

Immunology : History



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JANUARY (1) Thucydides! - (430 BC)

TUESDAY

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which had foundation

of immunity.

- In Athens.

- Pointed out that people once attacked with plague do not have fear of the 2nd attack by the disease.

Among the most famous parts of **Thucydides'** History of the Peloponnesian War is his account of the **plague** that killed nearly a third of the Athenian population in the summer of 430 and caused greater loss of human life than the rest of the Archidamian War

(2) Yi - Meishan (1000 AD)

- Chinese physician

- Successfully inoculated the emperor's grandson with dried crust of small pox to render him immune from the disease.

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EDWARD JENNER (1749-1823)

* English physician.

* His observation was based upon the observation on milk maids, namely those who often contracted cowpox were remarkably resistant to smallpox.

Notes

* In 1786, Jenner inoculated a boy with material he got from the lesions of milk maid who was attacked with cowpox. After few weeks the boy was again ~~into~~ inoculated

with infectious pus, but he did not get the disease.

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WEDNESDAY

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* He concluded:- Process of inoculation leads to the immunity against small pox.

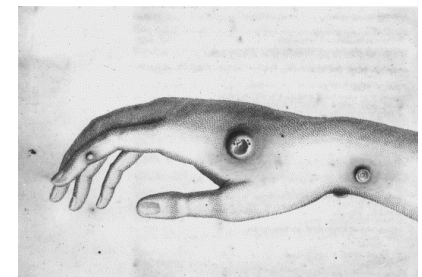
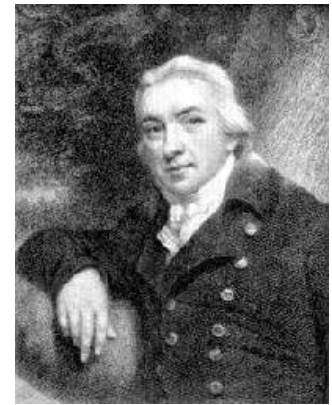
Edward Jenner (1749-1823).

- Born on May 17, 1749, in Berkeley, Gloucestershire, England, Died Jan. 26, 1823.
- As a teenager, while learning to be a physician, he heard a young farm girl tell a doctor that she could not contract smallpox because she had once had cowpox (a very mild disease). This started him thinking about a vaccine.

- After years of experimenting, on May 14, 1796, Edward Jenner carried out a famous experiment on a healthy 8-year-old boy, James Phipps, with cowpox.

- ✓ He took material from a burst pustule on the arm of Sarah Nelmes who had apparently contracted cowpox.
- ✓ Deliberately exposed the boy to virulent variola virus two months later and found that the child was protected, showing only a mild inflammation around the site where the variola was injected.

- Some record shows that in 1789 he had already experimented vaccination on his own son, then aged one-and-a-half, with the swine pox, followed by conventional smallpox inoculation.



