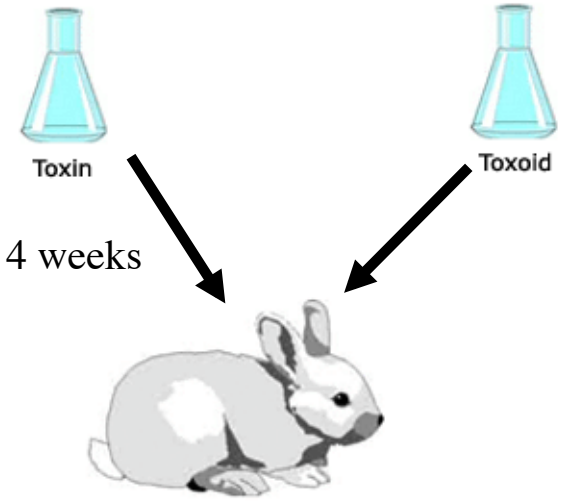
Von Behring and Kitsano

experiment 1



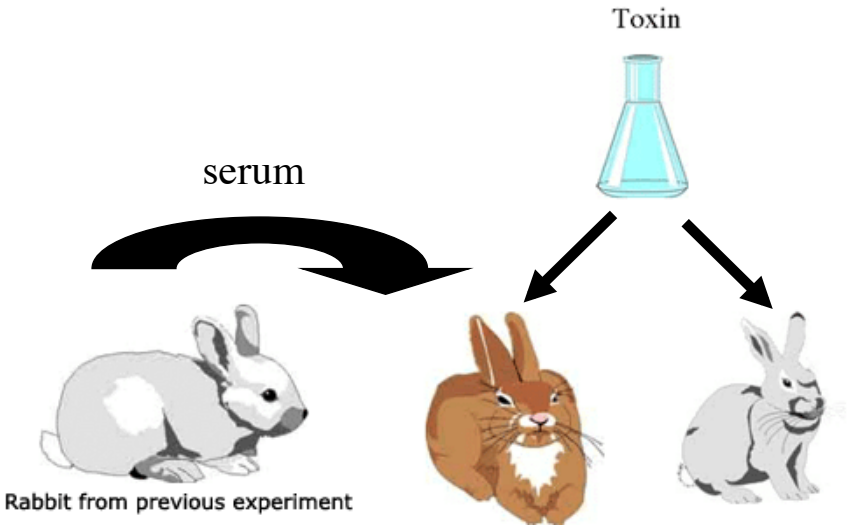
Rabbit dies

experiment 2



Rabbit survives

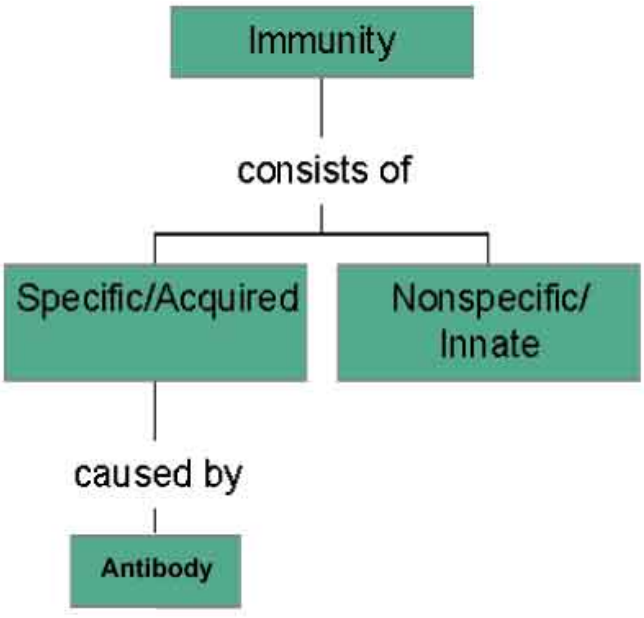
Von Behring and Kitsano, experiment 3



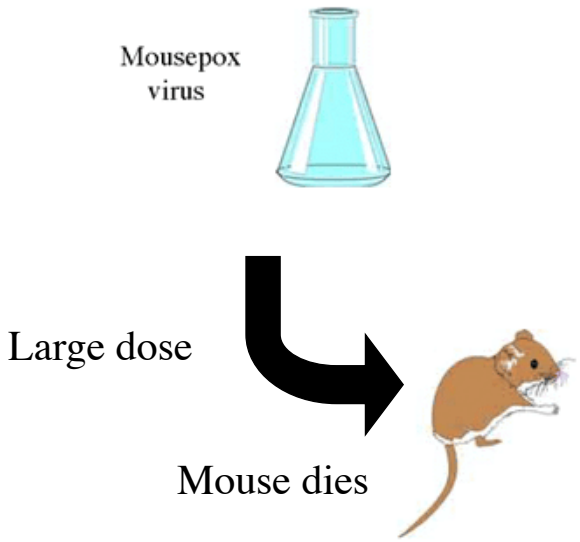
lives dies

By the end of the 1920s,