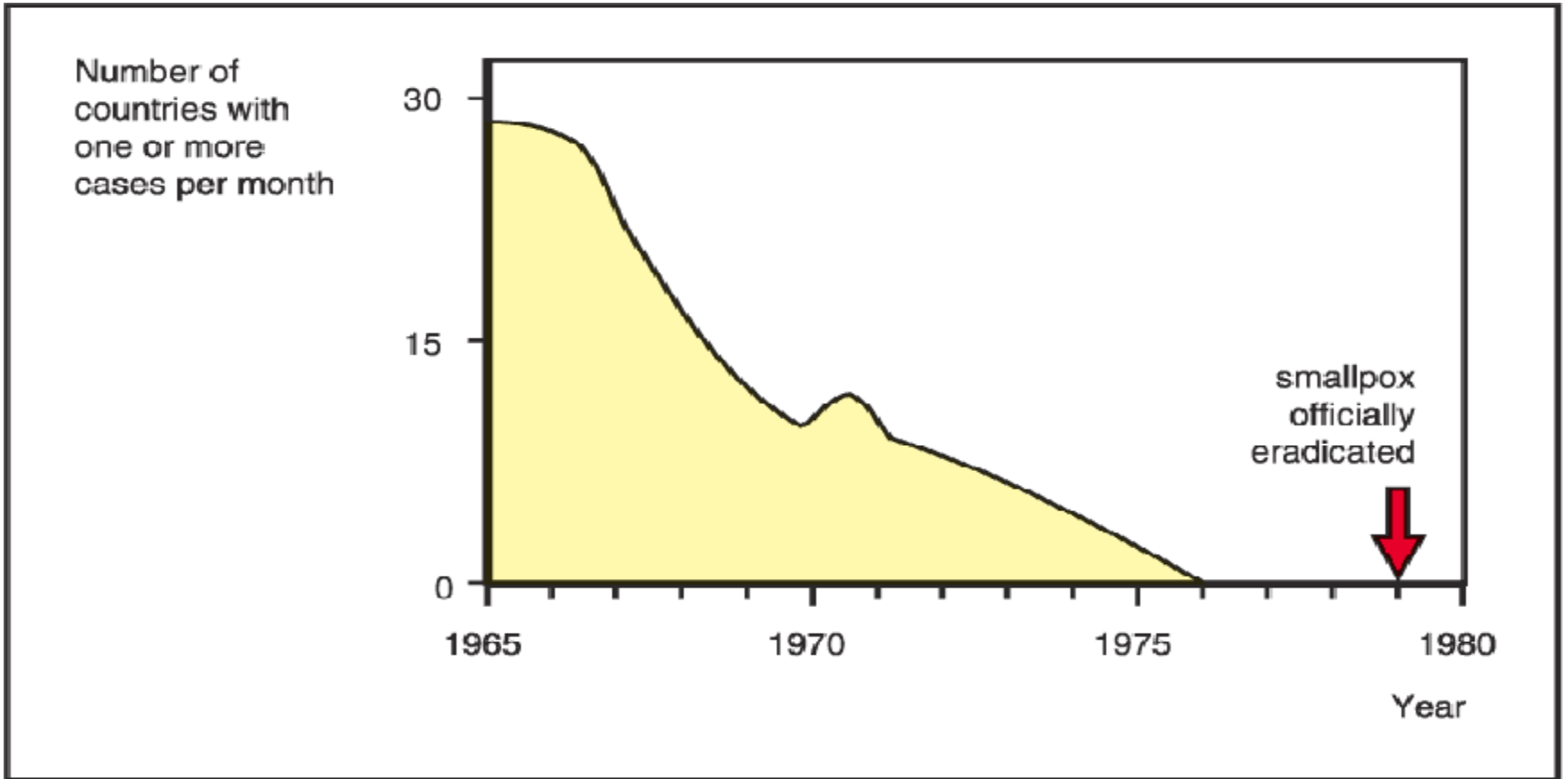
Sarah Nelmes' hand



In 1796 Edward Jenner infects a boy with cow pox to protect against small pox (before germ theory of disease)

- Jenner wrote a paper in 1798 explaining his experiments, and wanted to report his first case study in the “Transactions of the Royal Society of London” His study was rejected.
- He then went to London to demonstrate his theory. But he was discouraged . Jenner returned to Berkeley.
- In 1801, Jenner published “The Origin of the Vaccine Inoculation” describing how cowpox virus was prepared and used to protect ("vaccinate") healthy persons against smallpox. Material used as the vaccine was prepared from the arm of a vaccinated child, thus the distribution of vaccine involved the transportation of vaccinated children all over Europe. Orphans were often used for this purpose. Eventually, material from infected cows was used directly as vaccine. By 1840, the British government had banned other preventive treatments against smallpox.

“Vaccination,” the word Jenner invented for his treatment (from the Latin, *vacca*, a cow), was adopted by Louis Pasteur for immunization against any disease.



The last reported case of smallpox, Ali Maakin, in the world was in Somalia, on October 26, 1977

(4) Louis Pasteur :- (1822-1895)

- French chemist.

- Father of Immunology.

- Worked on common animal diseases like :-

(a) Pebrines (silk worm disease)

(c) Chicken Cholera.

(b) Anthrax (cattle disease)

(d) Rabies.

* He accidentally hit upon different methods of reducing the virulence of pathogenic microbes.

His contributions are :-

→ (A) Inoculated chickens with old cultures of bacillus namely Pasteurella aviseptica. He observed that inoculated chickens failed to develop illness.

- Through this chance observation he demonstrated that aged cultures lose virulence, but retain capacity to induce immunity against cholera.

- This he called ATTENUATION and the aged cultures of chicken cholera became the 1st ATTENUATED VACCINES.

[Attenuation :- Process of Weakening or reducing the virulence of pathogenic organisms without loosing the capacity to induce immunity]

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THURSDAY

Sheep were inoculated with Bacillus anthracis, cultivated at 42°C . Sheep do not develop the disease. At usual growth temperature 37°C , these were highly pathogenic.

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- He inferred that "pathogenic bacteria lose their virulence on cultivation at high temperatures".

- Based upon pastures method, few other methods were used to attenuate the pathogens.

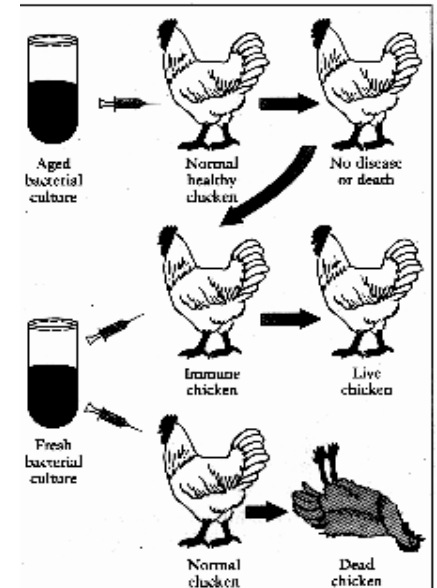
ef. :- (a) Unnatural hosts → Rabies virus when passed through rabbit & smallpox virus of human beings when passed through cow many times, viruses lose their capacity to produce serious diseases, but retained their capacity to induce immunity.

(c) Most important & interesting work is :- Production of vaccines for rabies. He injected spinal cord extracts from rabid dogs into healthy rabbits. From these rabbits, extracts from spinal cord were prepared and dried for several days. From these extracts which contained the attenuated viruses, the rabies vaccines were prepared.

He called these extracts as vaccines in honour of Edward Jenner who prepared 1st vaccine.
(Lt: Vacca → Cow)

Louis Pasteur (1822-1895)

- Stereochemist: molecular asymmetry
- Fermentation and silk worker disease
- Germ Theory of disease
- Attenuated vaccines for cholera, anthrax, and rabies
- On July 4, 1886, 9-year-old Joseph Meister was bitten repeatedly by a rabid dog. Pasteur treated him with his attenuated rabies vaccine two days later. Meister survived. Joseph Meister later became a gatekeeper for the Pasteur Institute. In 1940, when he was ordered by the German occupiers to open Pasteur's crypt, Joseph Meister refused and committed suicide!



Louie Louie...



Pasteur inoculating sheep at Msr. Rossignol's farm – May, 1881

Louis Pasteur

1879- discovered that aged bacterial cultures of *Pasteurella* lost virulence. Referred to injection of weakened culture a “vaccine” in honor of Jenner

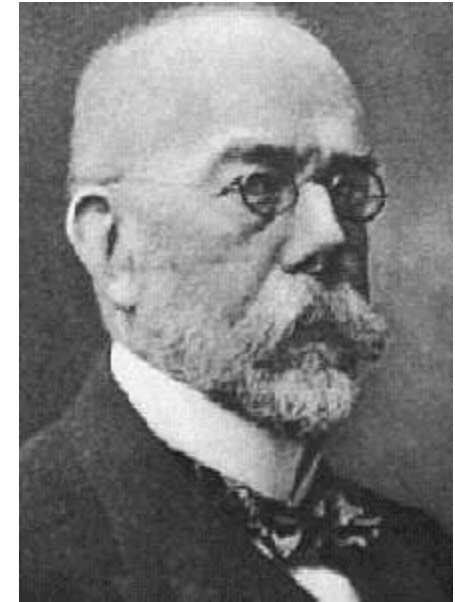
1881- He applied the same technique vs. anthrax
...and then rabies

Pasteur's contributions: The father of Immunology

- ❖ Changes in hospital practices to minimize hospital infections
- ❖ Attenuation and produced Vaccines
- ❖ Found that rabies was transmitted by agents so small that could not be seen under a microscope, thus revealing the world of viruses.
- ❖ Developed techniques to vaccinate dogs against rabies, and to treat humans bitten by rabid dogs.
- ❖ Developed "*pasteurization*," a process by which harmful microbes in perishable food products are destroyed by heat, without destroying the food.