vaccines for diphtheria, tetanus, pertussis (whooping cough) and tuberculosis (BCG) were all available.

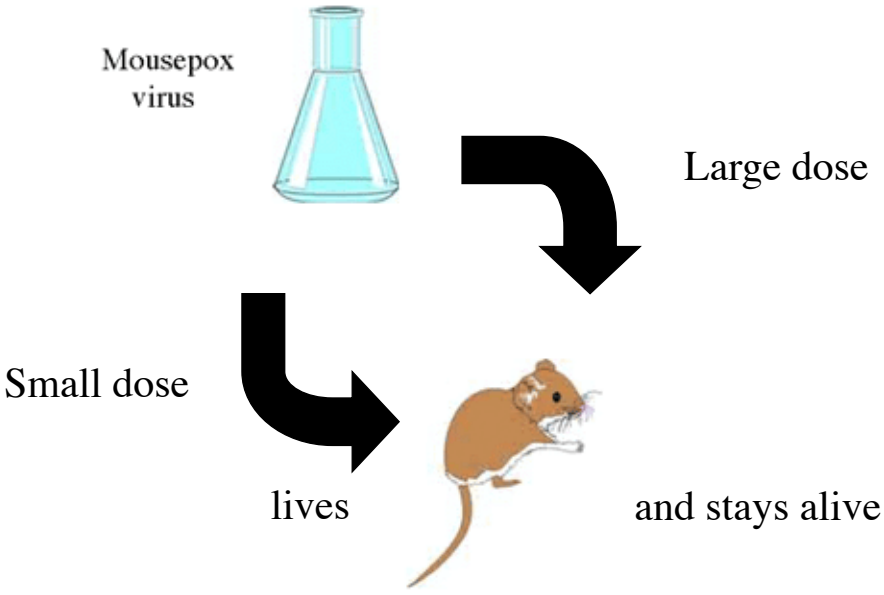
1930, the serum component transferring immunity was found to be in a fraction called γ-globulin (now immunoglobulin) and the active molecules are called antibodies.
Humoral immunity.