Robert Koch (1843-1910)

- German physician.
- Worked on Anthrax in 1870's. Identified the spore stage. First time the causative agent of an infectious disease was identified.
- Koch's postulates: conditions that must be satisfied before accepting that particular bacteria cause particular diseases.
- Discovered the tubercle bacillus and tuberculin.
- Identifies causative agent of cholera as *Vibrio cholerae*
- Studied life cycle of Anthrax bacilli.
- Developed staining and methods of obtaining pure culture using solid media



Detailed tuberculin skin test (DTH).

Awarded 1905 Nobel Prize.

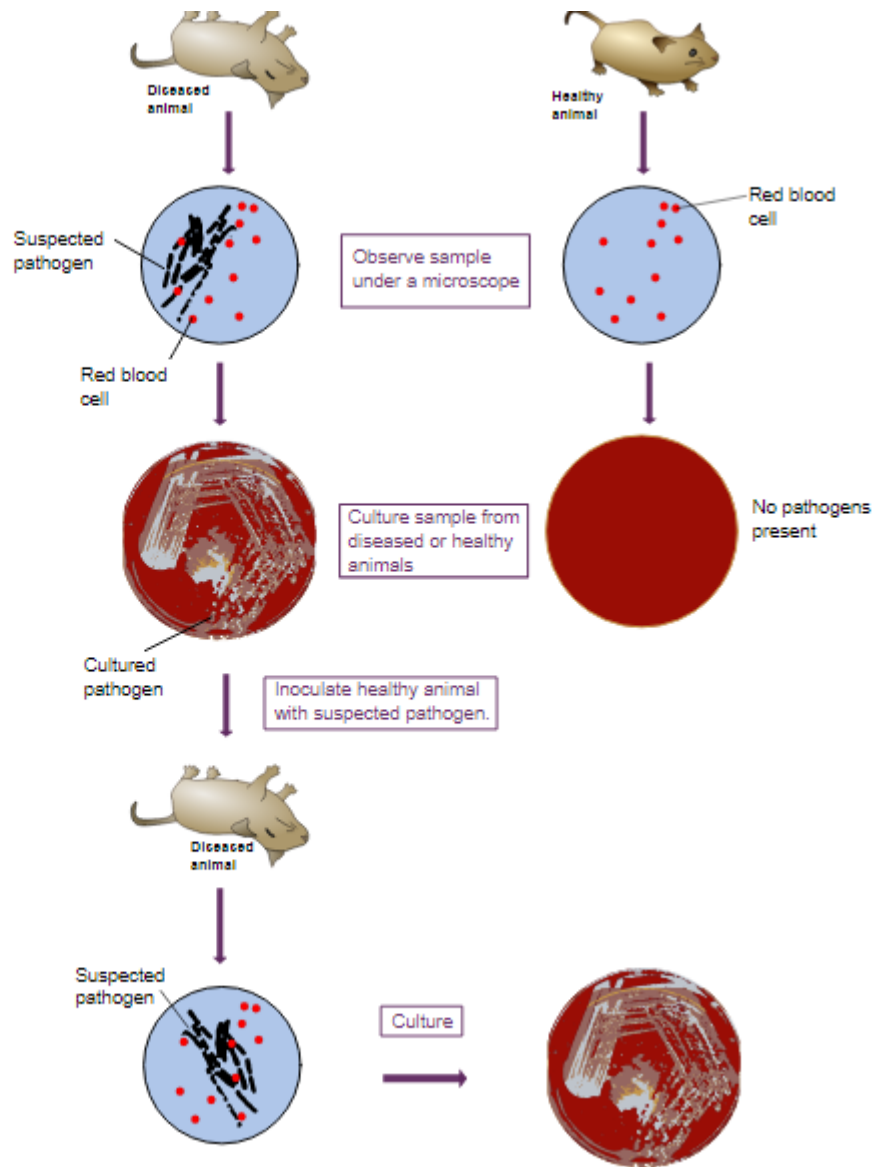
Koch's Postulates:

① The microorganism must be found in abundance in all organisms suffering from the disease, but should not be found in healthy organisms.