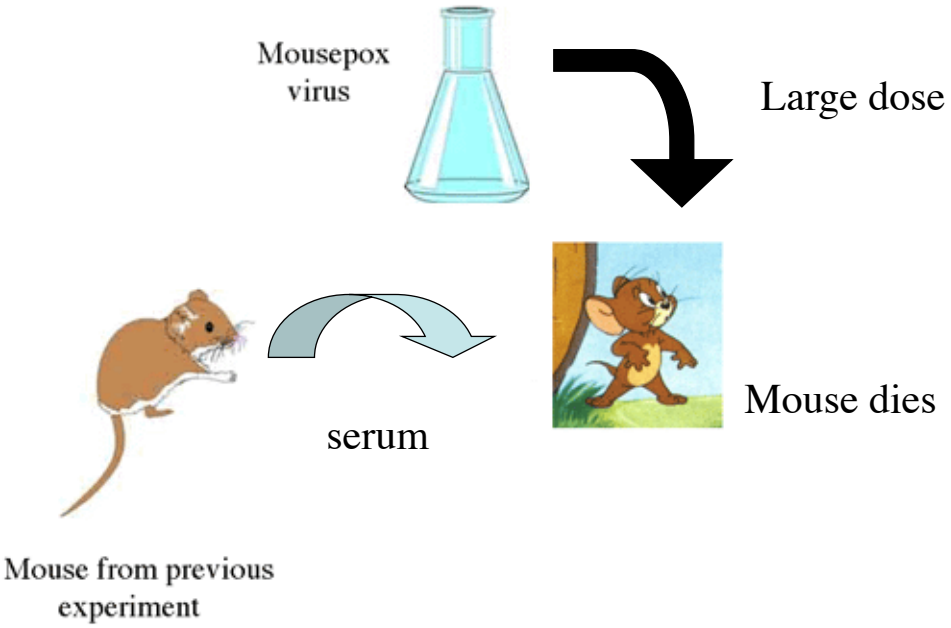
Mousepox, experiment 1



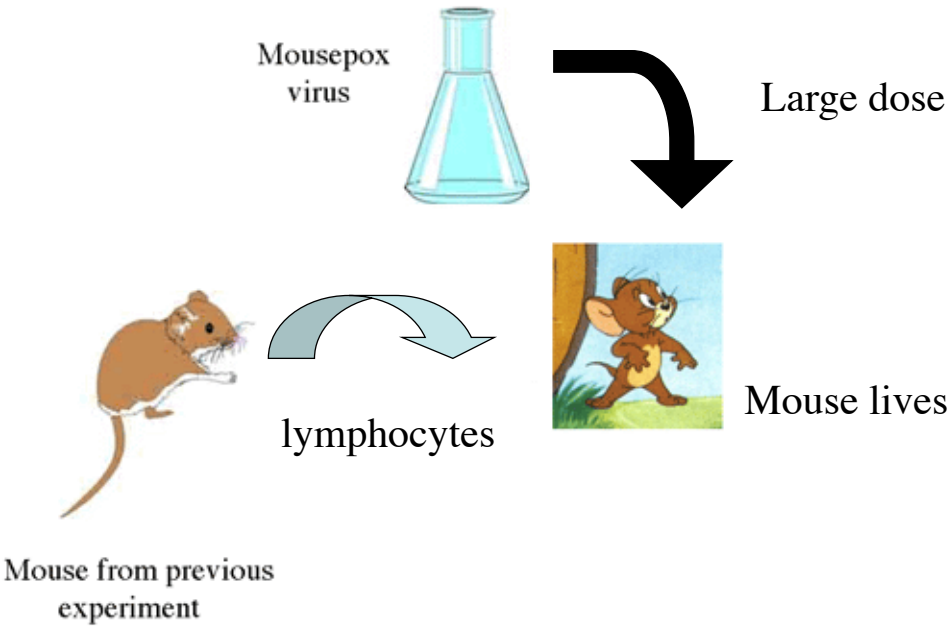
Mousepox, experiment 2

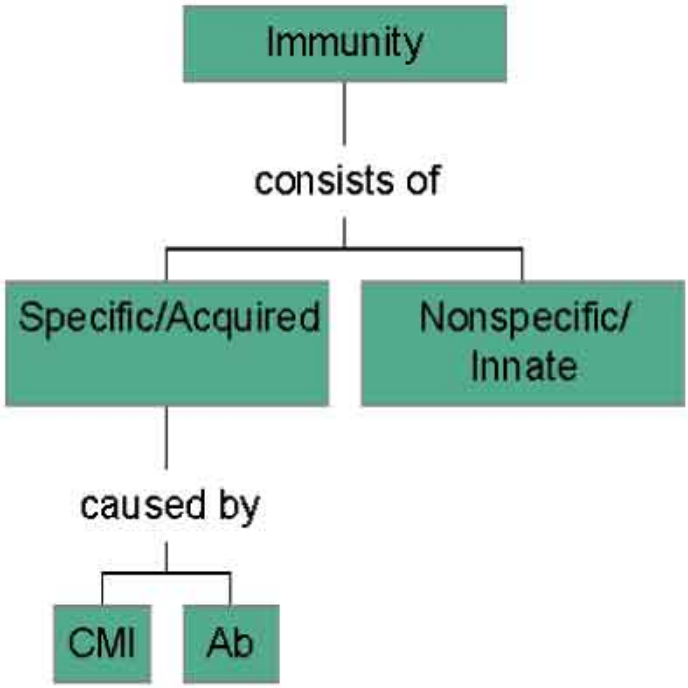


Mousepox, experiment 3



Mousepox, experiment 3





In 1940: M. Chase succeeded in transferring immunity to M. tuberculosis by transferring white blood cells.

Note: Already in 1883, Elie Metchnikow hypothesized that (phagocytic) cells could transfer immunity (concept of cell- mediated immunity).

In 1950, identification of two types of lymphocyte, B cells and T cells, which were responsible for humoral and cellular immunity.