② The microorganism must be isolated from a diseased organism and grown in pure culture.

③ The cultured microorganism should cause disease when introduced into a healthy organism.

④ The microorganism must be reisolated from the inoculated, diseased experimental host and identified as being identical to the original specific causative agent.



Emil Adolf Von Behring (1854 – 1917)

- Awarded first Nobel Prize in physiology, 1901
- Student of Koch
- Discovered anti-toxin for Diphtheria and Tetanus and applied as therapy.
- Supported Humoral theory



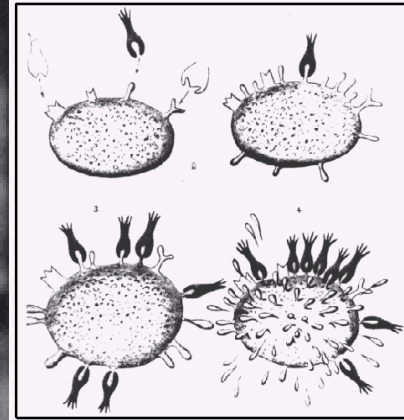
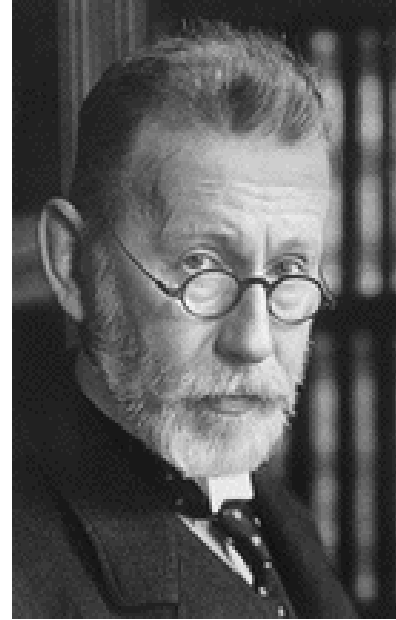
⑦ Emil Von Behring (1854-1917)

- German bacteriologist.
- Supported humoral theory.
- Showed the possibility to provide an animal with passive immunity against Tetanus by injecting into it the blood serum of another injected animal. He worked for immunity against diphtheria.

- He was given noble prize in 1901 for his work on antitoxins and principle of antiserum therapy.

Paul Ehrlich (1854 – 1915)

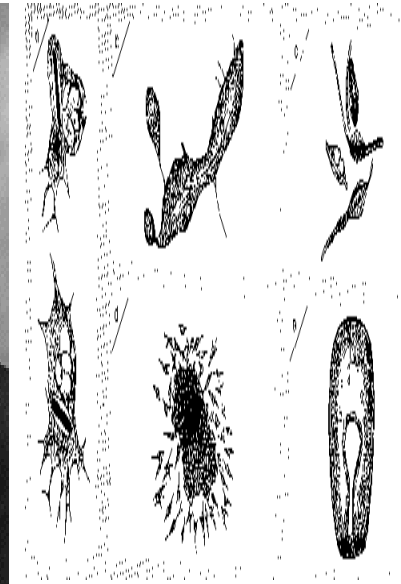
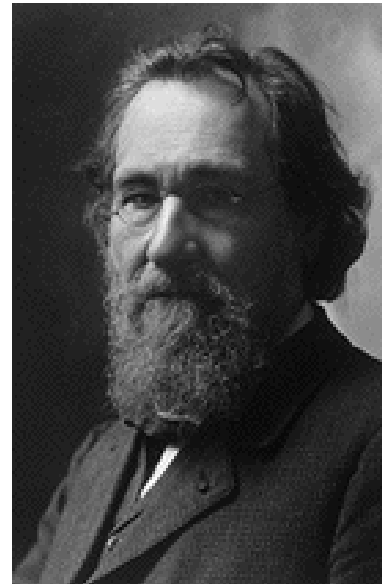
- Developed a series of tissue-staining dyes including that for tubercle bacillus.
- Developed anti-toxin (Diphtheria) and hemolysis
- Side-chain theory of antibody formation: "surface receptors bound by lock & key; Ag stimulated receptors"
- Renamed **Bordet alexins** as Complement
- Discovered Mast cells
- Shared 1908 Nobel Prize with Metchnikoff.



Paul Ehrlich, one of the pioneers of immunology at the beginning of the century, proposed the concept of receptors (which we now know as antibodies) secreted by cells of the immune system in response to foreign antigens. He foresaw their use as "magic bullets" to specifically attack a wide variety of diseases. This diagram, which is remarkably close to our present view of the formation of antibodies, comes from one of his early publications.

Elie Metchnikoff (1845-1916)

- Embryologist studying starfish development.
- Found phagocytosis. Formed the basis of leukocyte phagocytosis.
 - Birth of cellular immunology.
 - Suggested that inflammation might be a protective act rather than destructive
- Shared Nobel Prize with Ehrlich in 1908



First insights into mechanics of immunity...



Elie Metchnikoff



S. Kitasato

1890- von Behring and Kitasato discovered blood sera could transfer immunity

∴ liquid of blood conferred immunity

Q: Which confers immunity... cells or serum?

Both cells and serum contribute to immunity!

- **1930's – early techniques made it easier to study humoral elements [than cellular ones].**
 - discovery of active component of blood –
gamma globulin “protein”
- **1950's – discovery of T and B cells**
 - Later discoveries linked lymphocytes to both
cellular and humoral immunity

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Almóth wright :-

- British bacteriologist.

Notes - In 1903 discovered that metchnikoff's cellular or humoral theory was wrong.

- Together with Stewart Daughless, he formulated the theory of opsonization.

Opsonin :- An Ab that attaches to a cellular or particulate Ag and prepares it for phagocytosis.

Introduced antityphoid inoculations

Alexander Fleming (1881-1955)

- British bacteriologist
- Received noble prize in 1945 for discovery of penicillin.
- Contributions :-
 - Discovery of anti lysozyme.
 - " " antibacterial substance - penicillin

Widal Fernando (1862-1929)

- french bacteriologist
- introduced diagnosis by blood tests
- devised widal test for typhoid fever diagnosis
- Prepared antityphoid vaccine.

Sir Frank Macfarlane (1899-1985)

- Trained as MD
- Selection theory
- Important work on influenza. Discovery of an influenza viral enzyme with the specificity for particular forms of neuramic acid. Used today for detection.
- Acquired immunological tolerance
- Clonal selection theory to explain tolerance



Niels K. Jerne (1912-1994)

- Antibody avidity maturation
- Plaque forming assay
- Helped the formation of clonal selection theory.
- Host MHC is the driving force for the maturation and selection of T cells in the thymus.
- **Idiotypic network** (The variable part of an antibody including the unique antigen binding site is known as the idiotype.)
- Nobel Prize, 1984, for theories concerning "the specificity in development and control of the immune system" and the discovery of "the principle for production of monoclonal antibodies."



Isotypes, Allotypes, and Idiotypes of Immunoglobulins

1. ISOTYPES All the heavy chain constant region structures which give rise to classes and subclasses are expressed together in the serum of a normal subject are called Isotypic variants. (IgG, IgA, IgM, etc) Each of those is called Isotype.

2. ALLOTYPES Inherited small, functionally insignificant, structural differences, especially in the constant portion of the antibody cause by the difference of amino acid sequence. The variations in heavy chain genes are called Allotypes.

3. IDIOTYPE The variations of amino acid sequences within the variable domains on light and heavy chains are called Idiotypes.

to make things easy!

Isotype: Present in ALL members of the same species (ALL humans); ie., same for all humans.

Allotype: Present in members of the same family, same ethnic group, etc. Used for paternity testing.

Idiotype: Different for each and every individual.

JANUARY

(18)

Karl Landsteiner

TUESDAY

→ (1868 - 1943)

- Australian Scientist

- Discovered four primary blood groups in man. For this he was awarded nobel prize in 1930.

- Coined term Haptane for small chemical gr. which themselves are non-immunogenic.

- Discovered Rh-antigen in 1940.

- " delayed hypersensitivity.

Rodney R. Porter

(1917 - 1985)

- Given Chemistry of Immunoglobulins

↓

got nobel prize for this.

Burnet Macfarlane (1899-1985)

- Formulated 'clonal selection Theory'
- Got noble prize for the discovery of 'Acquired Immunological Tolerance' in 1960.

Isaacs & Lindenmann :-

- Discovered interferons in 1957.